Supporting information for: Understanding the self-assembly of amino ester-based benzene-1,3,5-tricarboxamides using molecular dynamics simulations

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Force field parameters

A description of the various atom types and their partial charges for all three derivatives are illustrated in Figures S1, S2 and S3. All the bonded and non-bonded potentials are listed in Tables S1, S2, S3 and S4. The total interaction energy is calculated as described below. For the hydrogen bonding potential, we have used D_{hb}=7.5 kcal/mol and R_{hb}=2.75 Å. DREIDING's[S1] mixing rules are used for non-bonded interactions between unlike atom types.

$$\begin{aligned} E = \sum^{bond} K_r(r - r_o)^2 + \sum^{angle} K_\theta(\theta - \theta_o)^2 + \sum^{dihedral} K(1 + \cos[n\phi - d])) \\ + \sum^{inversion} K(1 + d\cos(n\phi)) + E_{nb} \end{aligned} \tag{1}$$

$$\begin{aligned} E_{nb} &= E_{vdW} + E_Q + E_{hb} \\ E_{vdW} &= A\exp(-r_{ij}/\rho) - C/r_{ij}^6 \\ E_Q &= q_i q_j/(4\pi\epsilon_o r_{ij}) \\ E_{hb} &= D_{hb}[5(R_{hb}/R_{DA})^{12} - 6(R_{hb}/R_{DA})^{10}]\cos^4(\theta_{DHA}) \end{aligned} \tag{2}$$

here, E_{hb} is a three-body term that is used to describe hydrogen bond interactions.

Mixing rules for non-bonded interactions

$$A_{ij} = \sqrt{A_{ii} \times A_{jj}} \tag{3}$$

$$C_{ij} = \sqrt{C_{ii} \times C_{jj}} \tag{4}$$

$$\frac{1}{\rho} = \frac{1}{2\rho_{ii}} + \frac{1}{2\rho_{jj}} \tag{5}$$

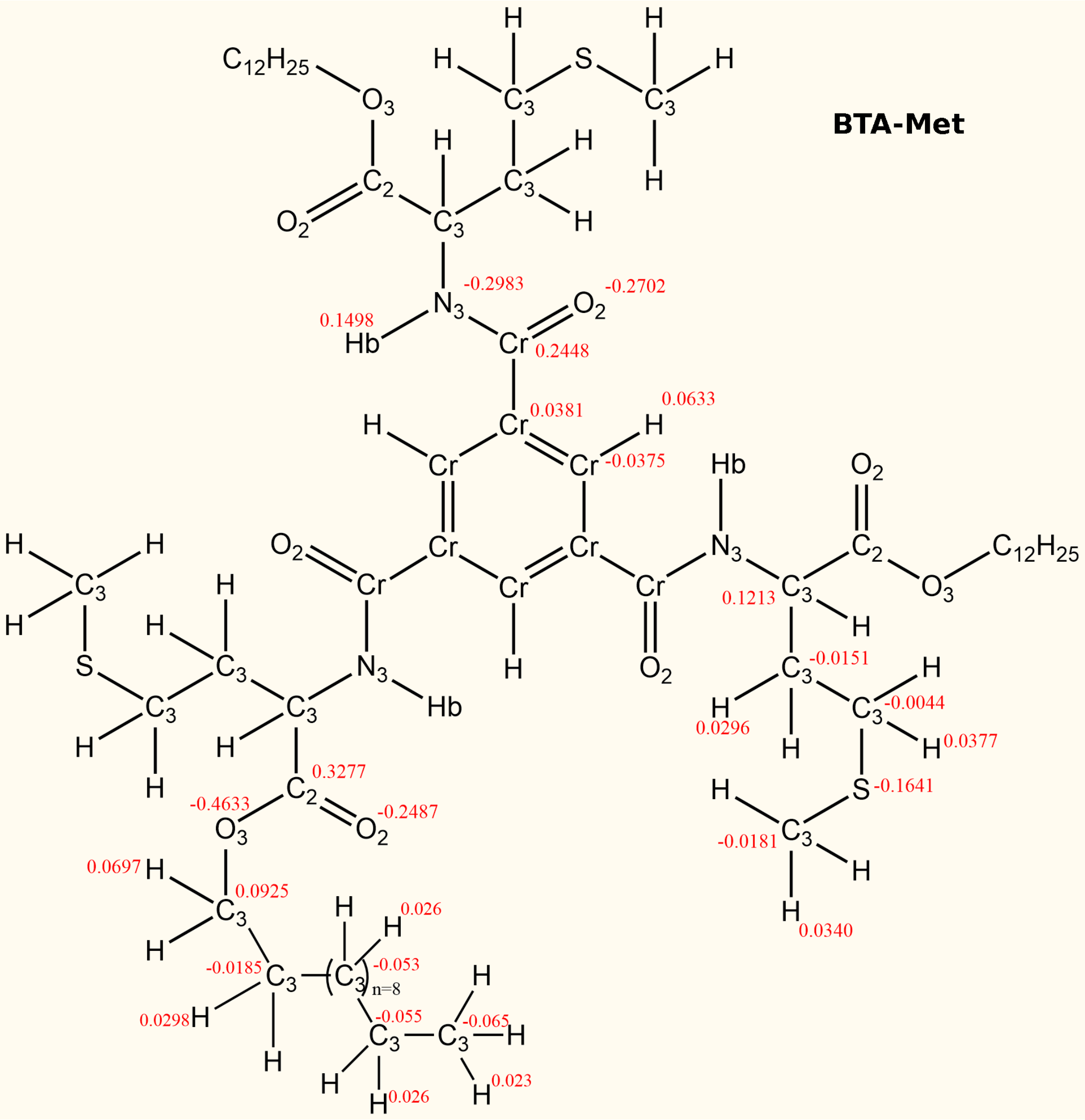


Figure S1: Atom types and their partial charges for BTA-Met molecule.

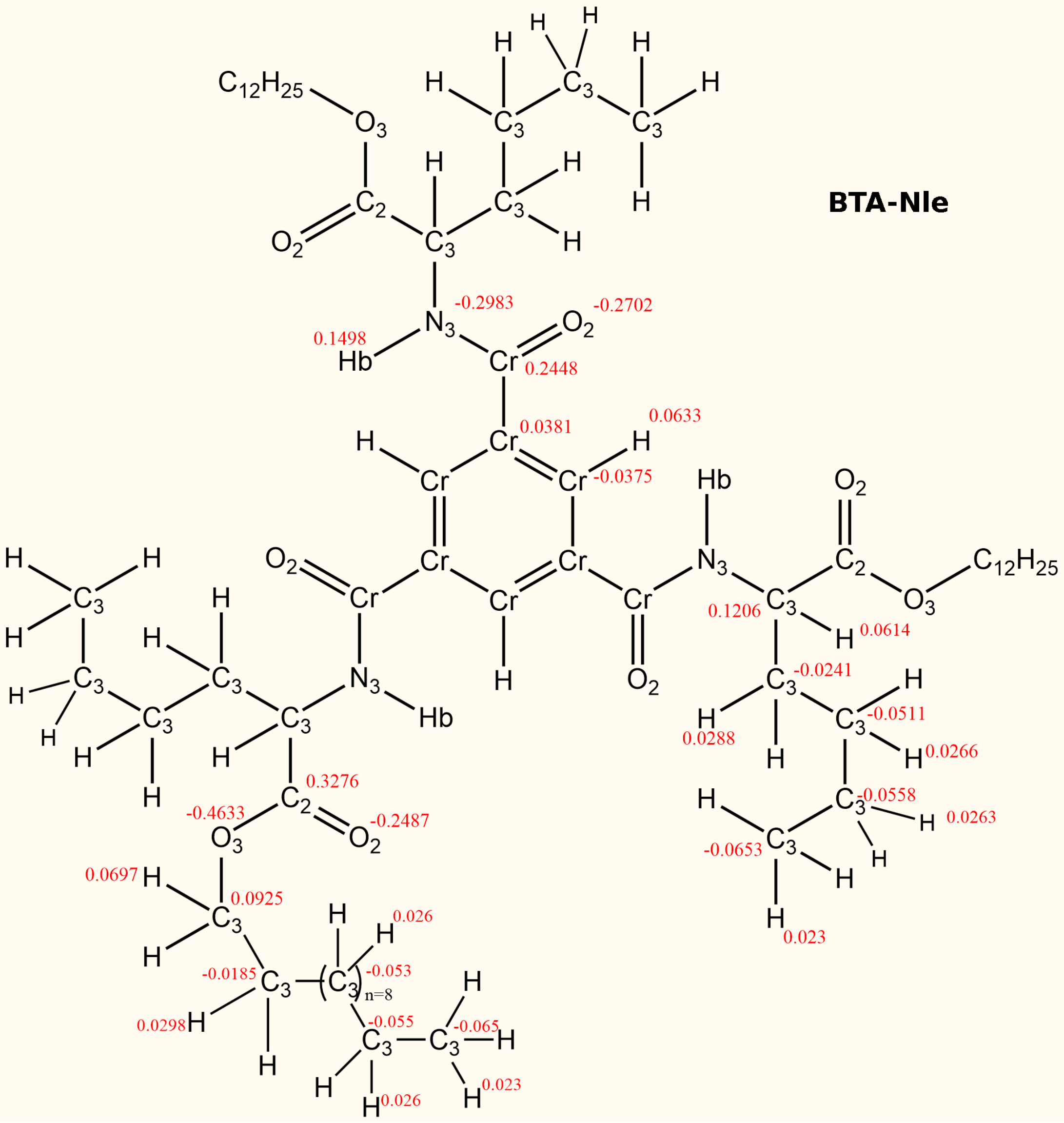


Figure S2: Atom types and their partial charges for BTA-Nle molecule.

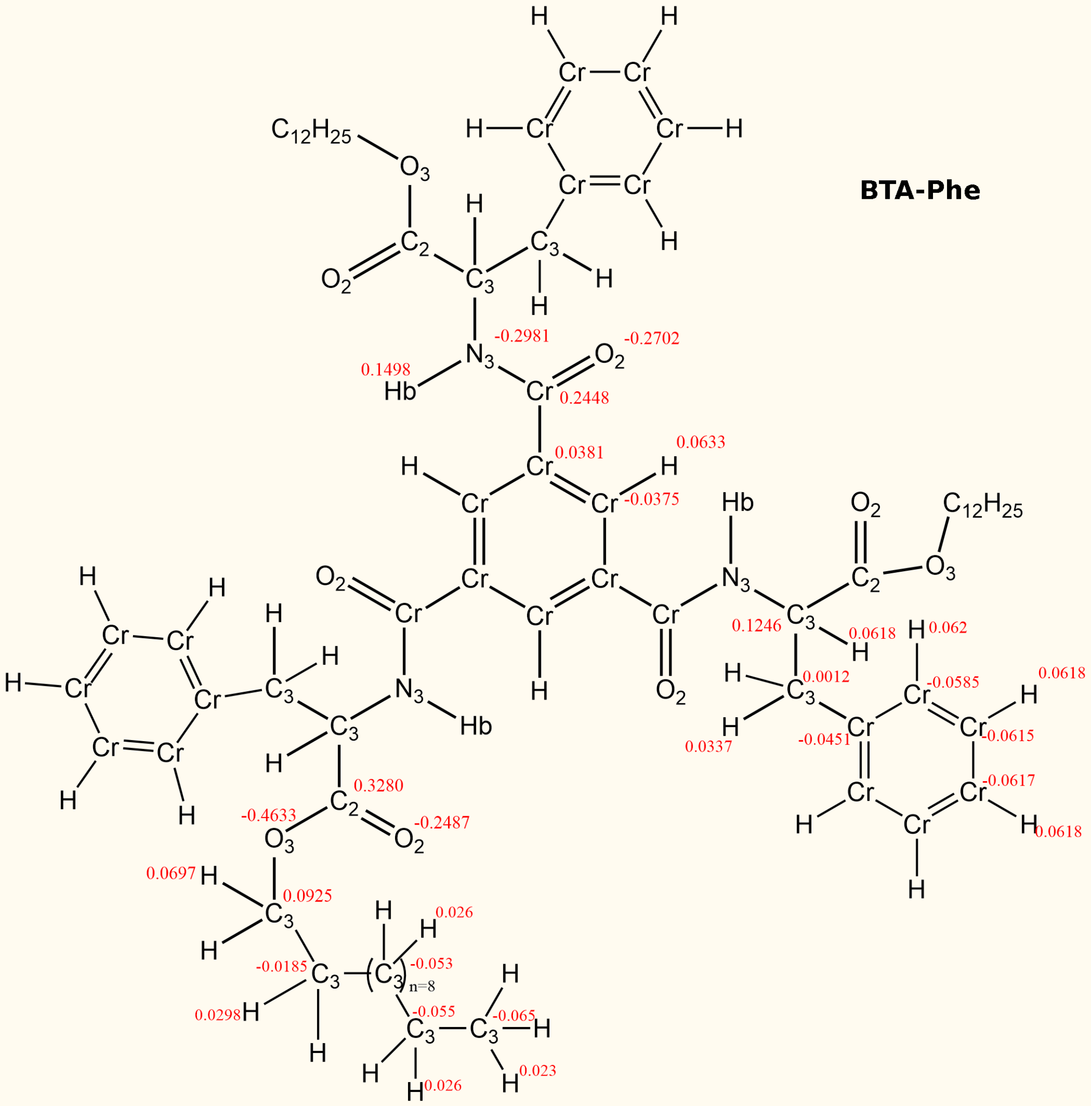


Figure S3: Atom types and their partial charges for BTA-Phe molecule.

Bonded parameters

Table S1: Bond parameters

Type	Force constant (in kcal/mol)	Equilibrium bond distance (r_o)(in Å)
C2-C3	350.00	1.43
N3-Hb	350.00	0.97
C3-O3	350.00	1.42
Cr-N3	525.00	1.34
C3-S	350.00	1.80
Cr-H	350.00	1.02
Cr-O2	525.00	1.35
C3-C3	350.00	1.53
N3-C3	350.00	1.41
C2-O2	700.00	1.22
C3-H	350.00	1.09
C2-O3	350.00	1.32
Cr-Cr	525.00	1.39
C3-Cr	350.00	1.46

Table S2: Angle parameters

Type	Force constant (kcal/mol)	Equilibrium angle (θ_o) (in °)
H-C3-H	50.00	109.471
C3-N3-Hb	50.00	120.0
O3-C2-O2	50.00	120.0
H-C3-O3	50.00	109.471
C3-C2-O2	50.00	120.0
N3-Cr-O2	50.00	120.0
C3-C3-N3	50.00	109.471
H-C3-S3	50.00	109.471
C3-C3-H	50.00	109.471
C2-O3-C3	50.00	104.51
C3-C3-O3	50.00	109.471
Cr-Cr-N3	50.00	120.0
Cr-Cr-H	50.00	120.0
Cr-Cr-O2	50.00	120.0
C2-C3-C3	50.00	109.471
C3-N3-Cr	50.00	120.0
C3-S3-C3	50.00	92.1
C3-C3-S3	50.00	109.471
C3-C3-C3	50.00	109.471
C2-C3-N3	50.00	109.471
C2-C3-H	50.00	109.471
Cr-Cr-Cr	50.00	120.0
Cr-N3-Hb	50.00	120.0
C3-C2-O3	50.00	120.0
H-C3-N3	50.00	109.471
C3-Cr-Cr	50.00	120.0
Cr-C3-H	50.00	109.471
C3-C3-Cr	50.00	109.471

Table S3: Dihedral parameters

Type	K (in kcal/mol)	n	d
O2-C2-C3-C3	0.0833	6	180
Cr-N3-C3-H	0.1666	3	0
H-C3-S3-C3	0.3333	3	0
H-C3-C3-S3	0.1111	3	0
C3-C3-O3-C2	0.3333	3	0
C3-C2-O3-C3	0.1666	6	180
O3-C2-C3-C3	0.0833	6	180
H-C3-C3-N3	0.1111	3	0
Hb-N3-C3-C2	0.1666	3	0
C3-C3-C3-O3	0.1111	3	0
H-C3-C3-H	0.1111	3	0
Hb-N3-C3-C3	0.1666	3	0
O2-Cr-N3-Hb	3.125	2	180
Cr-N3-C3-C3	0.1666	3	0
C3-C3-C3-C3	0.1111	3	0
C3-C3-S3-C3	0.3333	3	0
C3-C3-C3-S3	0.1111	3	0
Cr-Cr-N3-Hb	3.125	2	180
C2-C3-C3-H	0.1111	3	0
C3-C3-C3-N3	0.1111	3	0
O2-Cr-N3-C3	3.125	2	180
O2-C2-C3-N3	0.0833	6	180
C3-C3-C3-H	0.1111	3	0
O2-C2-C3-H	0.0833	6	180
Cr-Cr-Cr-N3	0.625	2	180
O3-C2-C3-N3	0.0833	6	180
Cr-Cr-Cr-H	3.125	2	180
Cr-Cr-Cr-O2	0.625	2	180
H-C3-O3-C2	0.333	3	0
O2-C2-O3-C3	0.1666	6	180
O3-C2-C3-H	0.0833	6	180
Cr-Cr-N3-C3	3.125	2	180
H-C3-C3-O3	0.1111	3	0
C2-C3-N3-Cr	0.1666	3	0
Hb-N3-C3-H	0.1666	3	0
C2-C3-C3-C3	0.1111	3	0
Cr-Cr-Cr-Cr	3.125	2	180
C3-Cr-Cr-Cr	3.125	2	180
H-C3-Cr-Cr	0.0833	6	180
Cr-C3-C3-N3	0.1111	3	0
Cr-C3-C3-H	0.1111	3	0
C3-C3-Cr-Cr	0.0833	6	180
C2-C3-C3-Cr	0.1111	3	0
C3-Cr-Cr-H	3.125	2	180

Improper Dihedral parameters: k=40 ; d = -1; n = 1

Table S4: Non-bonded parameters

Pair	A (kcal/mol)	ρ (Å)	C (kcal/mol - Å^6)
C2-C2	88366.712630	0.277775	583.017658
C3-C3	88366.712630	0.277775	583.017658
Cr-Cr	88366.712630	0.277775	583.017658
H-H	3407.785992	0.258036	31.369151
Hb-Hb	16.275479	0.266250	0.212743
N3-N3	60862.320828	0.264545	329.511185
O3-O3	55027.520269	0.252511	268.546376
O2-O2	55027.520269	0.252511	268.546376
S-S	55987.648248	0.335833	2947.261800

Table S5: Details of the simulated systems. [a] Temperature is 350 K. All other simulations are at 298.15 K. [b] Free energy simulations performed at 298.15 K and length of the trajectory corresponds to the duration in each window.

System	Total No. of atoms	No. of cyclohexane molecules	Mean box length (in Å)	Trajectory length (in ns)
Hexamer (BTA-Met)	16080	2500	76.9	40
Hexamer (BTA-Phe)	16134	2500	76.9	40
AC dimer (BTA-Met)	11724	1894	69.8	25
AA dimer (BTA-Met)	11700	1890	69.7	25
AC dimer (BTA-Nle)	11670	1883	69.7	25
AA dimer (BTA-Nle)	11514	1857	69.4	25
AC dimer (BTA-Phe)	11586	1868	69.5	25
AA dimer (BTA-Phe)	11616	1873	69.6	25
AC dimer (BTA-Met)[a]	11724	1894	71.3	25
AA dimer (BTA-Met)[a]	11700	1890	71.3	25
AC dimer (BTA-Nle)[a]	11670	1883	71.2	25
AA dimer (BTA-Nle)[a]	11514	1857	70.9	25
AC dimer (BTA-Phe)[a]	11586	1868	71.0	25
AA dimer (BTA-Phe)[a]	11616	1873	71.1	25
Dimer (BTA-Met)[b]	11724	1894	69.8	20
Dimer (BTA-Nle)[b]	11670	1883	71.2	20
Dimer (BTA-Phe)[a]	11586	1868	71.0	20
Tetramer (BTA-Met)[b]	23370	3775	87.9	10
Tetramer (BTA-Nle)[b]	23544	3800	88.1	10
Tetramer (BTA-Phe)[b]	23610	3809	88.2	10
Hexamer (BTA-Phe)[b]	17430	2716	79.0	10

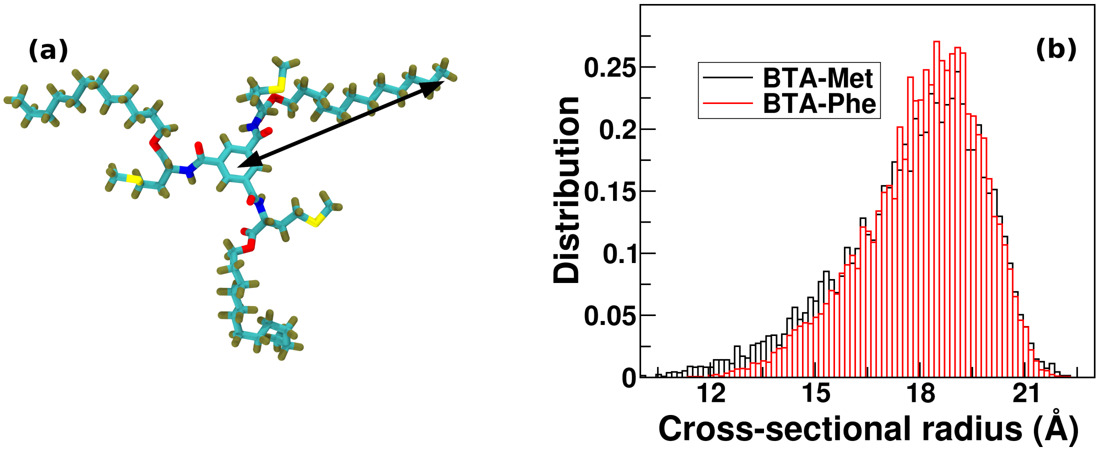


Figure S4: (a) Schematic showing the measurement for cross-sectional radius, the distance between the benzene ring and the last carbon of the dodecyl chain. (b) Distribution of the distance averaged over the two molecules in the core of a hexamer in solution.

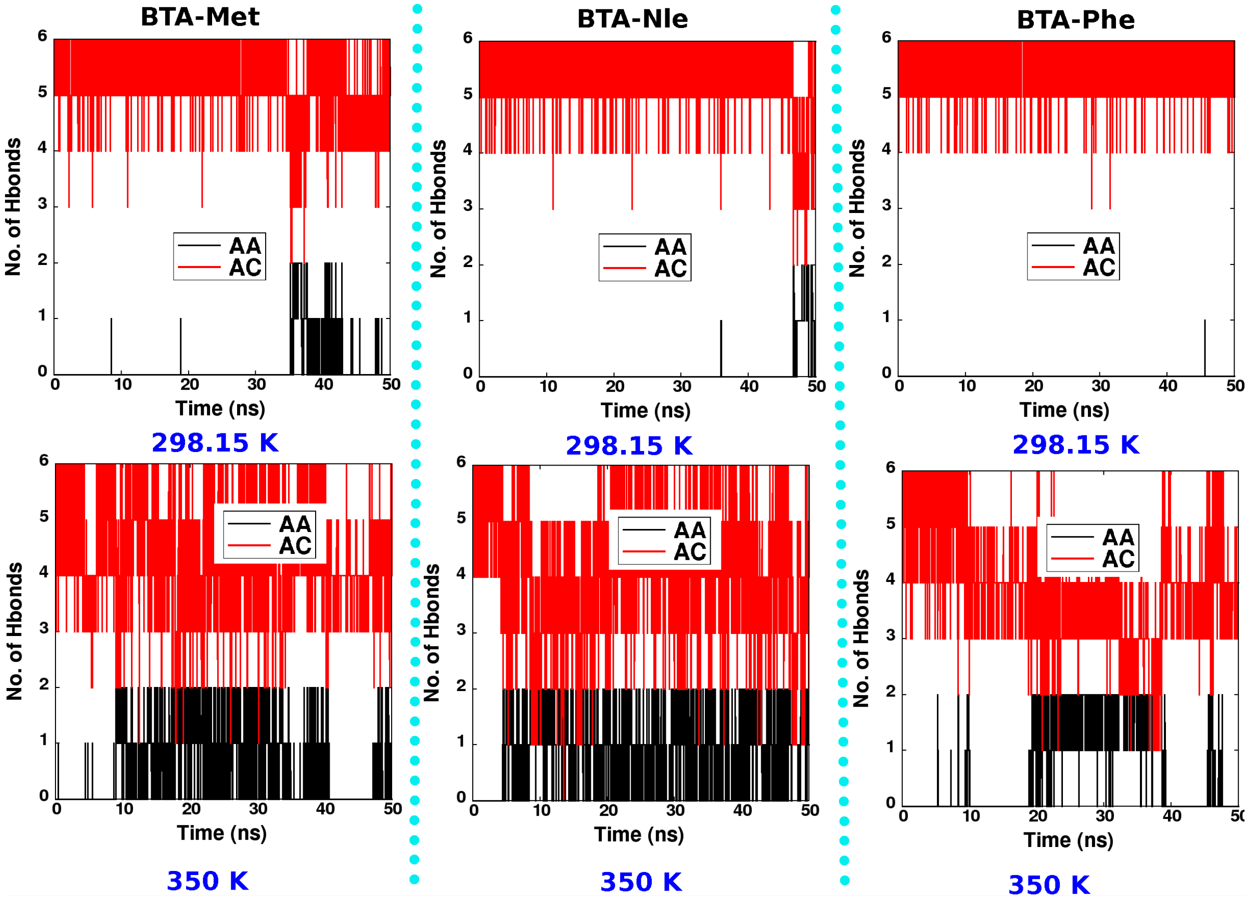


Figure S5: MD simulations started from an AC dimer (six AC hydrogen bonds) configuration soaked in explicit cyclohexane solution were performed in the NPT ensemble. The number of AA and AC hydrogen bonds as a function of time for the three derivatives at 298.15 K (top panel) and at 350 K (bottom panel) are shown. For BTA-Met: R’=$CH_2CH_2SCH_3$, BTA-Nle: R’=$CH_2CH_2CH_2CH_3$, BTA-Phe:R,=$CH_2C_6H_5$ and R”=dodecyl.

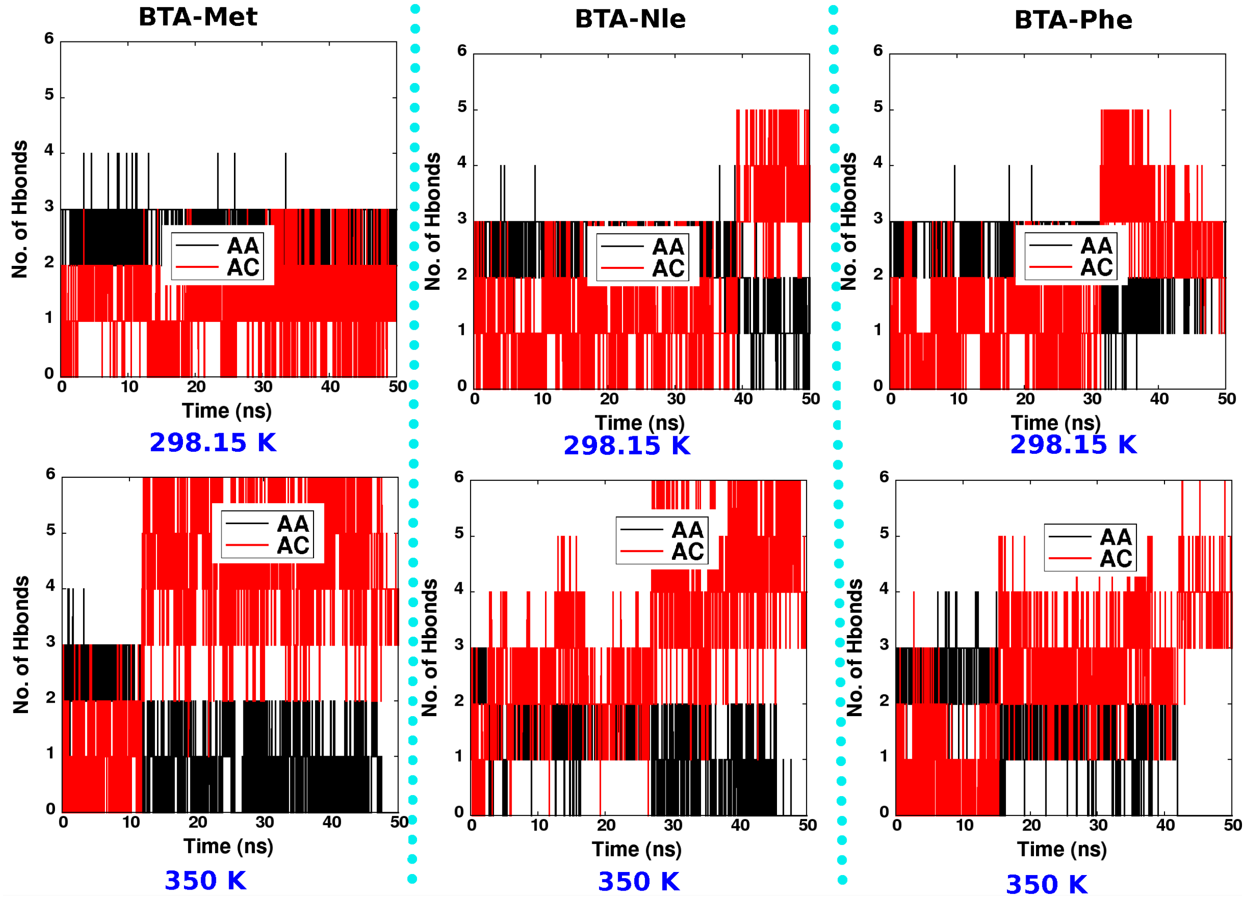


Figure S6: MD simulations started from an AA dimer (three AA hydrogen bonds) configuration soaked in explicit cyclohexane solution were performed in the NPT ensemble. The number of AA and AC hydrogen bonds as a function of time for the three derivatives at 298.15 K (top panel) and 350 K (bottom panel) are shown. For BTA-Met: R’=$CH_2CH_2SCH_3$, BTA-Nle: R’=$CH_2CH_2CH_2CH_3$, BTA-Phe:R,=$CH_2C_6H_5$ and R”=dodecyl.

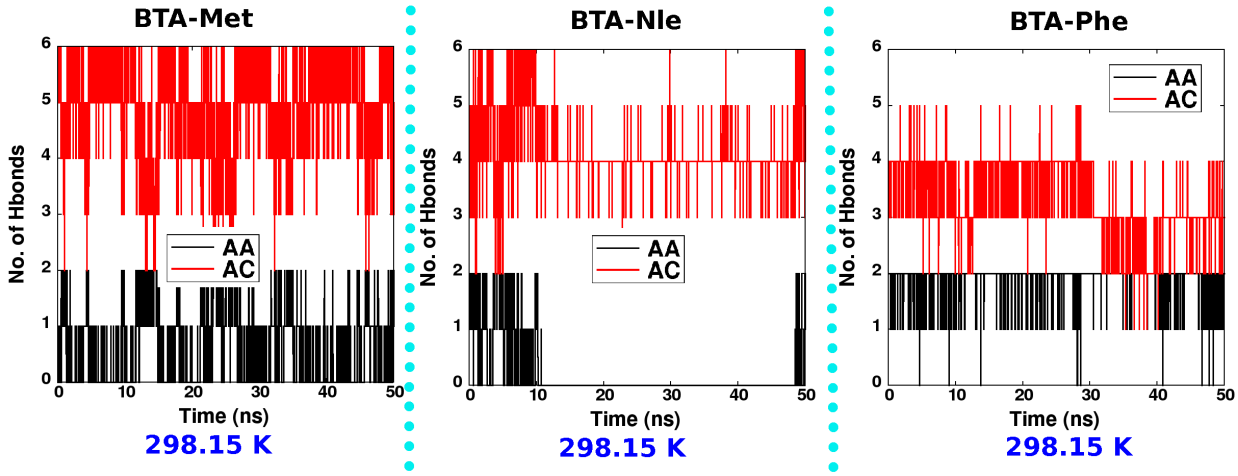


Figure S7: Configurations obtained from simulations at 350 K initiated from an AC dimer configuration were cooled to 298.15 K over a duration of 2.5 ns. MD simulations were extended for 50 ns at 298.15 K. The number of AA and AC type hydrogen bonds in such a run at 298.15 K are displayed. For BTA-Met: R’=$CH_2CH_2SCH_3$, BTA-Nle: R’=$CH_2CH_2CH_2CH_3$, BTA-Phe:R,=$CH_2C_6H_5$ and R”=dodecyl.

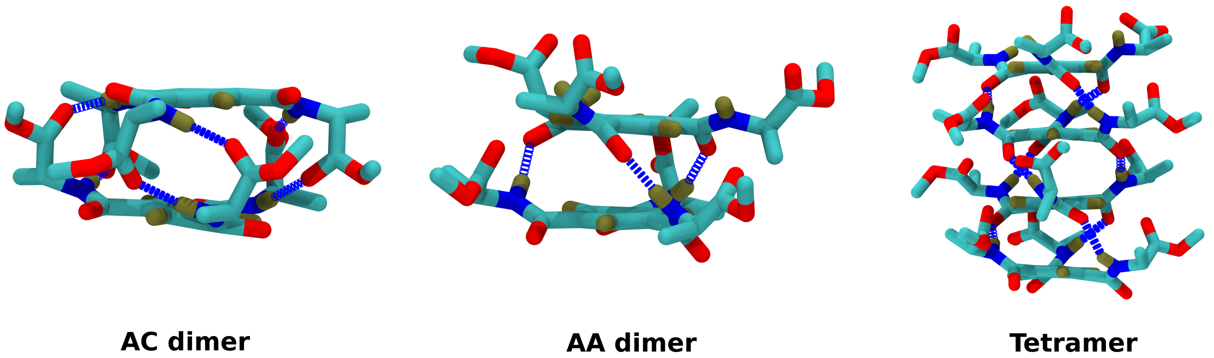

AC dimer **AA dimer** **Tetramer**

Figure S8: Snapshots of an AC dimer, an AA dimer and a tetramer that were considered as reference structures to determine RMSD. These structures were chosen from unbiased simulations carried out in explicit solution at 298.15 K.

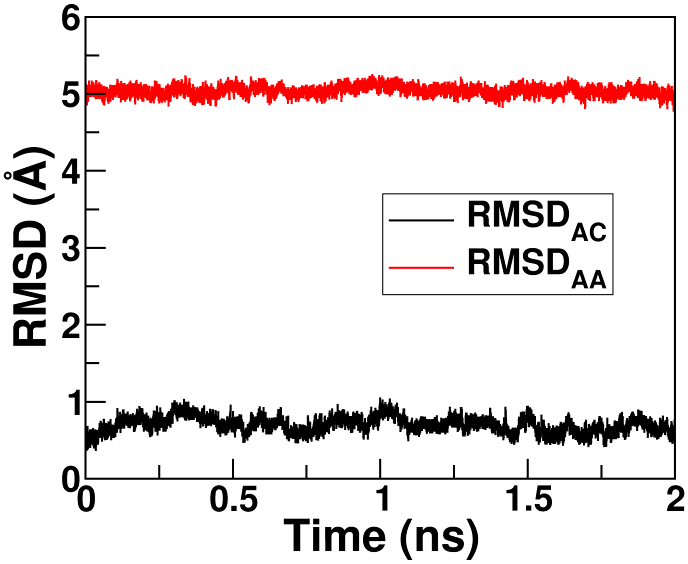


Figure S9: RMSD of an AC dimer with respect to AC and AA dimer reference configurations (see Figure S8) obtained from an unbiased MD simulation trajectory.

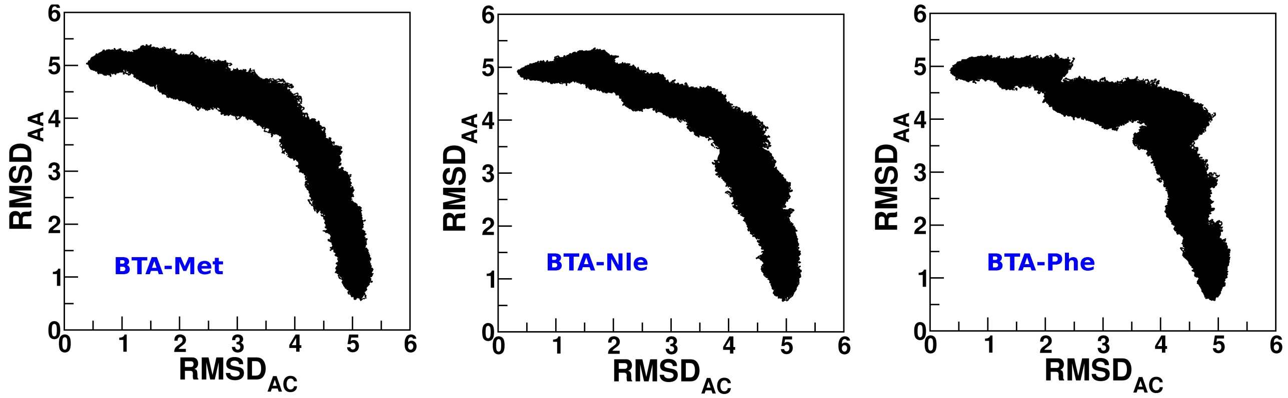


Figure S10: Overlap of the probability distributions along the two-dimensional reaction coordinate (Ref. Figure 5 of the main manuscript).

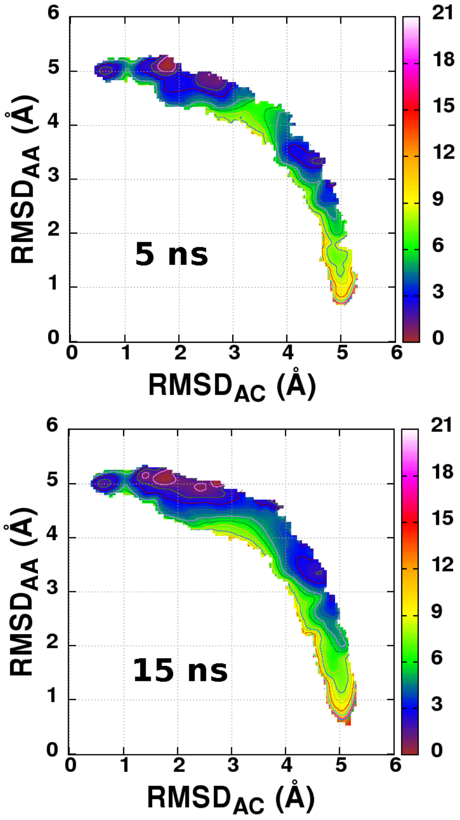


Figure S11: Evolution of the free energy surface as a function of time for BTA-Met derivative. From 15 ns to 20 ns, free energy surface does not vary much.

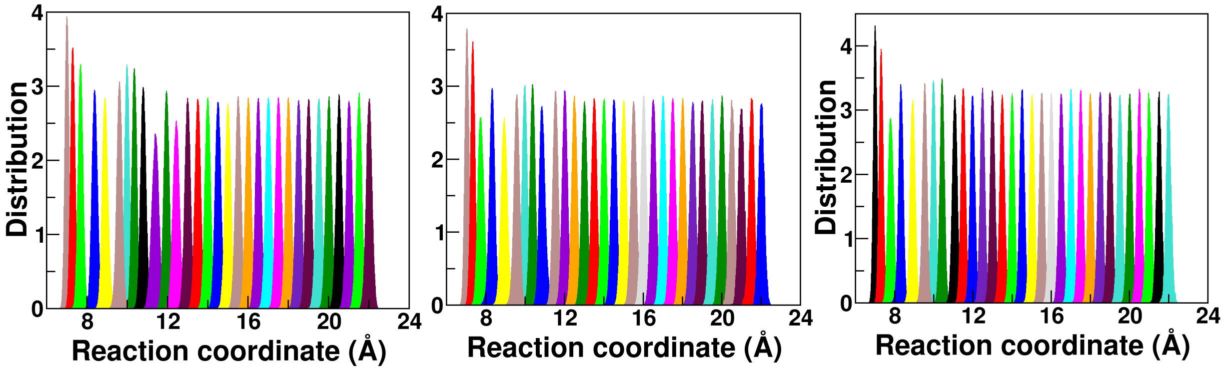
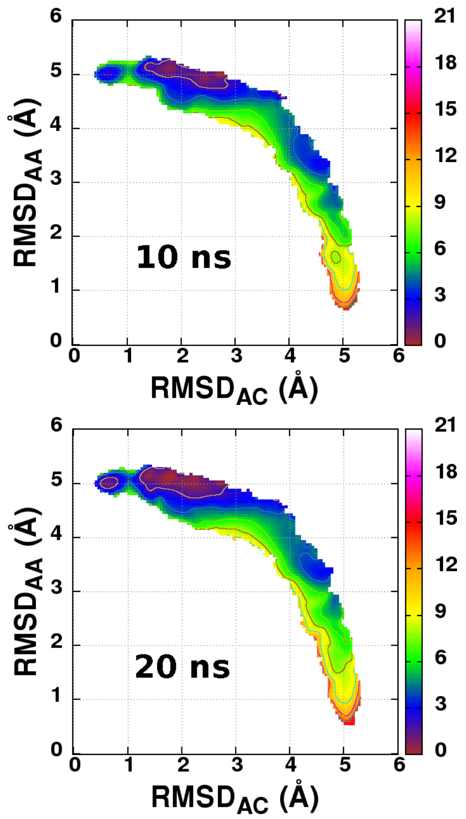


Figure S12: Overlap of probability distributions along the reaction coordinate (Ref. Figure 7 of the main manuscript).



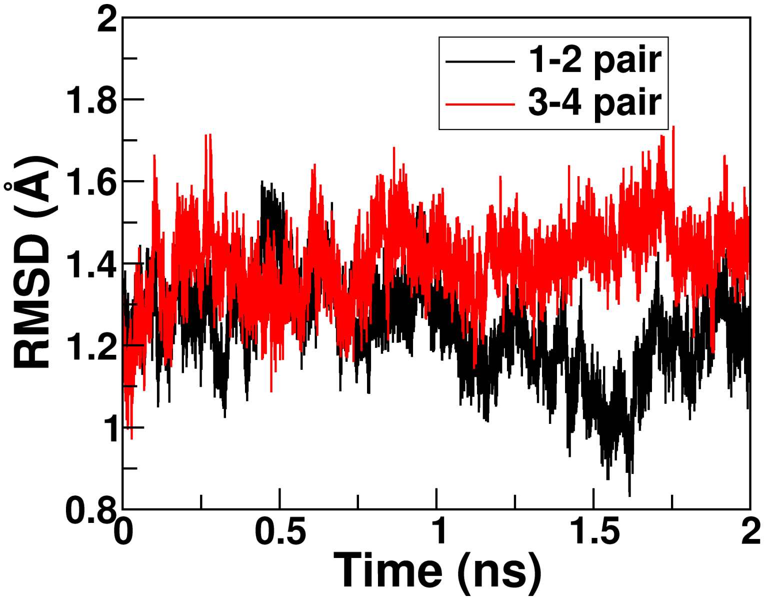


Figure S13: MD simulations of a tetramer in cyclohexane solution at 298.15 K. A pair of neighbouring molecules in a tetramer resembles an AA dimer. RMSD of two pair of dimers with respect to an AA dimer (see Figure S8).

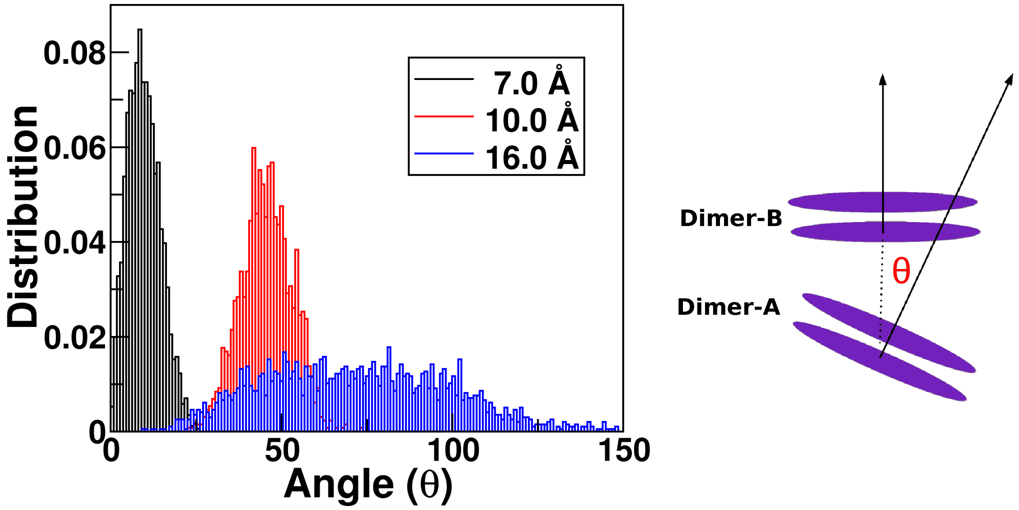


Figure S14: Distributions of the angle between two dimers which were pulled apart from a tetramer. Vector-1 is the vector joining the centers of mass of molecules in Dimer-A. Vector-2 is the vector joining the centers of mass of molecules in Dimer-B. θ is the angle between these two vectors. Legend displays the inter-dimer distances at which these distributions were calculated.

Free energy simulations of a tetramer

The geometry of the two dimers was restrained by imposing that the RMSD variable has an upper boundary of 1.3 Å. For BTA-Met, we have also carried out simulations relaxing the RMSD value from 1.3 Å to 1.5 Å. The colvar value for two dimers as a function of time for different restraint values are shown in Figure S16. A comparison of the free energy profiles for different restraints are shown in Figure S17.

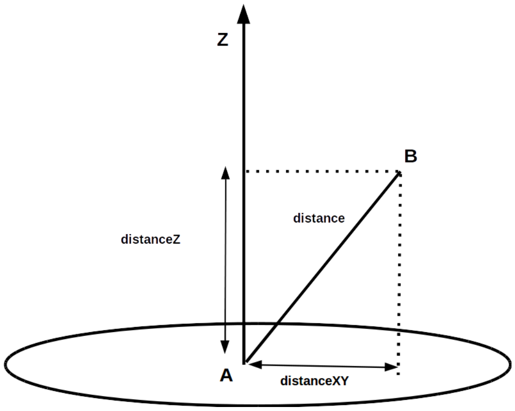


Figure S15: DistanceXY: It is the projection component of the distance between two groups onto a plane. DistanceZ is the projection component of the distance between two group onto an axis.

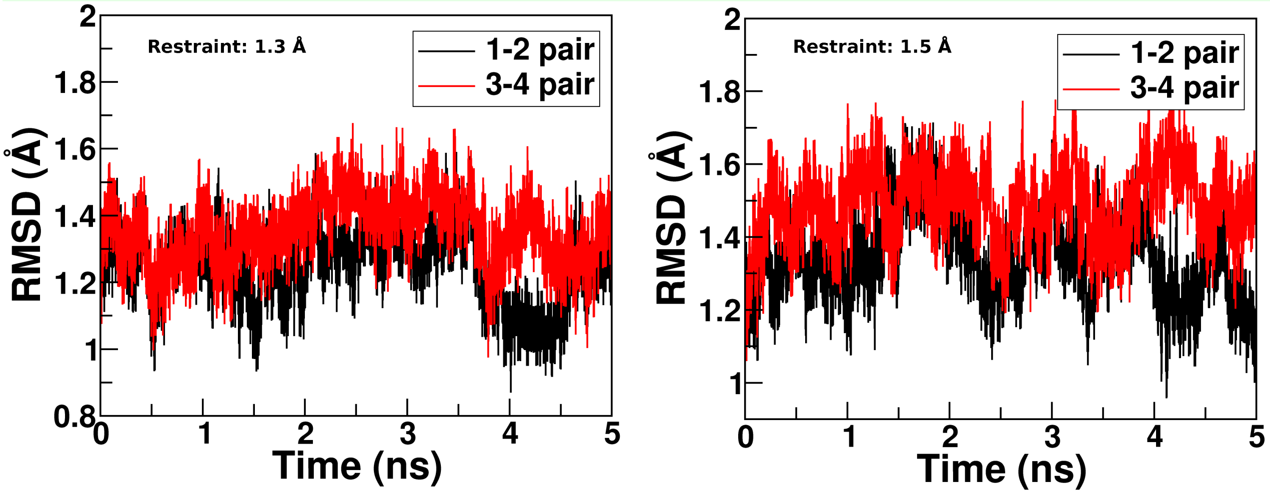


Figure S16: RMSD value of two pairs of dimers with respect to an AA dimer (see Figure S8). Simulations were performed in cyclohexane solvent at 298.15 K.

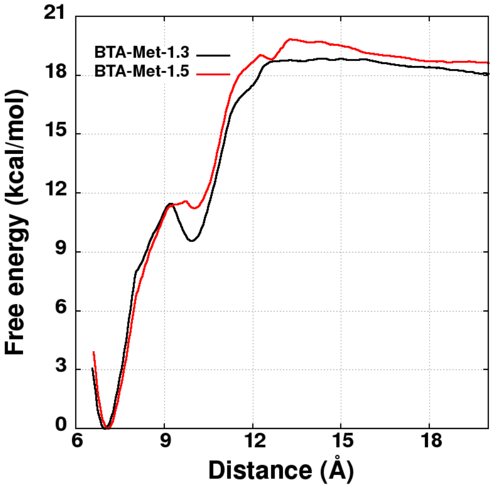


Figure S17: Free energy profiles associated with pulling two AA dimers apart from an AA tetramer. The geometry of each dimer is restrained with a RMSD variable.

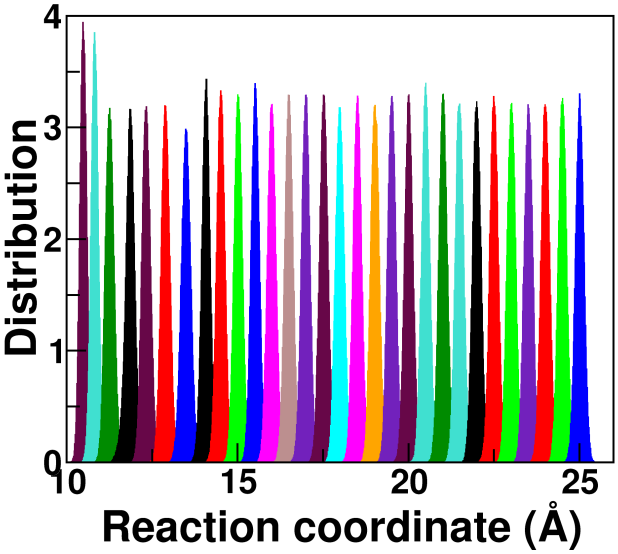


Figure S18: Overlap of probability distributions along the reaction coordinate (Ref. Figure 8 of the main manuscript).

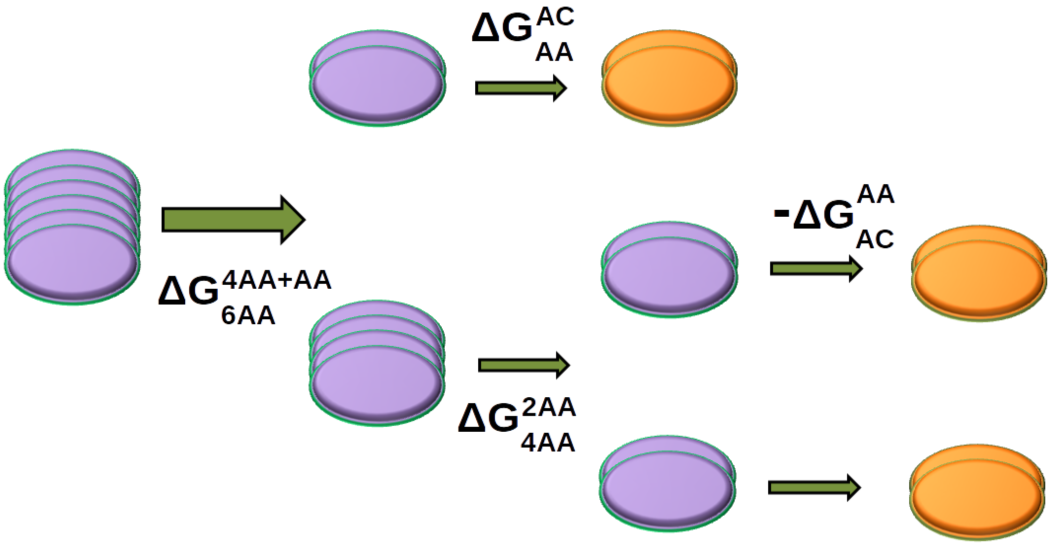


Figure S19: Scheme to determine the free energy difference ΔG_{6AA}^{3AC}, between a hexamer with AA hydrogen bonding and three AC dimers.

References

(S1) Mayo, S. L.; Olafson, B. D.; Goddard, W. A. DREIDING: a generic force field for molecular simulations. *J. Phys. Chem.* **1990**, *94*, 8897–8909.