Supplementary information.

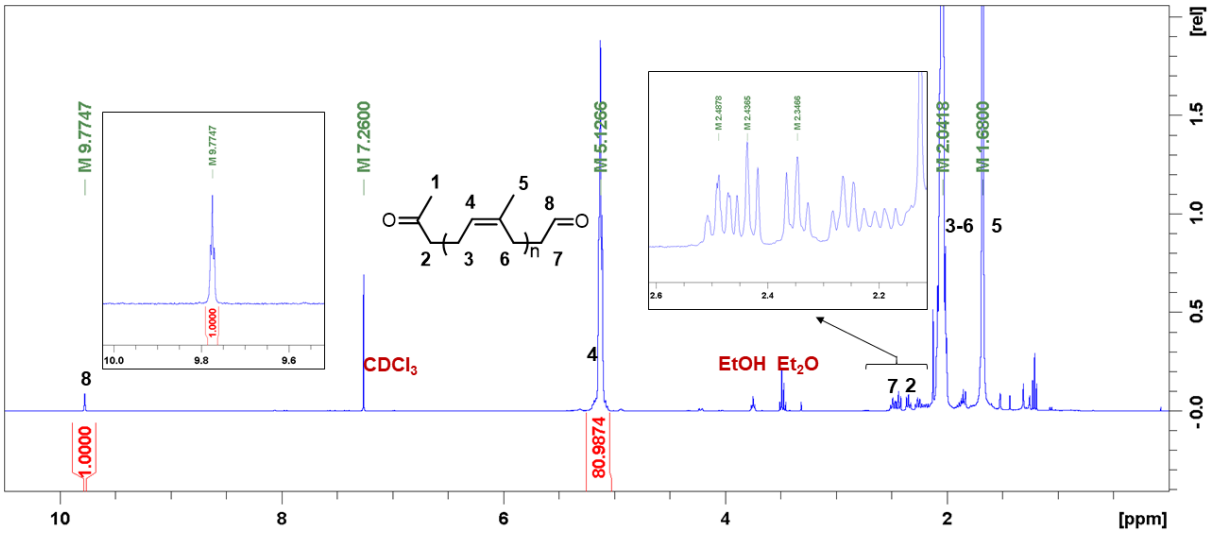

Figure S1. NMR spectrum of purified heterotelechelic keto/aldehyde PI (PIEG). 15 mg of purified PIEG were dissolved into 500 µL of $CDCl_3$ and analyzed with a Bruker AVANCE III HD 400 MHz Spectrometer. Insets: zoomed regions 9.8-10 ppm (left) and 2.2-2.8 ppm (right).

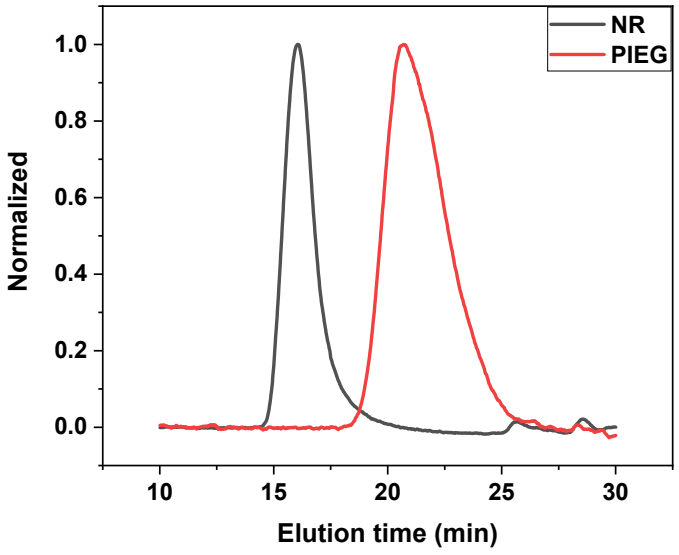

Figure S2. SEC analysis of purified PIEG. 10 mg of purified PIEG or NR were dissolved in 2 mL THF, the solution was passed through 0.45 µm PTFE filter, and was analyzed by SEC. The result obtained with PIEG (red line) was compared to that of the initial NR (black line).

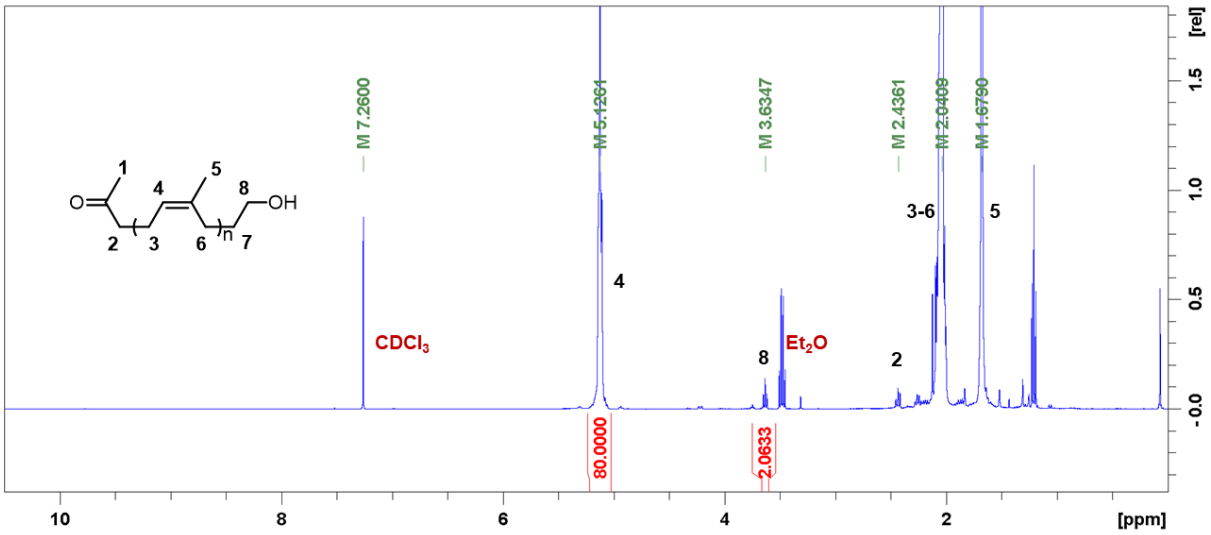

Figure S3. NMR spectrum of purified heterotelechelic keto/hydroxyl PI (PIOH). 15 mg of purified PIOH were dissolved into 500 µL of $CDCl_3$ and analyzed with a Bruker AVANCE III HD 400 MHz Spectrometer.

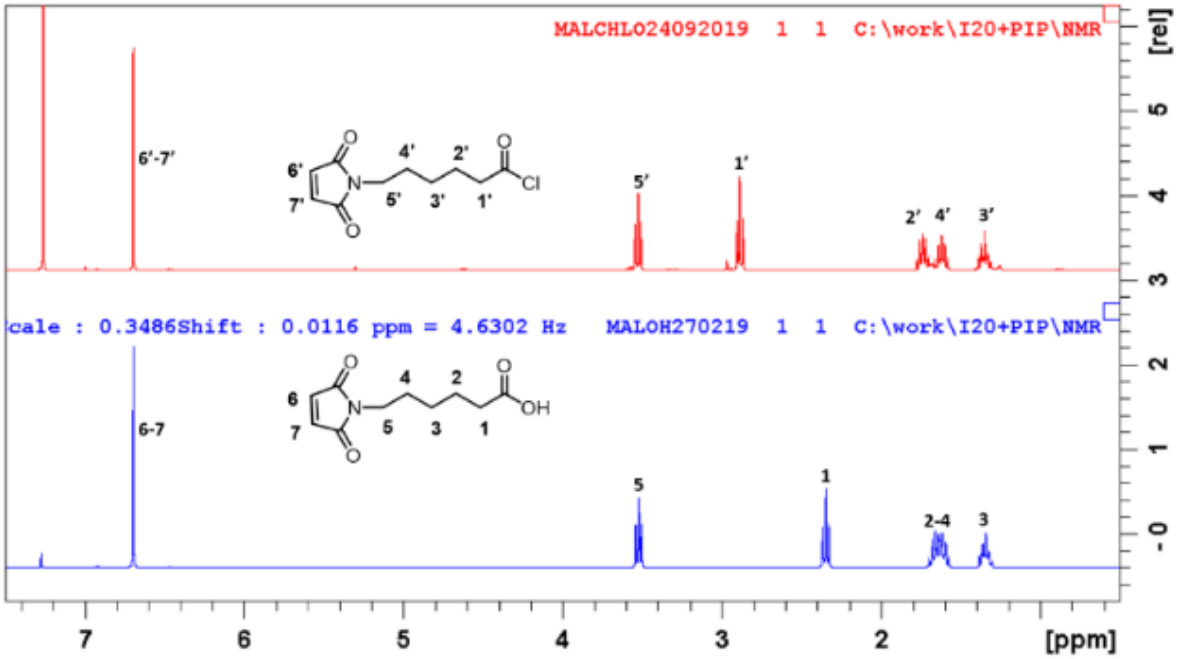

Figure S4. NMR spectrum of maleimidohexanoic chloride. Maleimido hexanoic acyl chloride was dissolved in 500 µL anhydrous $CDCl_3$, then analyzed with a Bruker AVANCE III HD 400 MHz Spectrometer (Top spectrum in red). In parallel, 30 mg of maleimidohexanoic acid was analyzed under the same conditions (Bottom spectrum in blue).

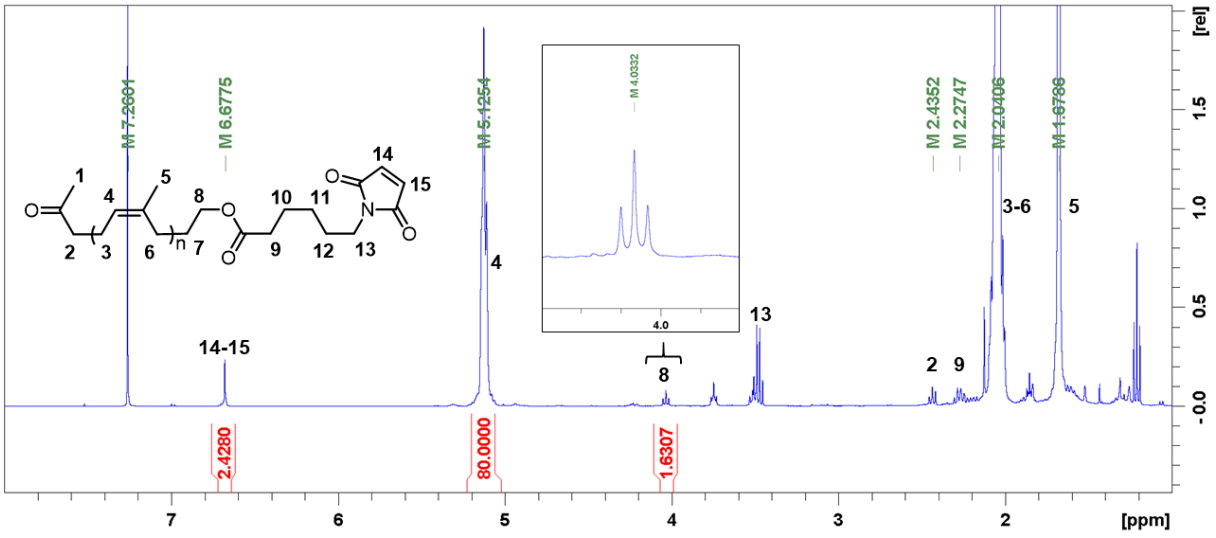

Figure S5. NMR analyses of purified N-polyisoprene-maleimide (PIMAL). NMR spectrum of PIMAL in $CDCl_3$. 30 mg of dried PIMAL was dissolved into 1 mL $CDCl_3$, then 500 µL solution was analyzed by Bruker AVANCE III HD 400 MHz Spectrometer. Inset: zoomed region 3.8-4.6 ppm

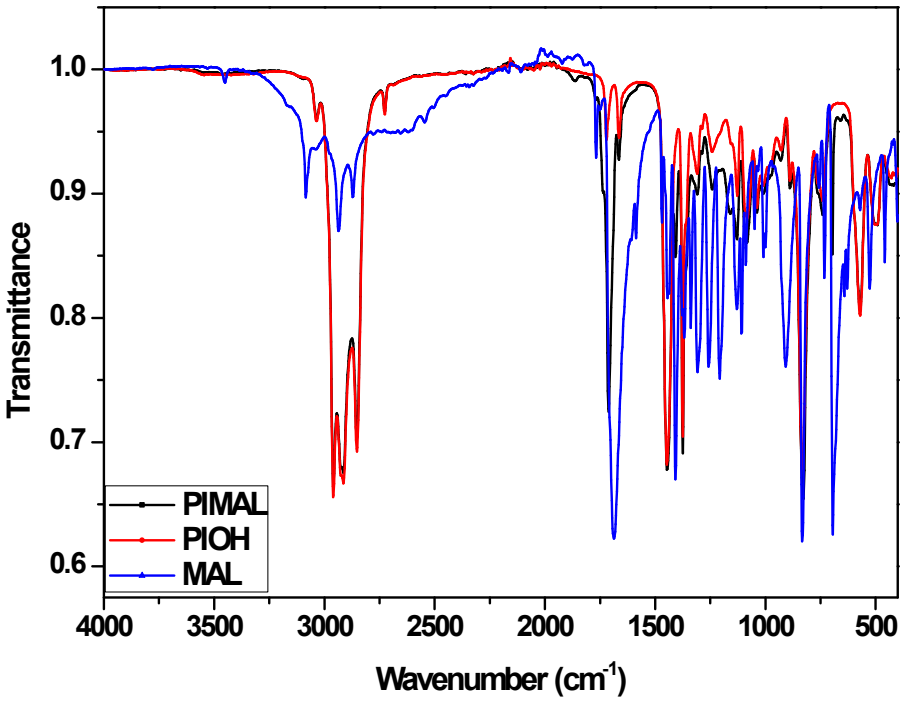

Figure S6. Comparison of infrared spectra of purified PIMAL, PIOH and Maleimide chloride. Purified PIMAL was analyzed with a Fourier Transform Infrared Spectrometer (FT-IR). PIMAL (black trace), PIOH (red trace), and Maleimide chloride (blue trace).

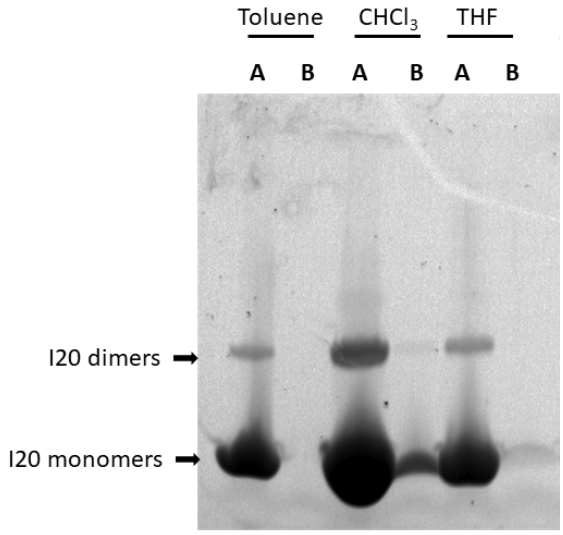

Figure S7: Solubilization assays of I20 monitored by SDS-PAGE analysis. Toluene, chloroform or tetrahydrofurane were added to a glass vial containing dried I20. After 48 h of incubation under magnetic agitation, the liquid fractions were passed through a 0.45 µm nylon filter, dried and solubilized by 1X SDS-PAGE loading buffer (lanes B). The non-solubilized aggregates that remains in the initial vial were dried, and solubilized by 1X SDS-PAGE loading buffer (lanes A). SDS-PAGE electrophoresis was performed with 4-20% gels, and gels were stained with InstantBlue™. The loading buffer did not contain reducing agents.

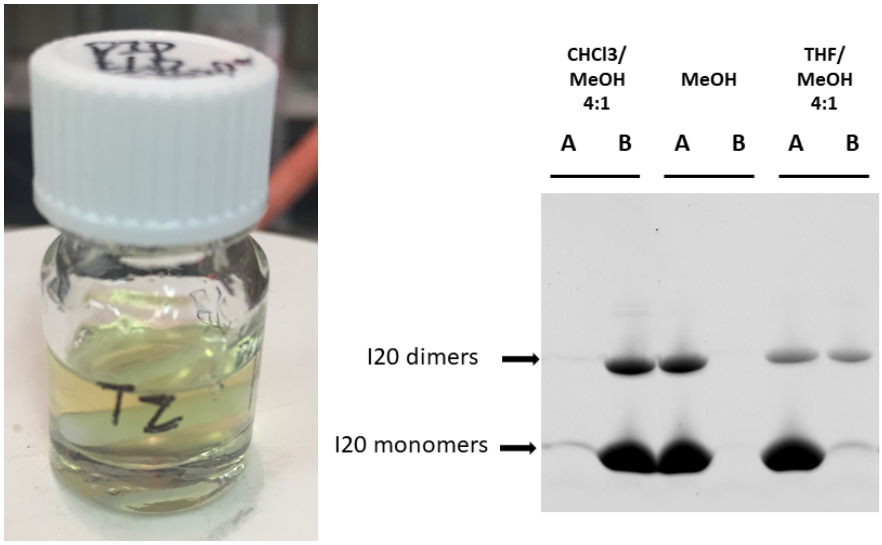

Figure S8. Solubilization of PIMAL (right) and I20 (left) by chloroform/methanol mixtures. 50 mg PIMAL was dissolved in 1 mL of $CHCl_3$/MeOH 4:1 (vol/vol) in a glass vial. Total solubilization was assessed by visual inspection (right). Dried I20 was dissolved in the corresponding solutions for 48 hours at RT under stirring. The solubilized fractions were passed through a 0.45 µm nylon filter, dried and solubilized by SDS-PAGE loading buffer (lanes B). The non-solubilized aggregates that remains in the initial vial were dried, and resuspended in SDS-PAGE loading buffer (lanes A). Electrophoresis was performed with 4-20% gels, and staining was performed InstantBlue™. The loading buffer did not contain reducing agents.

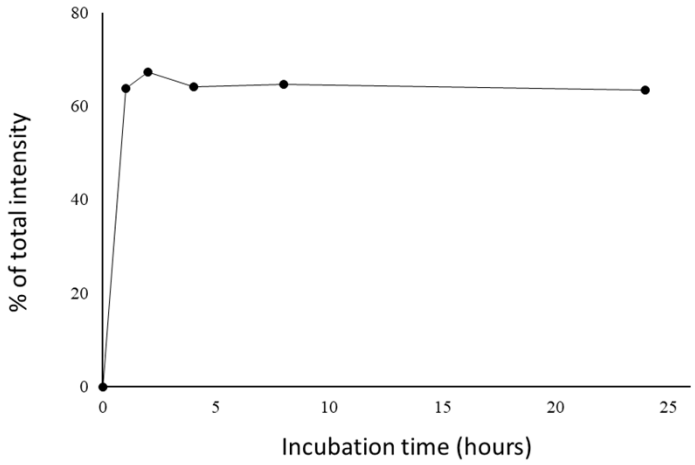

Figure S9. Time-course study of I20-*b*-PI formation. Reaction time varied between 1 and 24 h. From each sample, 50 µL was analyzed by SDS-PAGE. Densitometric analysis of the gel by Image Lab software allowed the quantification of each polypeptide band (I20 monomer, I20 dimer, and I20-*b*-PI). The total intensity/lane was set to 100%, and the calculated % for I20-*b*-PI was plotted.

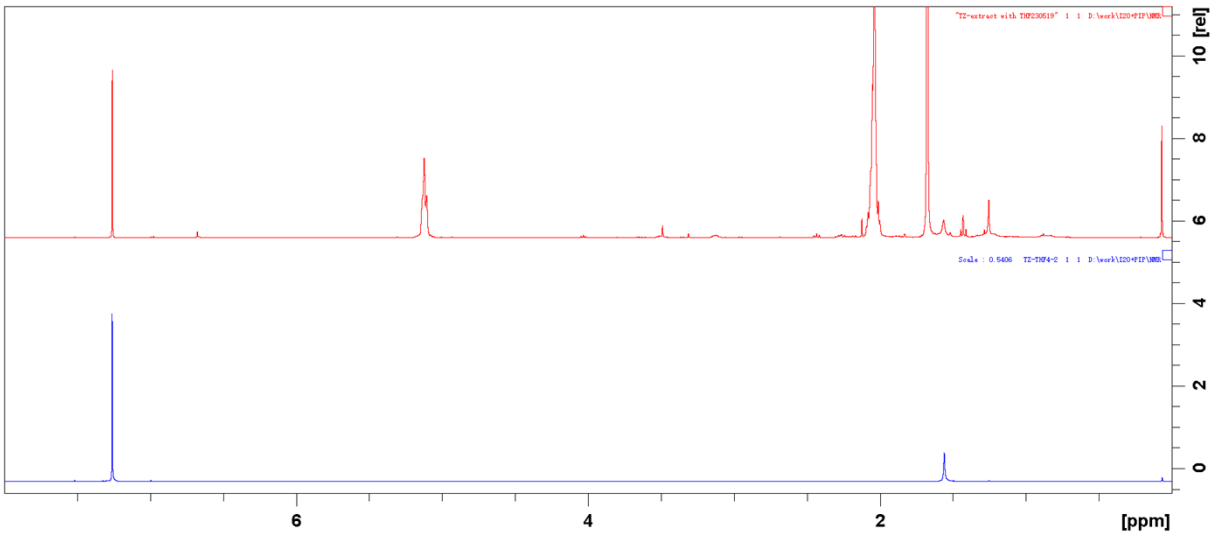

Figure S10. Evaluation of the elimination of the unreacted PIMAL from the reaction product. After the coupling reaction, the dried product was washed three times with THF to eliminate the excess of unreacted PI. The washing fractions were collected, dried, and dissolved in deuterated THF for proton NMR analysis to determine their PIMAL content. Top: First THF wash. Bottom: Third THF wash.

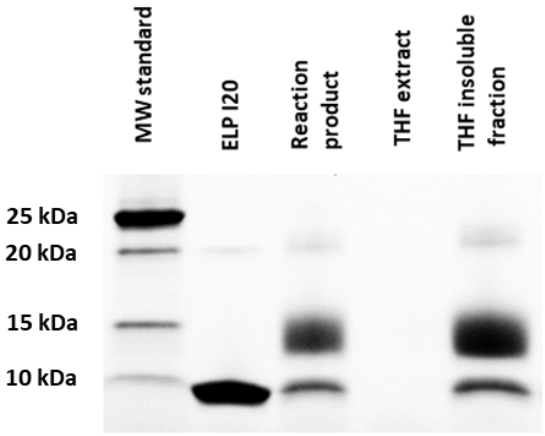

Figure S11. SDS-PAGE analysis after reaction and extracted with THF. After evaporation of the chloroform/methanol solvent the dried residues from the coupling reaction were re-suspended in THF. Non-solubilized materials were eliminated by centrifugation for 10 min at 10000 g and 20 ºC. The corresponding pellet was analyzed by SDS-PAGE (THF insoluble fraction). From the THF extact, 100 µL was evaporated and the residues were dissolved in 50 µL SDS-PAGE loading buffer and analyzed (THF extract). Pure I20 and a sample of the non-purified reaction product were analyzed as controls.

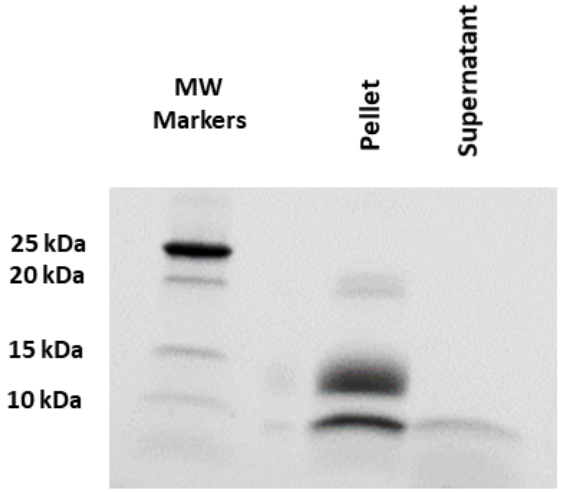

Figure S12. Evaluation of the elimination of the unreacted I20 from the reaction product by cold-water. After the coupling reaction between, chloroform/methanol was evaporated and the dry extract was washed with THF to eliminate the PIMAL in excess. After drying, the reaction products were incubated for 24 h in cold water (4°C) under agitation. The sample was then centrifuged for 10 min at 10 000g and 4°C, and samples from the pellet and the supernatant were analyzed by SDS-PAGE.

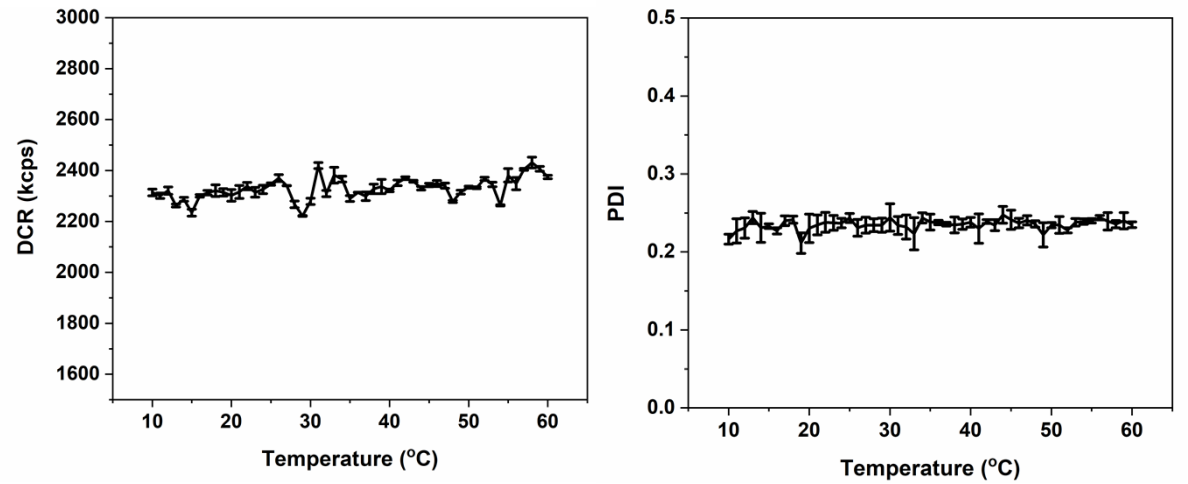

Figure S13. Stability of the I20-*b*-PI nanoparticles upon heating. A water solution containing I20-*b*-PI nanoparticles was analyzed by DLS. Scattered intensity (derived count rate, DCR) and polydispersity (PDI) of the sample were plotted as a function of temperature upon heating. Results are mean values ± SD (n=3)

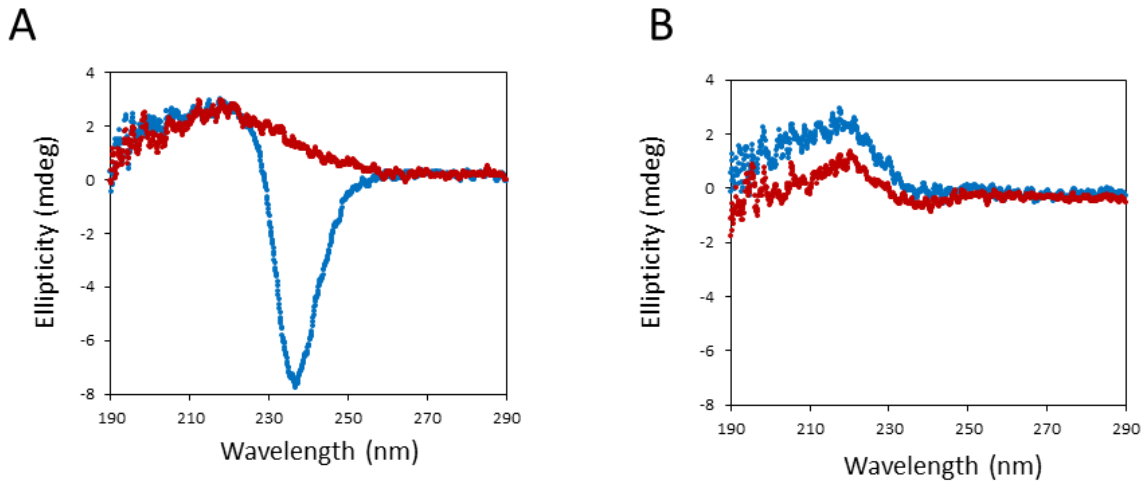

Figure S14: **Circular dichroism spectra of 10 µM solutions of A: ELP I20, B: I20-*b*-PI**. The spectra were recorded at two temperatures, 15°C (blue) and 30°C (red).

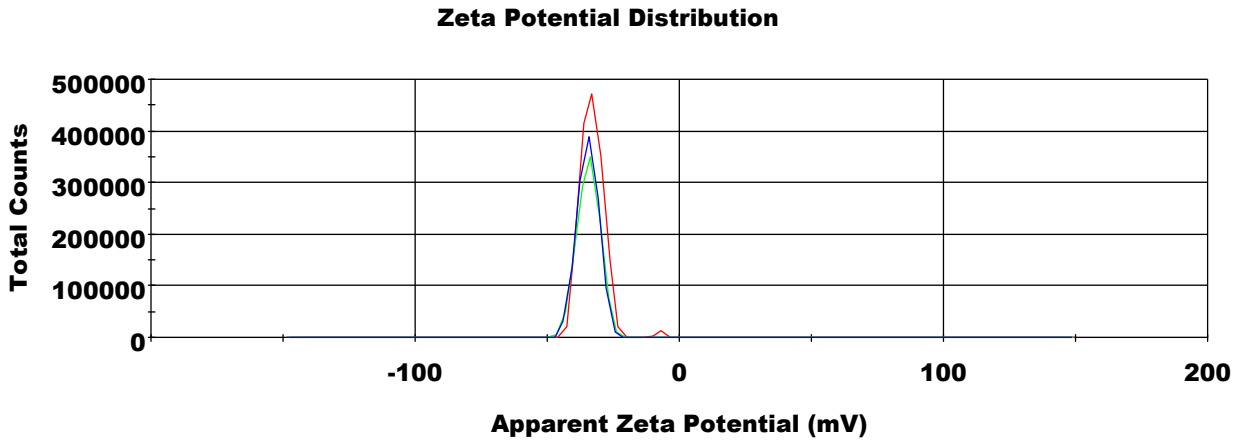

Figure S15. Zeta measurement of I20-*b*-PI nanoparticles. Zeta measurement was done with a Nano ZS instrument (Malvern U.K.) using the signal processing M3-PALS technique. Zeta potential range was > +/- 500 mV, and maximum sample concentration was 40% w/v. Data were analyzed with the Zetasizer software. The figure shows the results obtained after three measurements of the same sample.

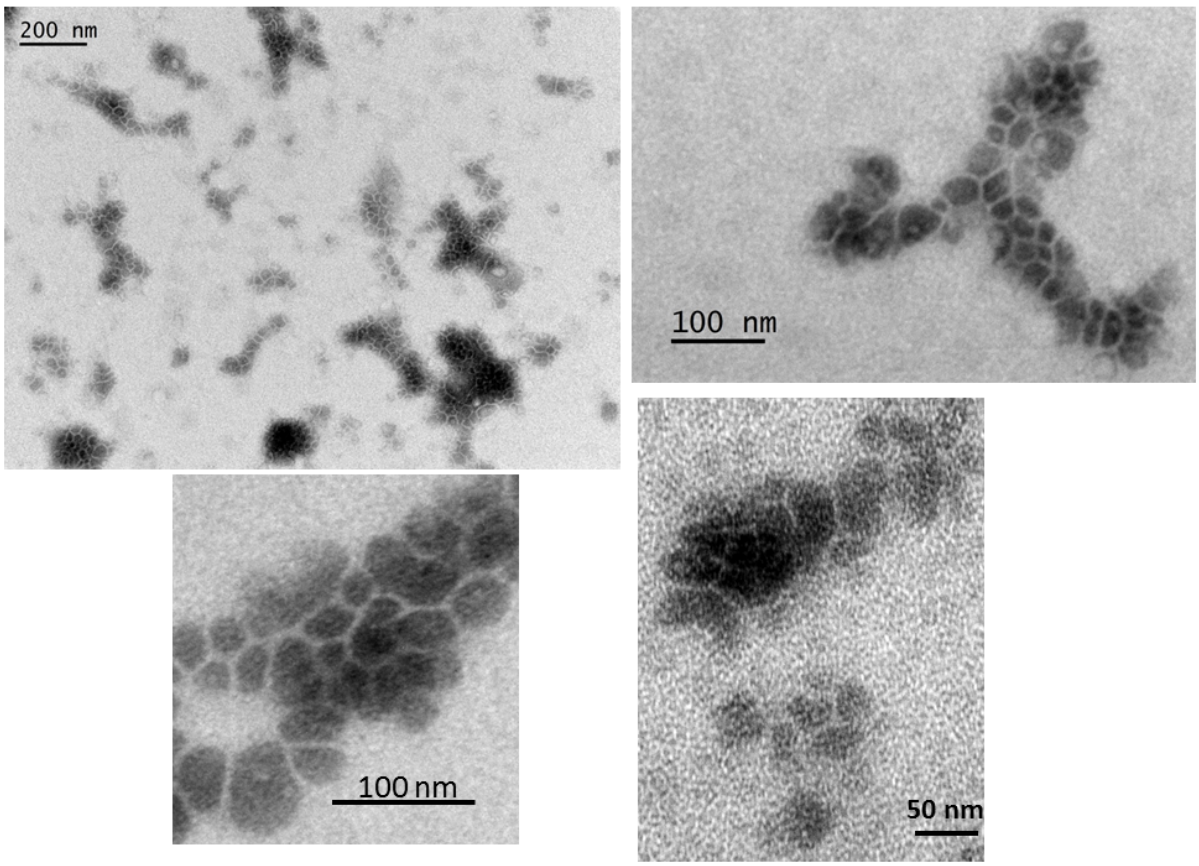

Figure S16. TEM images of I20-*b*-PI nanoparticles at different magnification. 20 µL of the polymer dispersion at 0.27 mg/mL were deposited onto lacey carbon grids, and then water was evaporated at room temperature. The grid was incubated with vapor of osmium tetroxide (OsO4, 4% in aqueous solution) for 12 h at room temperature.

Solvent	Respective % of I20-*b*-PI in the soluble (supernatant) and insoluble (pellet) fractions	
	Supernatant	Pellet
Chloroform/methanol 4 :1	100%	0%
Dichloromethane	68%	32%
dimethylsulfoxide	0%	100%
dimethylformamide	91%	9%
Toluene	12%	88%
Cyclohexane	14%	86%
Diethyl ether	8%	92%
Ethyl acetate	10%	90%
Acetonitrile	11%	89%
DMF/THF 1 :4	95%	5%

Table S1. Solubilization of I20-PI by different solvents. Dried purified I20-*b*-PI was incubated overnight at room temperature with each solvent. After centrifugation at 10 000 g for 10 min and 25°C, 100 µL of the supernatant was filtered through 0.45 µm devices, and dried. These samples were then solubilized by SDS-PAGE loading buffer. In parallel, pellets from the centrifugation step were dried and solubilized by SDS-PAGE loading buffer. All samples were submitted to electrophoresis, and the corresponding gels were stained with InstantBlue™. Quantification of the I20-PI bands from each sample was performed with the Image Lab software (BioRad).

	Initial	**7 days**	**25 days**	**28 days**	**46 days**
DCR	1621	1658	1806	1771	1815
PDI	0.130	0.256	0.242	0.240	0.250

Table S2. Stability of the I20-*b*-PI upon storage at 4°C. Nanoprecipitated I20-*b*-PI sample was stored for 46 days at 4°C. Measurement were made at 25°C. Scattered intensity (derived count rate, DCR) and polydispersity (PDI) were recorded.