SUPPORTING INFORMATION

I. COARSE-GRAINED MOLECULAR MODEL

A. Bonded interactions

Bond and angle interactions were treated as harmonic potentials:

$$u^{bond}(r) = \frac{1}{2} k_{bond} (r - r_0)^2 \tag{A.1}$$

$$u^{angle}(r) = \frac{1}{2} k_{angle} (\theta - \theta_0)^2 \tag{A.2}$$

where k_{bond} and k_{angle} correspond to the spring constants, and are set to large values in order to maintain all bonds and angles close to their minimum values (r_0 and θ_0, respectively). Table S1 provide the values used here for these parameters.

TABLE S1. Force field parameters for two- and three-body forces forces (i.e., bond and angle) used in the working CG model. All parameters are expressed in the intrinsic units (see main text).

Two-body interactions (bonds)		
	r_0 $[\mathcal{L}]$	k_{bond} $[\mathcal{E}/\mathcal{L}^2]$
NC_α	1.455	
$C_\alpha C'$	1.510	
$C'N$	1.325	300.0
$C_\alpha C_\beta$	1.530	
$C'C_1$, $C'C_3$	1.430	
C_1C_2, C_2C_3, C_3C_1	1.540	
Three-body interactions (angles)		
	θ_0 [deg]	k_{angle} $[\mathcal{E}/\text{deg}^2]$
$NC_\alpha C_\beta$	108.0	
$C_\beta C_\alpha C'$	113	
$NC_\alpha C'$	111.0	10.0
$C_\alpha C'N$	116.0	
$C'NC_\alpha$	122.0	
$C_1C_2C_3$, $C_2C_3C_1$, $C'C_1C_2$, C_3C_1C'	112.0	

The structural flexibility of the molecule is then provided through the torsional angles which allow the different beads to rotate around a bond. Generally, any torsional angle for a set of beads *ijkl* describes the angle between the planes *ijk* and *jkl*, and is such that the

counterclockwise rotation of the plane *ijk* with respect to *jkl* defines a positive rotational angle. For polypeptides, four different torsional angles were considered: (i) ϕ between beads C'NC$_\alpha$C'; (ii) ψ between beads NC$_\alpha$C'N; (iii) ω between beads C$_\alpha$C'NC$_\alpha$; and (iv) γ between beads NC$_\alpha$C'C$_\beta$. The first three dihedral angles define the structure of the protein backbone (see Fig. 1 in the main text), while γ is an improper angle and indicates the chirality of a given amino acid. In particular, ϕ and ψ allow one to determine the secondary structure propensity of the backbone (i.e., the formation of helical or β-stranded structure) and ω provides the balance between the *cis* ($\omega = 0°$) and *trans* ($\omega = 180°$) conformations of the peptide bond.

Here, dihedral angles are represented as a Fourier series in the rotational angle φ as

$$u^{dih}(\varphi) = \sum_n k_n \left[1 - \cos\left(n\varphi - \varphi_{n,0}\right)\right] \tag{A.3}$$

Each term in the Fourier series in eq. A.3 corresponds to a possible equilibrium orientation of the dihedral angle, and thus k_n and $\varphi_{n,0}$ represent the strength parameter and the phase angle for each of the equilibrium states, respectively. Because rotation around the bond between sp^3-hybridized atoms has a relative low energy barrier at room temperatures, ϕ and ψ were set to a single equilibrium position ($n = 1$) with a small value for the strength parameter. The equilibrium orientations for ϕ and ψ were selected to favor the dipole interaction between the amine and carboxylic groups rather than the rotation of both dihedral angles. Similarly, the *cis* conformation is rather unfavorable for most of the amino acids, and the equilibrium orientation for ω was set to the *trans* conformation except for proline that can adopt any of those conformations. Thus, for a peptide bond located before a proline, two energy minima are considered to map both *cis* and *trans* configurations. Given that the L-form is the naturally occurring isoform of all non-glycine amino acids, γ was also set to a single energy minimum. Nevertheless, the two stereoisomers only differ by the sign of γ, and both can be modeled with eq. A.3. Table S2 summarizes the different values of k_n and $\varphi_{n,0}$ used here.

In the case of polymer chains, there are three dihedral angles in the working CG model. Similar arguments than those used for modeling ϕ and ψ also hold for representing these dihedral angles as all of them occur around sp^3-hybridized atoms; however, there are no dipolar interactions between the atoms that form these torsional angles. In order to allow these bonds to freely rotate, the present CG model does not consider any explicit interaction

TABLE S2. Interaction parameters for four-body forces (i.e., dihedral angles) used in the working CG model. k, n, and φ_0 corresponds to the strength constant, the mode, and the phase angle in the Fourier series (eq. A.3). In the case of ω, the second mode of the Fourier series is only considered for the peptide bond around proline residues. For the L-form of an amino acid, the negative sign for the equilibrium value of γ is adopted.

	k_n [$\mathcal{E}$]	$\varphi_n, 0$ [deg]	n
ϕ	-0.3	0	1
ψ	-0.3	0	1
ω	67.0	180	1
	3.0	0	2
γ	17.0	$\pm$120	1

for the dihedral angles either within a polymer chain or involving a bead from a polymer chain (e.g., at the interface between a peptide and a polymer block).

B. Non-bonded interactions

1. Steric interactions

Steric interactions provide the main constrains in terms of excluded volume effects, and thus they play a key role on determining the secondary structure adopted by a polypeptide chain as well as the overall packing of the conjugated molecules. These interactions were modeled here via a purely repulsive Weeks-Chandler-Andersen potential

$$u^{sterics}(r) = \begin{cases} 4\epsilon_{sterics}\left[\left(\frac{\sigma_{ij}}{r}\right)^{12} - \left(\frac{\sigma_{ij}}{r}\right)^{6}\right] & \text{if } r \leq r_c\,, \\ 0 & \text{otherwise}\,. \end{cases} \tag{B.1}$$

where $r_c = 2^{1/6}\sigma_{ij}$ is the arithmetic mean between the two bead sizes involved in the interaction. $\epsilon_{sterics}$ represents the strength parameter for steric interactions regardless the type of interacting beads. Following a common practice in atomistic simulations, steric interactions are calculated between beads that are more than three bonds apart. Furthermore, steric interactions are considered for all beads except when it occurs between two C_β beads as this type of interaction is already implicitly considered in the hydrophobic interactions (see below). Table S3 summarizes the values of the free parameters used for steric interactions

as well as other non-bonded interactions considered in the working CG model.

TABLE S3. Non-bonded interaction parameters used in the working CG model. σ and ϵ values are in intrinsic units of length ($\mathcal{L}$) and energy ($\mathcal{E}$). σ_{C_i} corresponds to the excluded diameter of any of the beads in polyacrylic acid.

Steric interactions				
σ_N	σ_{C_α}	$\sigma_{C'}$	σ_{C_i}	$\epsilon_{sterics}$
2.9	3.7	3.5	3.95	0.02

Hydrophobic interactions	
σ_{C_β}	ϵ_{hp}
5.0	4.5

Hydrogen bond interactions	
σ_{hb}	ϵ_{hb}
4.11	6.0

2. Hydrophobic interactions

Attractive interactions between amino acids depend, at least in part, on their hydrophobicity and hydrogen-bonding capability (i.e., their water "affinity")[1–3]. Thus, the magnitude of the attractions between residues on adjacent proteins is described primarily in terms of the relative hydrophobicity of the two residues that are interacting. This level of specificity is achieved by considering two parameters in the model. The first parameter provides a relative hydrophobicity score, ϵ_i, which is dimensionless and ranges from 0 for the most hydrophilic residue to 1 for the most hydrophobic. The values of ϵ_i are those used by Bereau and Deserno[4] based on Miyazawa and Jernigan's statistical analysis[5] of residue-residue contacts within the crystal structures of multiple proteins. The second free parameter, ϵ_{hp}, accounts for translating the strength of the attractive interaction into an absolute scale -i.e., ϵ_{hp} has units of energy. Thus, hydrophobic interactions are treated as

$$u^{hp}(r) = \begin{cases} 4\epsilon_{hp}\left[\left(\frac{\sigma_{C_\beta}}{r}\right)^{12} - \left(\frac{\sigma_{C_\beta}}{r}\right)^{6}\right] + \epsilon_{hp}(1-\epsilon_{ij}) & \text{if } r \le r_c\,, \\ 4\epsilon_{hp}\epsilon_{ij}\left[\left(\frac{\sigma_{C_\beta}}{r}\right)^{12} - \left(\frac{\sigma_{C_\beta}}{r}\right)^{6}\right] & \text{otherwise}\,. \end{cases} \tag{B.2}$$

where σ_{C_β} is the van der Waals diameter of the C_β side chain. For simplicity, the excluded volume of all non-glycine side chains is kept constant. r_c is the same as defined for eq. B.1 and corresponds to the distance at which the interaction potential switches from being repulsive to attractive. This value is such that both the potential and its first derivative are continuous. The use of this form for the potential allows all types of residues to have the same strength for the short-ranged steric repulsion, whereas the attractive force depends on the relative affinity ϵ_{ij} between the i-th and j-th residues, and this form is also amenable to molecular dynamics simulations. The value of ϵ_{ij} is calculated from the geometric average of the relative hydrophobic score of the residues i and j (i.e. $\epsilon_{ij} = \sqrt{\epsilon_i \epsilon_j}$). Table S4 provides the values for ϵ_i for all type of side-chains. Note that hydrophobic interactions are only modeled between C_β beads.

TABLE S4. Relative hydrophobic scores[4] (ϵ_i) for each type of natural occurring amino acid. Although glycine (marked with an asterisk) has a non-negligible hydrophobic score, its side chain is not considered in the working coarse-grained model.

Residue	ϵ_i	Residue	ϵ_i
Lys	0.00	His	0.25
Glu	0.05	Ala	0.26
Asp	0.06	Tyr	0.49
Asn	0.10	Cys	0.54
Ser	0.11	Trp	0.64
Arg	0.13	Val	0.65
Gln	0.13	Met	0.67
Pro	0.14	Ile	0.84
Thr	0.16	Phe	0.97
Gly*	0.17	Leu	1.00

3. Hydrogen bonding

Hydrogen bonding constitutes one of the main attractive forces that affect the structure of biomolecules. The interaction depends on the relative distance and orientation between a H-donor group and a H- acceptor, and is such that the force is a maximum when these two groups are aligned. For instance, in the case of polypeptides, hydrogen bonding typically occurs between the amine group (H-donor; composed of a nitrogen and a hydrogen) and the carbonyl group (H-acceptor; with a carbon double-bonded to an oxygen), and is favored when the N, H, and O atoms are aligned. Conversely, polyacrylic acid interacts through hydrogen

bonding via the carboxylic group, which works as both H-donor (with the hydroxy group) and H-acceptor (with the carbonyl group). However, for simplicity and given the adopted geometrical representation of PAA here, the H-acceptor and H-donor were assigned to beads C_1 and C_2, respectively (cf. Fig. 1 in main text). Although neither oxygen nor hydrogen are explicitly considered in the present CG model, the position of these particles were calculated via the local geometry of the neighbor beads (Fig. S2). Hydrogen bonds are then modeled here as:

$$u^{hb}(r) = \epsilon_{hb}\left[5\left(\frac{\sigma_{hb}}{r}\right)^{1} 2 - 6\left(\frac{\sigma_{hb}}{r}\right)^{1} 0\right] \times \begin{cases} \cos^2\theta_d \cos^2\theta_a & \text{if } |\theta_d|,|\theta_a| < 90^\circ\,, \\ 0 & \text{otherwise}\,. \end{cases} \tag{B.3}$$

where r is the distance between the H-donor and H-acceptor beads, σ_{hb} is the equilibrium distance for hydrogen bonding. θ_d (θ_a) corresponds to the angle formed by the H-donor (H-acceptor) group and r (Fig. S2). ϵ_{hb} is a free parameter that provides the interaction strength for hydrogen bonding. In the case of polypeptides, hydrogen bonding is considered for all type of amino acids except for the amine group of proline as its side chain is typically connected to the nitrogen of the backbone.

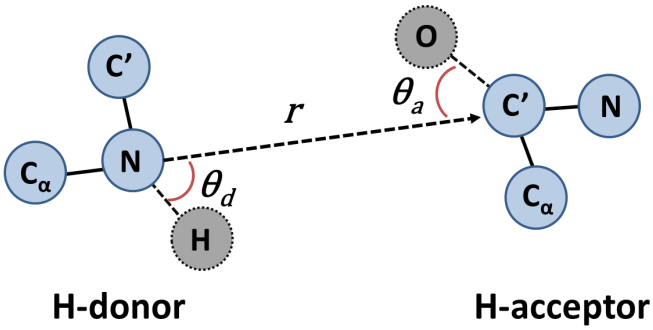

FIG. S1. Schematic illustration of the hydrogen bond interaction between amino acids. Similar interaction model is also considered between polymer units with N, C_α and C' replaced by C_1, C_2, and C_3, respectively. Hydrogen (H) and oxygen (O) beads are not explicitly modeled, but their position is inferred from neighbor beads.

C. Thermodynamic variables of CG model

Thermodynamic properties were calculated from the REMD simulations via implementation of WHAM[6,7]. Thus, the free-energy of a given state is calculated as

$$A_T(X) = -k_B T \ln \left[\frac{\sum_E \omega(E,X) \exp(-E/k_B T)}{\sum_X \sum_E \omega(E,X) \exp(-E/k_B T)} \right] \tag{C.1}$$

where X denotes any order parameter for a given configuration such as the radius of gyration or specific hydrogen-bond interactions. $\omega(E,X)$ is the density of states and corresponds to the number of configurations that give a value for the interaction energy of E and for the order parameter of X regardless the temperature. $A_T(X)$ represents the Helmholtz free-energy at a temperature T for all the configurations that yield a value of X. Note that the term in the logarithm in eq. C.1 is effectively the probability of finding a configuration at a temperature T that yields a value for the order parameter of X.

Therefore, it follows from eq. C.1 that the average value of X can be calculated as

$$\langle X \rangle = \frac{\sum_E X \omega(E,X) e^{-E/k_B T}}{\sum_X \sum_E \omega(E,X) e^{-E/k_B T}} \tag{C.2}$$

where $\langle ... \rangle$ represents the ensemble average.

From a statistical mechanical standpoint, the heat-capacity C_v is calculated as the variance of the internal energy[8]. That is,

$$\frac{C_v}{k_B} = \beta^2 \left(\langle E^2 \rangle - \langle E \rangle^2 \right) \tag{C.3}$$

II. SIMULATED POLYMER SIZE

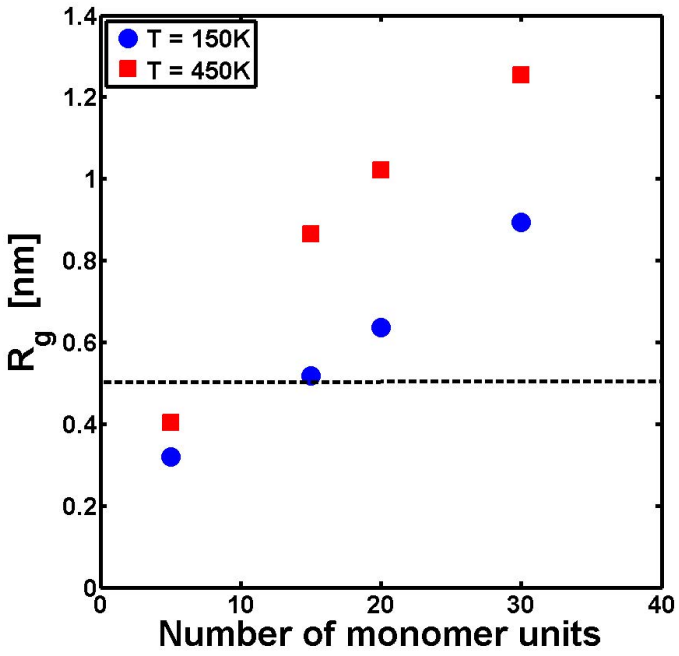

FIG. S2. Radius of gyration (R_g) as a function of the number of monomeric units in polyacrylic acid at two different temperatures: (circles) 150 K and (squares) 450 K. These two temperature correspond to conditions where the structure of the polymer is collapsed or folded (low temperatures) and as a random coil (high temperatures). R_g is obtained by simulating a single polymer molecule using the CG model and methodology described in this work. The dashed line indicate half of the size of the polymer block used for the experimental analysis, and thus the selected size for the simulated polymer block.

III. R_g FOR POINT-MUTATIONS

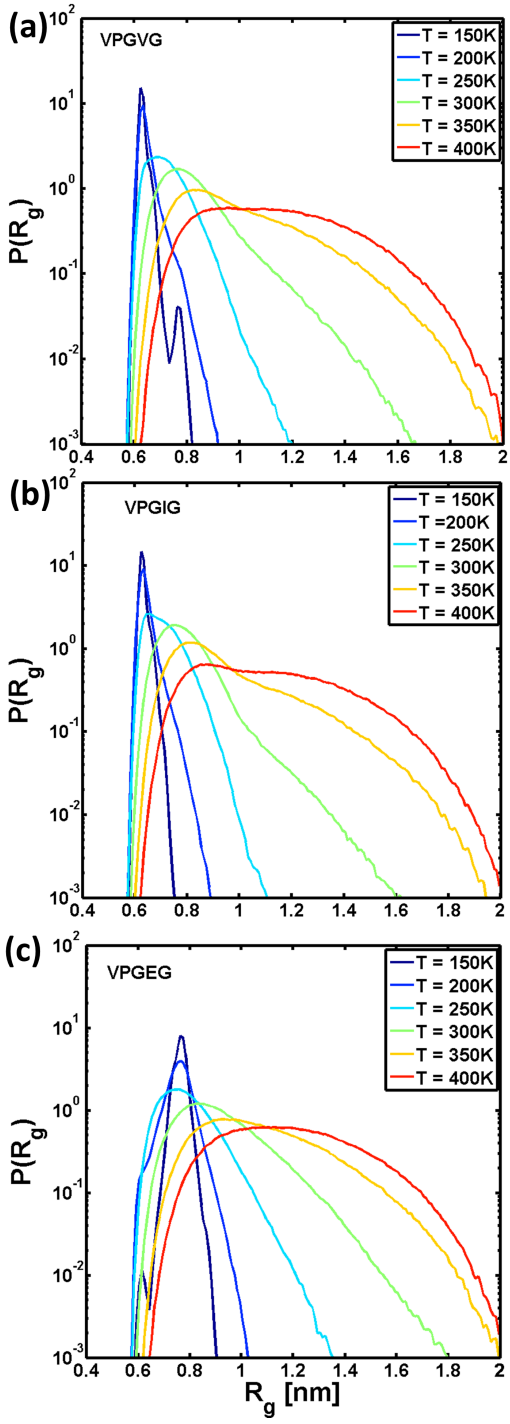

FIG. S3. Probability distribution functions of molecular configurations as a function of the radius of gyration (Rg) at temperatures ranging from 150 to 400 K for the triblock molecules with different variants of the polypeptide blocks: (a) VPGVG-PAA-VPGVG; (b) VPGIG-PAA-VPGIG; and (c) VPGEG-PAA-VPGEG. PAA block consists of 15 monomers for all the variants.

IV. NMR OF CONJUGATED MATERIALS

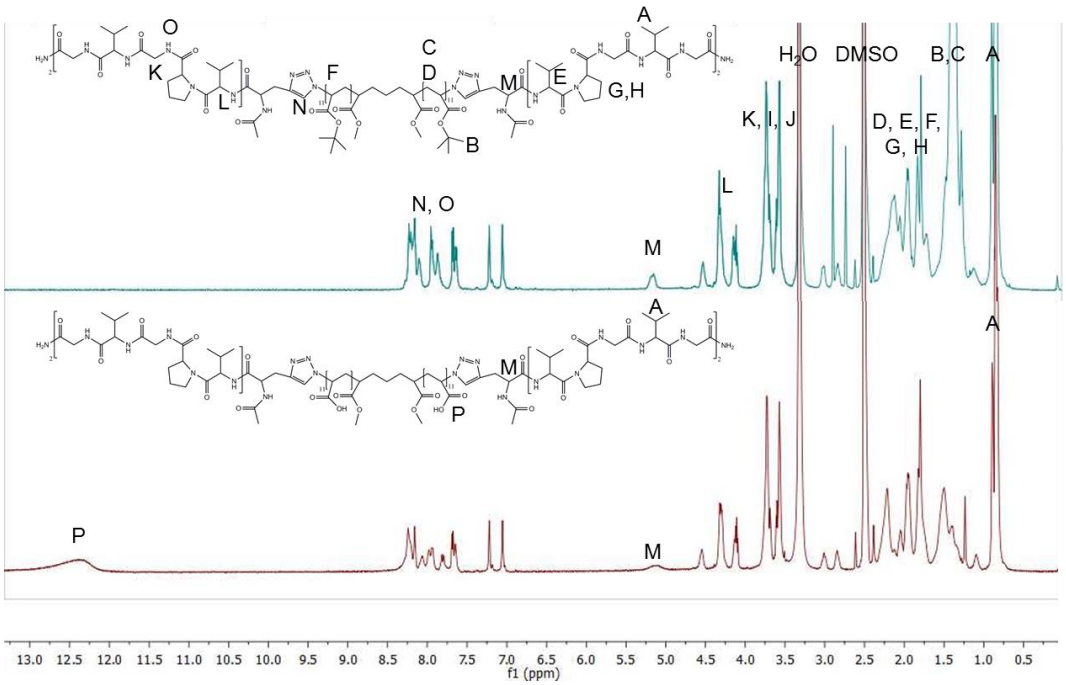

FIG. S4. NMR spectra of the $PtBA_{22}$-VG_2 PAA_{22}-VG_2 triblock in DMSO-d_6. Cleavage of the *tert*-butyl groups and the presence of the COO***H*** shows successful removal. The integration of the peaks correspond to the molar ratios of the components within the conjugate and was found to be 2:1, and the presence of the triazole-C***H***$(NHCOCH_3)$CO proton with an integration of two shows that cleavage conditions did not degrade the triblock.

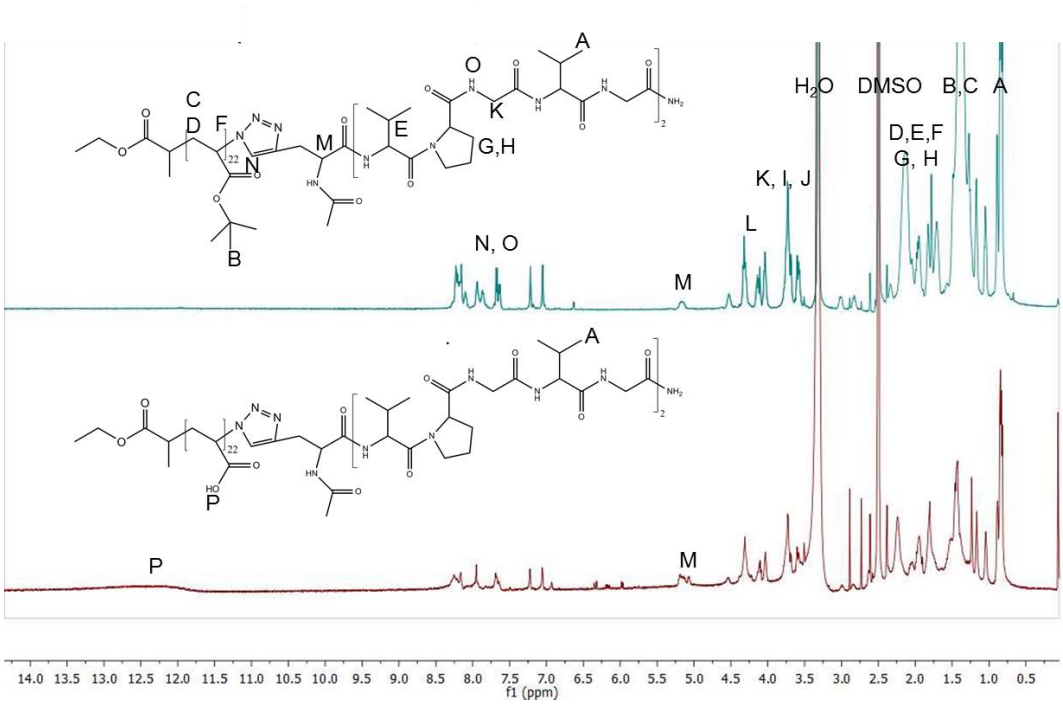

FIG. S5. NMR spectra of the $PtBA_{22}$-VG_2 PAA_{22}-VG_2 diblock in DMSO-d_6. Cleavage of the *tert*-butyl groups and the presence of the COO***H*** shows successful removal. The integration of the peaks corresponds to the molar ratios of the components with in the conjugate and was found to be 1:1, and the presence of the triazole-C***H***$(NHCOCH_3)$CO proton with an integration of one shows that cleavage conditions did not degrade the diblock.

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