Supplementary Information (SI) for Nanoscale.

Electronic Supporting Information

of the article

Radiopaque Poly(5-acrylamido-2,4,6-triiodoisophthalic acid)-Based Copolymers as Theranostic Carriers for Image-Guided Drug Delivery

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S1.1. NMR analysis of homopolymers

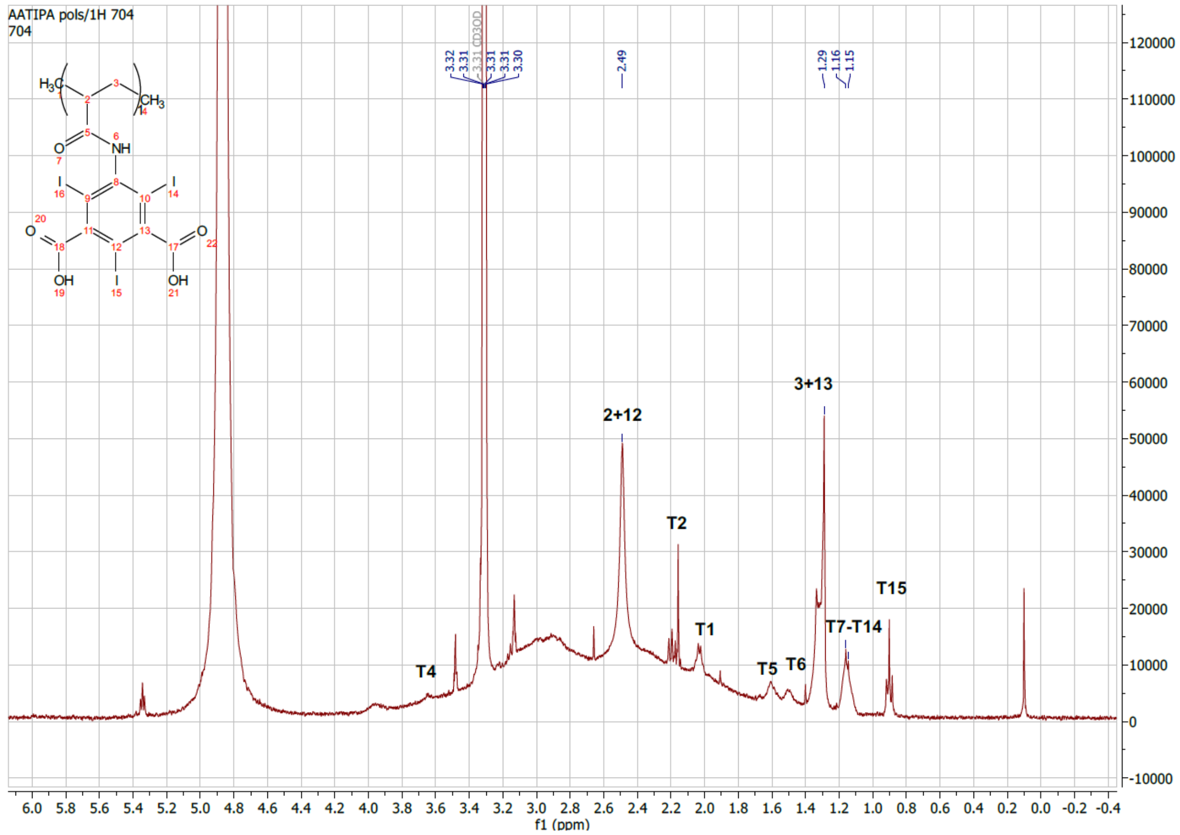

Figure S1. [1]H NMR (400 MHz, CD_3OD) spectrum of **PAATIPA** synthesized via RAFT polymerization using CDPA as CTA (peaks of the CTA were allocated as T1-T14 as previously described[1]).

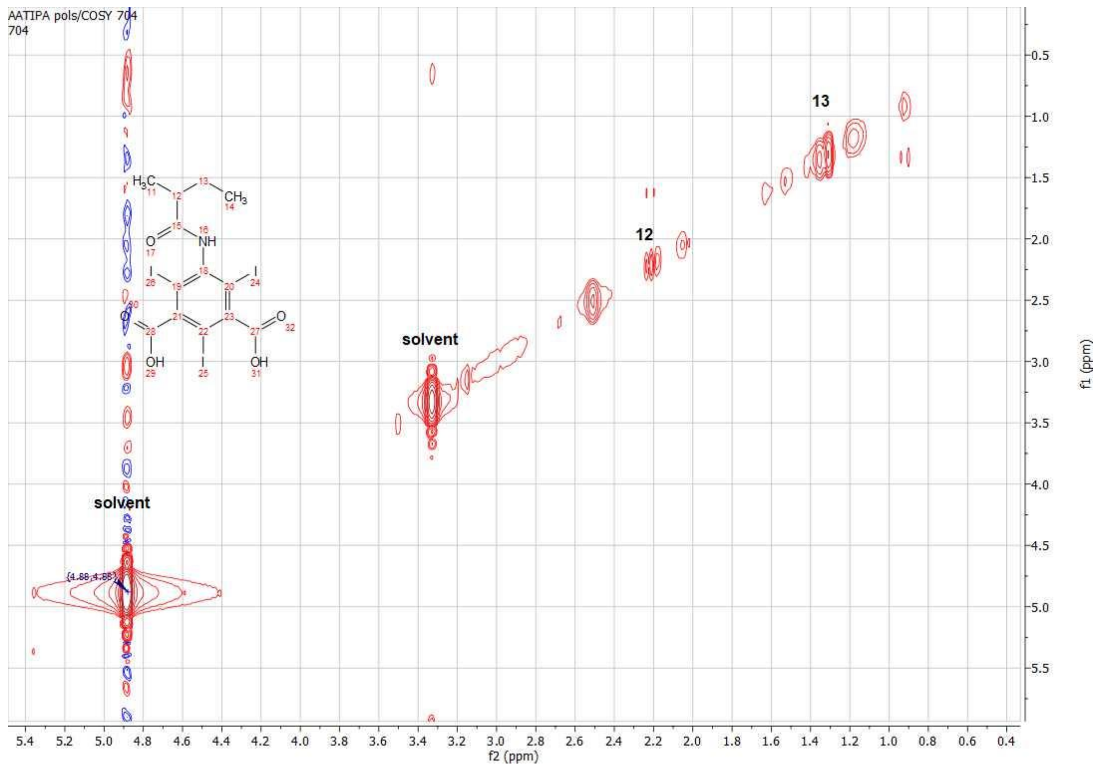

Figure S2. [1]H-[1]H COSY NMR (400 MHz, CD_3OD) spectrum of **PAATIPA**.

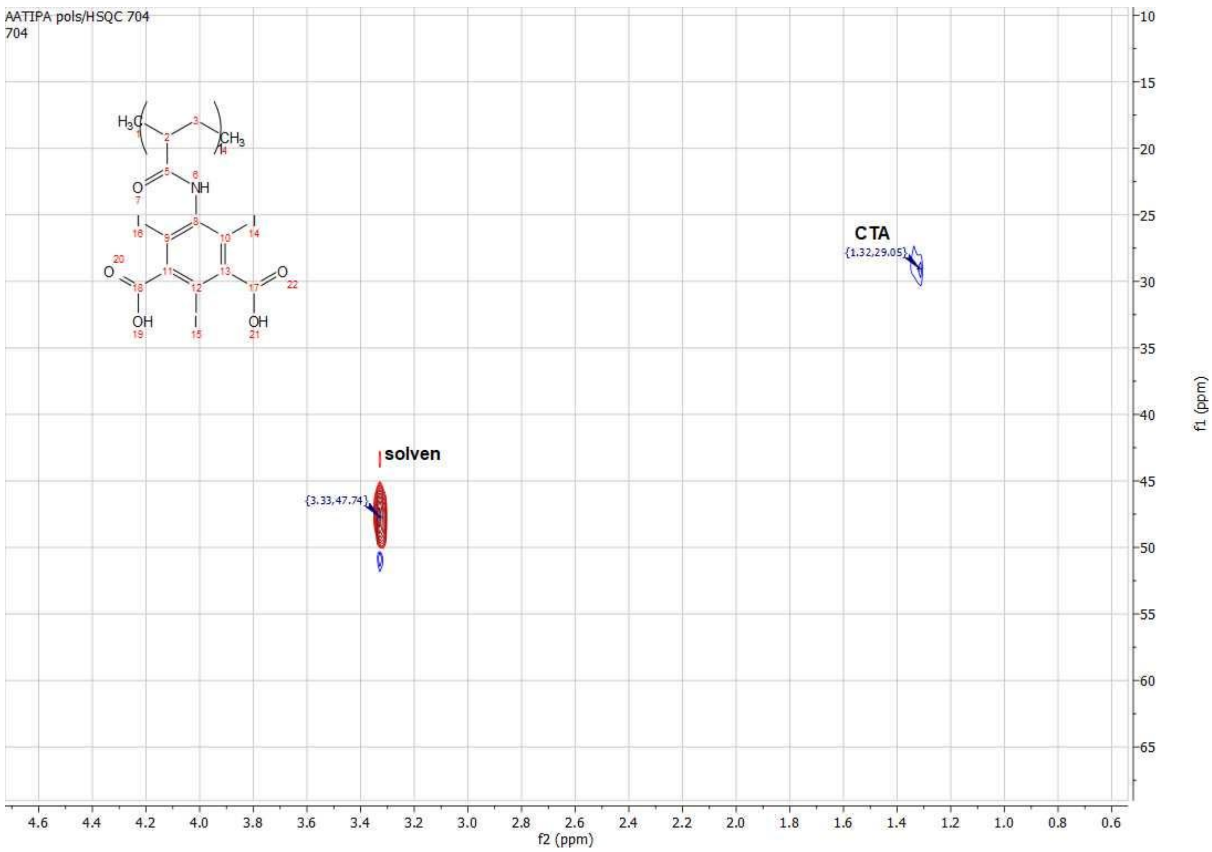

Figure S3. ^{1}H-^{13}C HSQC NMR (400 MHz, CD_3OD) spectrum of **PAATIPA**.

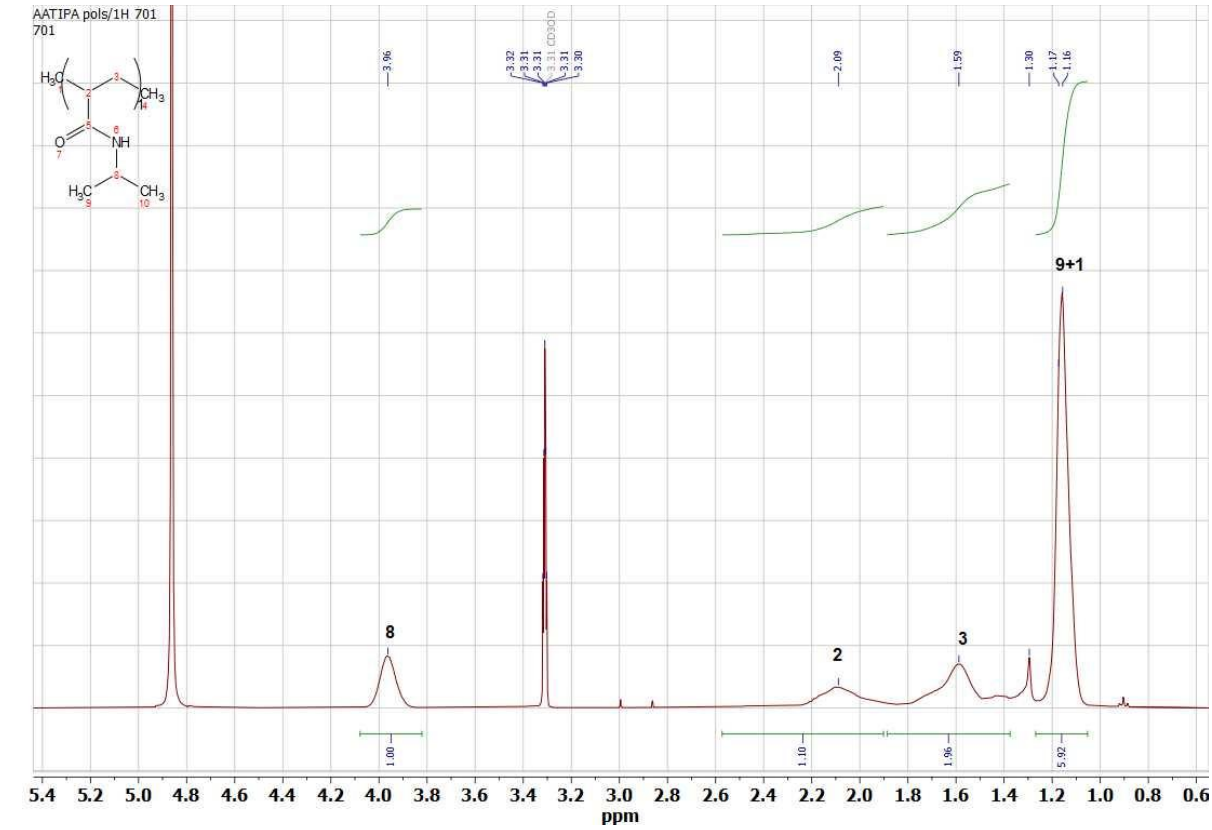

Figure S4. ^{1}H NMR (400 MHz, CD_3OD) spectrum of **PNIPAM 1**.

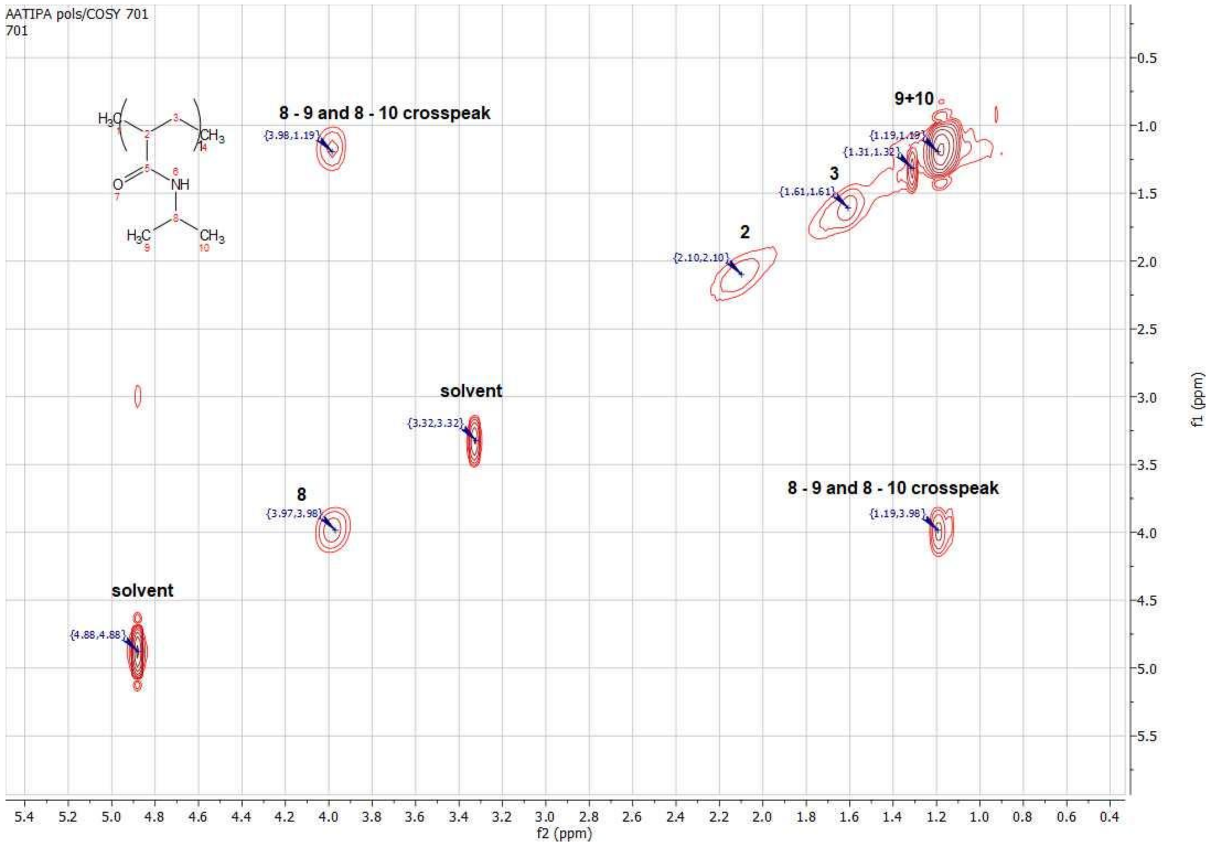

Figure S5. ^{1}H-^{1}H COSY NMR (400 MHz, CD_3OD) spectrum of **PNIPAM 1**.

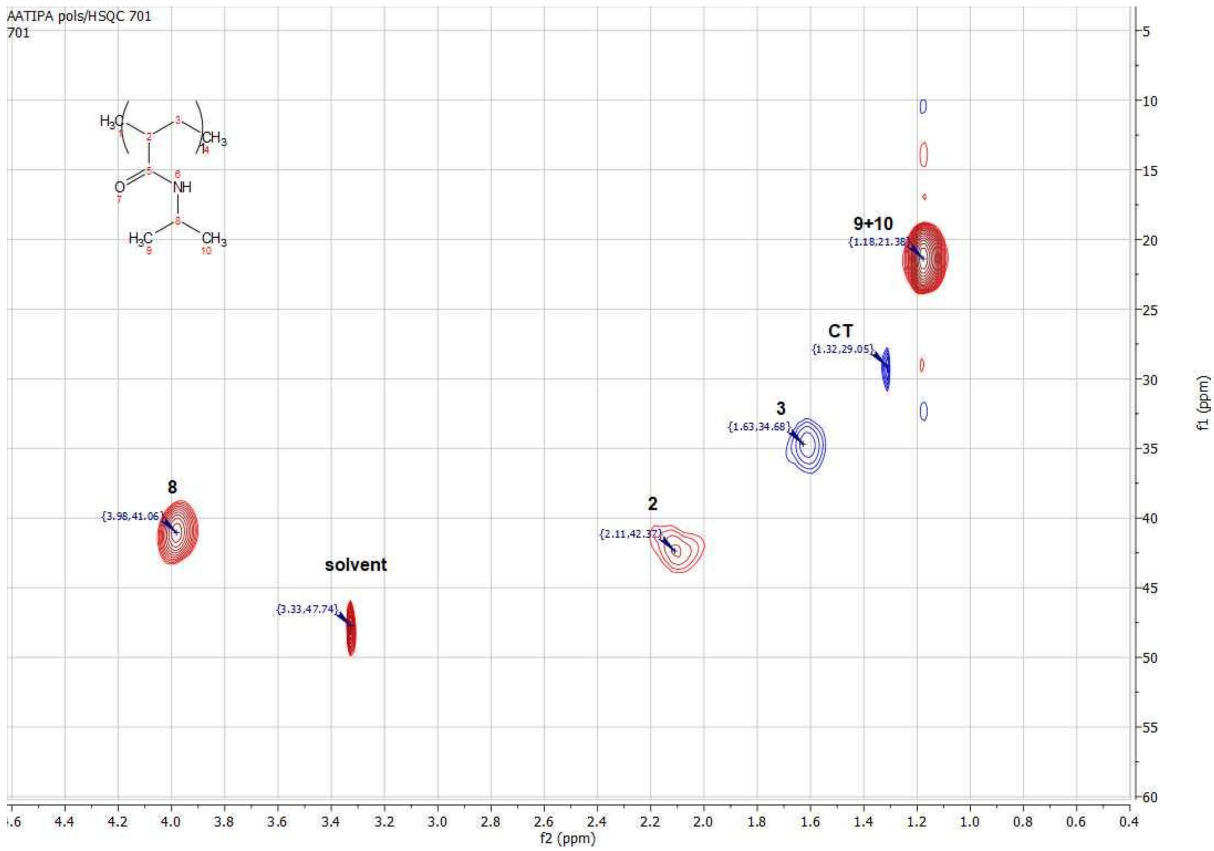

Figure S6. ^{1}H-^{13}C HSQC NMR (400 MHz, CD_3OD) spectrum of **PNIPAM 1**.

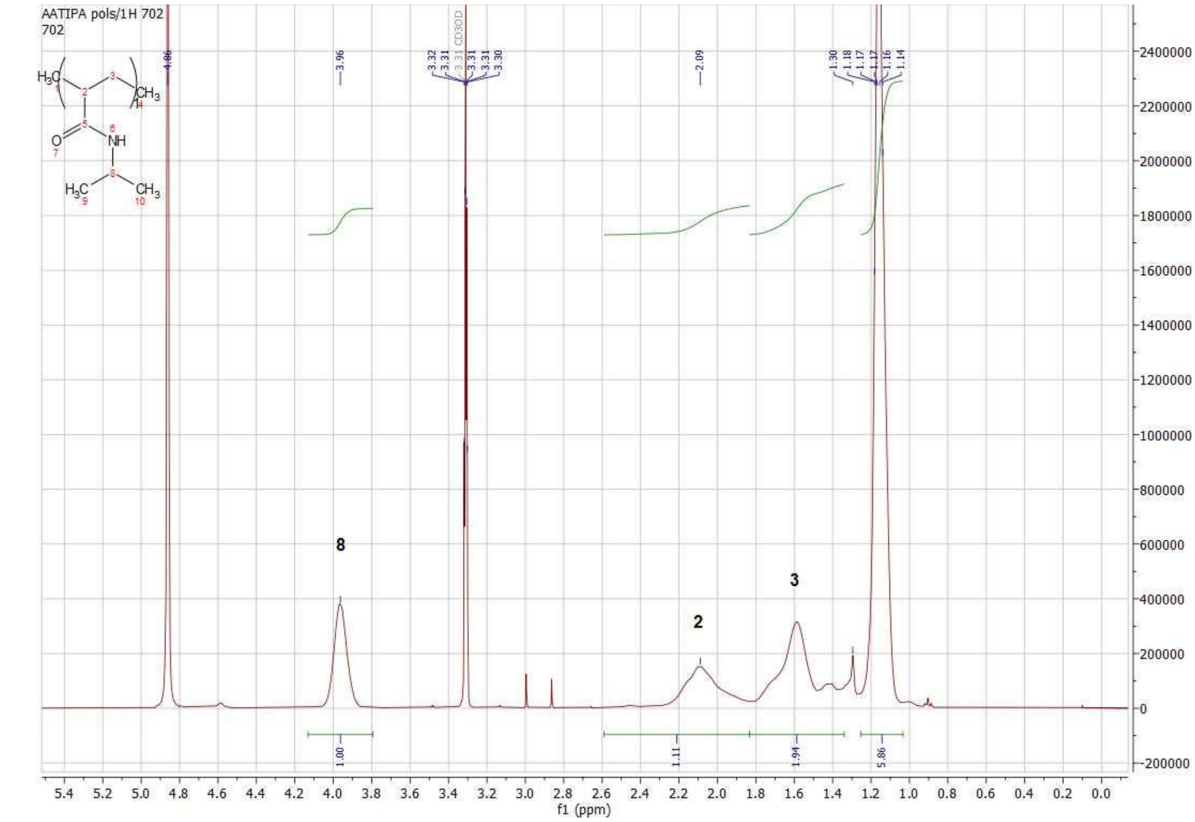

Figure S7. ^{1}H NMR (400 MHz, CD_3OD) spectrum of **PNIPAM 2**.

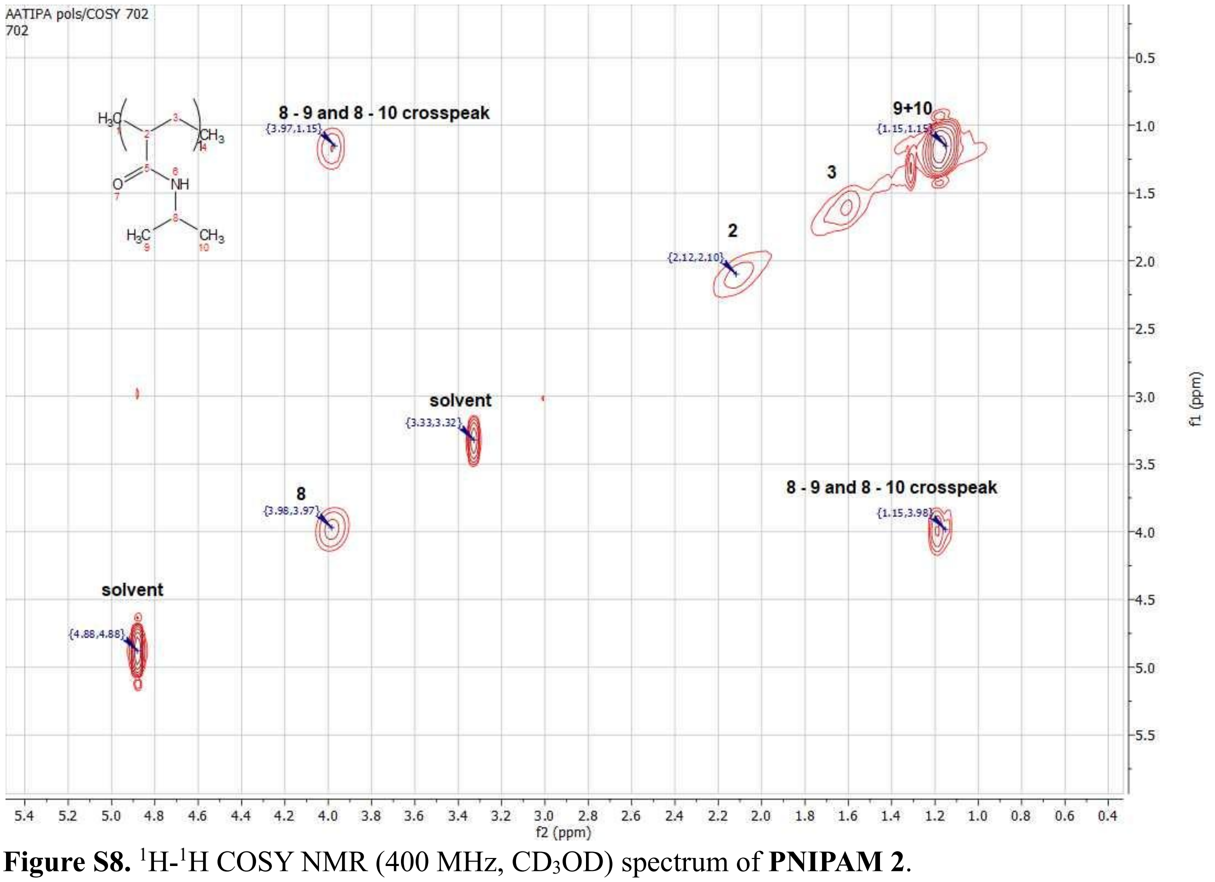

Figure S8. ^{1}H-^{1}H COSY NMR (400 MHz, CD_3OD) spectrum of **PNIPAM 2**.

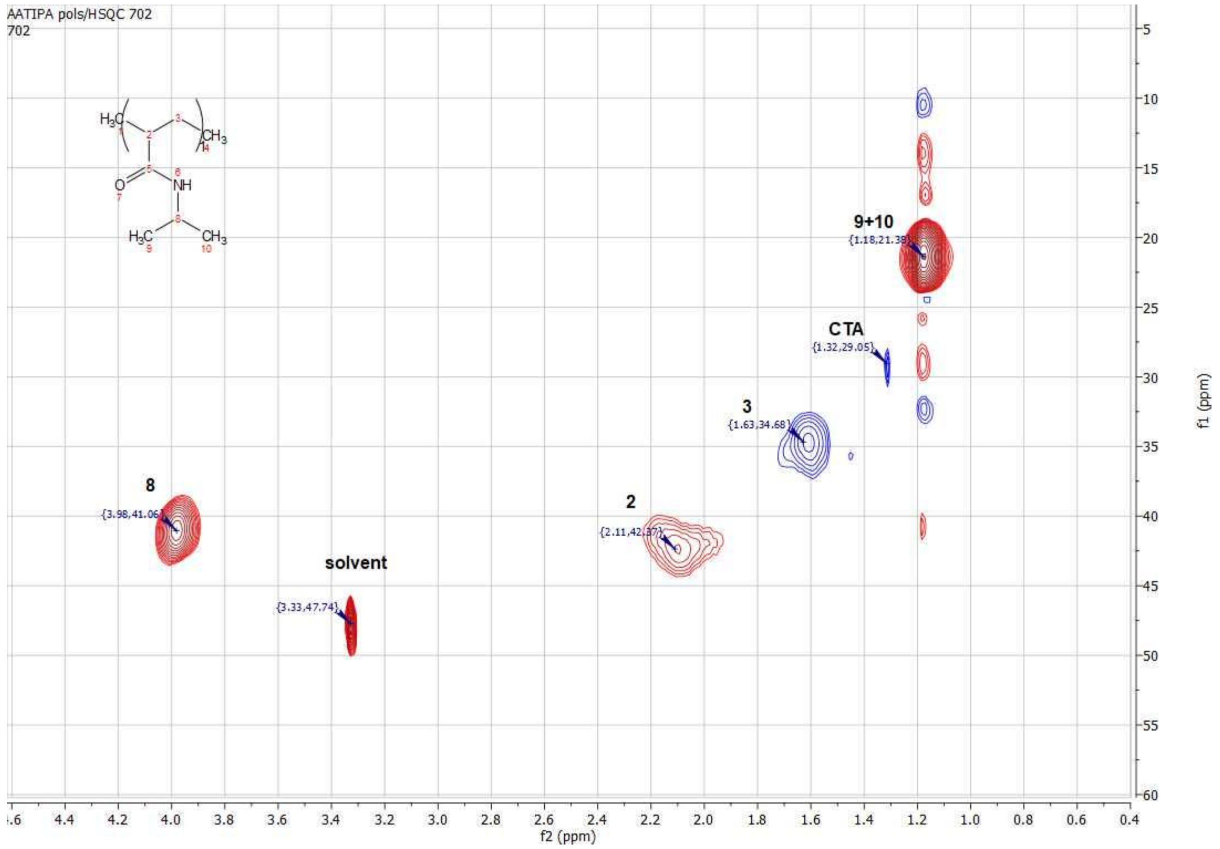

Figure S9. ^{1}H-^{13}C HSQC NMR (400 MHz, CD_3OD) spectrum of **PNIPAM 2**.

S1.2. NMR analysis of block copolymers

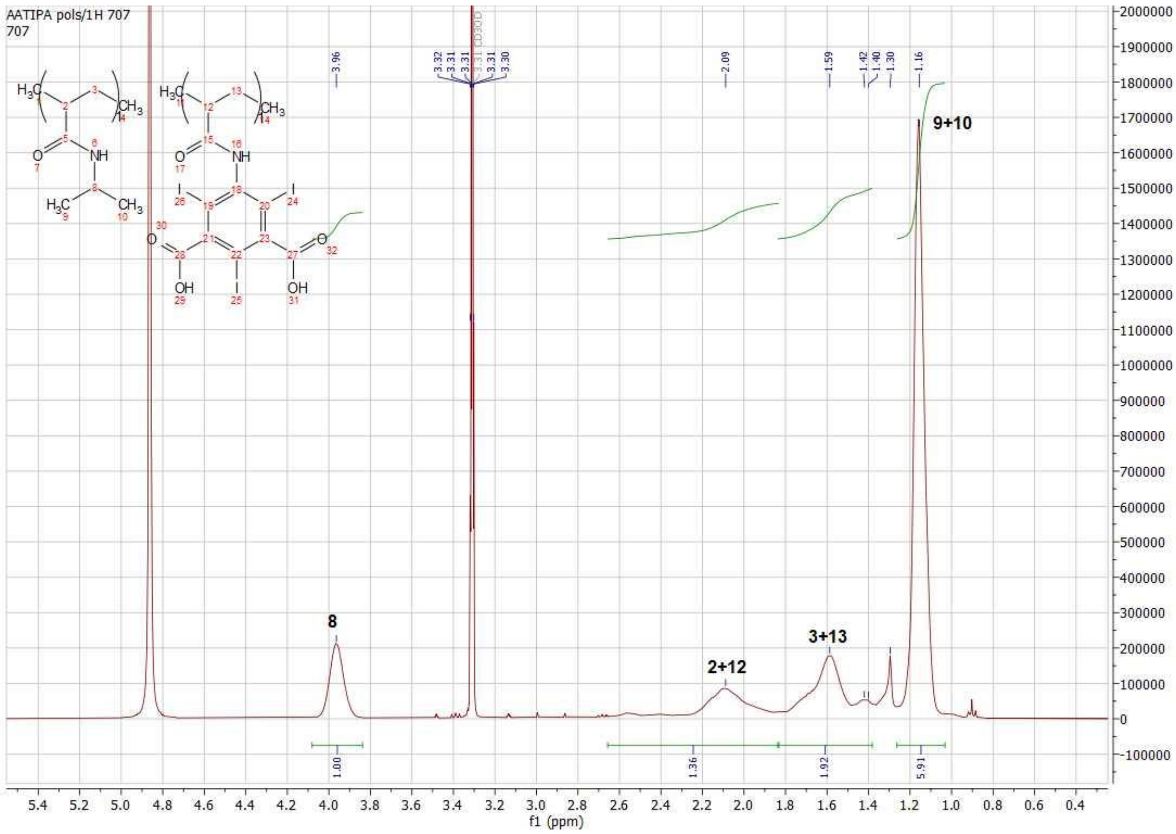

Figure S10. ^{1}H NMR (400 MHz, CD_3OD) spectrum of **B1**.

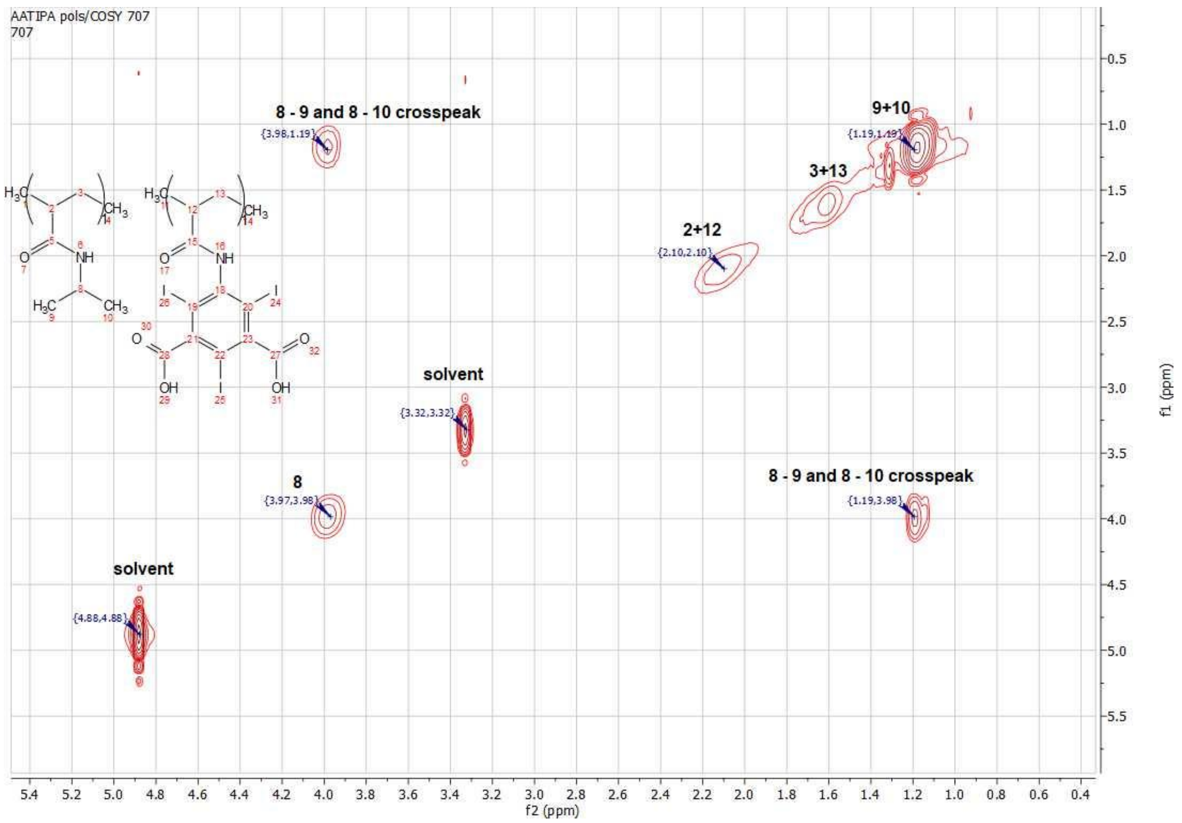

Figure S11. ^{1}H-^{1}H COSY NMR (400 MHz, CD_3OD) spectrum of **B1**.

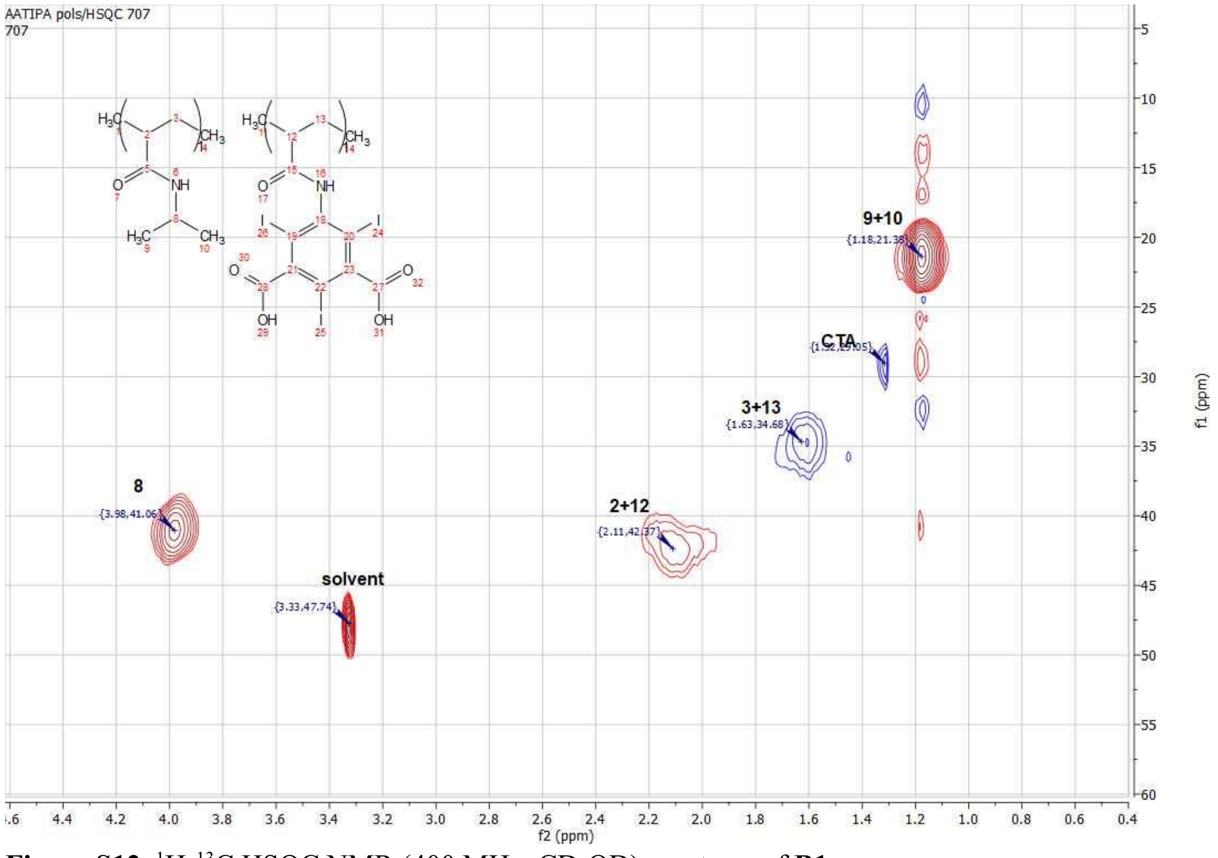

Figure S12. ^{1}H-^{13}C HSQC NMR (400 MHz, CD_3OD) spectrum of **B1**.

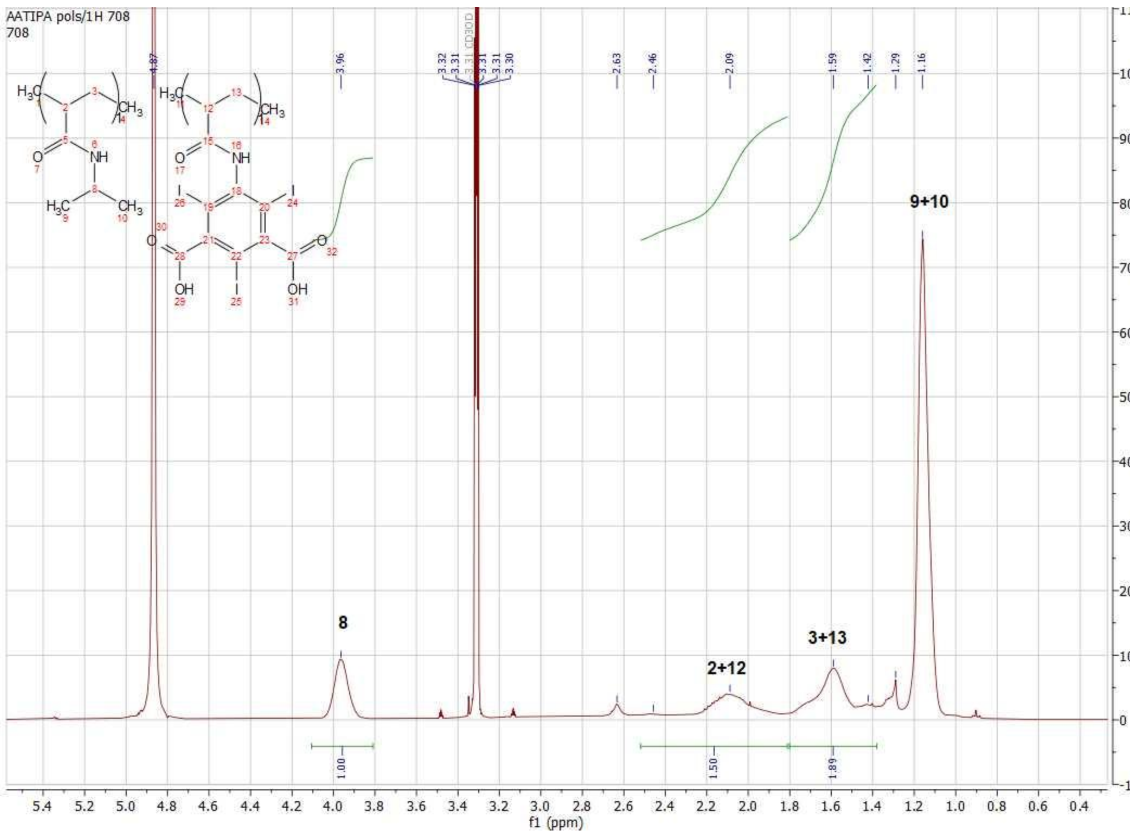

Figure S13. ^{1}H NMR (400 MHz, CD_3OD) spectrum of **B2**.

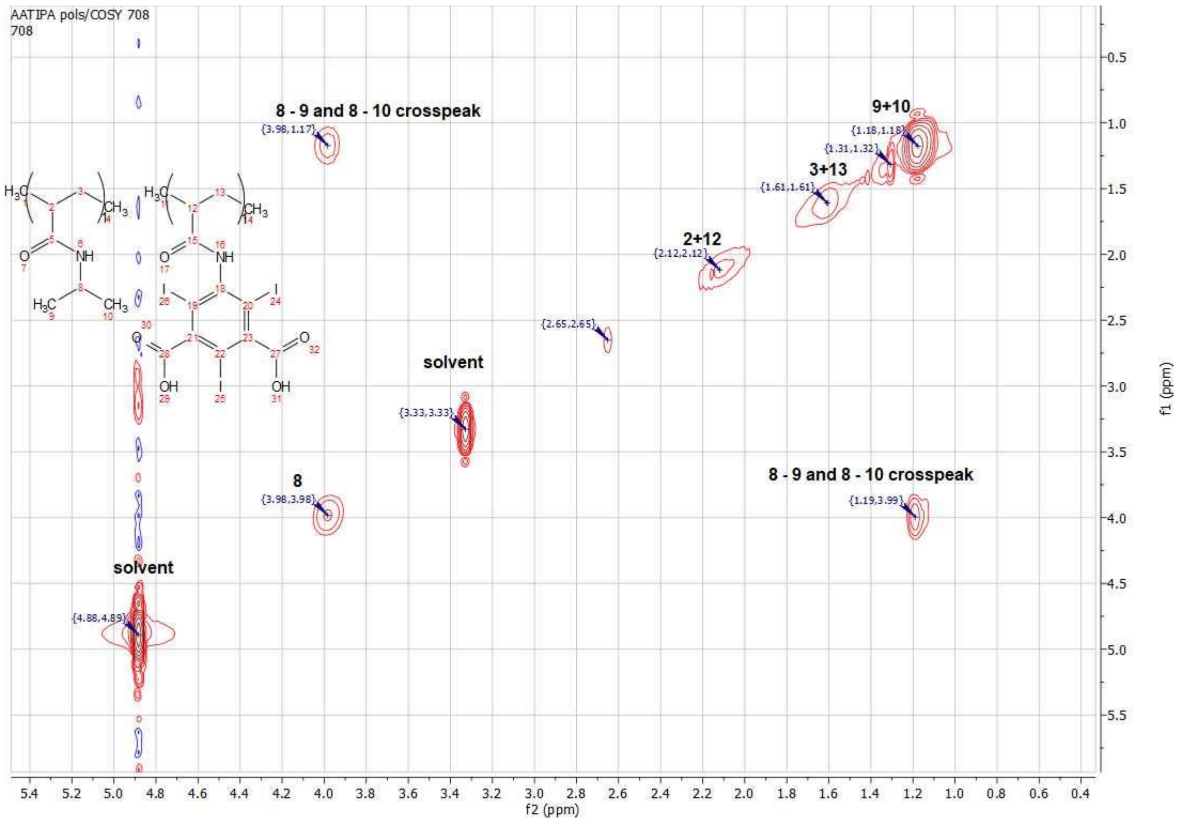

Figure S14. ^{1}H-^{1}H COSY NMR (400 MHz, CD_3OD) spectrum of **B2**.

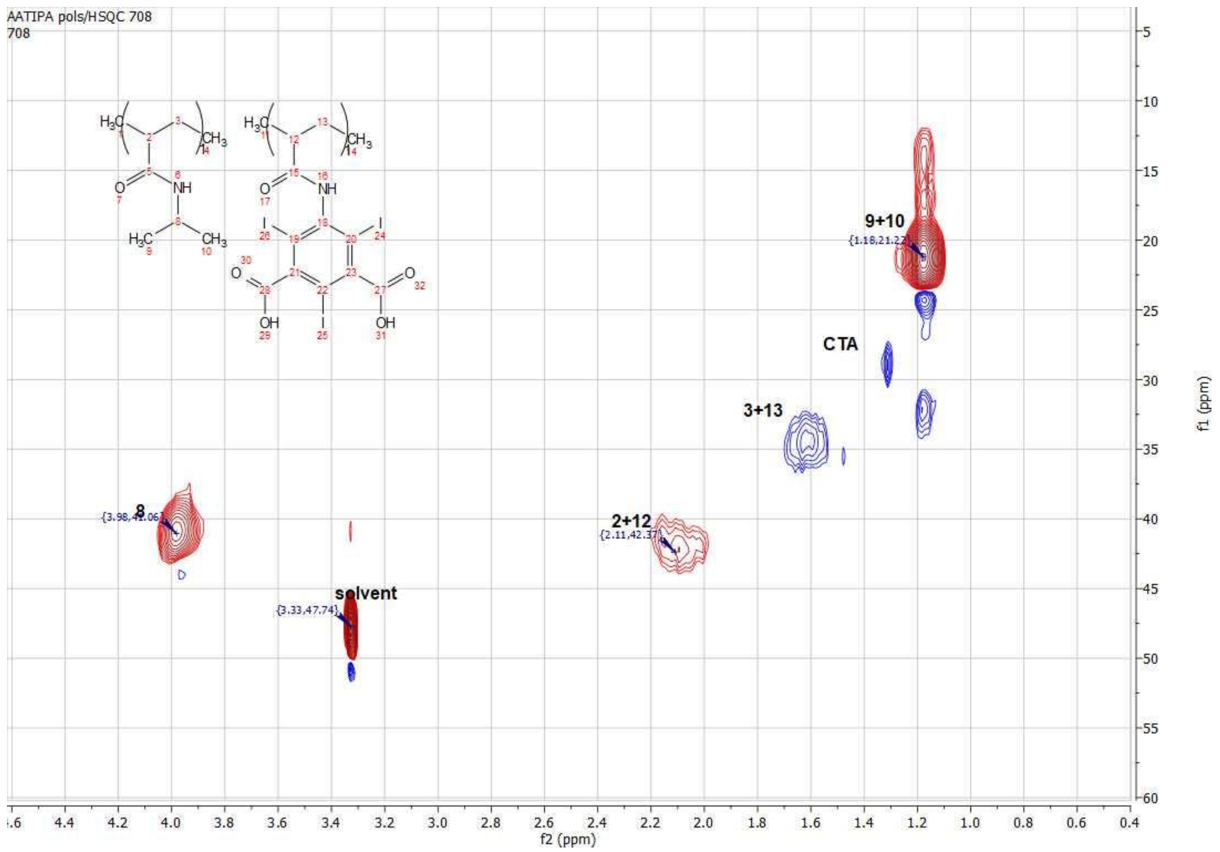

Figure S15. ^{1}H-^{13}C HSQC NMR (400 MHz, CD_3OD) spectrum of **B2**.

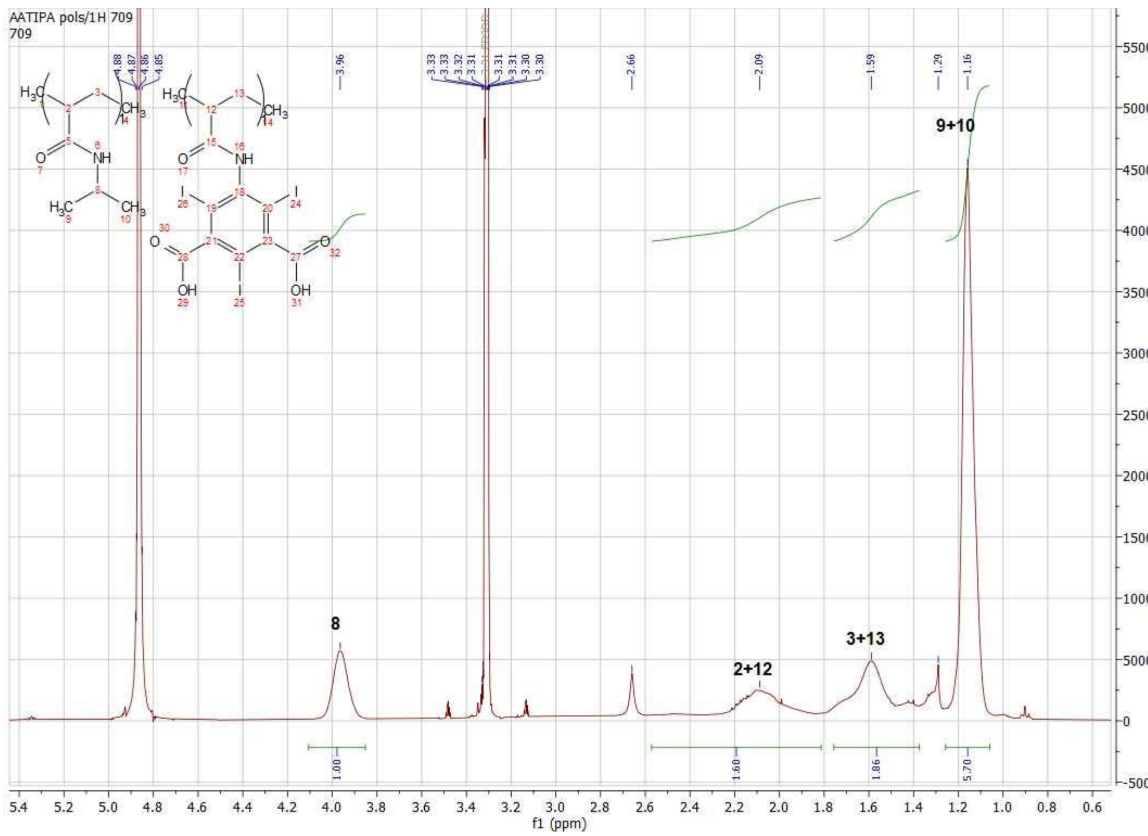

Figure S16. ^{1}H NMR (400 MHz, CD_3OD) spectrum of **B3**.

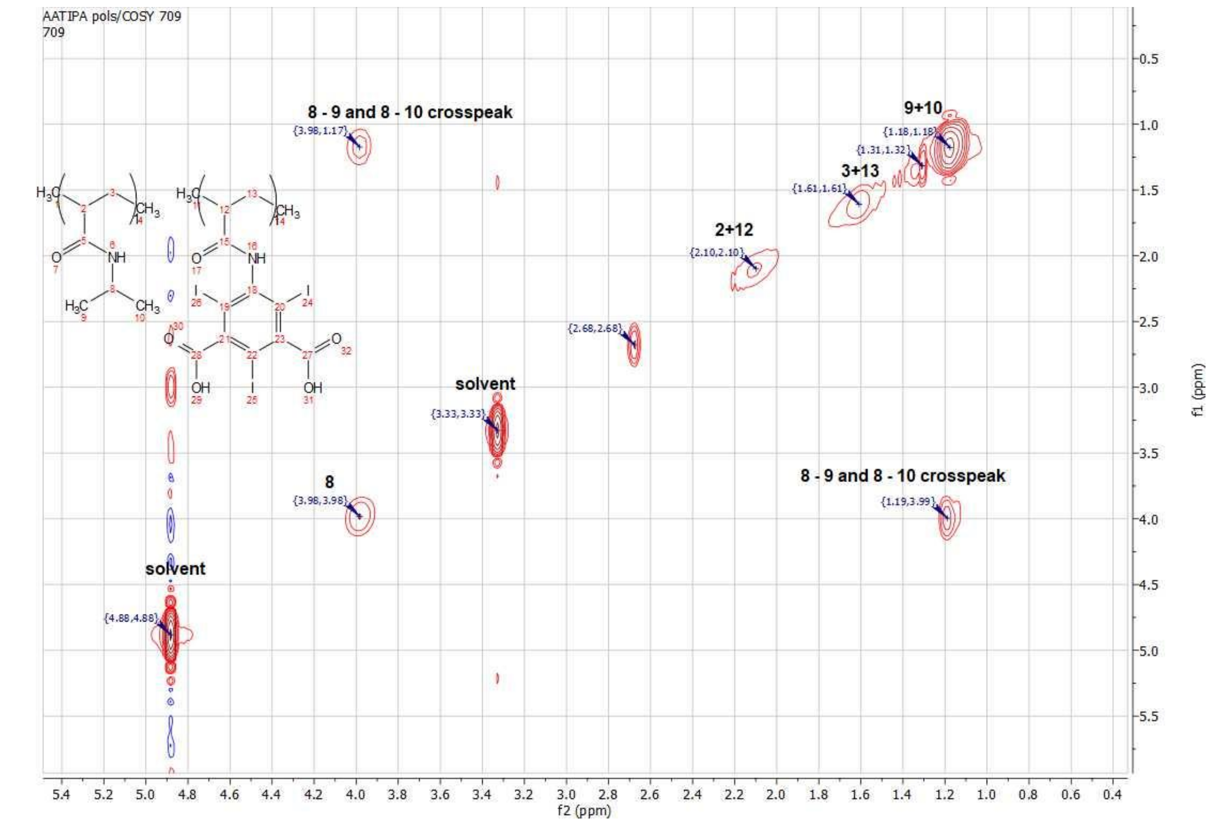

Figure S17. ^{1}H-^{1}H COSY NMR (400 MHz, CD_3OD) spectrum of **B3**.

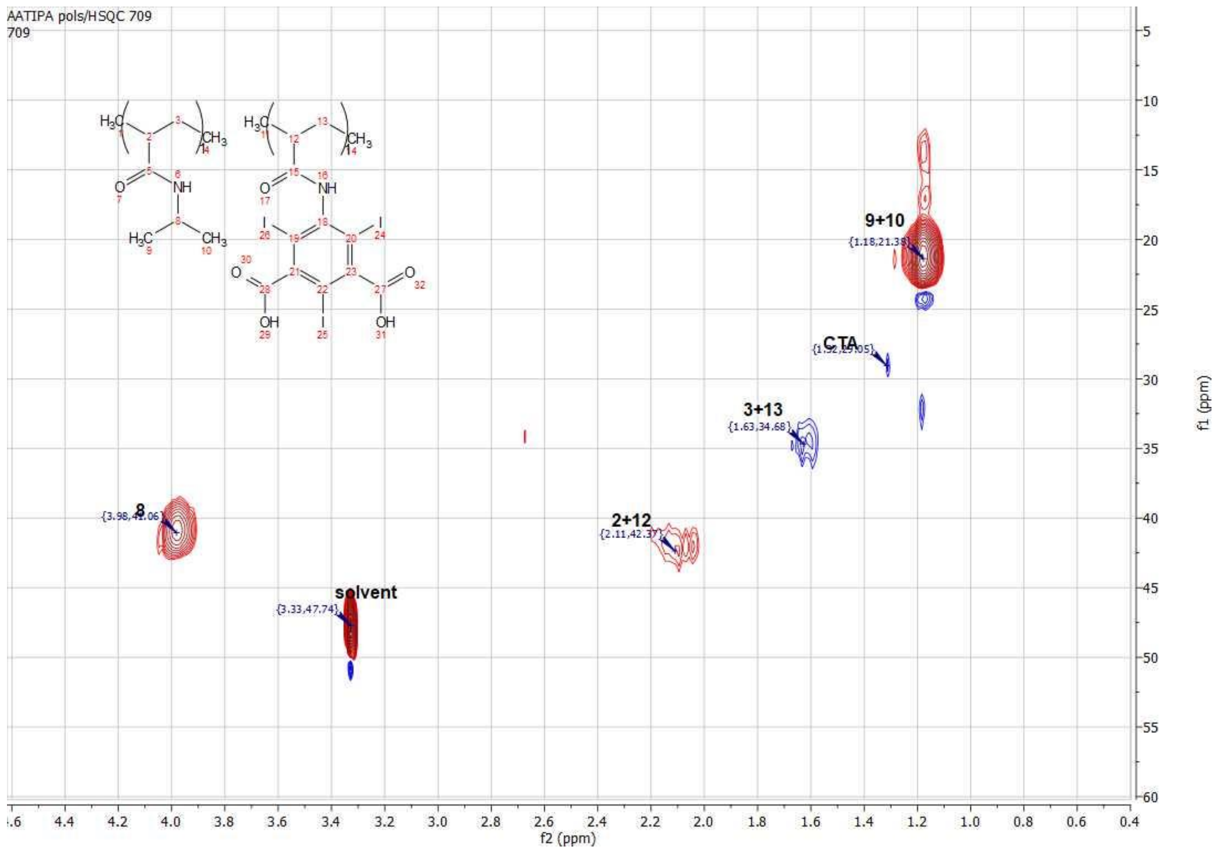

Figure S18. ^{1}H-^{13}C HSQC NMR (400 MHz, CD_3OD) spectrum of **B3**.

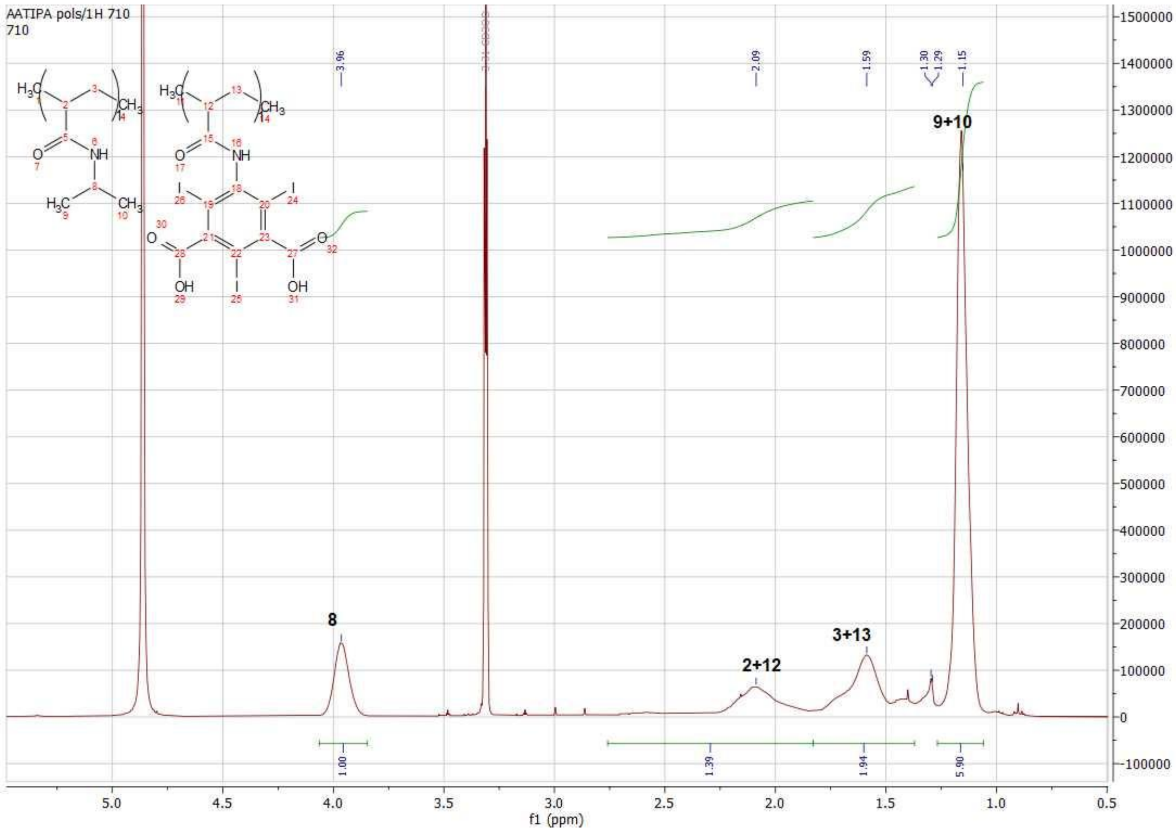

Figure S19. ^{1}H NMR (400 MHz, CD_3OD) spectrum of **B4**.

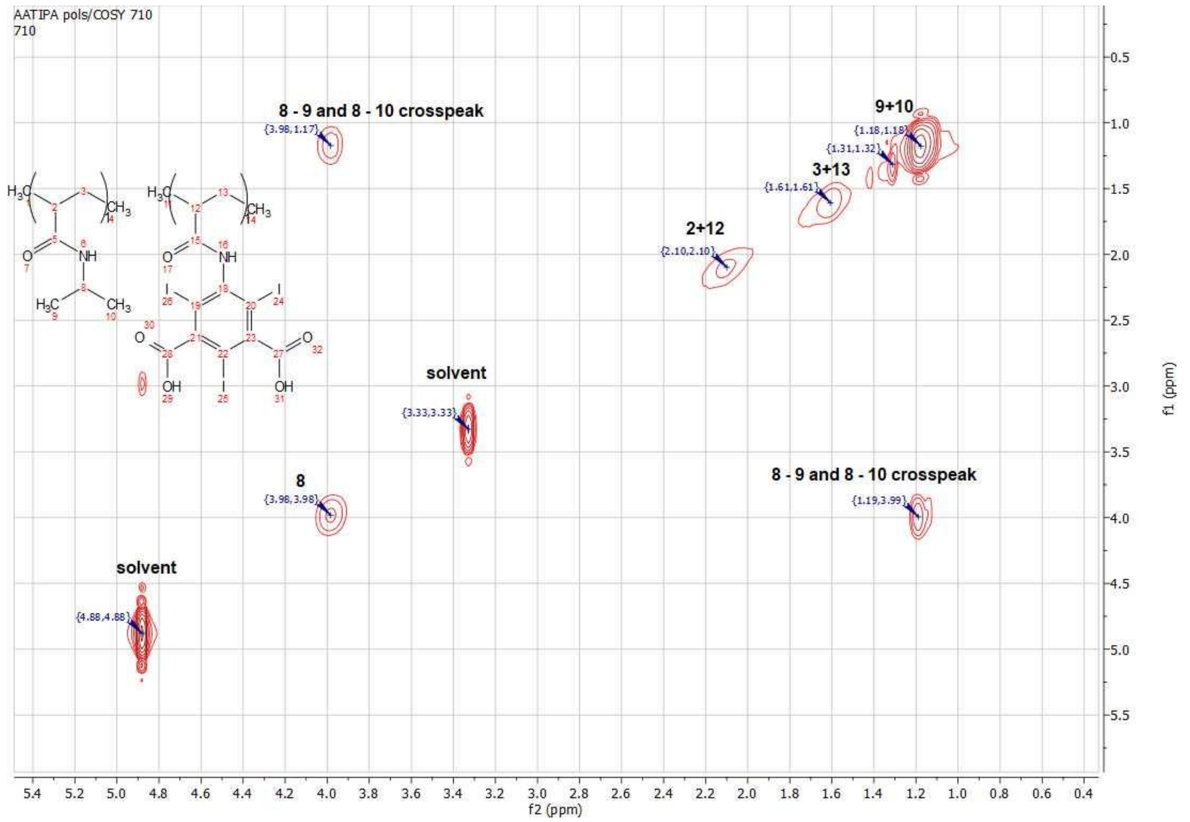

Figure S20. ^{1}H-^{1}H COSY NMR (400 MHz, CD_3OD) spectrum of **B4**.

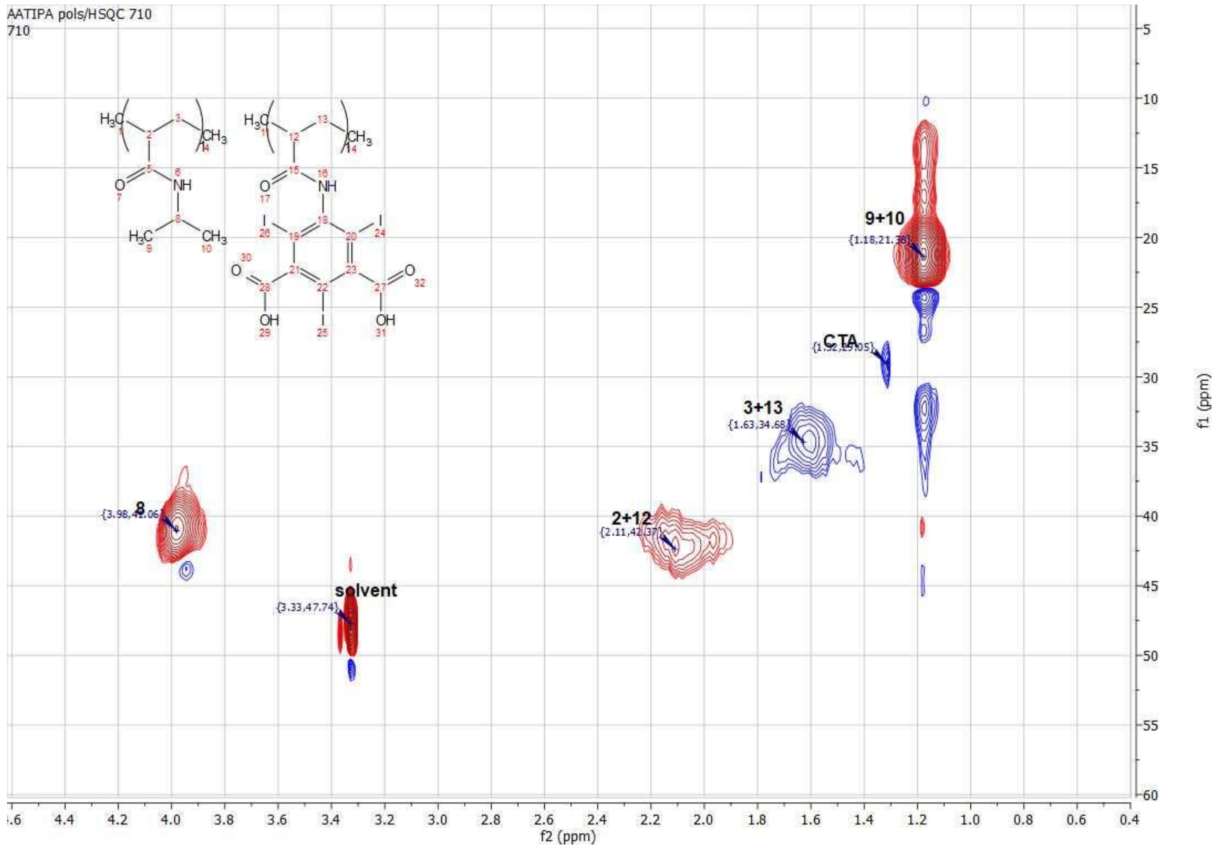

Figure S21. ^{1}H-^{13}C HSQC NMR (400 MHz, CD_3OD) spectrum of **B4**.

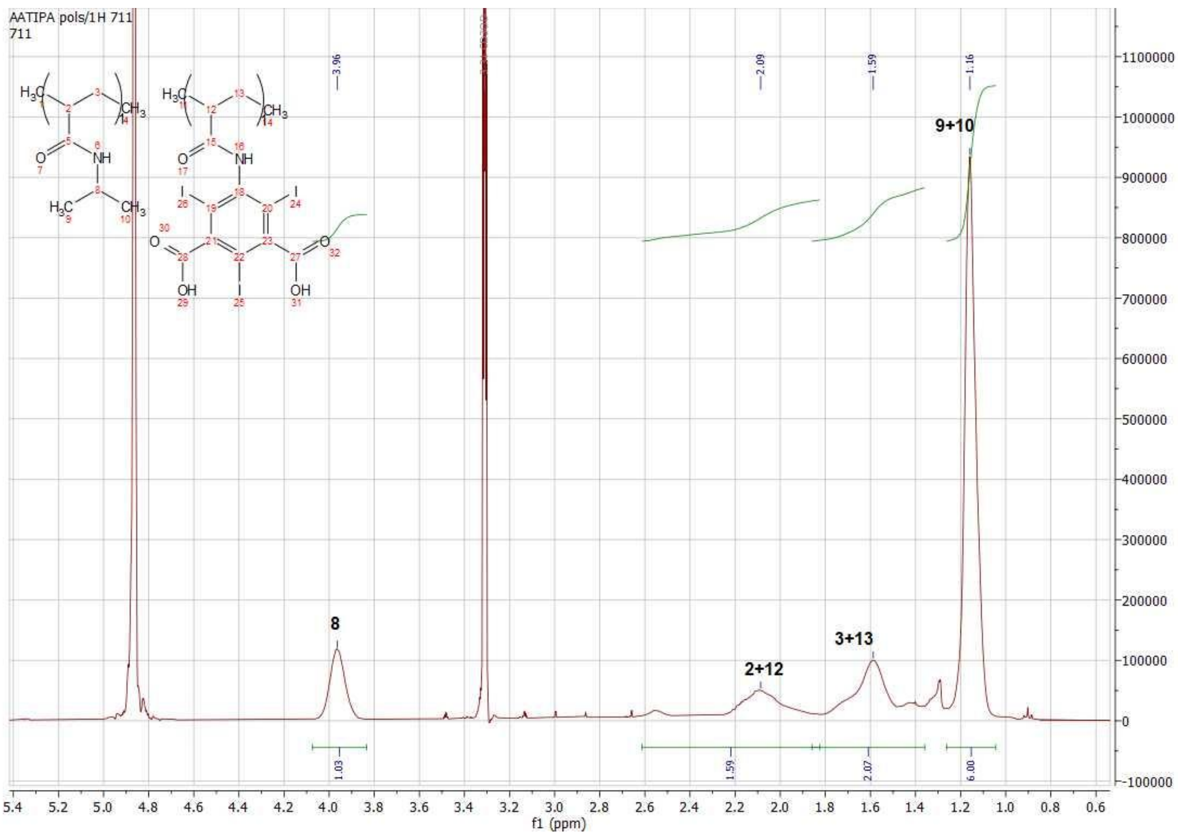

Figure S22. ^{1}H NMR (400 MHz, CD_3OD) spectrum of **B5**.

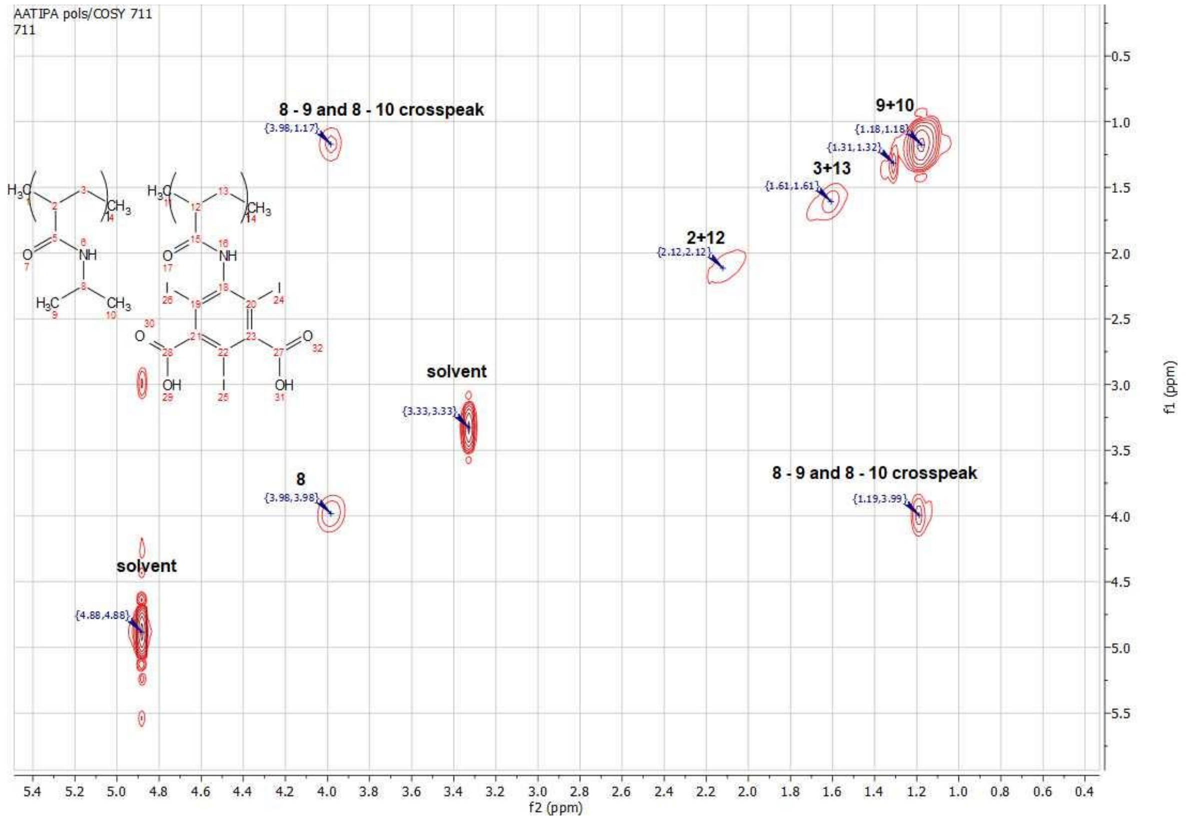

Figure S23. ^{1}H-^{1}H COSY NMR (400 MHz, CD_3OD) spectrum of **B5**.

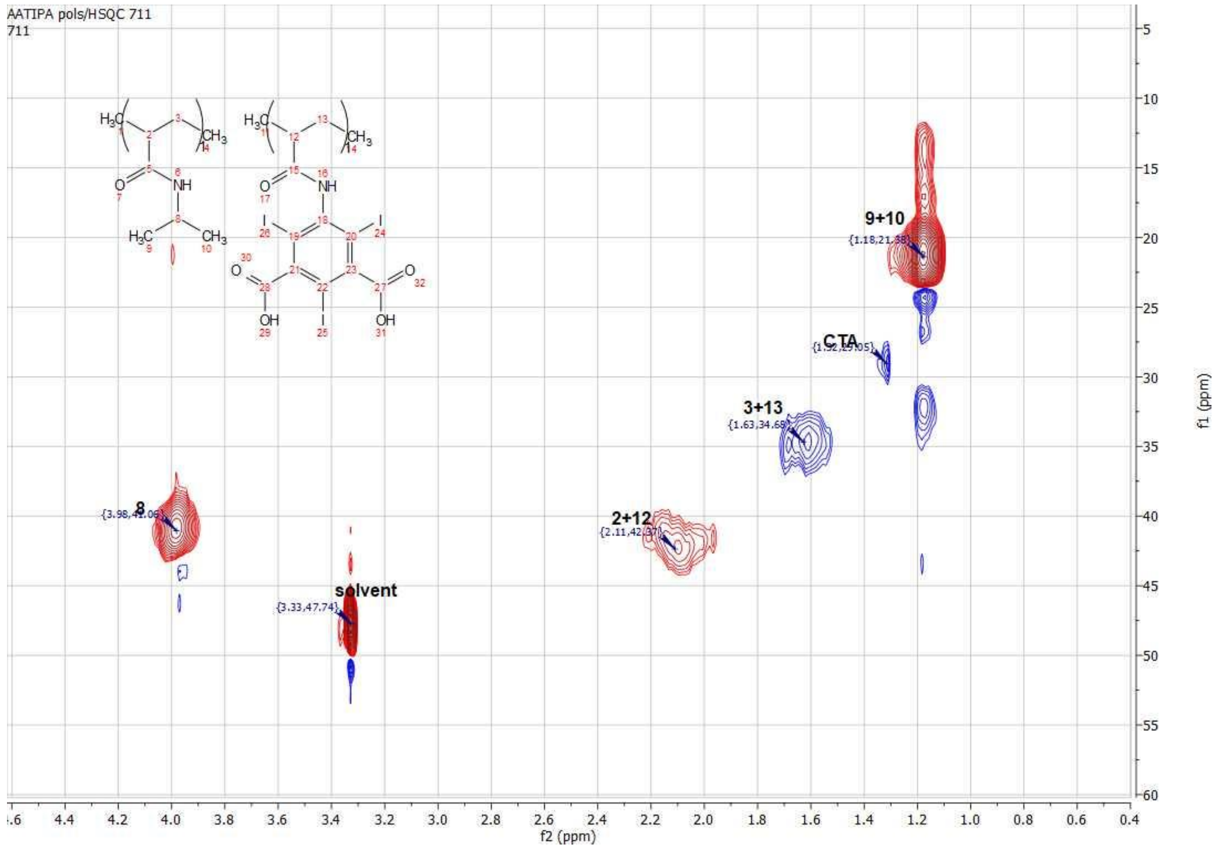

Figure S24. ^{1}H-^{13}C HSQC NMR (400 MHz, CD_3OD) spectrum of **B5**.

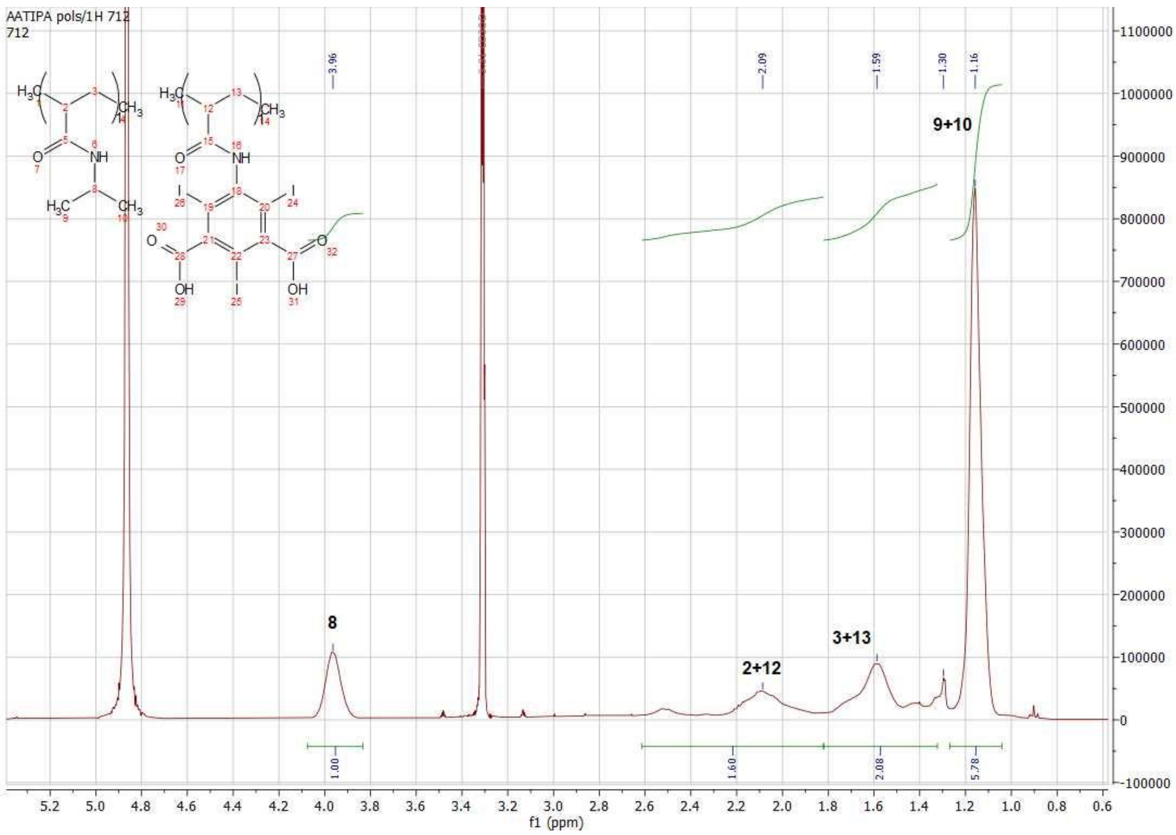

Figure S25. ^{1}H NMR (400 MHz, CD_3OD) spectrum of **B6**.

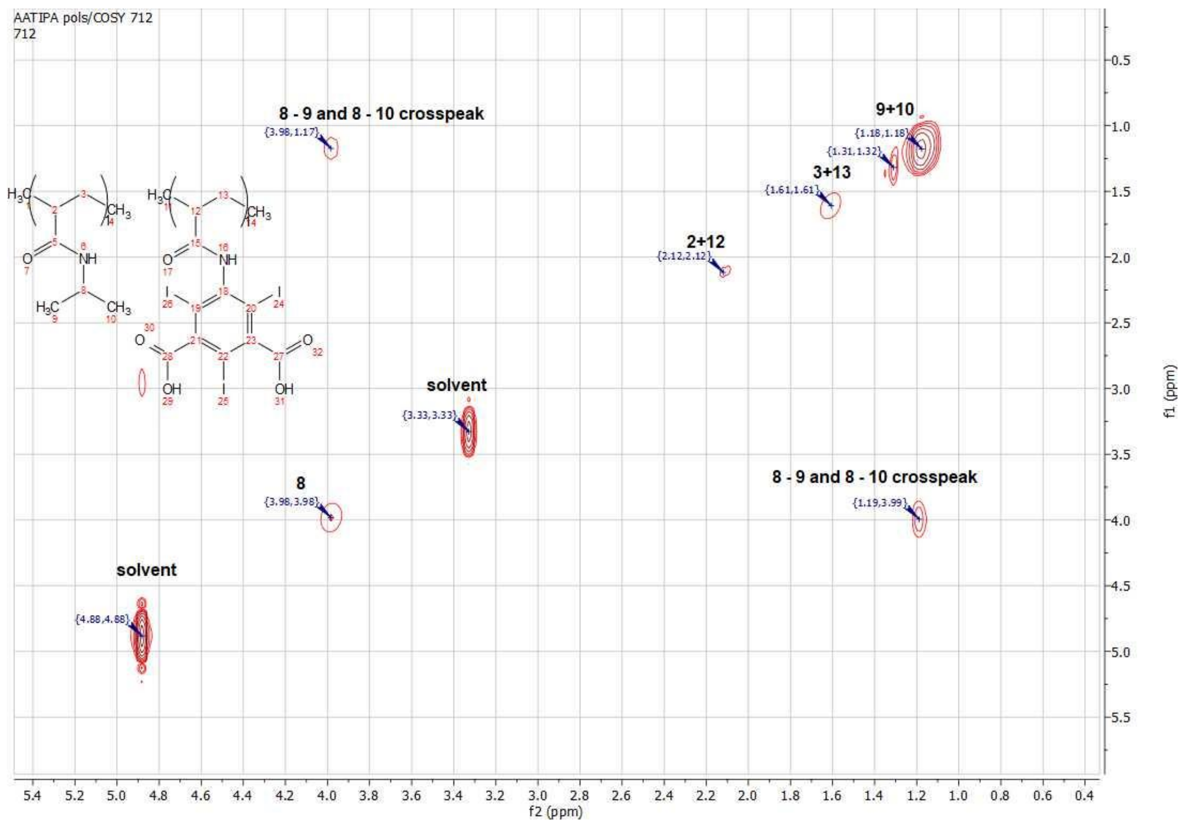

Figure S26. ^{1}H-^{1}H COSY NMR (400 MHz, CD_3OD) spectrum of **B6**.

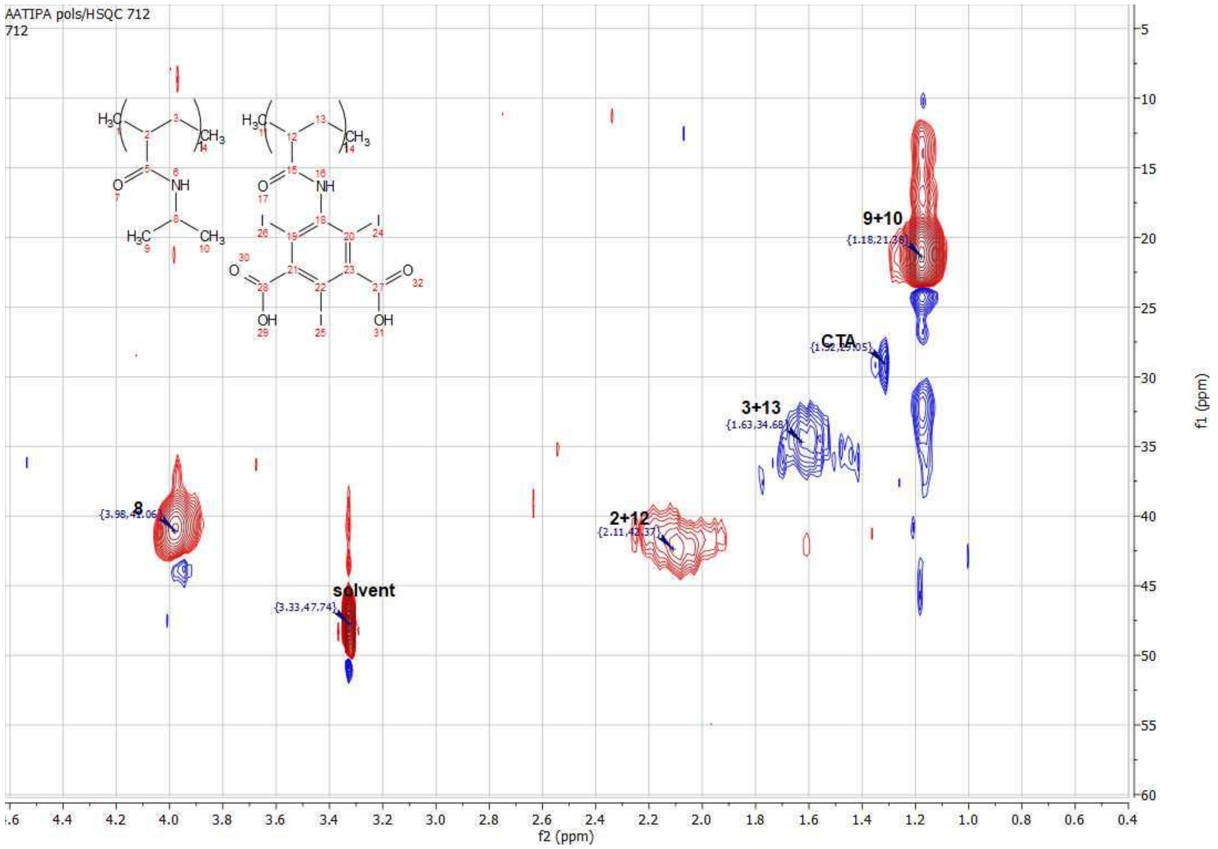

Figure S27. ^{1}H-^{13}C HSQC NMR (400 MHz, CD_3OD) spectrum of **B6**.

S1.2. NMR analysis of statistical copolymers

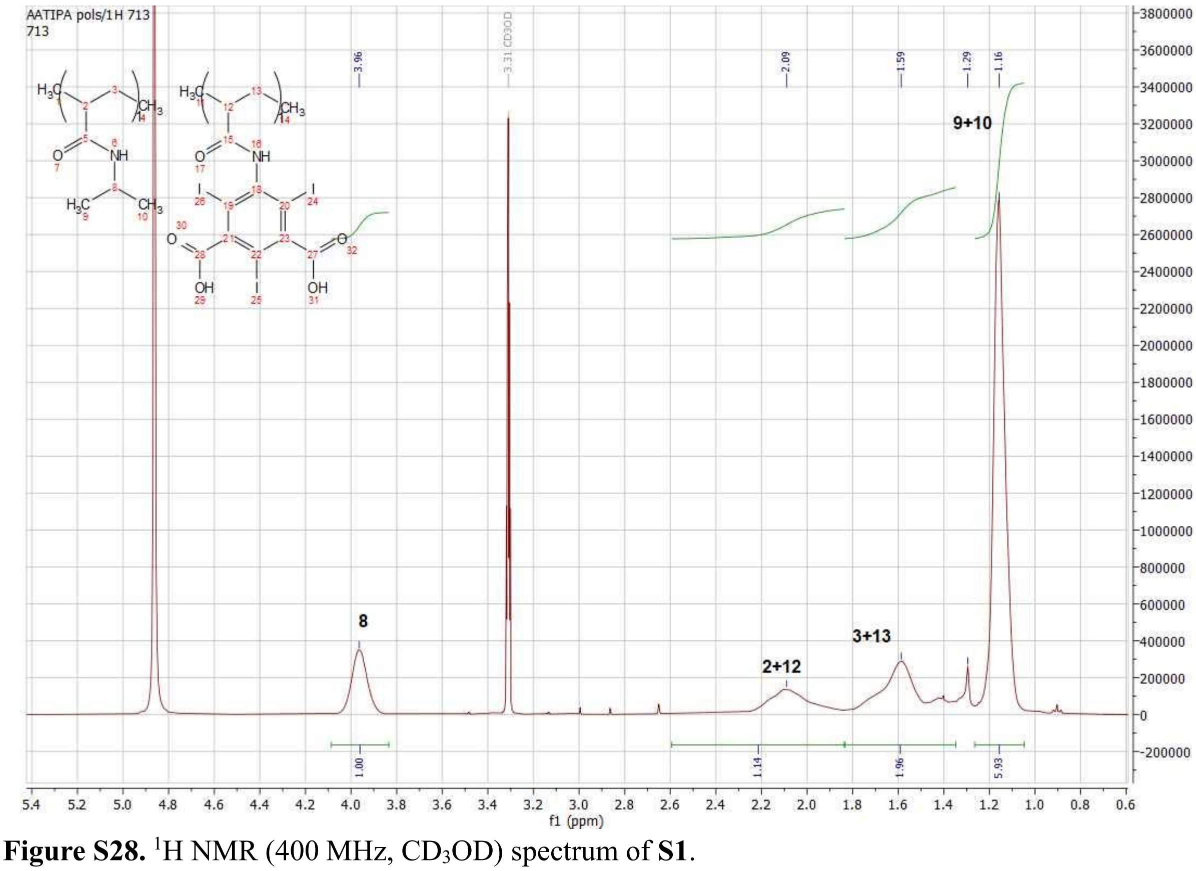

Figure S28. ^{1}H NMR (400 MHz, CD_3OD) spectrum of **S1**.

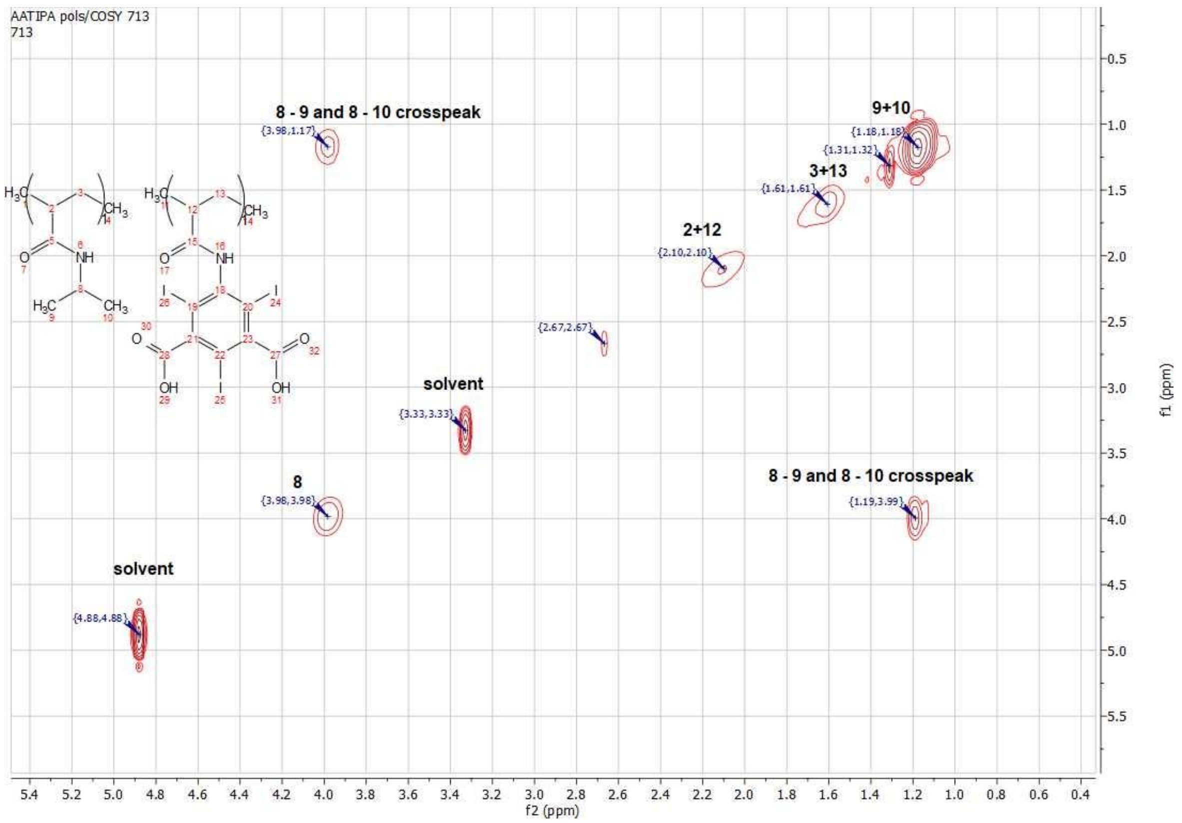

Figure S29. ¹H-¹H COSY NMR (400 MHz, CD_3OD) spectrum of **S1**.

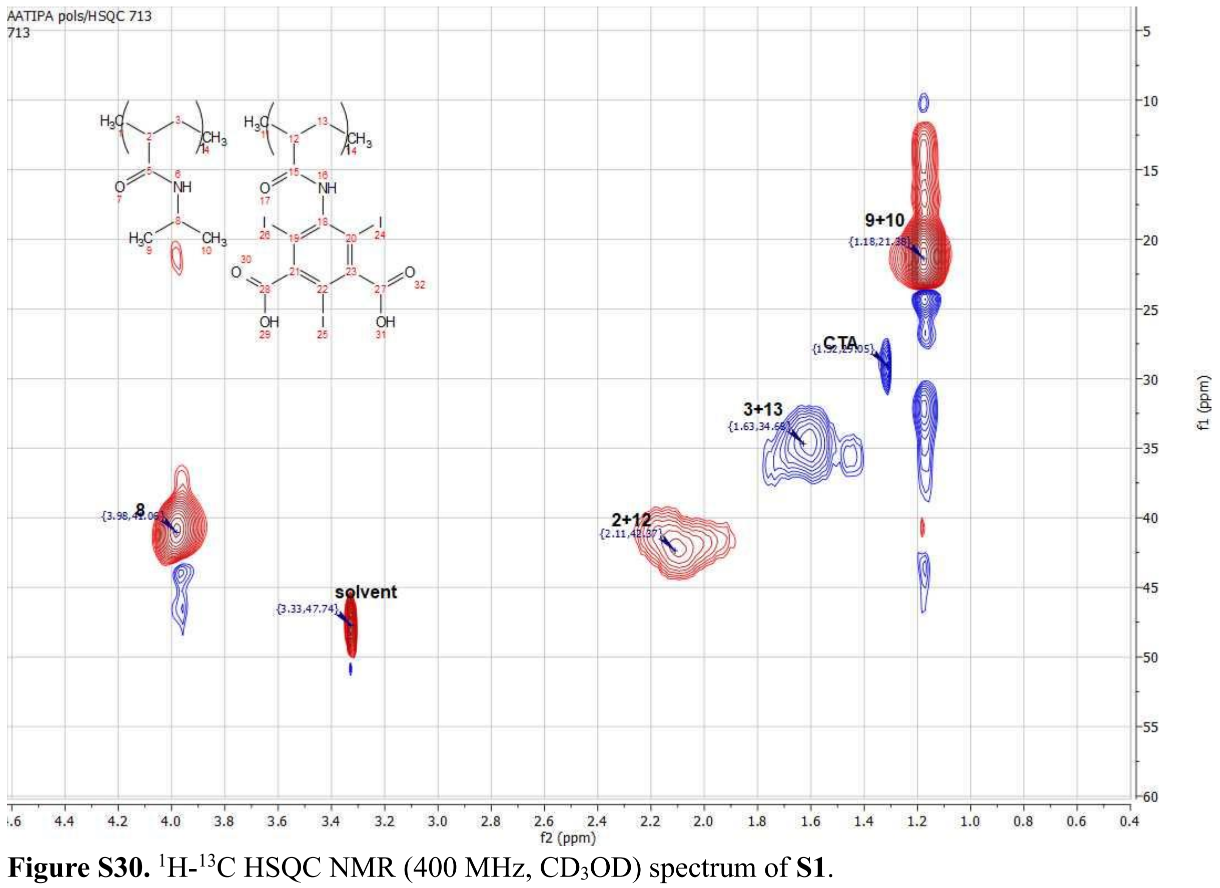

Figure S30. ¹H-¹³C HSQC NMR (400 MHz, CD_3OD) spectrum of **S1**.

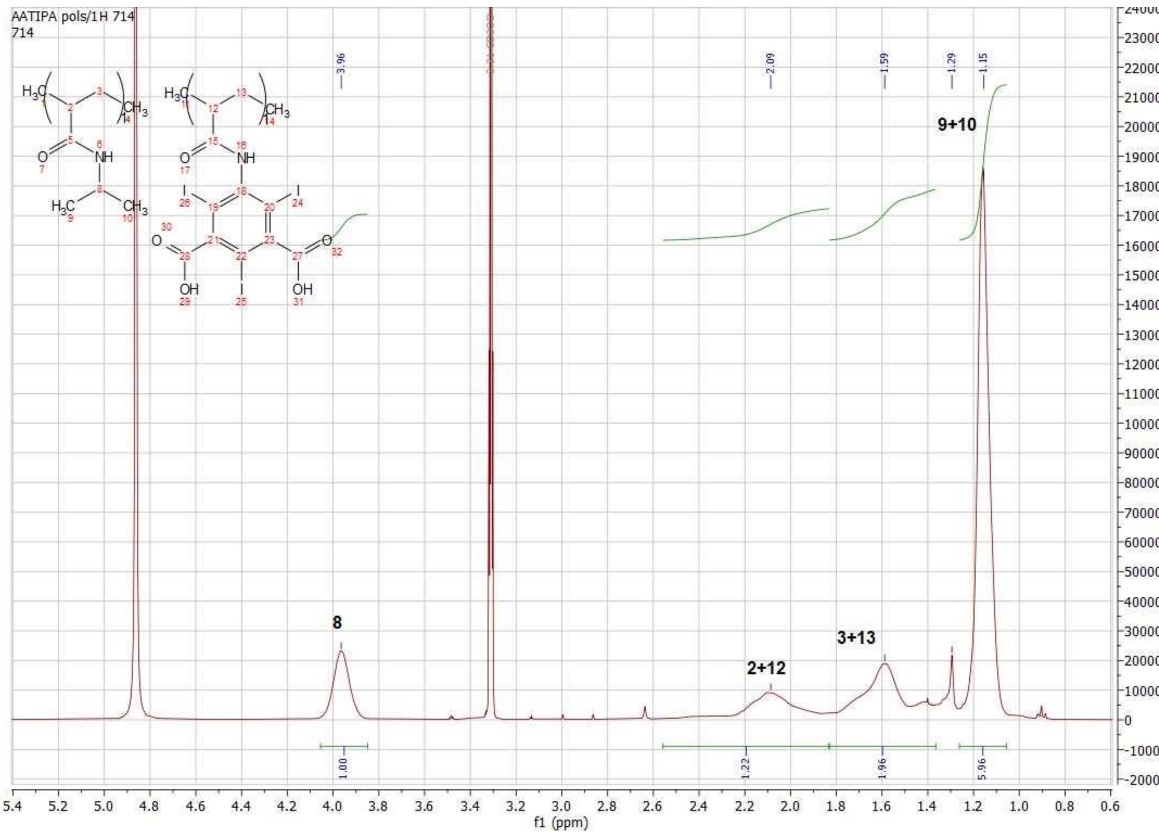

Figure S31. ^{1}H NMR (400 MHz, CD_3OD) spectrum of **S2**.

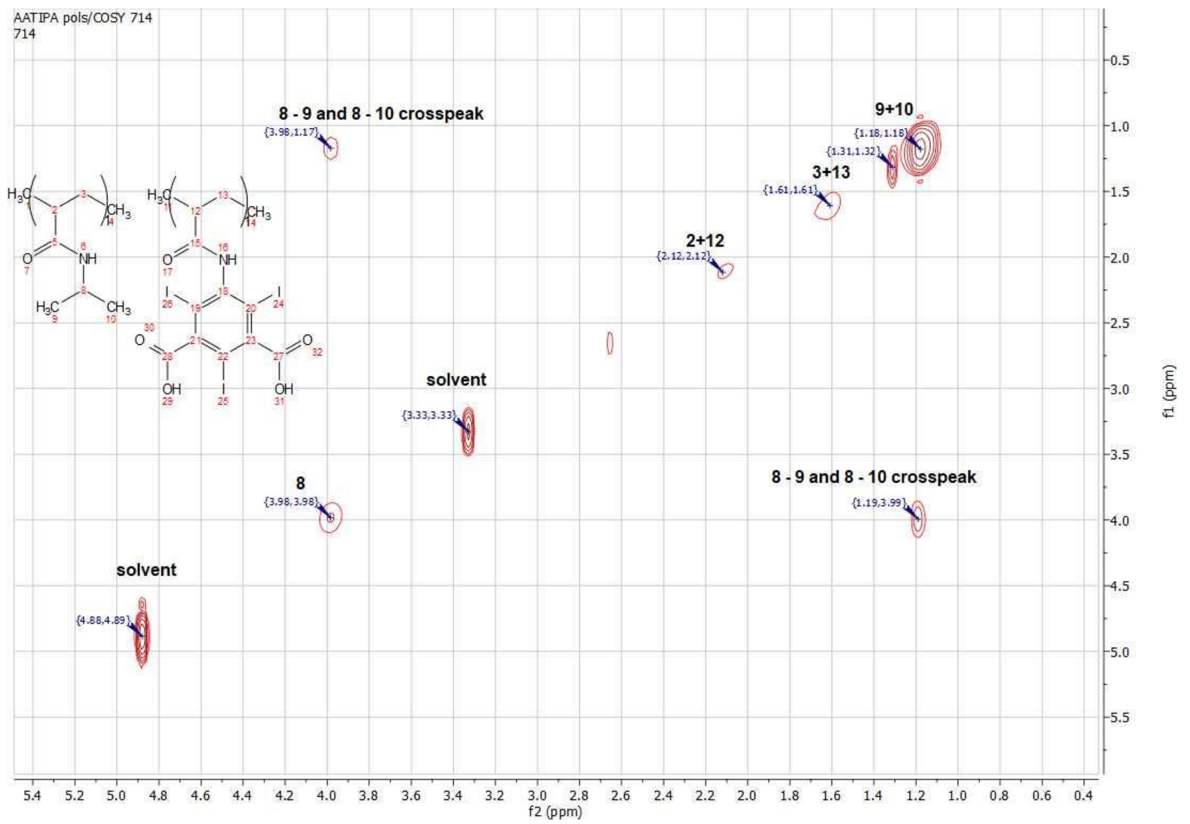

Figure S32. ^{1}H-^{1}H COSY NMR (400 MHz, CD_3OD) spectrum of **S2**.

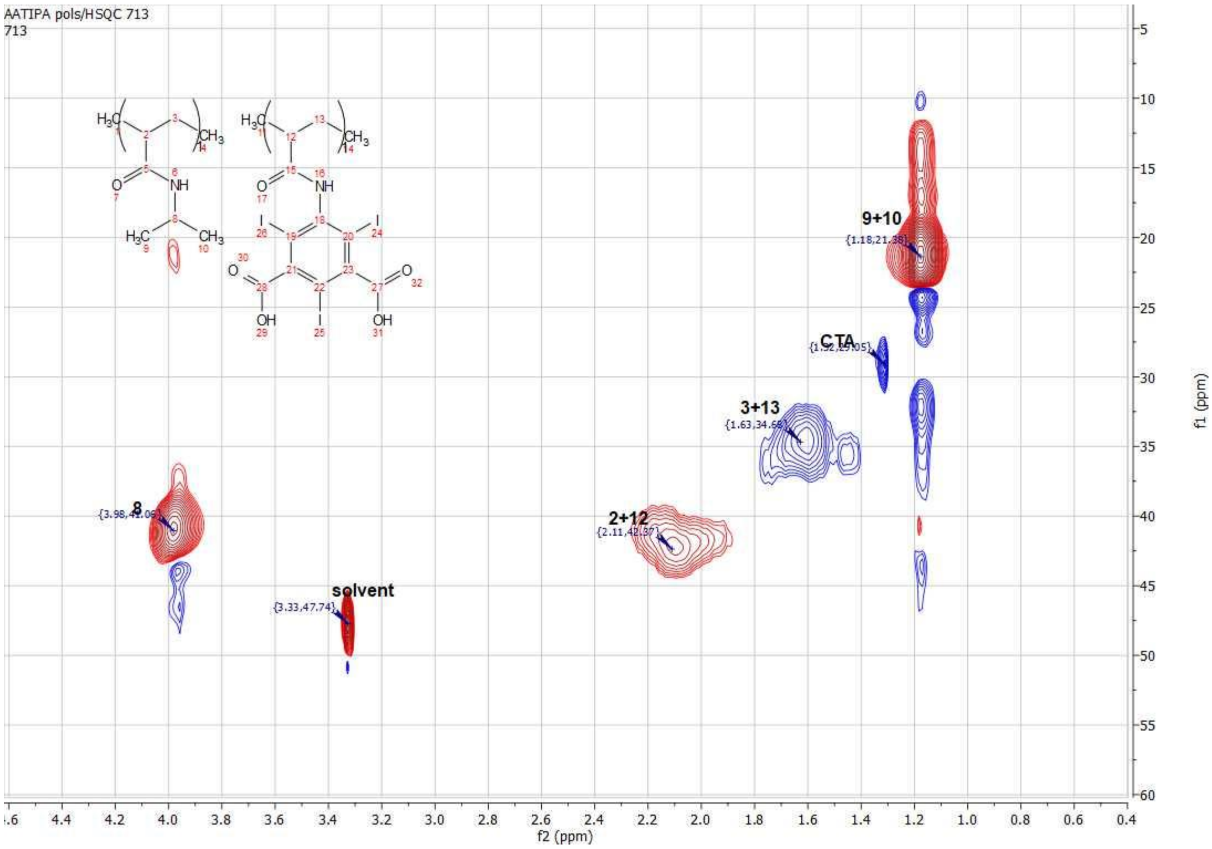

Figure S33. ^{1}H-^{13}C HSQC NMR (400 MHz, CD_3OD) spectrum of **S2**.

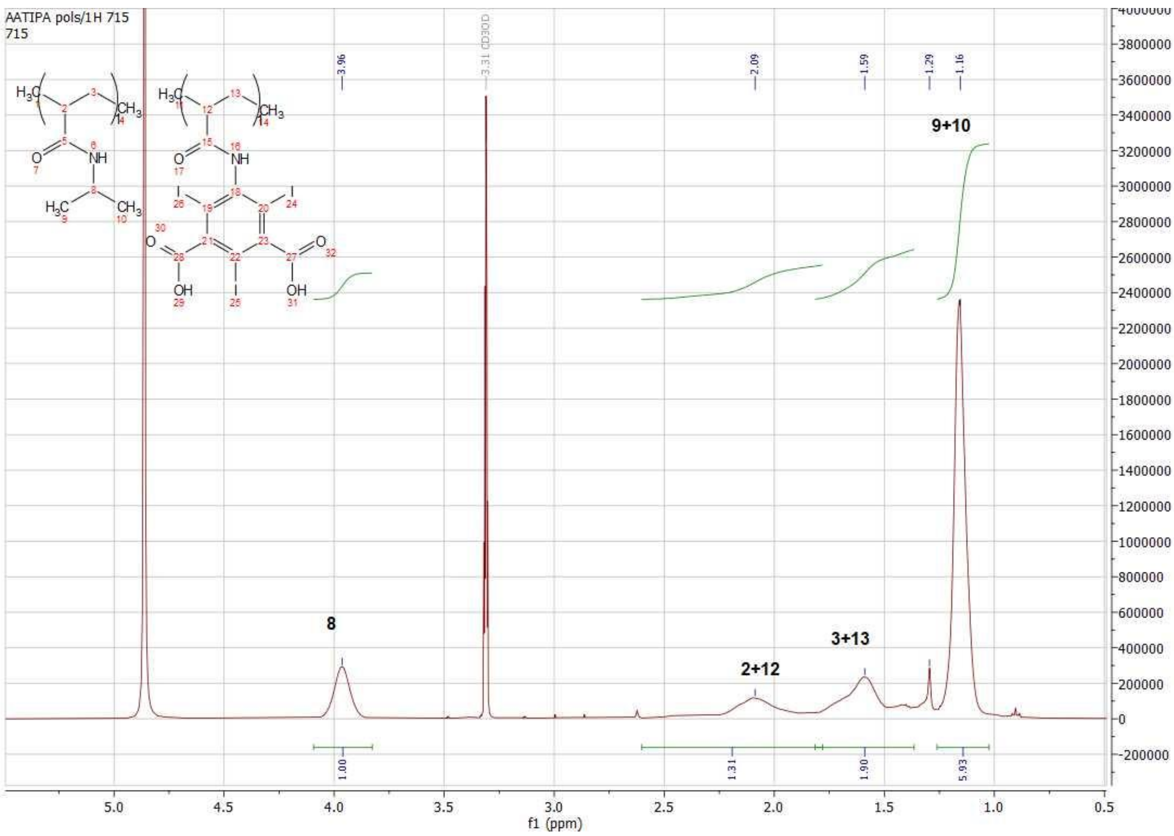

Figure S34. ^{1}H NMR (400 MHz, CD_3OD) spectrum of **S3**.

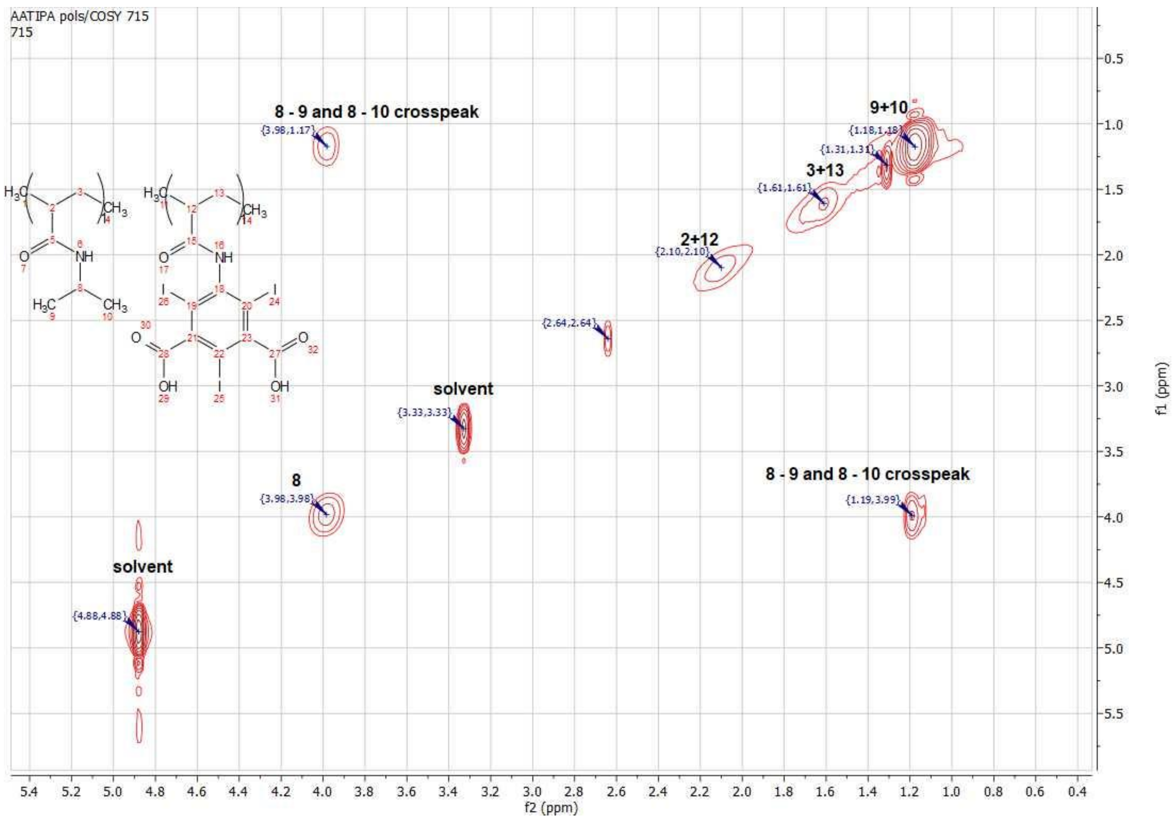

Figure S35. ^1H-^1H COSY NMR (400 MHz, CD_3OD) spectrum of **S3**.

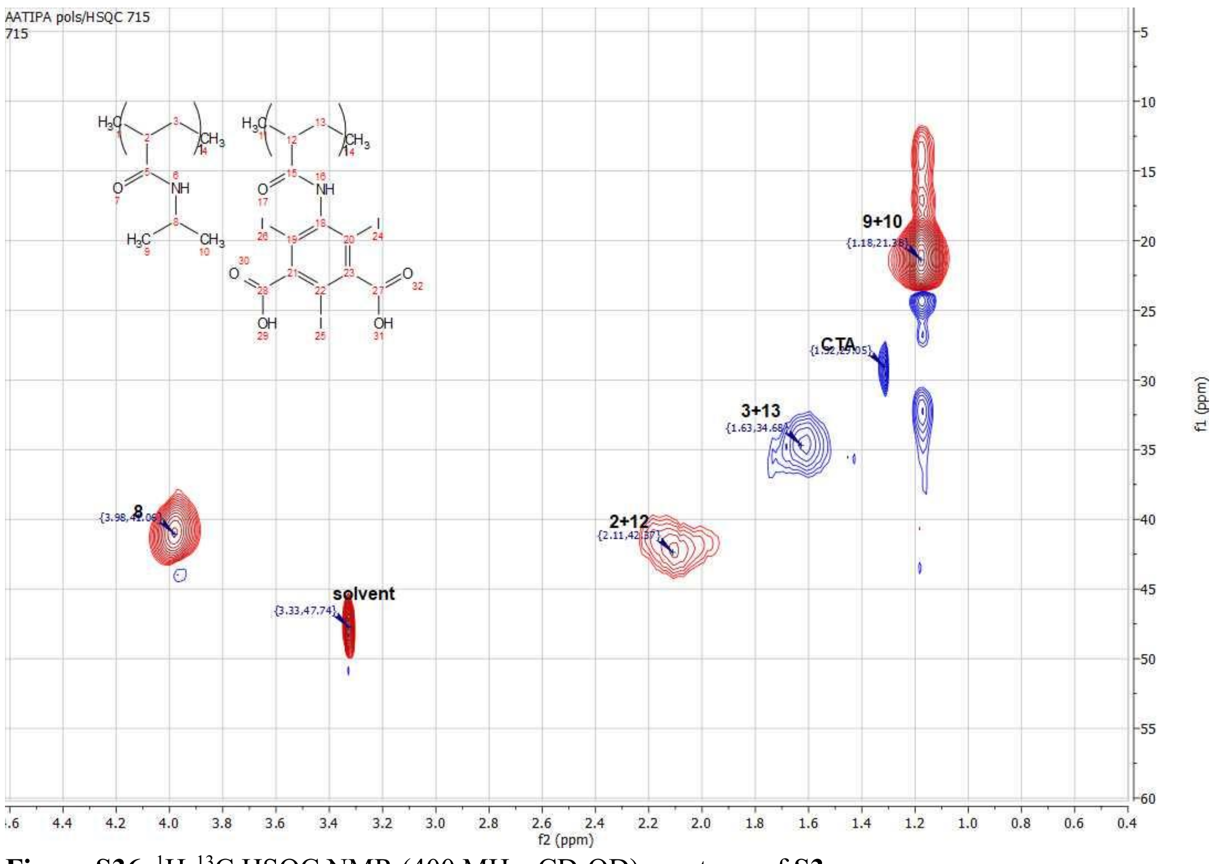

Figure S36. ^1H-^{13}C HSQC NMR (400 MHz, CD_3OD) spectrum of **S3**.

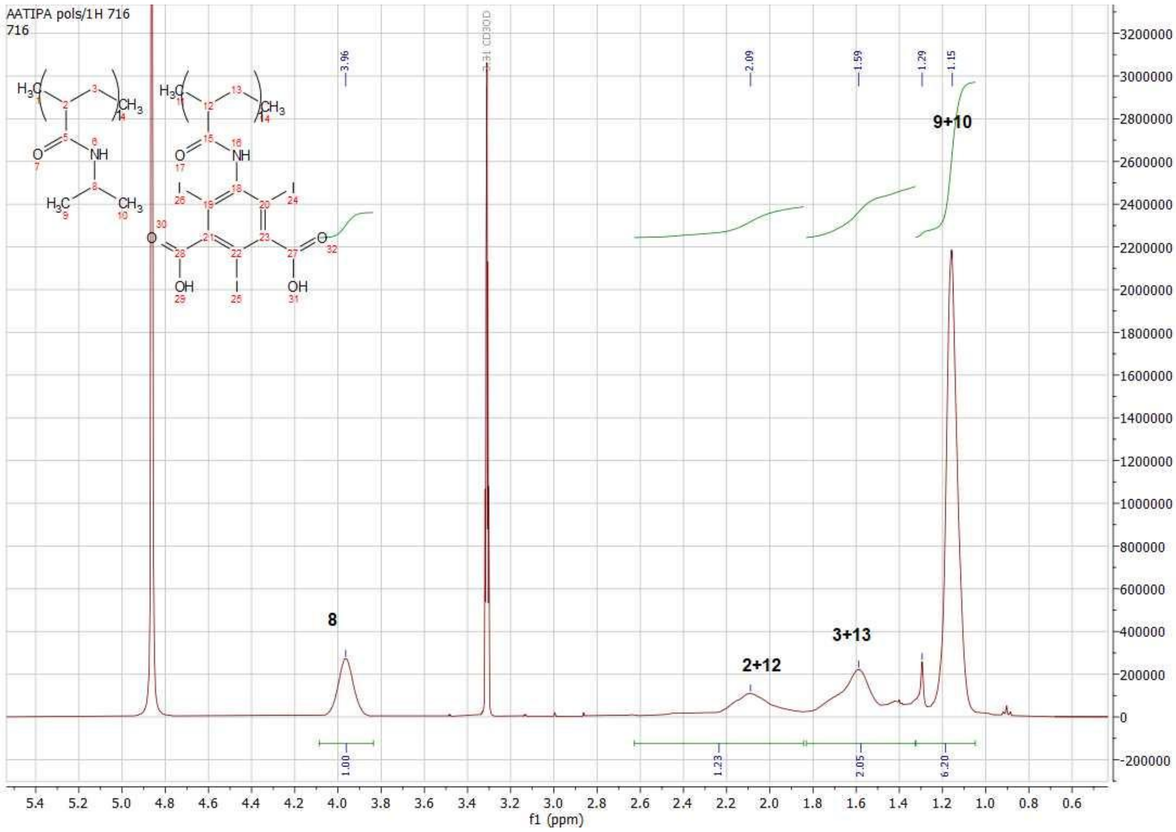

Figure S37. ^{1}H NMR (400 MHz, CD_3OD) spectrum of **S4**.

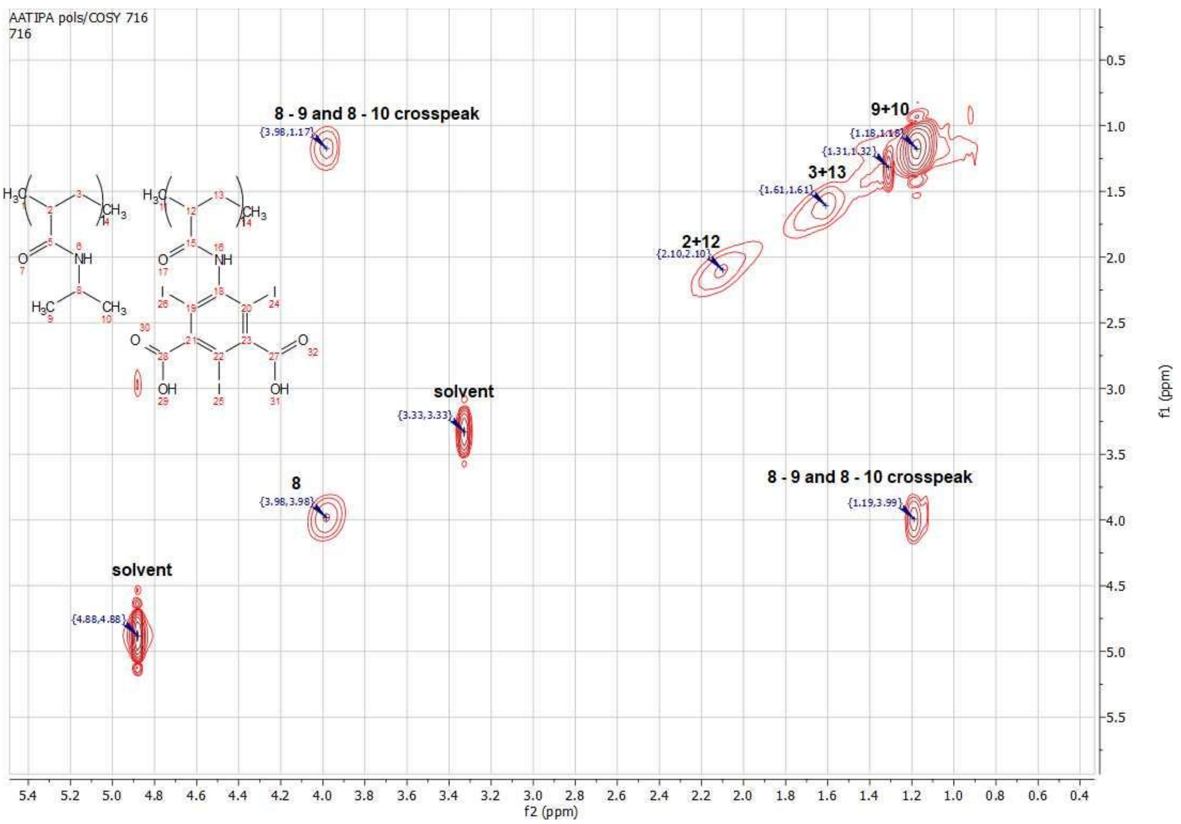

Figure S38. ^{1}H-^{1}H COSY NMR (400 MHz, CD_3OD) spectrum of **S4**.

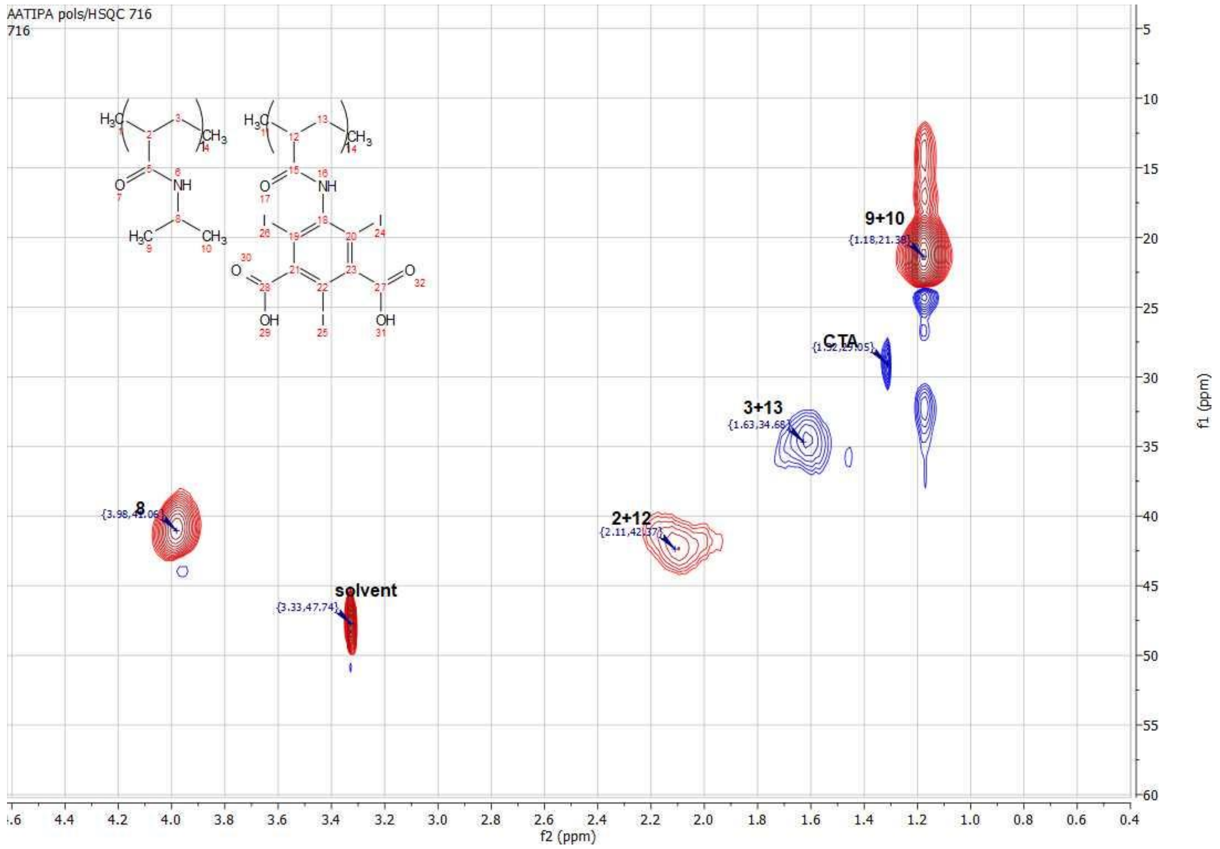

Figure S39. ^{1}H-^{13}C HSQC NMR (400 MHz, CD_3OD) spectrum of **S4**.

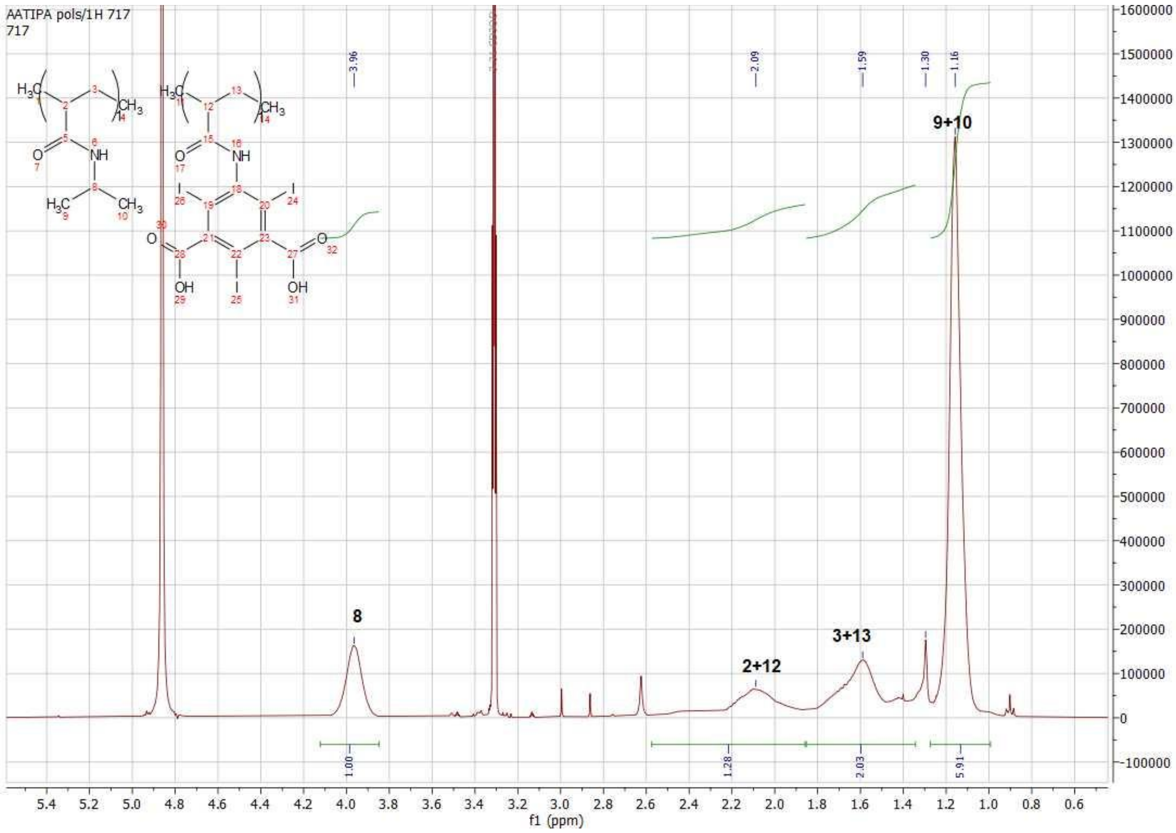

Figure S40. ^{1}H NMR (400 MHz, CD_3OD) spectrum of **S5**.

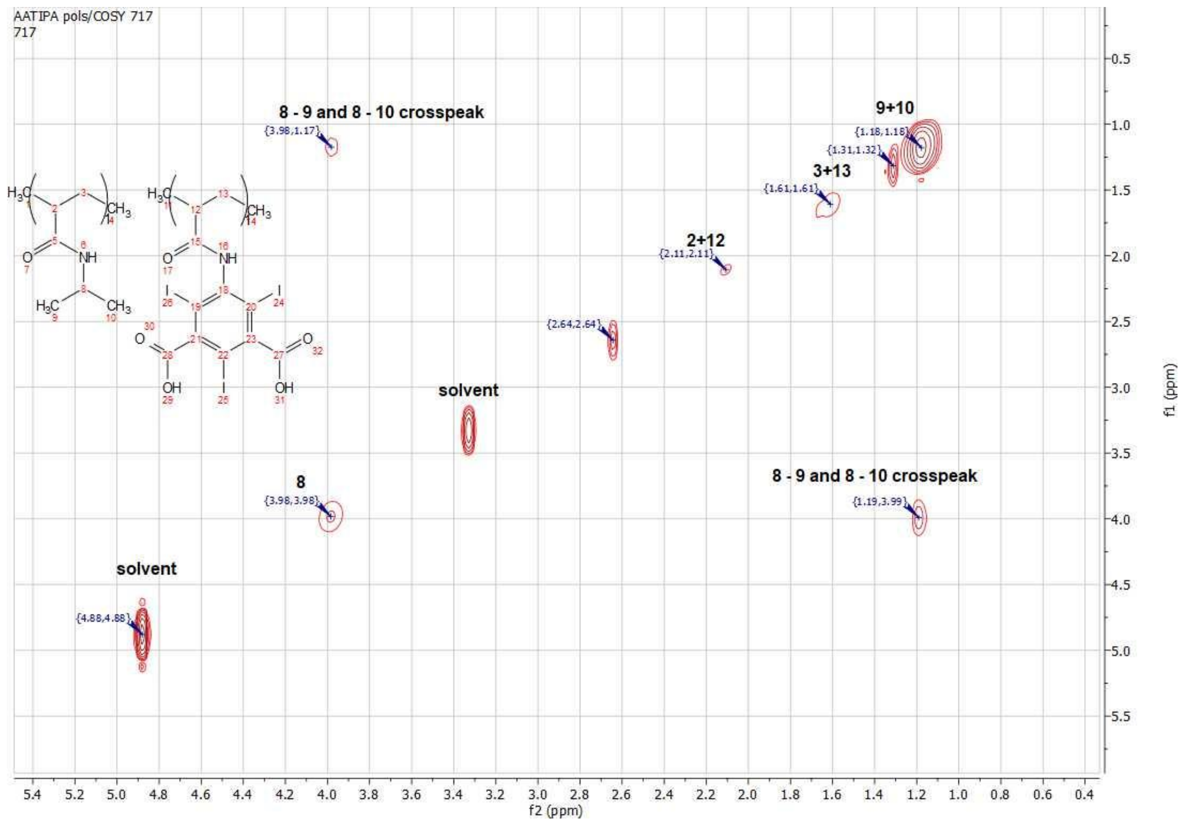

Figure S41. ^{1}H-^{1}H COSY NMR (400 MHz, CD_3OD) spectrum of **S5**.

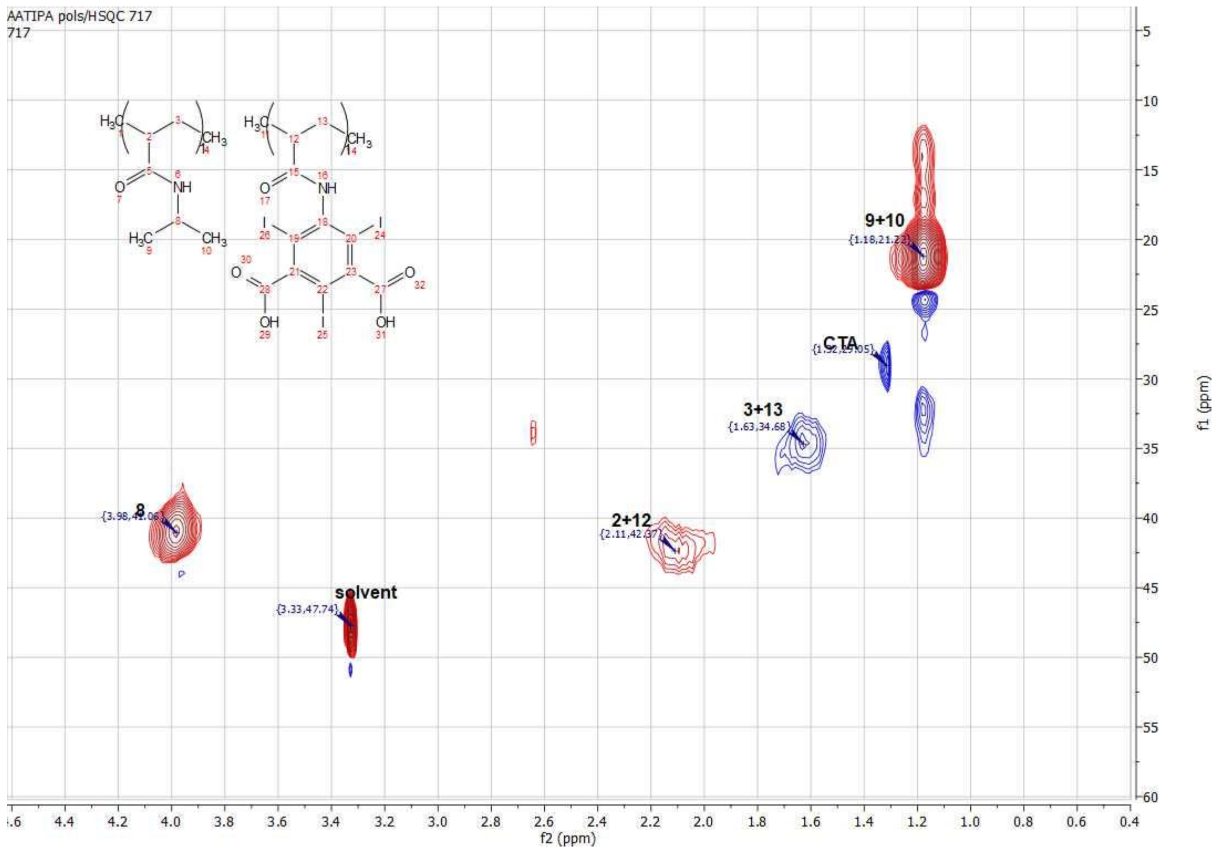

Figure S42. ^{1}H-^{13}C HSQC NMR (400 MHz, CD_3OD) spectrum of **S5**.

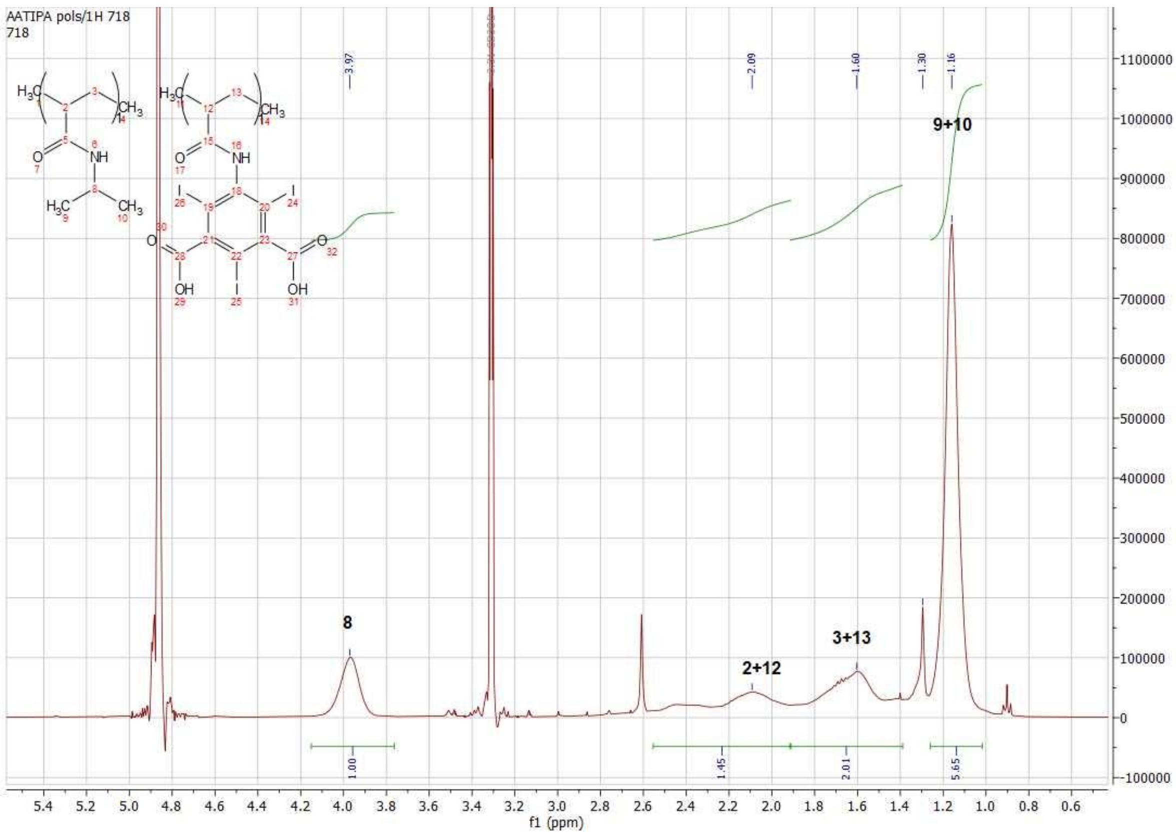

Figure S43. ^{1}H NMR (400 MHz, CD_3OD) spectrum of **S6**.

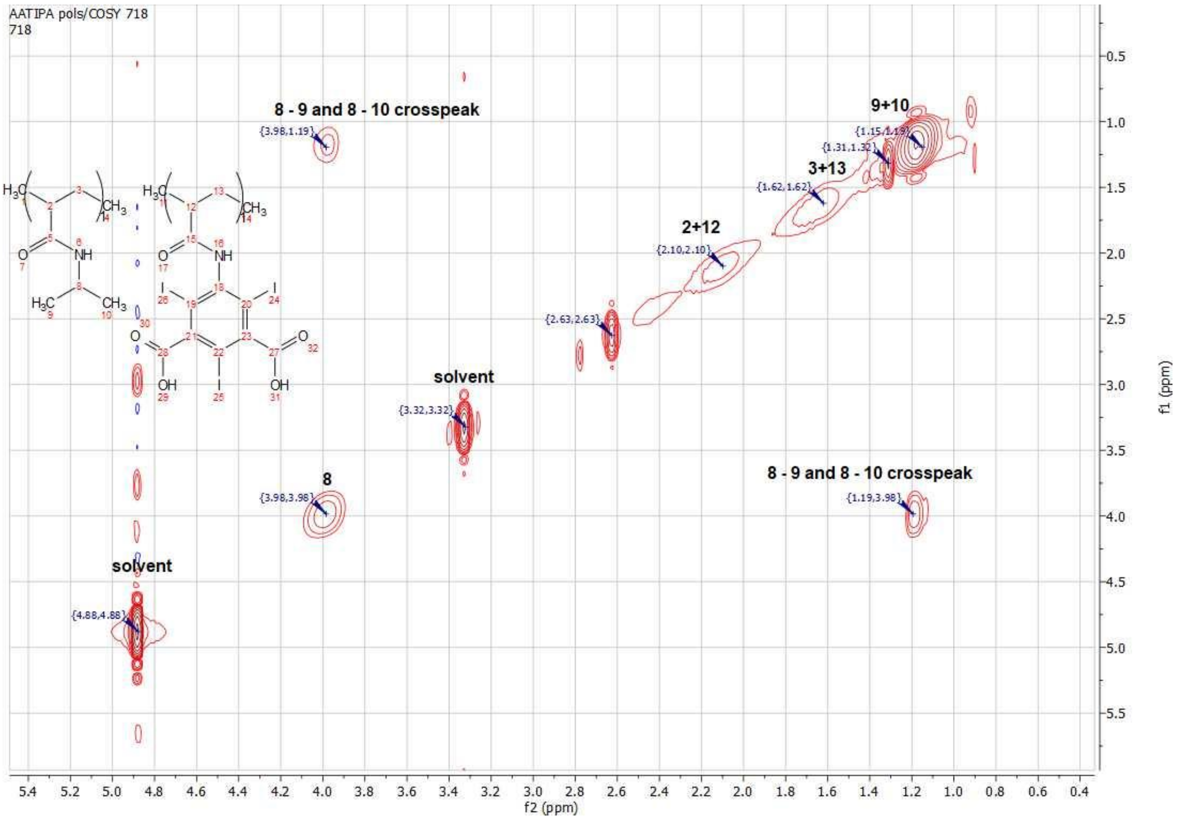

Figure S44. ^{1}H-^{1}H COSY NMR (400 MHz, CD_3OD) spectrum of **S6**.

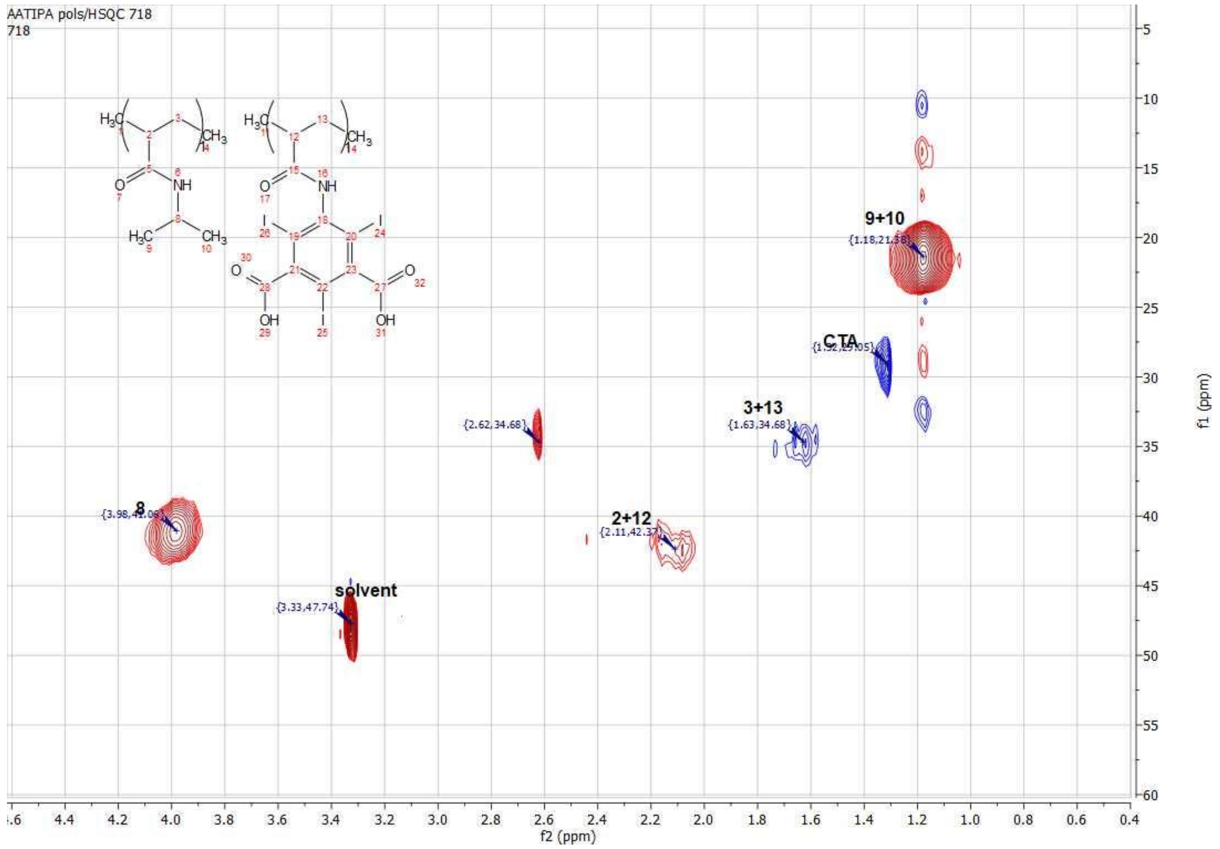

Figure S45. ^{1}H-^{13}C HSQC NMR (400 MHz, CD_3OD) spectrum of **S6**.

S1.2. NMR analysis of statistical copolymers S1m-S6m.

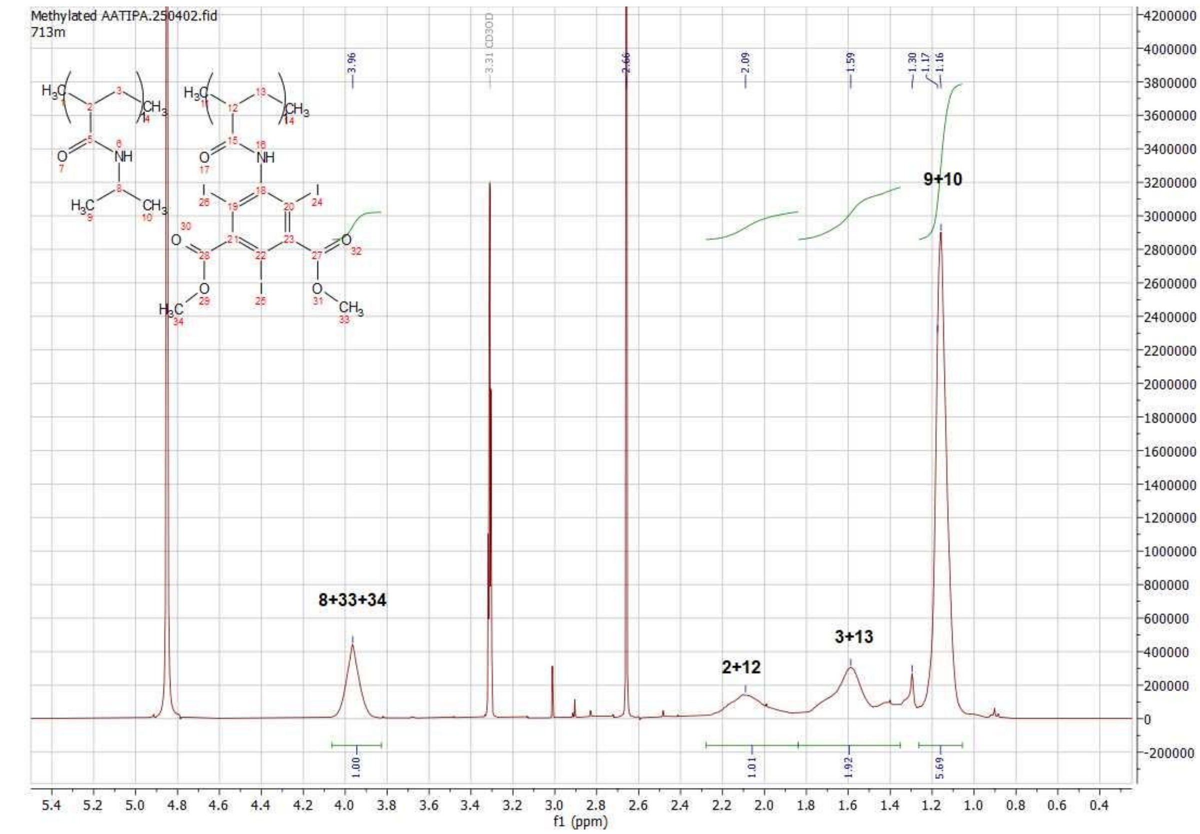

Figure S46. ^{1}H NMR (400 MHz, CD_3OD) spectrum of **S1m**.

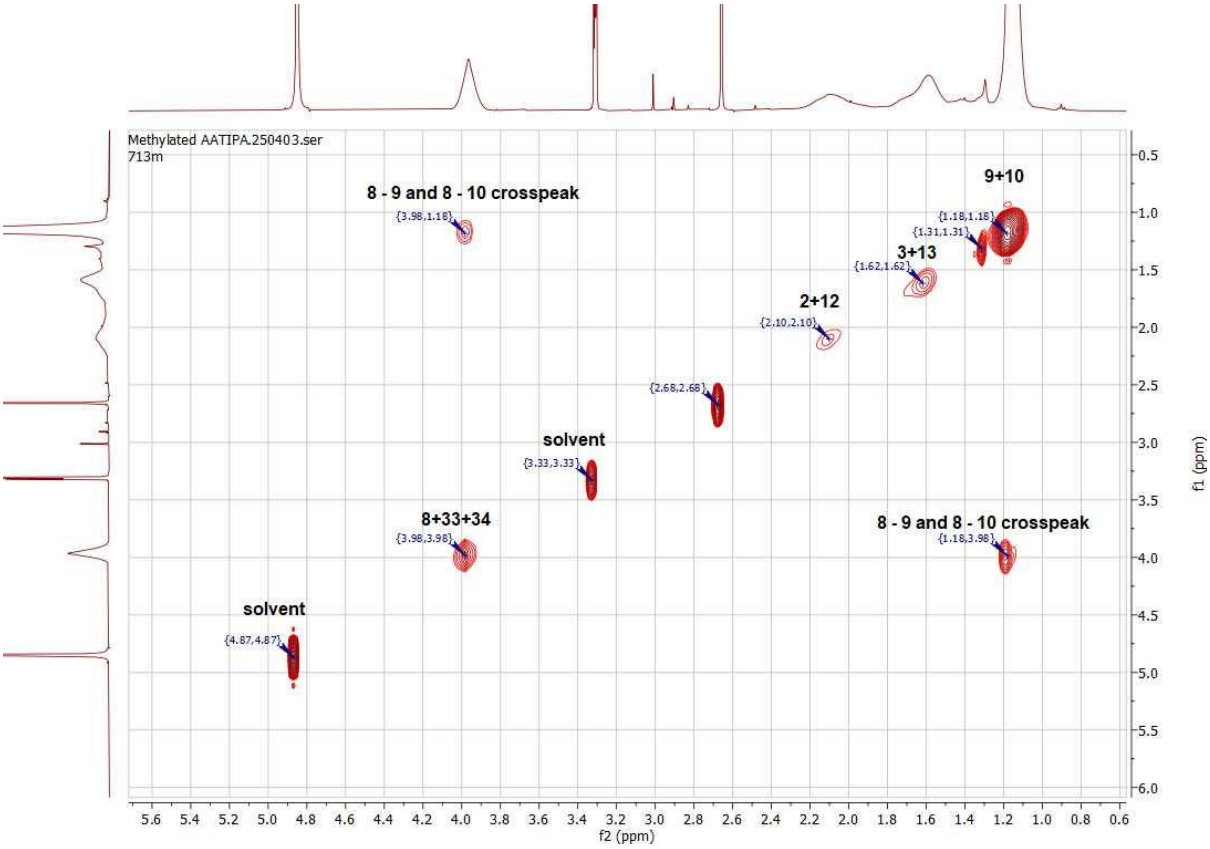

Figure S47. ^{1}H-^{1}H COSY NMR (400 MHz, CD_3OD) spectrum of **S1m**.

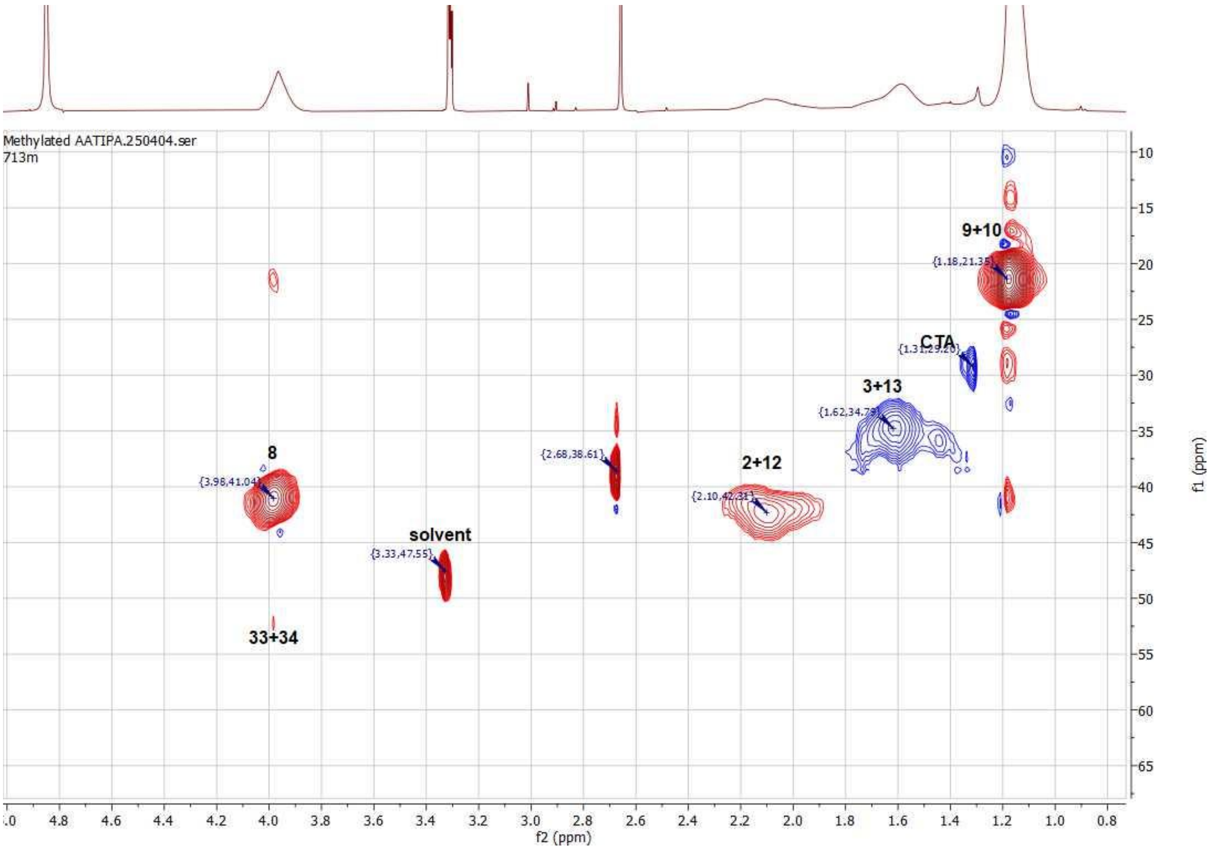

Figure S48. ^{1}H-^{13}C HSQC NMR (400 MHz, CD_3OD) spectrum of **S1m**.

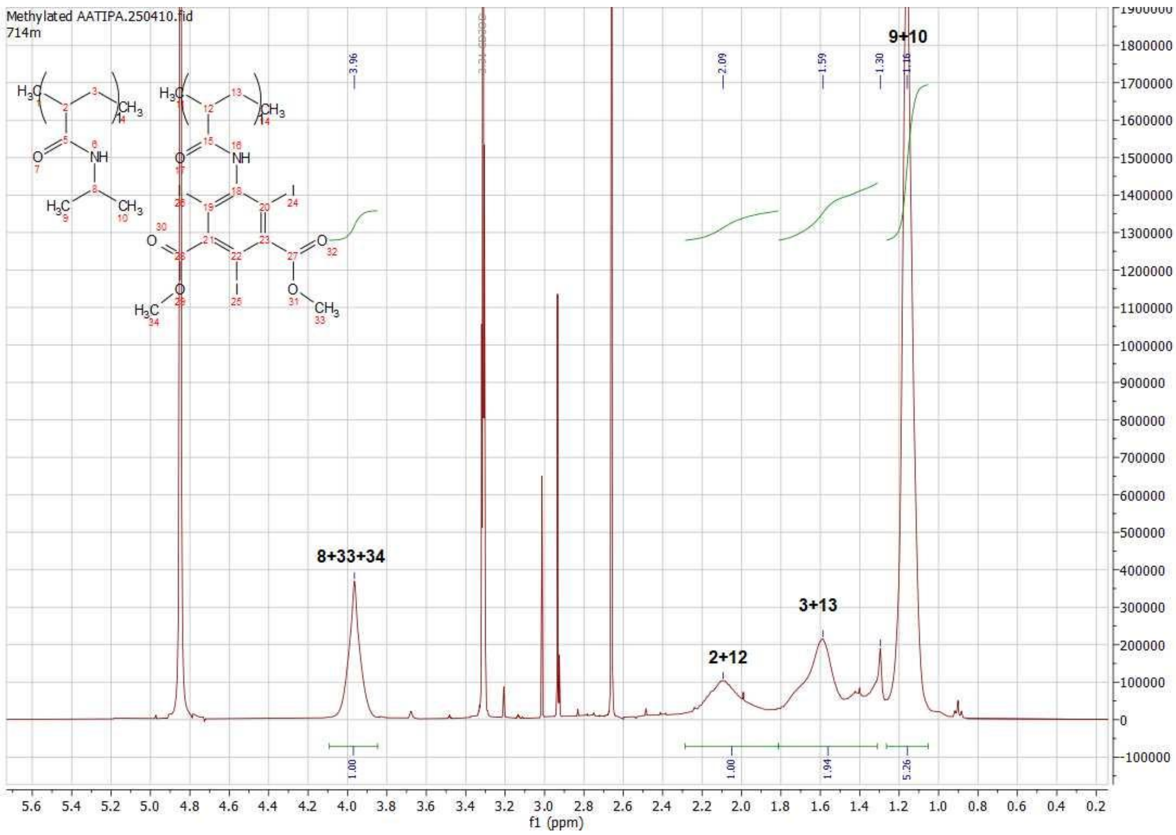

Figure S49. ^{1}H NMR (400 MHz, CD_3OD) spectrum of **S2m**.

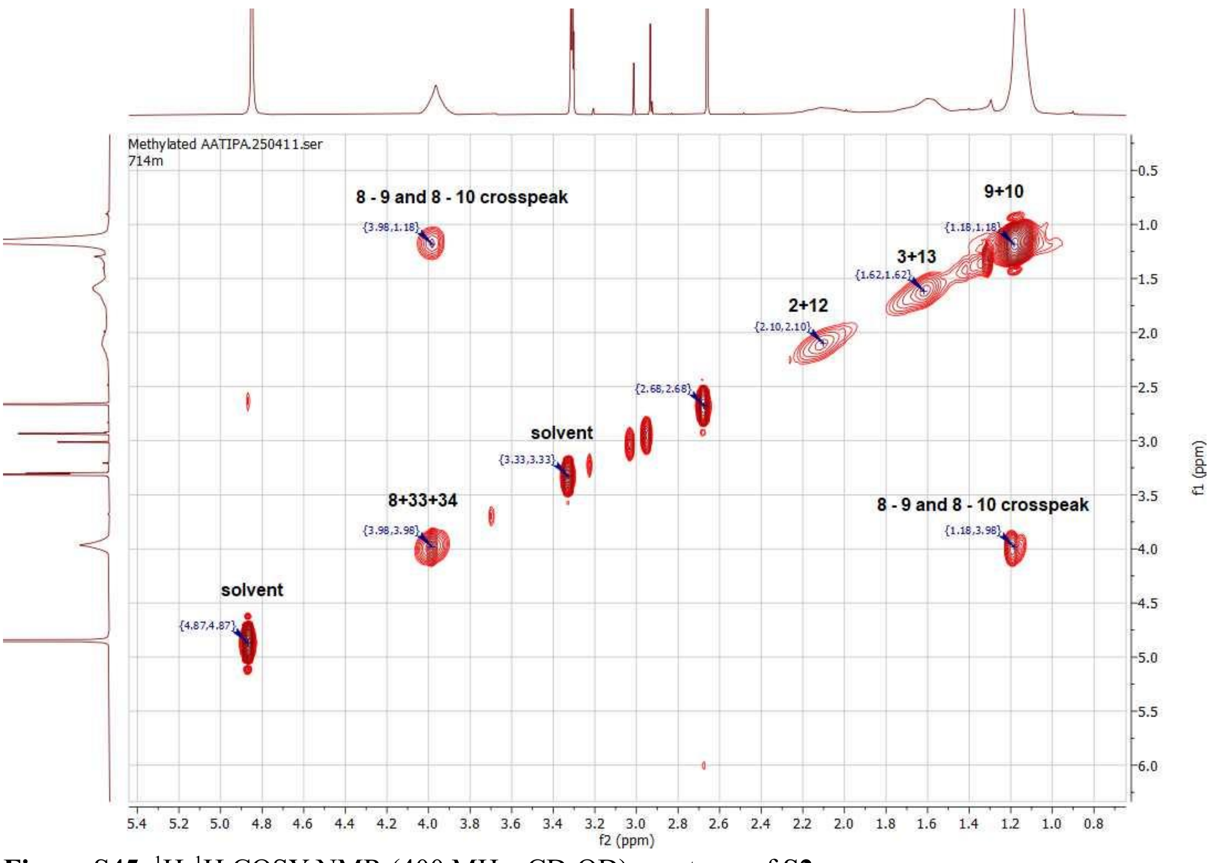

Figure S45. ^{1}H-^{1}H COSY NMR (400 MHz, CD_3OD) spectrum of **S2m**.

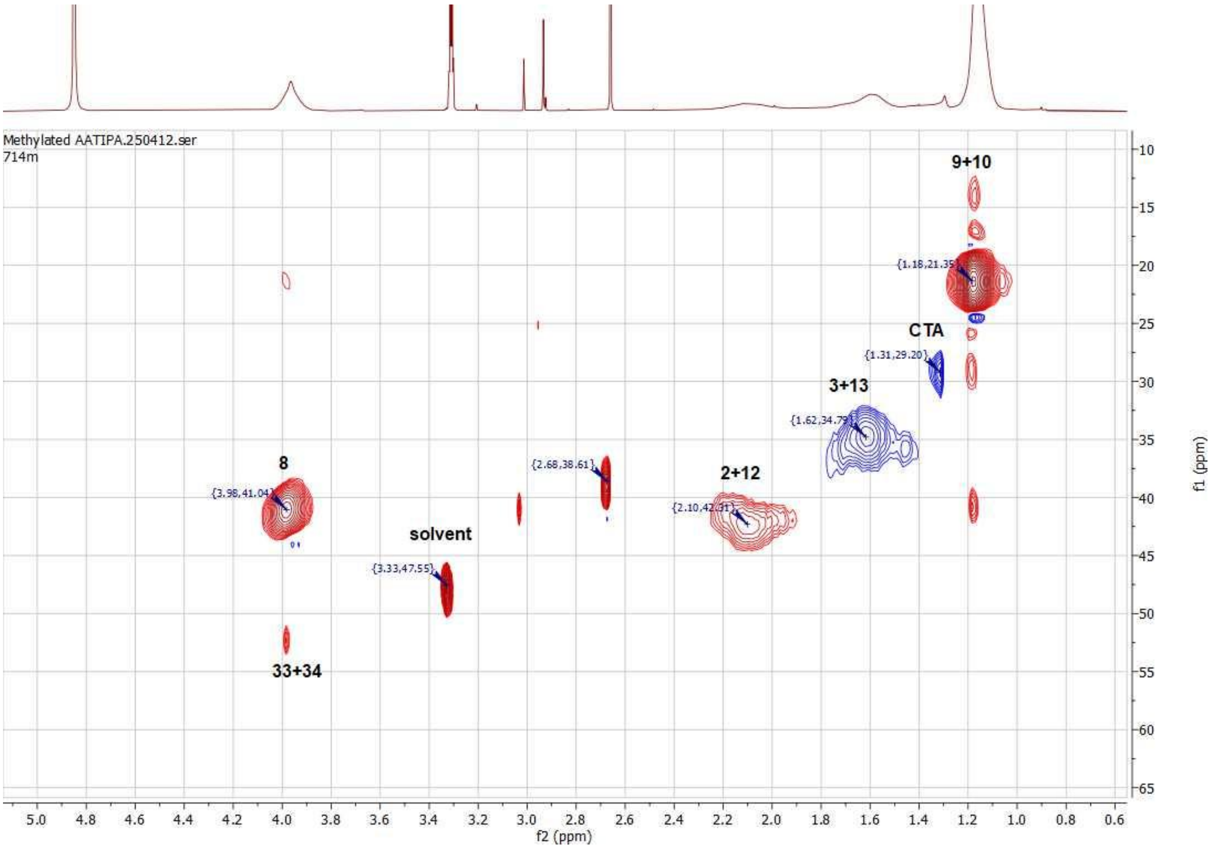

Figure S46. ^{1}H-^{13}C HSQC NMR (400 MHz, CD_3OD) spectrum of **S2m**.

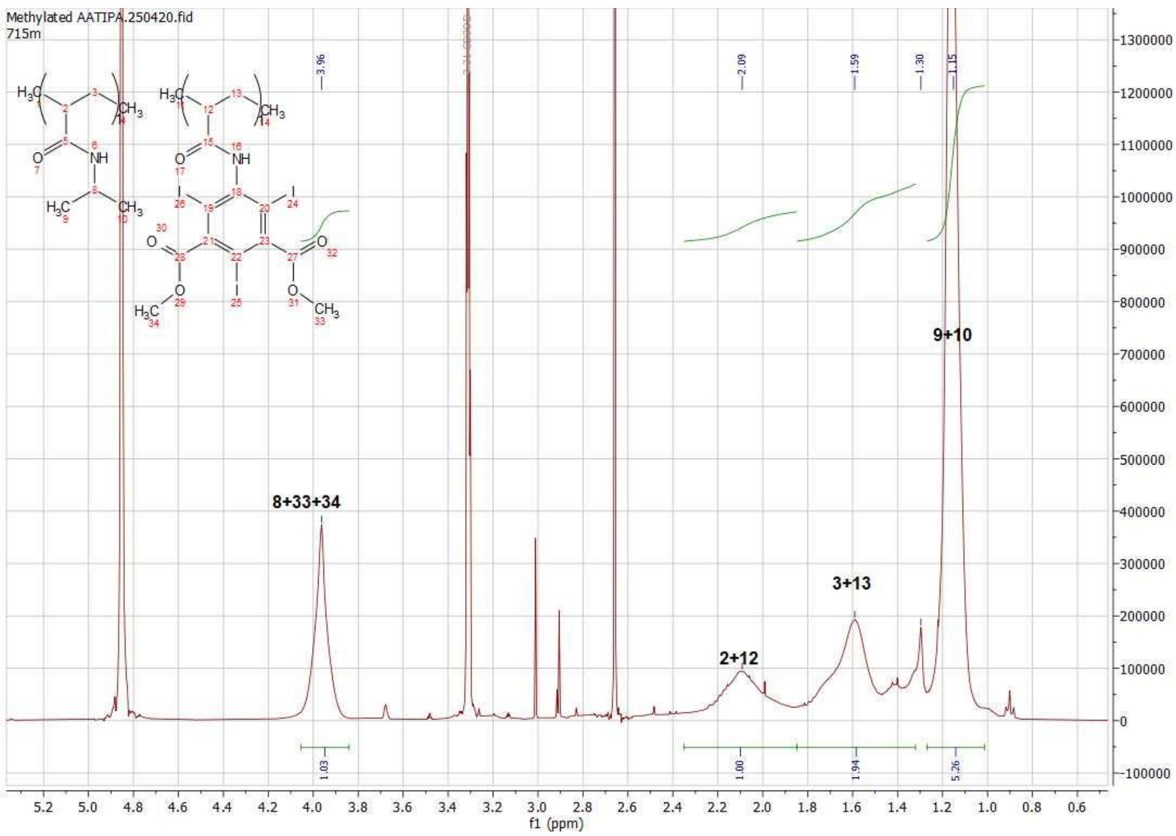

Figure S47. ^{1}H NMR (400 MHz, CD_3OD) spectrum of **S3m**.

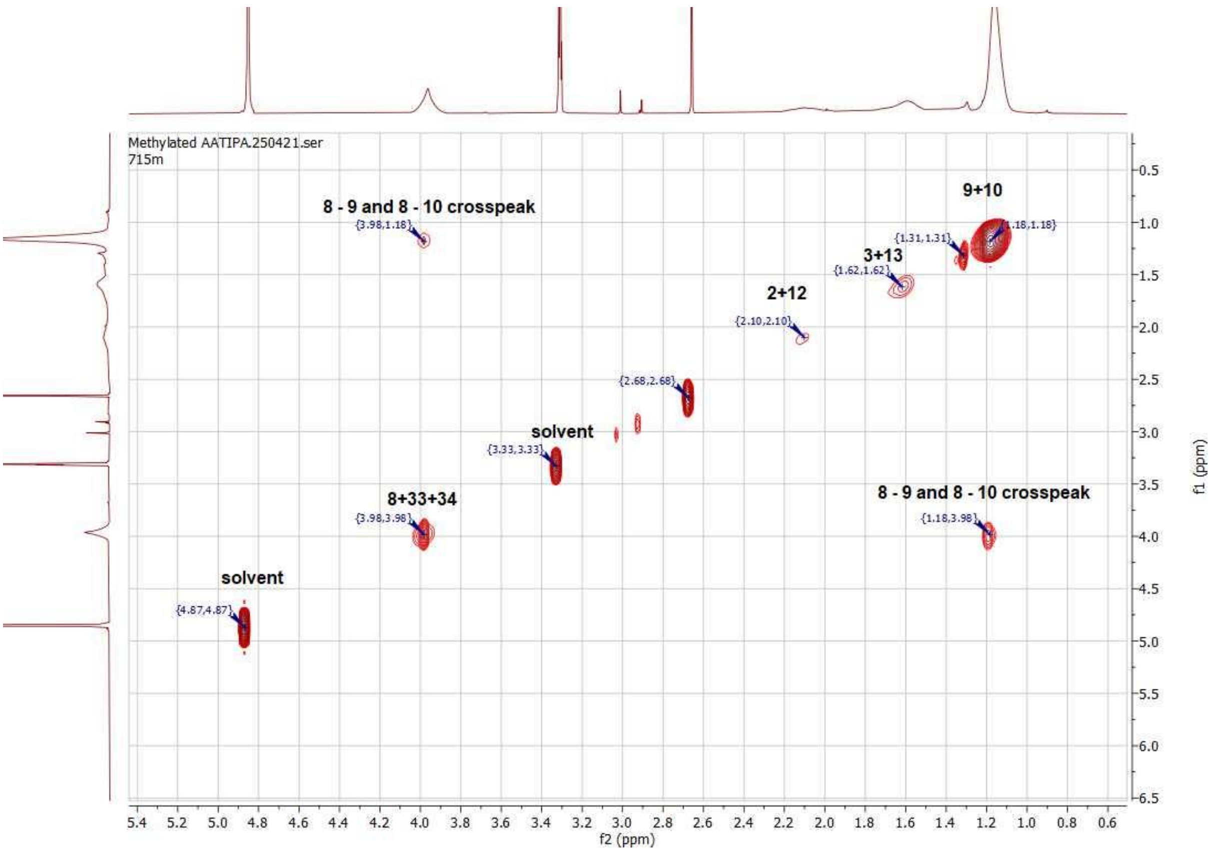

Figure S48. ^{1}H-^{1}H COSY NMR (400 MHz, CD_3OD) spectrum of **S3m**.

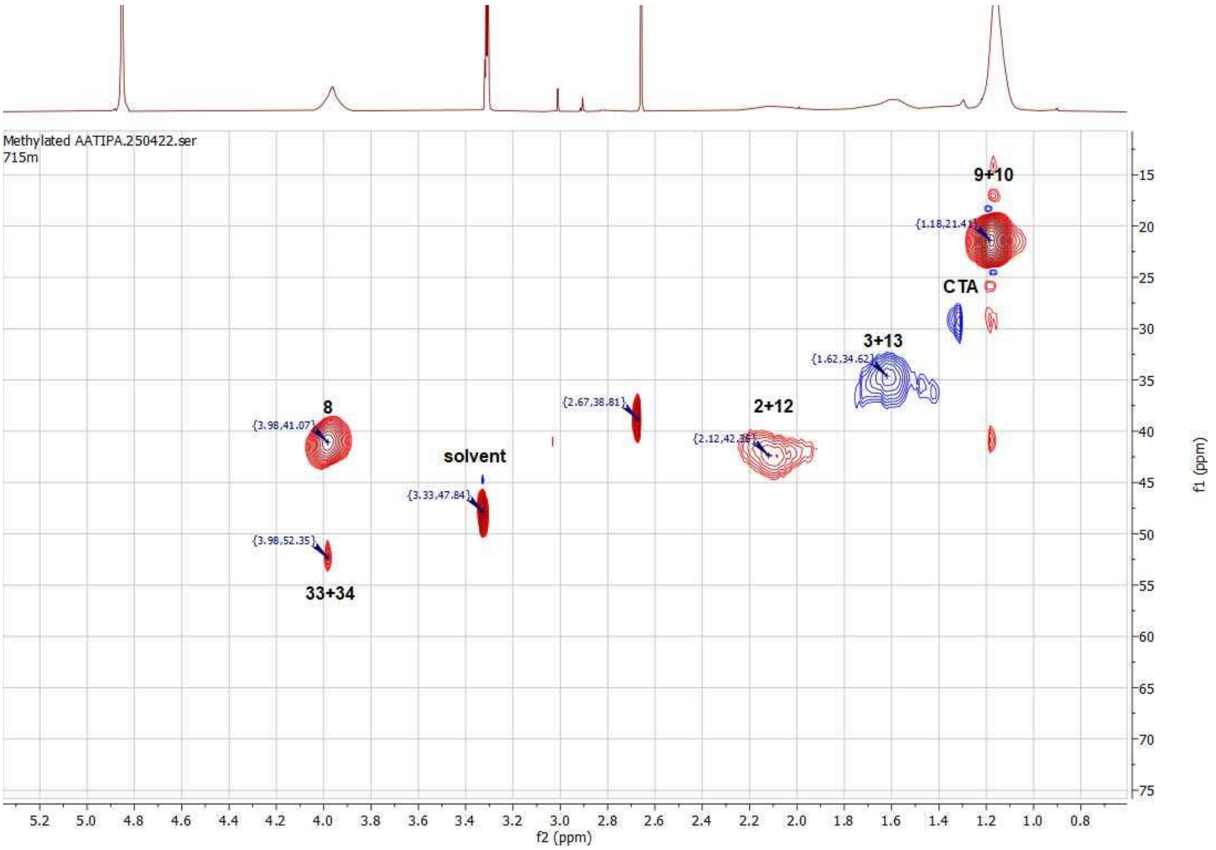

Figure S49. ^{1}H-^{13}C HSQC NMR (400 MHz, CD_3OD) spectrum of **S3m**.

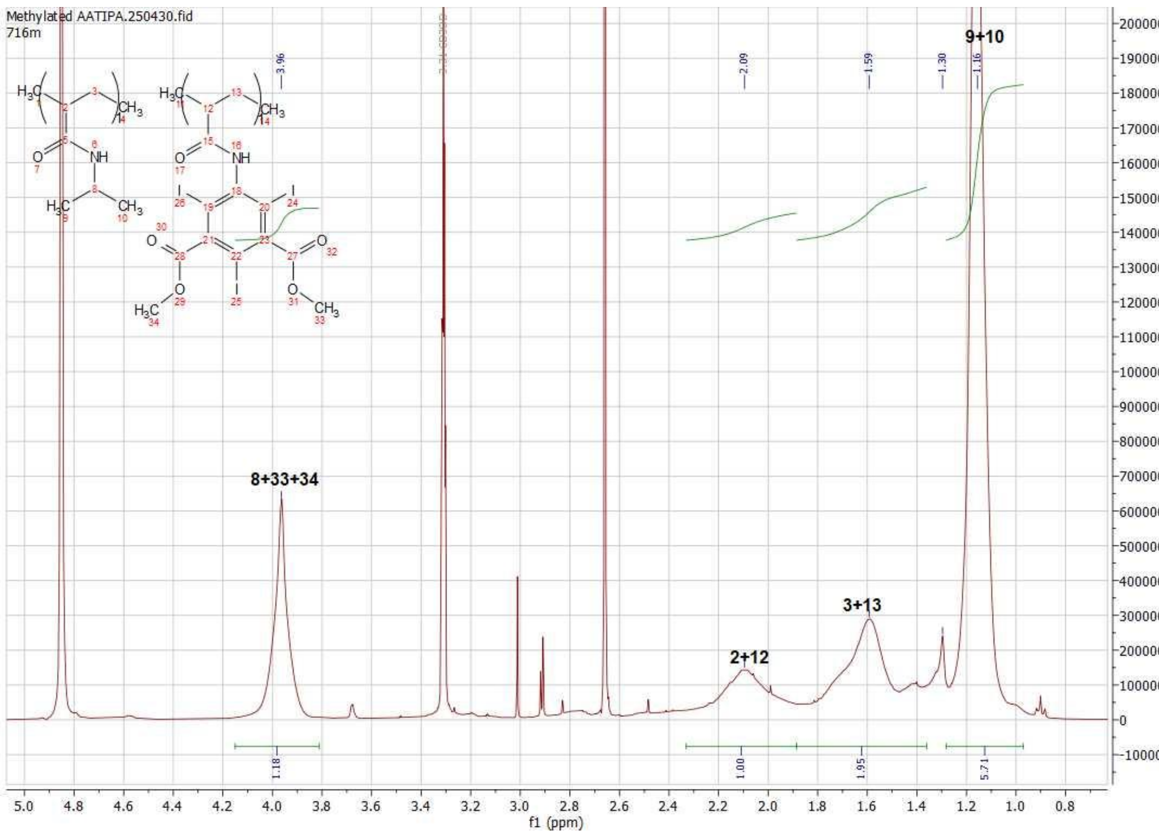

Figure S50. ^{1}H NMR (400 MHz, CD_3OD) spectrum of **S4m**.

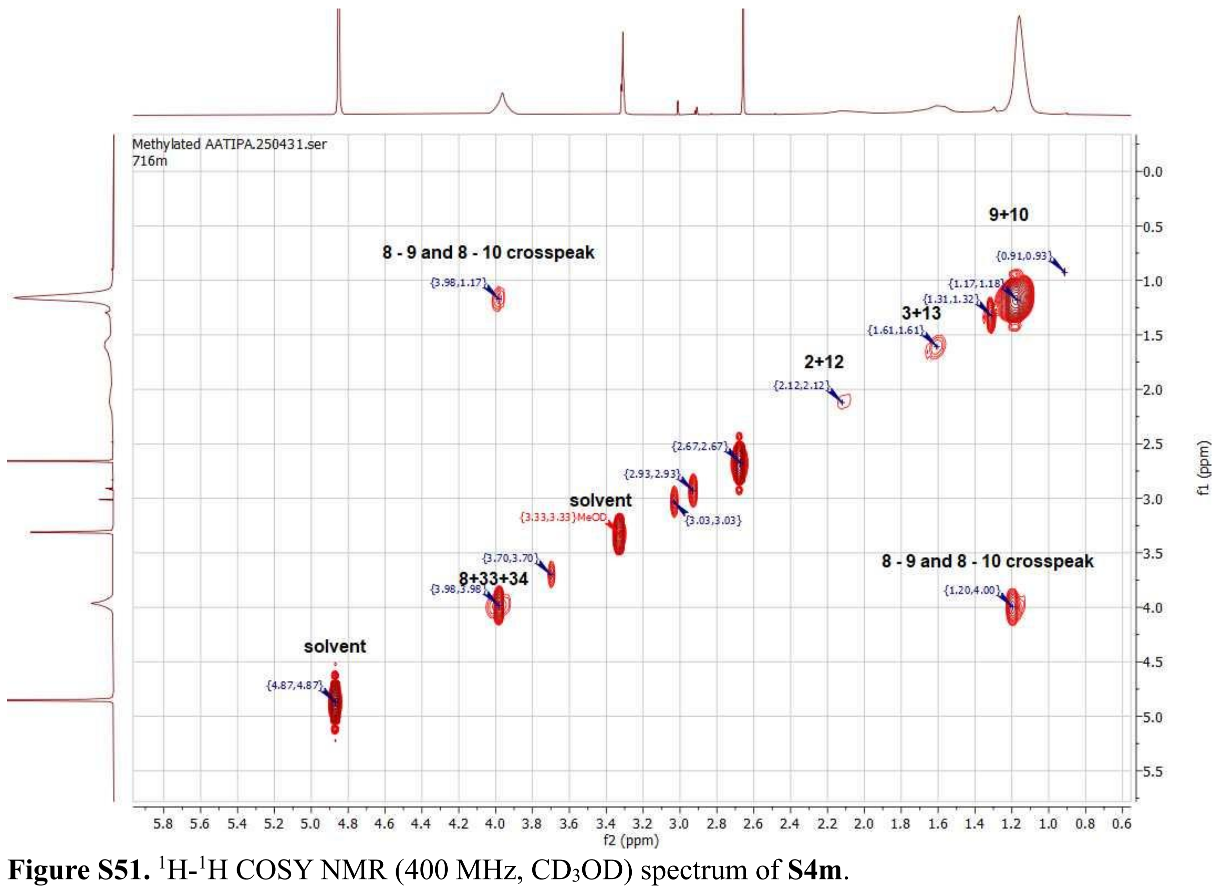

Figure S51. ^{1}H-^{1}H COSY NMR (400 MHz, CD_3OD) spectrum of **S4m**.

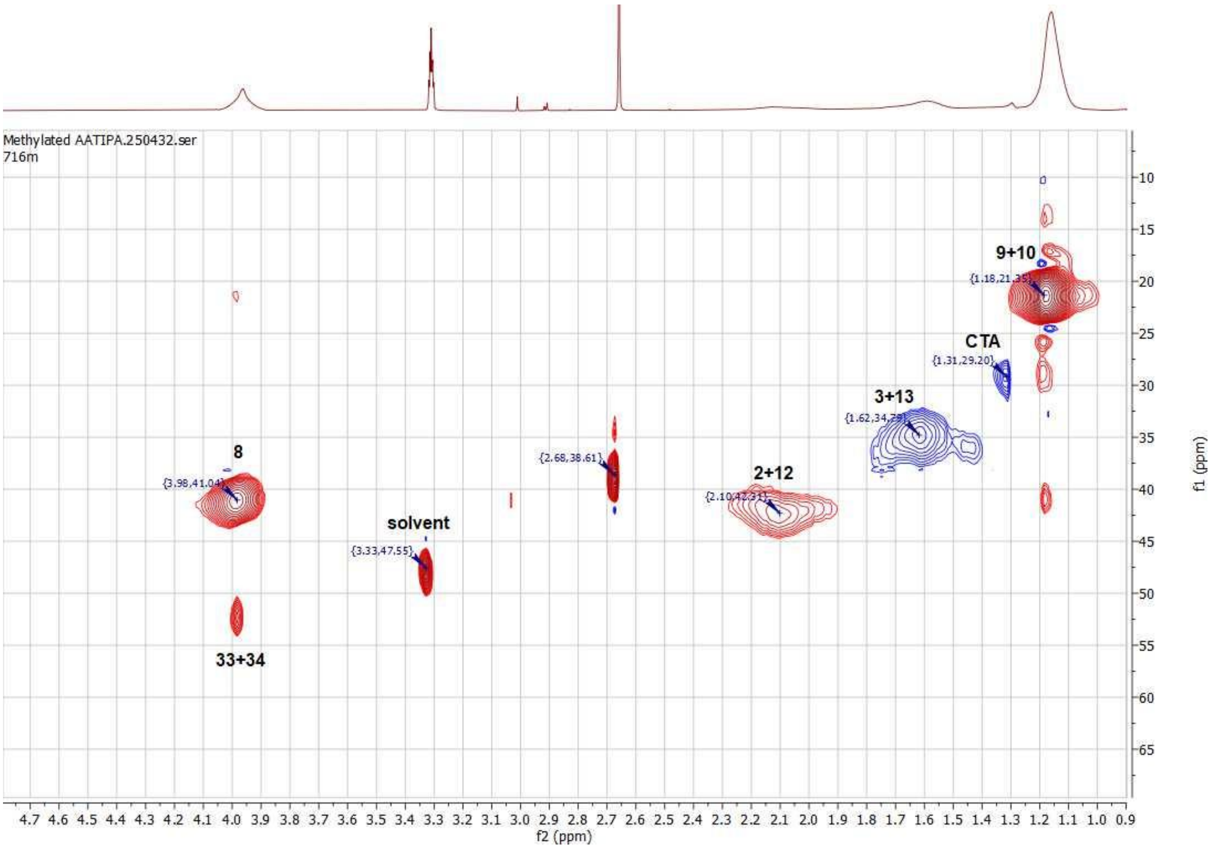

Figure S52. ^1H-^{13}C HSQC NMR (400 MHz, CD_3OD) spectrum of **S4m**.

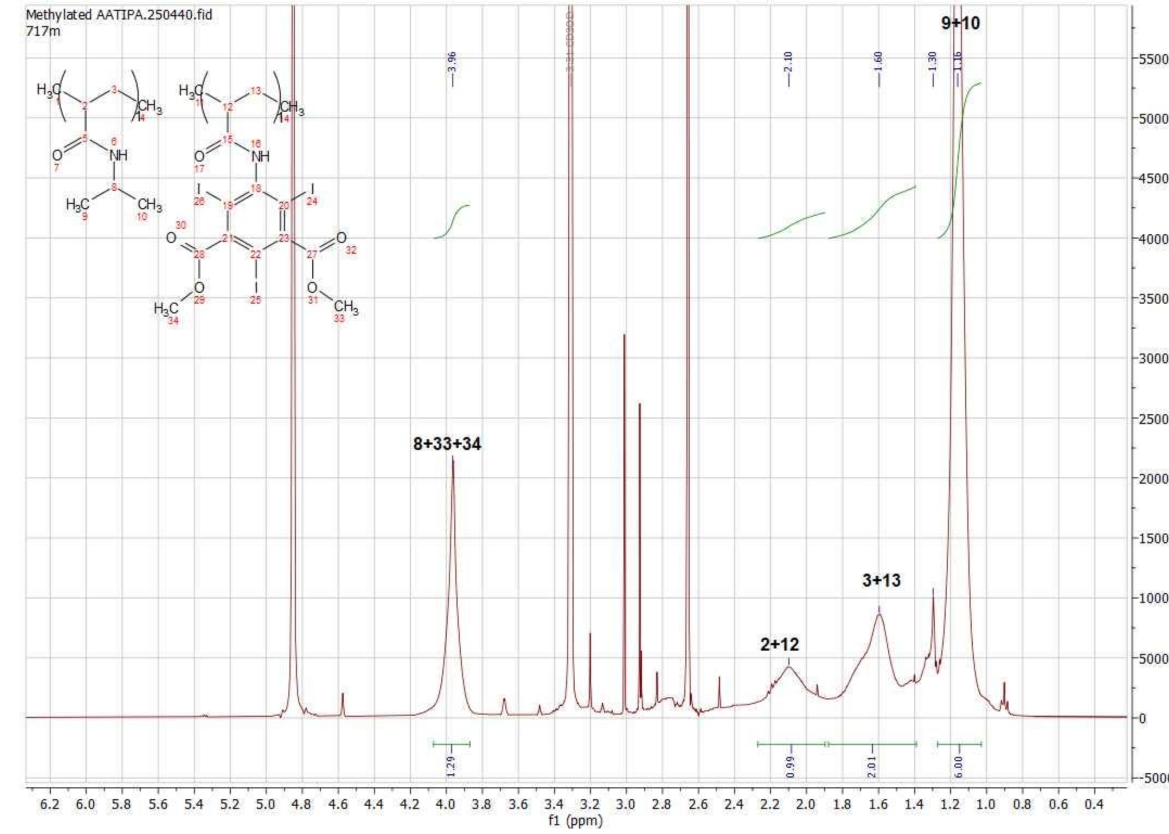

Figure S53. ^1H NMR (400 MHz, CD_3OD) spectrum of **S5m**.

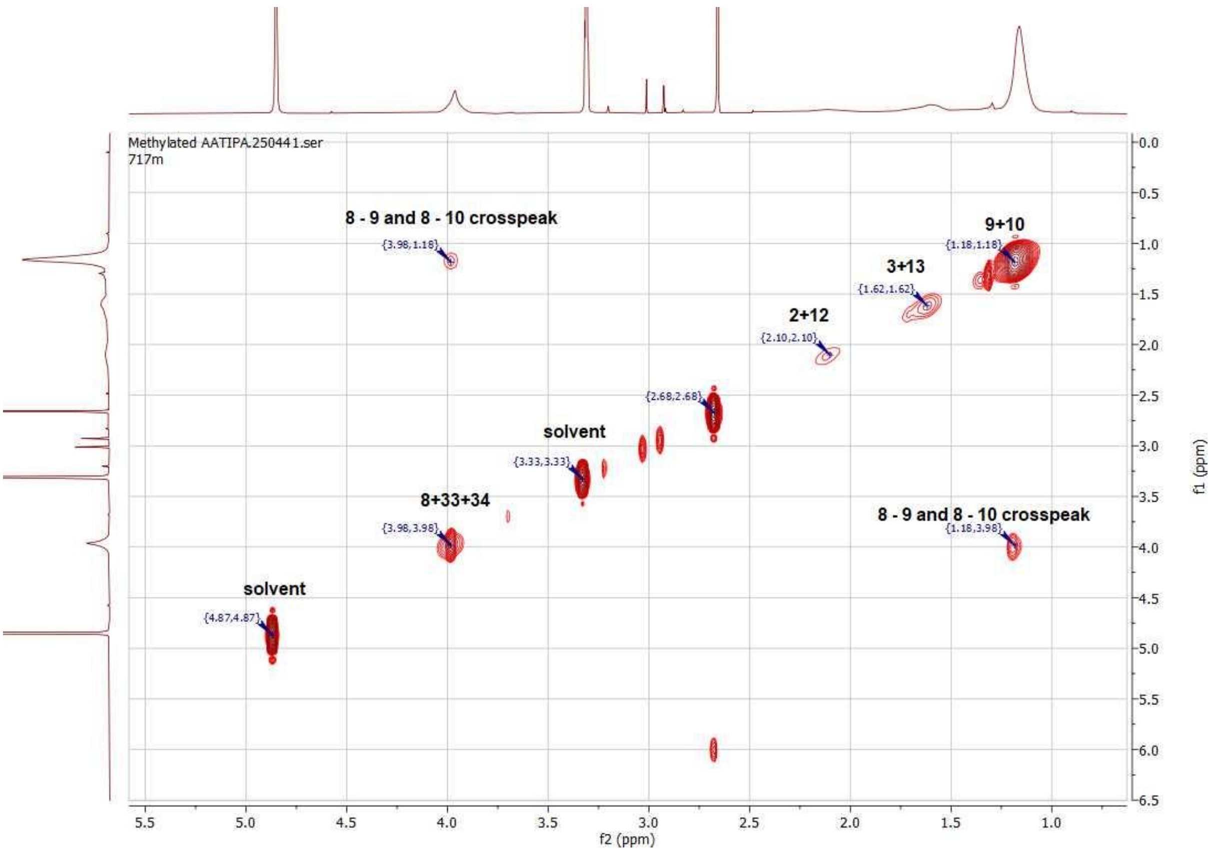

Figure S54. ^{1}H-^{1}H COSY NMR (400 MHz, CD_3OD) spectrum of **S5m**.

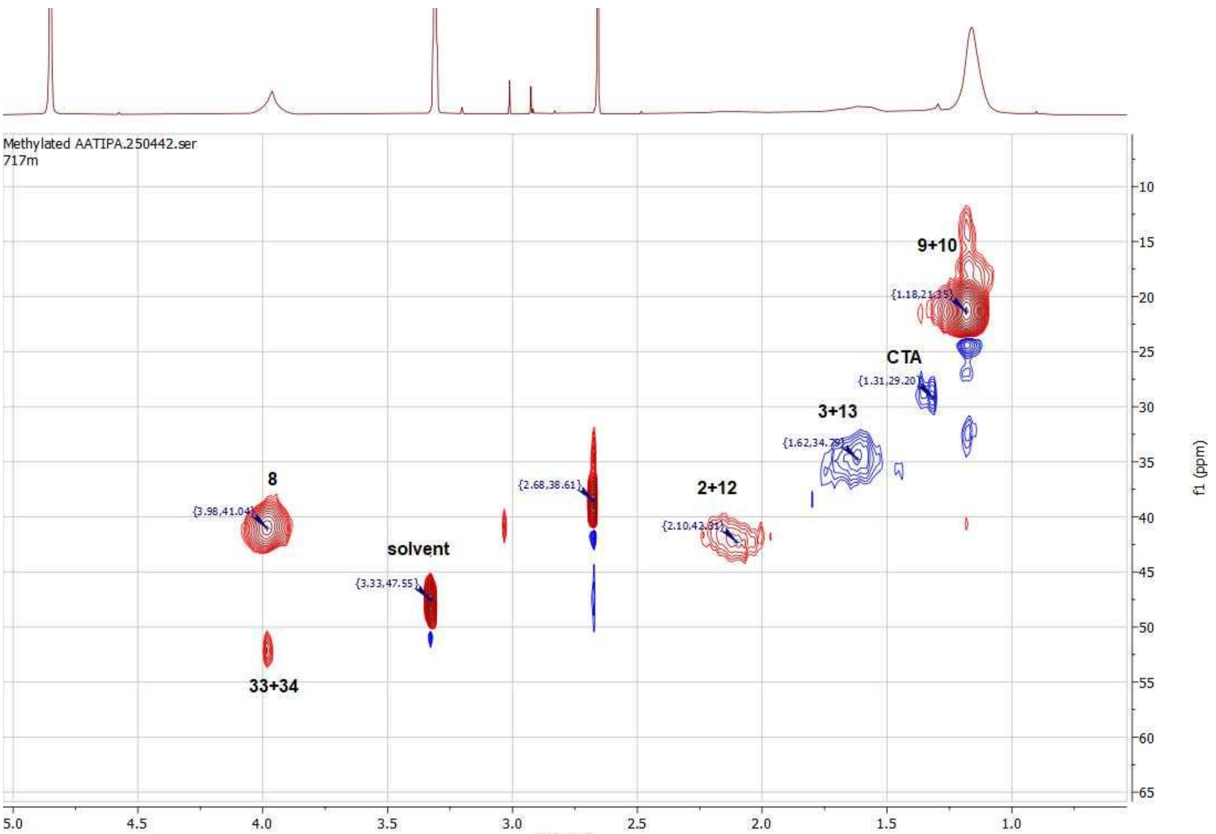

Figure S55. ^{1}H-^{13}C HSQC NMR (400 MHz, CD_3OD) spectrum of **S5m**.

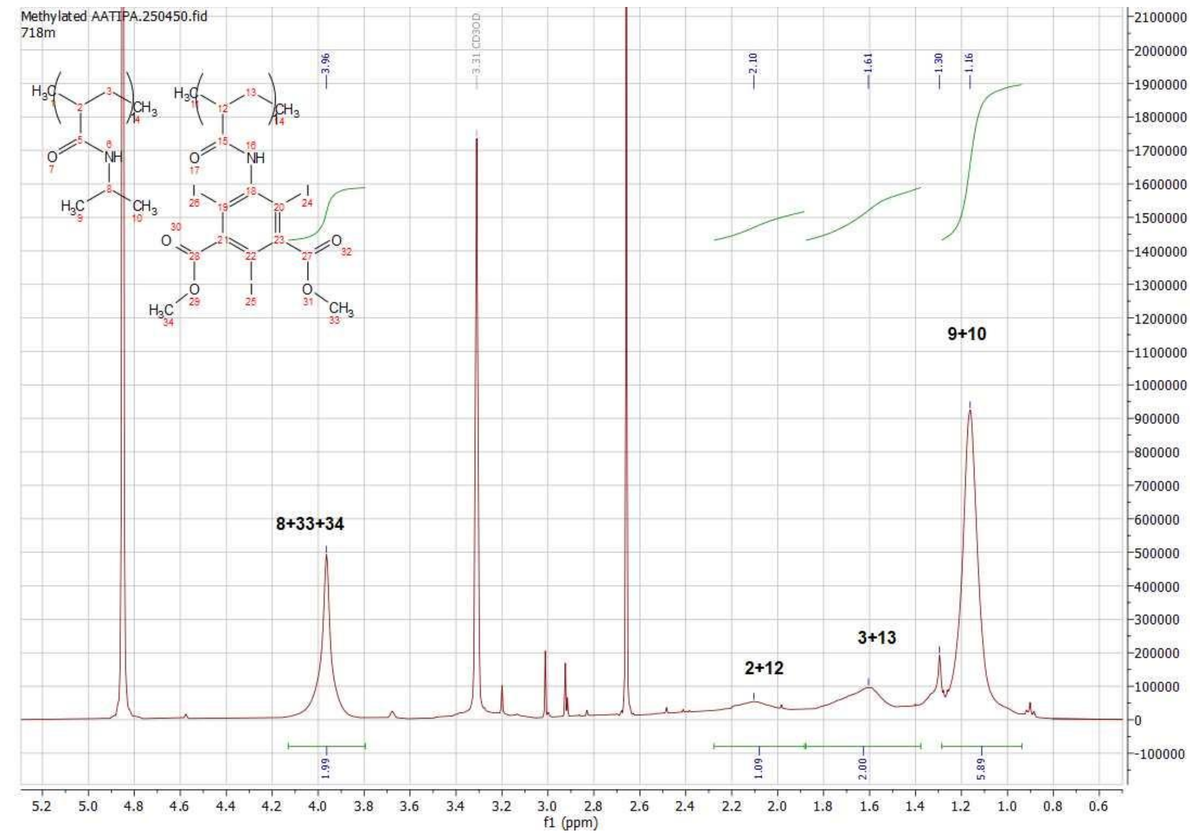

Figure S56. ^{1}H NMR (400 MHz, CD_3OD) spectrum of **S6m**.

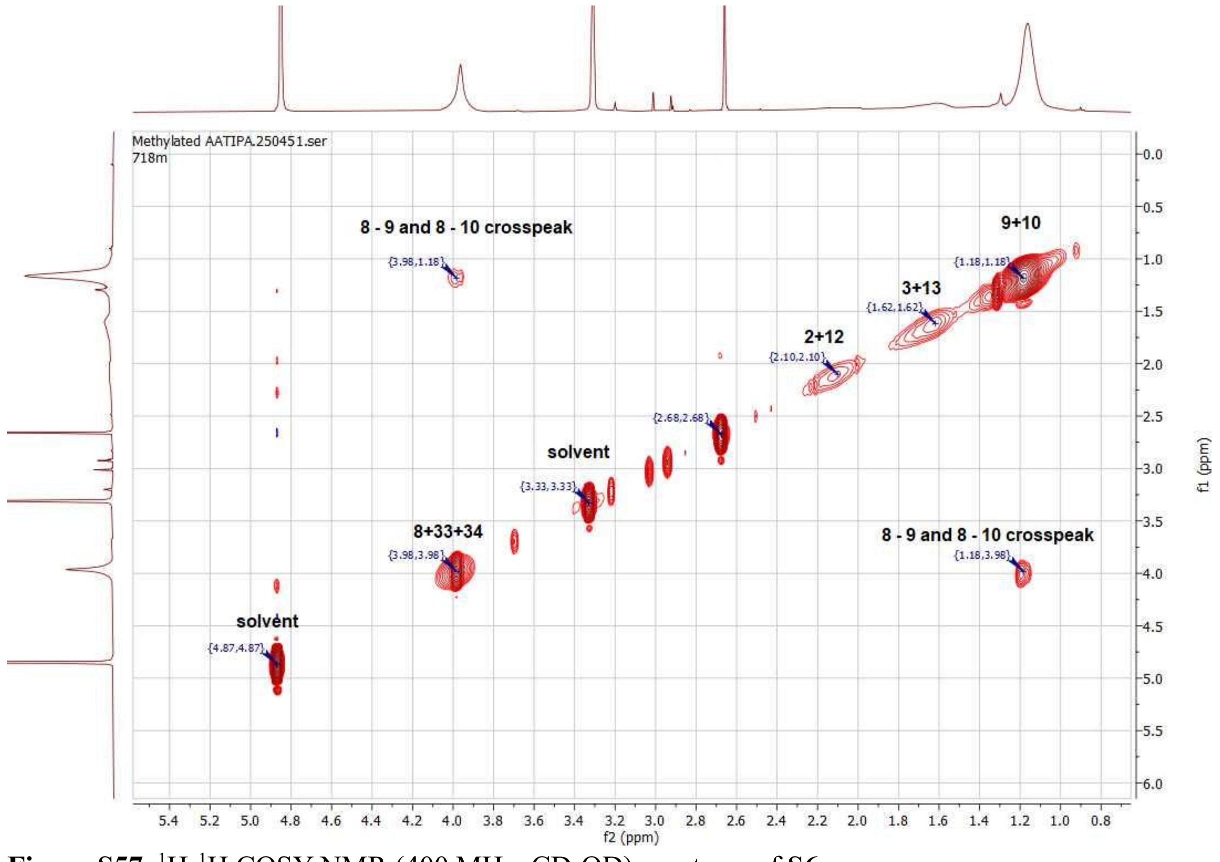

Figure S57. ^{1}H-^{1}H COSY NMR (400 MHz, CD_3OD) spectrum of **S6m**.

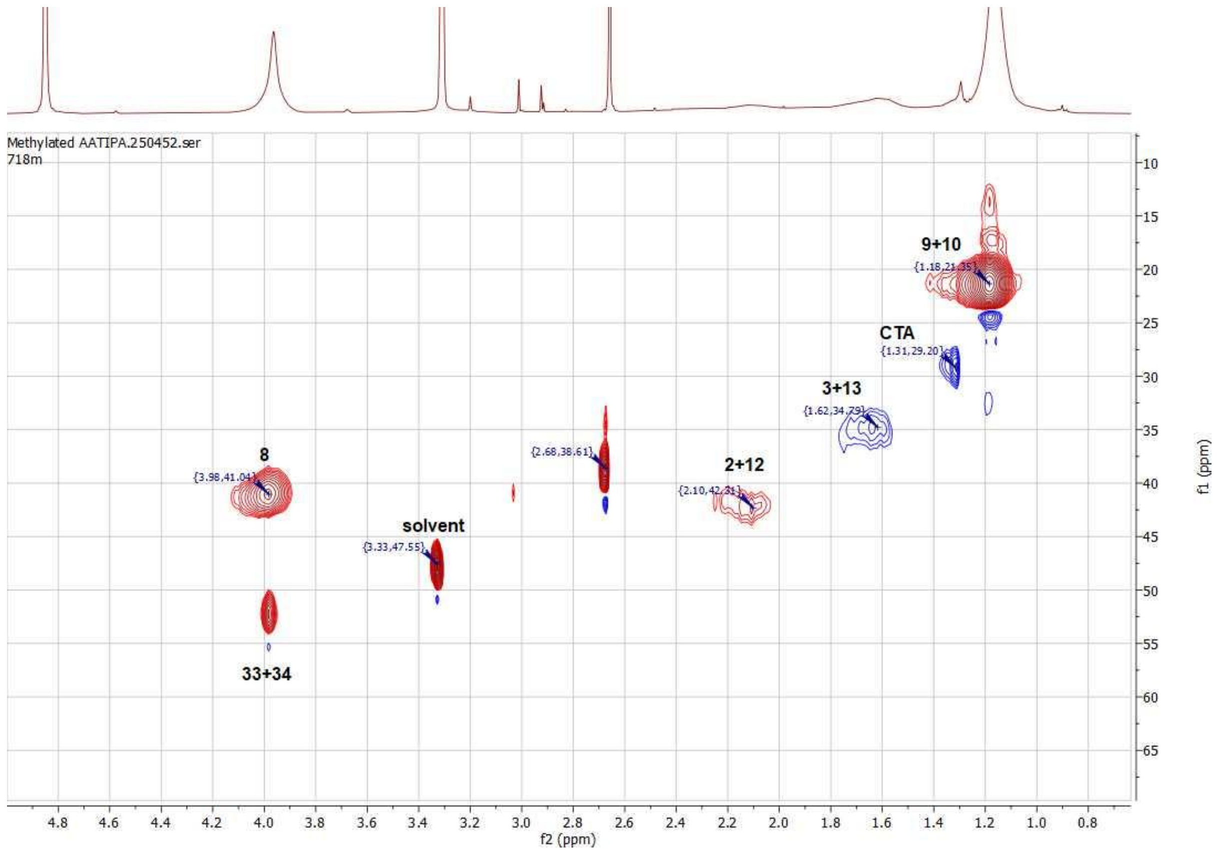

Figure S58. ^1H-^{13}C HSQC NMR (400 MHz, CD_3OD) spectrum of **S6m**.

Table S1. The *wt* % of PAATIPA in the synthesized polymers obtained from ^1H NMR spectroscopy compared to the *wt* % of PAATIPA obtained from elemental analysis (EA).

Pol.	PAATIPA (*wt* %, EA)	PAATIPA (*wt* %, NMR)	Pol.	PAATIPA (*wt* %, EA)	PAATIPA (*wt* %, NMR)
B1	26.8	29.2	**S1**	3.96	7.61
B2	50.1	38.0	**S2**	8.25	18.6
B3	58.2	42.6	**S3**	12.2	22.1
B4	26.5	33.5	**S4**	16.9	29.2
B5	40.8	52.6	**S5**	19.4	31.8
B6	45.4	53.4	**S6**	38.7	42.6

S2. SEC analysis

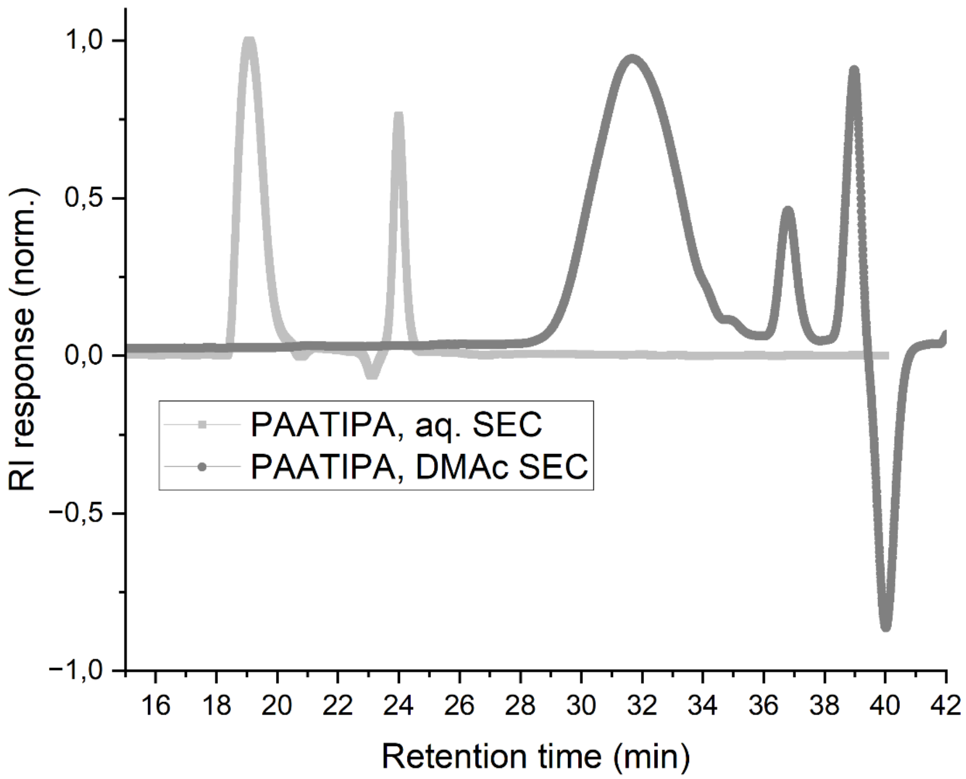

Figure S59. Size exclusion chromatograms of the block copolymers. Two different SEC systems were used. The first system had a mobile phase consisting of DMAc with 50 mM LiCl at a flow rate of 0.5 mL/min. Molar mass and dispersity values were calculated using PMMA standards. The chromatograms were analysed using Agilent GPC Data Analysis Software (Agilent Technologies, CA). To prepare samples for this system, the carboxylic acids of the AATIPA monomeric units were methylated with MeI in the presence of KOH. The second system had a mobile phase consisting of an aqueous buffer containing 80 v/v % of phosphate-nitrate buffer (0.01 M $NaH_2PO_4 \cdot 2H_2O$, Chemlab and 0.2 M $NaNO_3$, Acros in ultrapure water at pH 7) and 20 v/v % of MeOH.

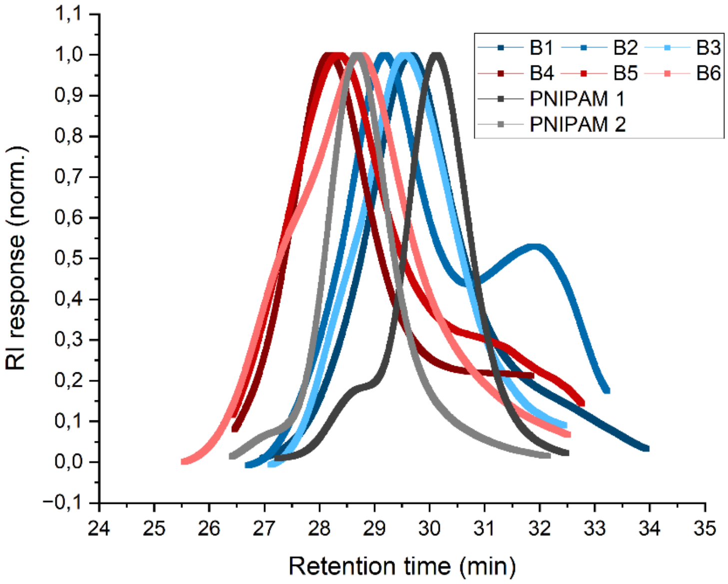

Figure S60. Size exclusion chromatograms of the block copolymers exploiting as mobile phase DMAc containing 50 mM LiCl at a flow rate of 0.5 mL/min. Molar mass and dispersity values were calculated using PMMA standards. The chromatograms were analysed using Agilent GPC Data Analysis Software (Agilent Technologies, CA). In order to prepare samples for this system, the carboxylic acids of the AATIPA monomeric units were methylated with MeI in the presence of KOH.

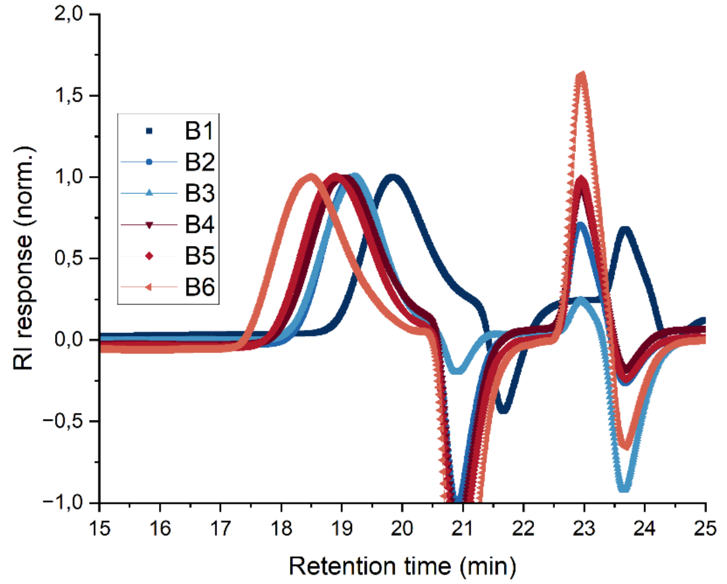

Figure S61. Size exclusion chromatograms of block copolymers exploiting as mobile phase an aqueous buffer containing 80 v/v % of phosphate-nitrate buffer (0.01 M $NaH_2PO_4 \cdot 2H_2O$, Chemlab and 0.2 M $NaNO_3$, Acros in ultrapure water at pH 7) and 20 v/v % of MeOH.

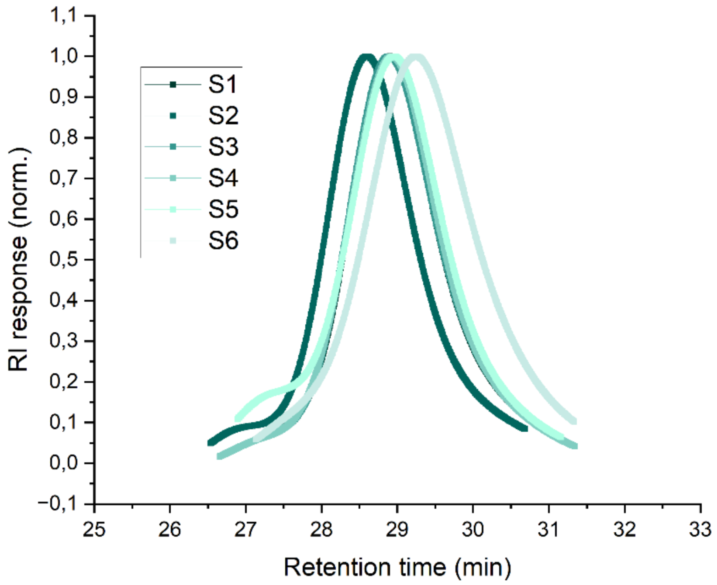

Figure S62. Size exclusion chromatograms of the statistical copolymers exploiting as mobile phase DMAc containing 50 mM LiCl at a flow rate of 0.5 mL/min. Molar mass and dispersity values were calculated using PMMA standards. The chromatograms were analysed using Agilent GPC Data Analysis Software (Agilent Technologies, CA). In order to prepare samples for this system, the carboxylic acids of the AATIPA monomeric units were methylated with MeI in the presence of KOH.

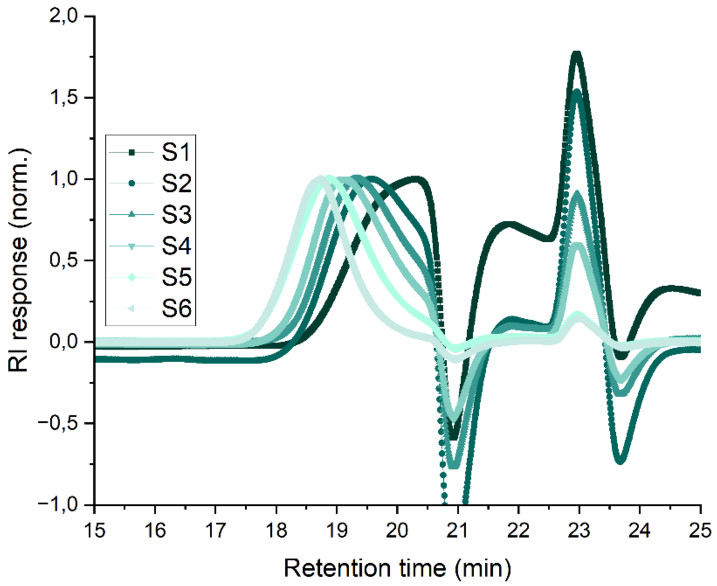

Figure S63. Size exclusion chromatograms of the statistical copolymers exploiting as mobile phase an aqueous buffer containing 80 v/v % of phosphate-nitrate buffer (0.01 M $NaH_2PO_4 \cdot 2H_2O$, Chemlab and 0.2 M $NaNO_3$, Acros in ultrapure water at pH 7) and 20 v/v % of MeOH.

Table S2. SEC characterization of the resulting PNIPAM-PAATIPA copolymers: M_n, M_w, and $Đ_M$ evaluated from aqueous SEC.

Pol.	M_n (kg/mol)	M_w (kg/mol)	$Đ_M$	Pol.	M_n (kg/mol)	M_w (kg/mol)	$Đ_M$
B1	2.11	3.09	1.46	**B1**	2.22	3.76	1.70
B2	5.79	8.48	1.46	**B2**	3.21	5.70	1.77
B3	6.16	8.89	1.44	**B3**	4.60	7.03	1.54
B4	7.64	11.2	1.46	**B4**	6.00	9.04	1.52
B5	8.83	13.3	1.51	**B5**	8.50	14.5	1.71
B6	15.1	23.9	1.58	**B6**	11.7	17.5	1.50

Table S3. Characteristics of the resulting PAATIPA determined by two different SEC systems. Targeted and resulting DPs, M_n, M_w, and $Đ_M$.

SEC type	DP_{theor}	DP	M_n (kg/mol)	M_w (kg/mol)	$Đ_M$
DMAc	20	15	8.88	10.5	1.19
Aqueous	20	10	5.85	7.01	1.20

S3. Characterization of the self-assembled particles

S3.1. DLS of block copolymers

S3.1.1. Intensity distribution

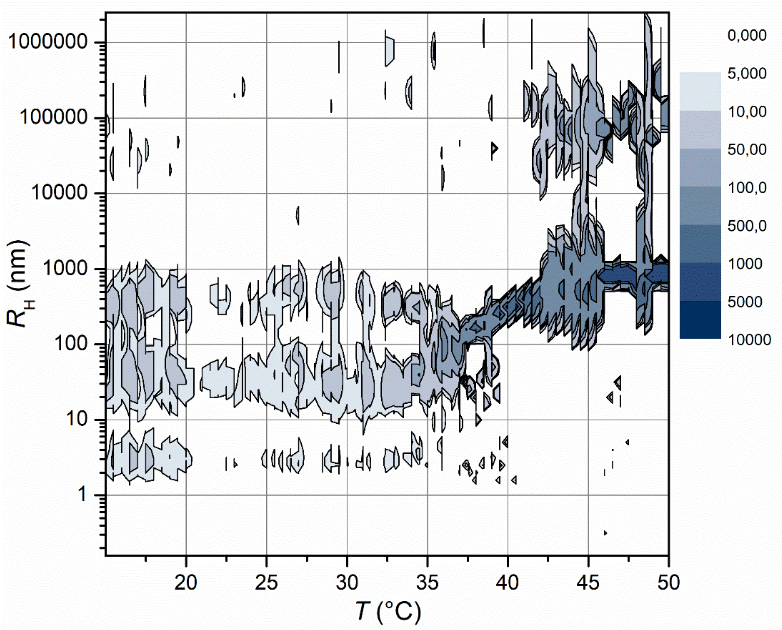

Figure S64. Temperature dependence of the self-assembly of **B2** in PBS measured via DLS. The equal-area representation (the vertical axis shows $R_h \cdot A(R_h)$, where $A(R_h)$ is the intensity distribution function of hydrodynamic radii R_h of particles in the sample).

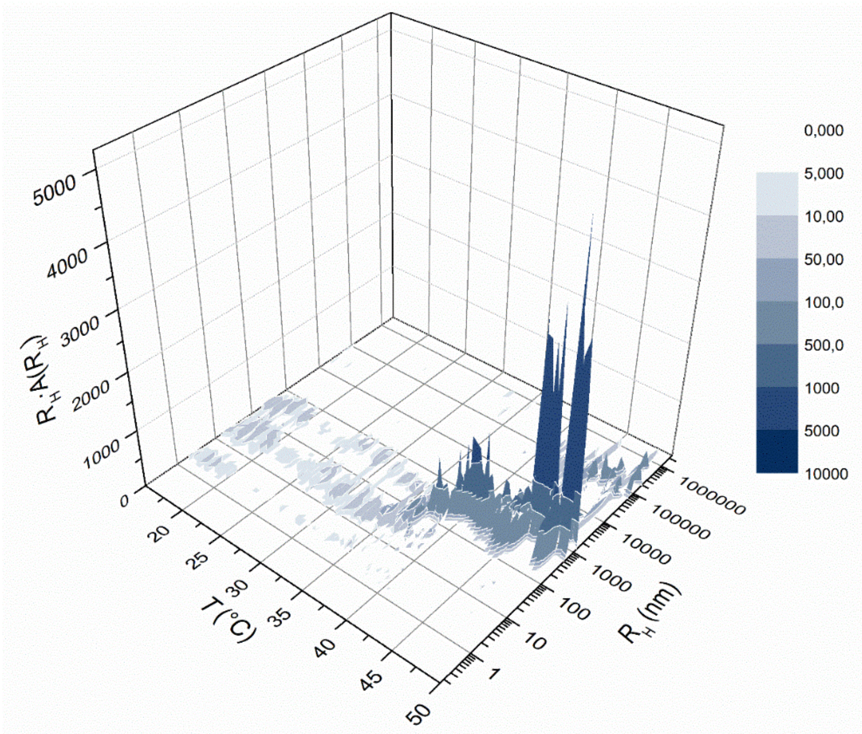

Figure S65. Temperature dependence of self-assembly of **B2** in PBS measured by DLS. The equal-area representation (the vertical axis shows $R_h \cdot A(R_h)$, where $A(R_h)$ is the intensity distribution function of hydrodynamic radii R_h of particles in the sample).

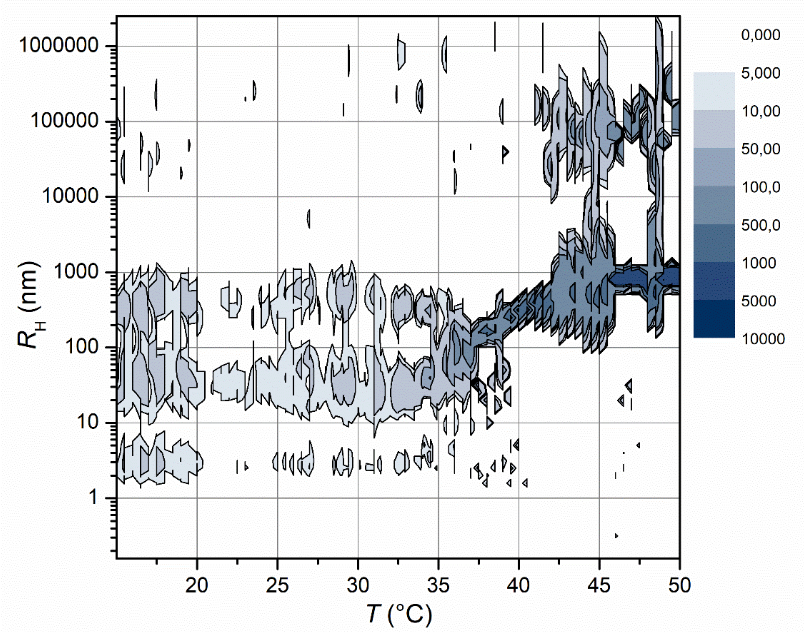

Figure S66. Temperature dependence of the self-assembly of **B3** in PBS measured via DLS. The equal-area representation (the vertical axis shows $R_h \cdot A(R_h)$, where $A(R_h)$ is the intensity distribution function of hydrodynamic radii R_h of particles in the sample).

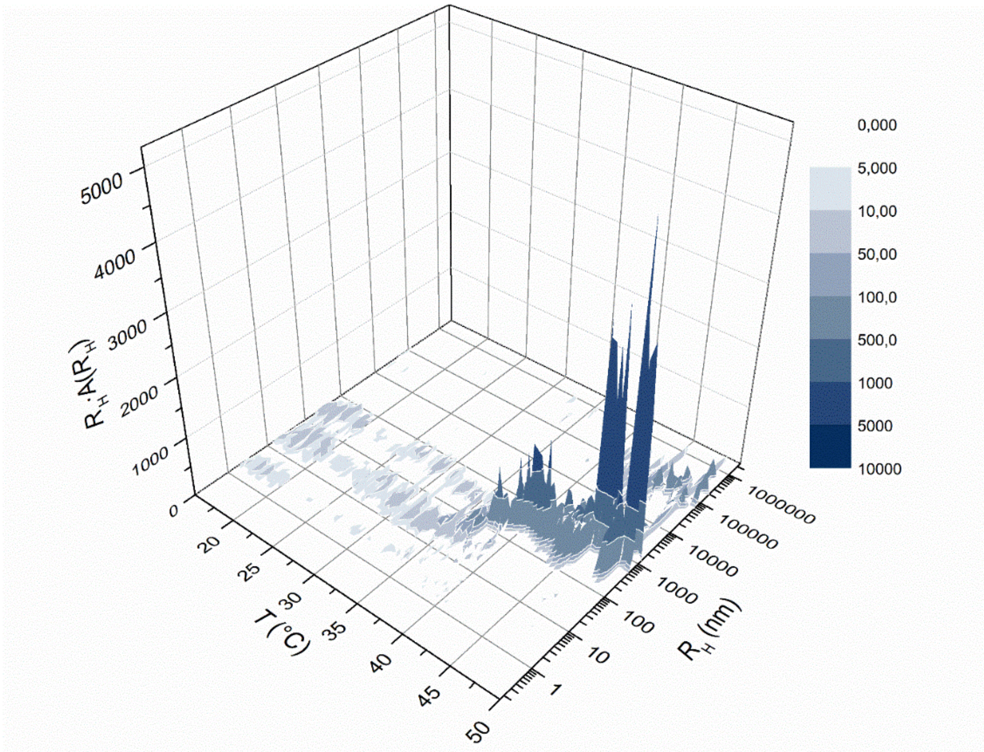

Figure S67. Temperature dependence of the self-assembly of **B3** in PBS measured via DLS. The equal-area representation (the vertical axis shows $R_h \cdot A(R_h)$, where $A(R_h)$ is the intensity distribution function of hydrodynamic radii R_h of particles in the sample).

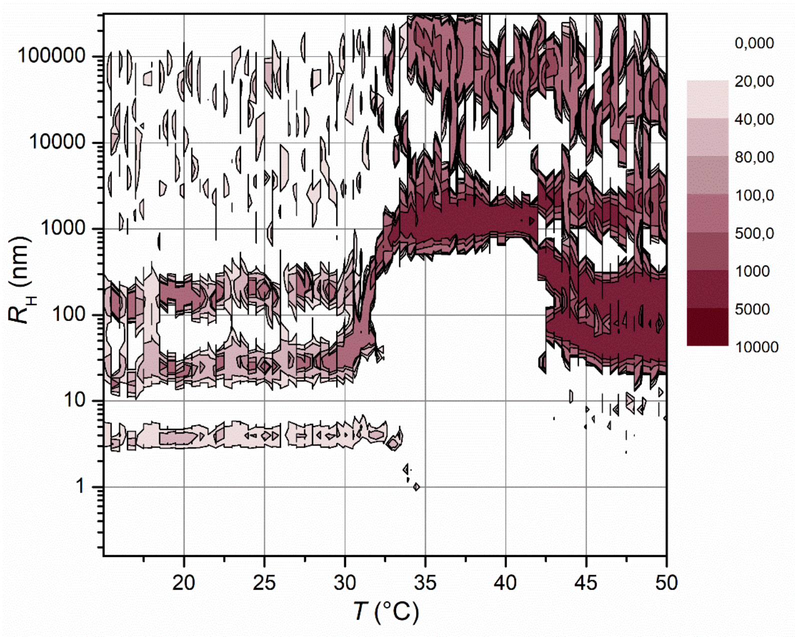

Figure S68. Temperature dependence of the self-assembly of **B5** in PBS measured via DLS. The equal-area representation (the vertical axis shows $R_h \cdot A(R_h)$, where $A(R_h)$ is the intensity distribution function of hydrodynamic radii R_h of particles in the sample).

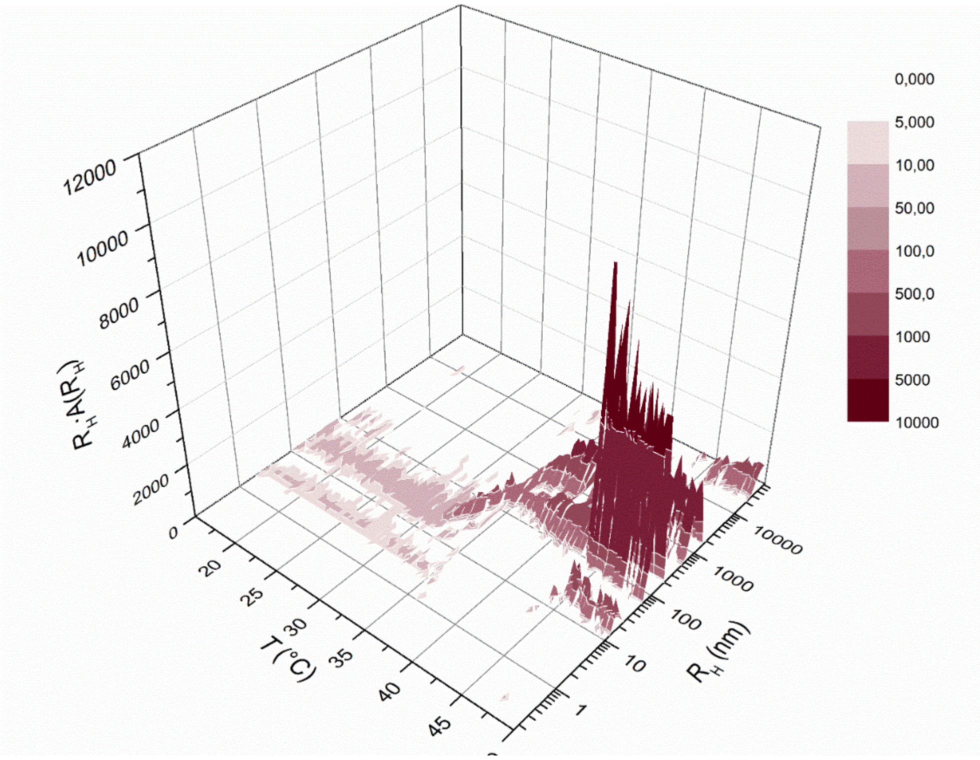

Figure S69. Temperature dependence of the self-assembly of **B5** in PBS measured via DLS. The equal-area representation (the vertical axis shows $R_h \cdot A(R_h)$, where $A(R_h)$ is the intensity distribution function of hydrodynamic radii R_h of particles in the sample).

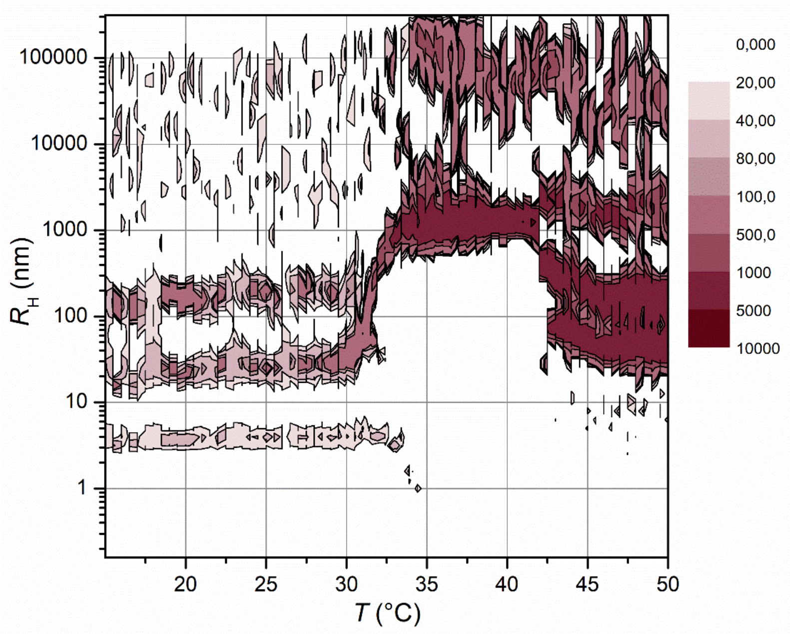

Figure S70. Temperature dependence of the self-assembly of **B6** in PBS measured via DLS. The equal-area representation (the vertical axis shows $R_h \cdot A(R_h)$, where $A(R_h)$ is the intensity distribution function of hydrodynamic radii R_h of particles in the sample).

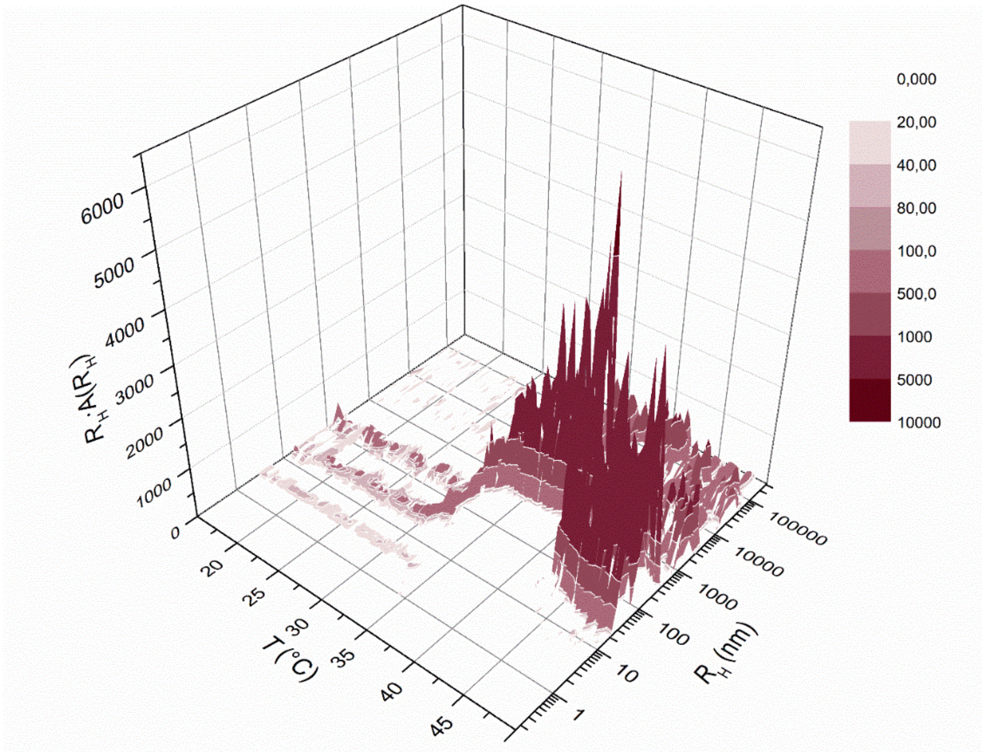

Figure S71. Temperature dependence of the self-assembly of **B6** in PBS measured via DLS. The equal-area representation (the vertical axis shows $R_h \cdot A(R_h)$, where $A(R_h)$ is the intensity distribution function of hydrodynamic radii R_h of particles in the sample).

S3.1.1. Volume- and number-weighted distribution

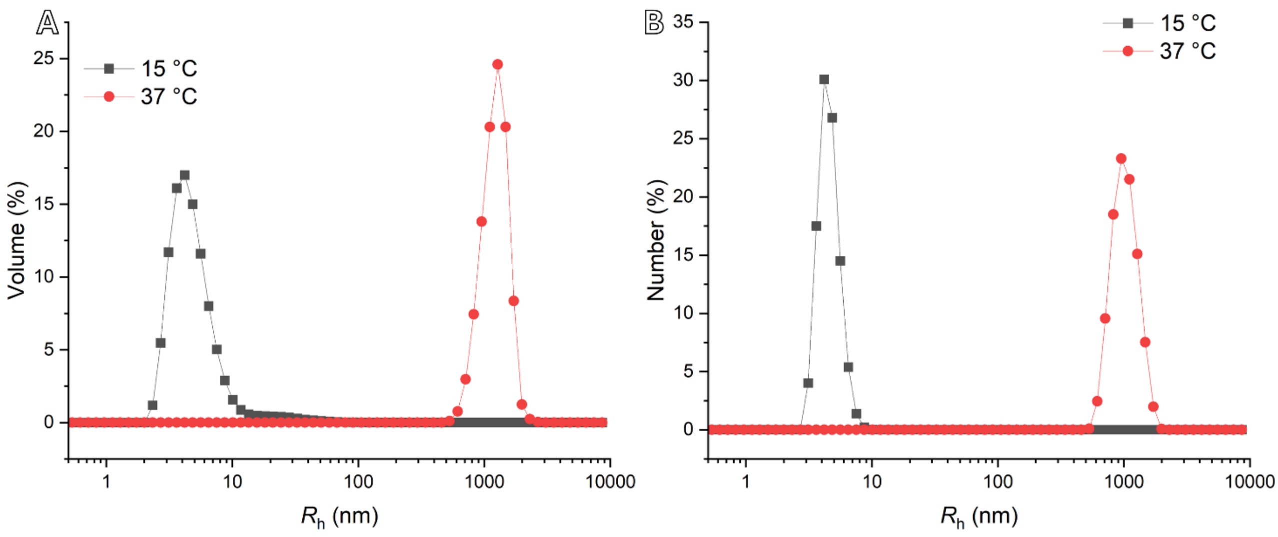

Figure S72. (A) Volume-weighted and (B) number-weighted particle size distributions of **B1** measured at 15 °C and 37 °C by DLS.

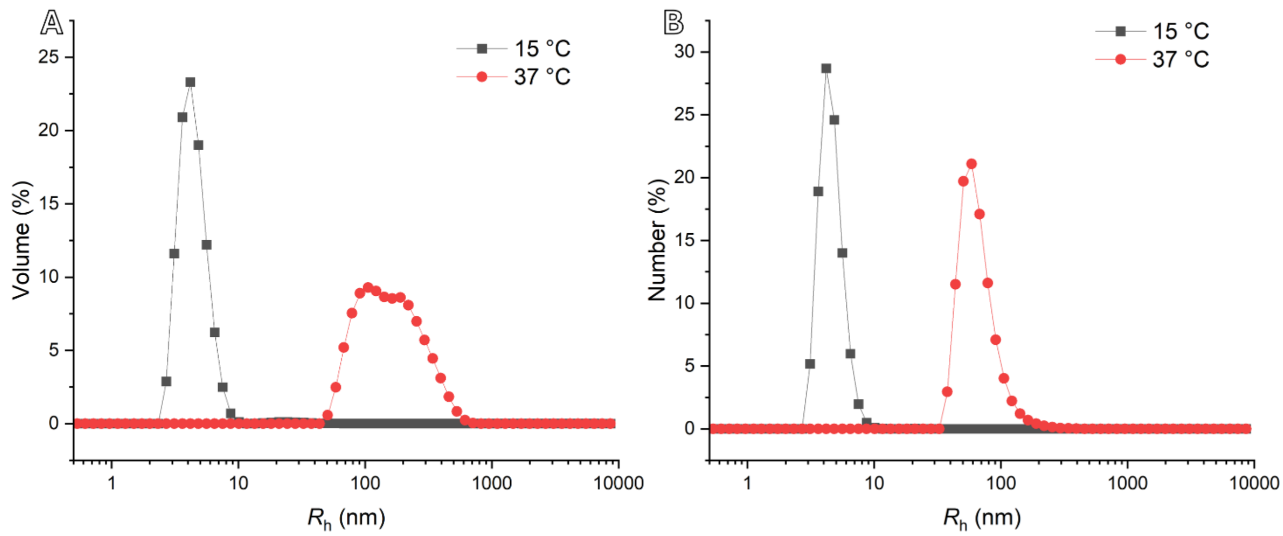

Figure S73. (A) Volume-weighted and (B) number-weighted particle size distributions of **B2** measured at 15 °C and 37 °C by DLS.

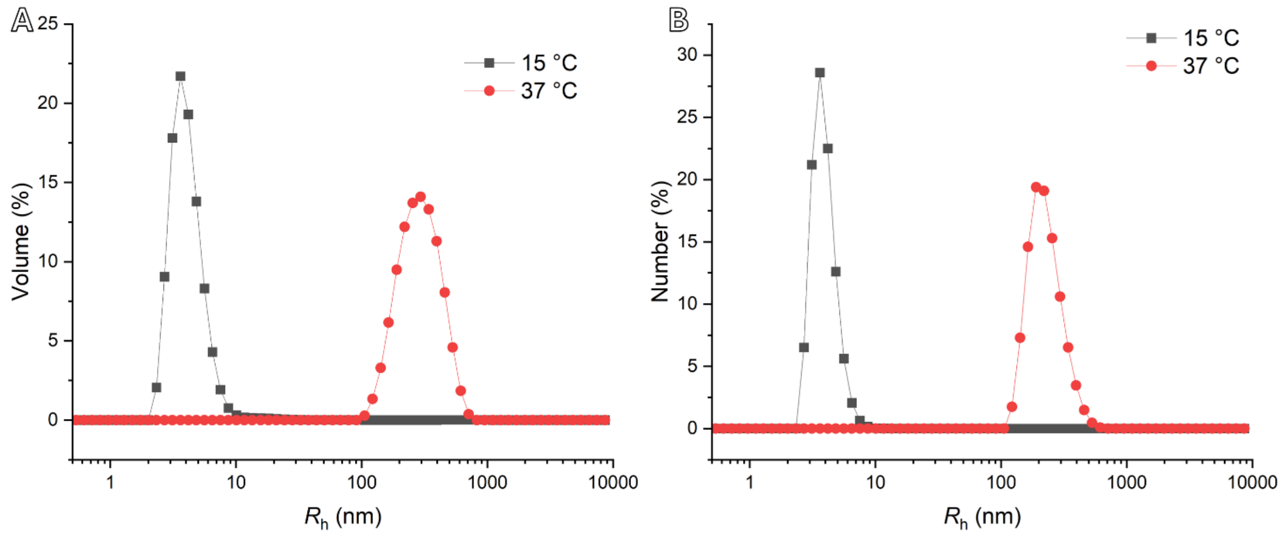

Figure S74. (A) Volume-weighted and (B) number-weighted particle size distributions of **B3** measured at 15 °C and 37 °C by DLS.

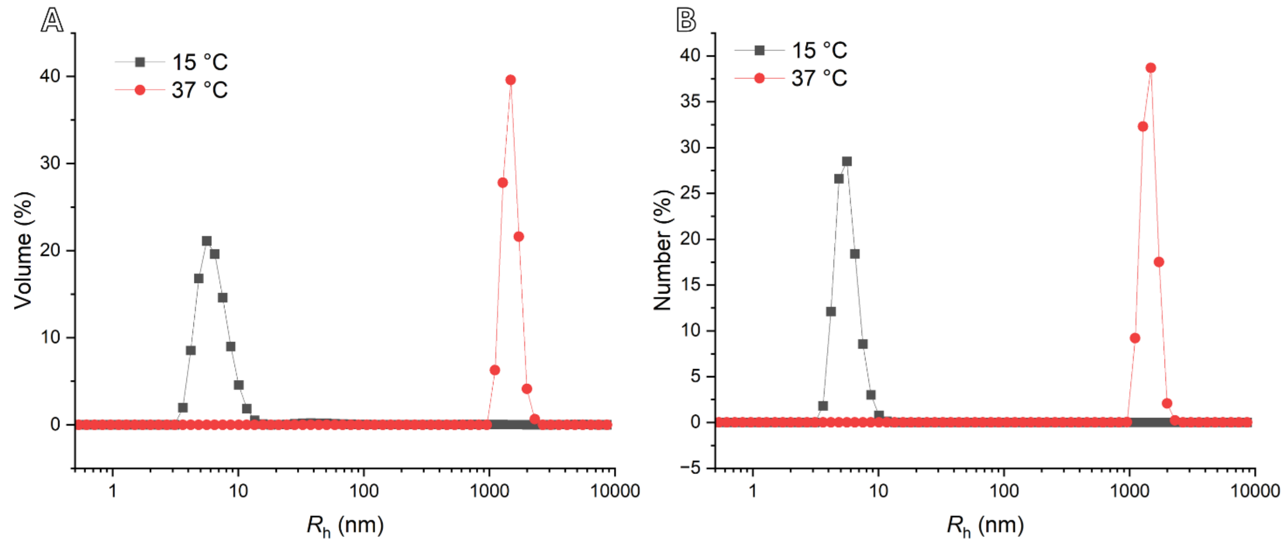

Figure S75. (A) Volume-weighted and (B) number-weighted particle size distributions of **B4** measured at 15 °C and 37 °C by DLS.

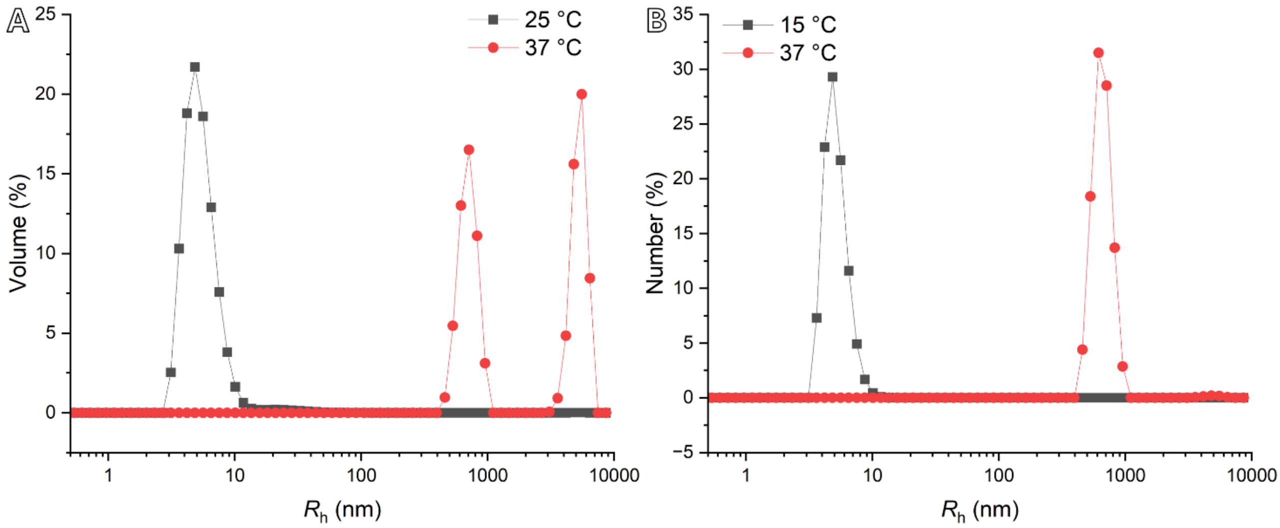

Figure S76. (A) Volume-weighted and (B) number-weighted particle size distributions of **B5** measured at 15 °C and 37 °C by DLS.

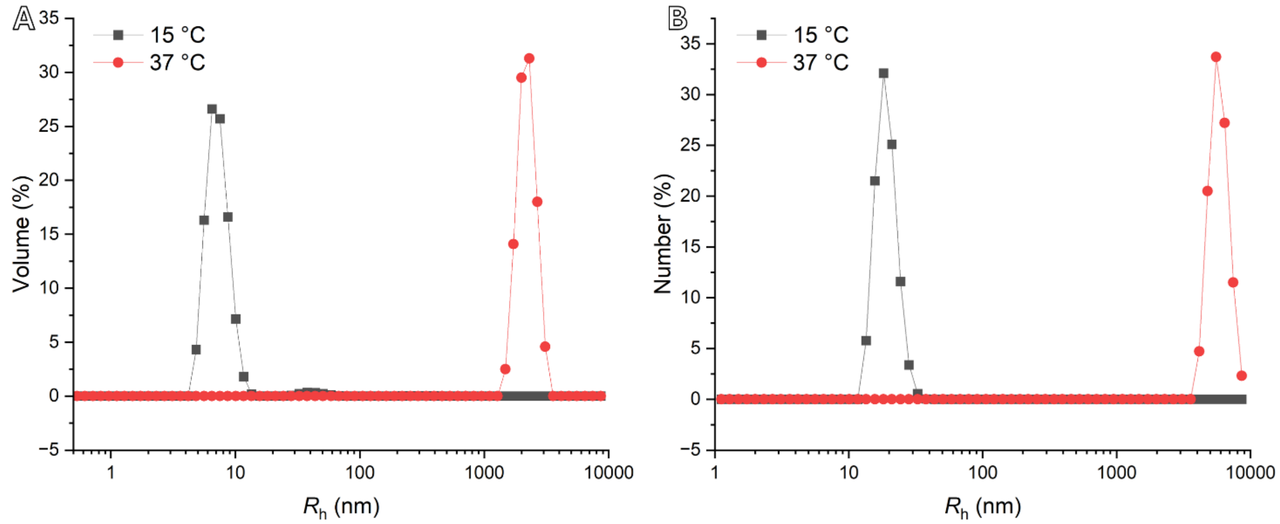

Figure S77. (A) Volume-weighted and (B) number-weighted particle size distributions of **B6** measured at 15 °C and 37 °C by DLS.

S3.2. TEM of block copolymers

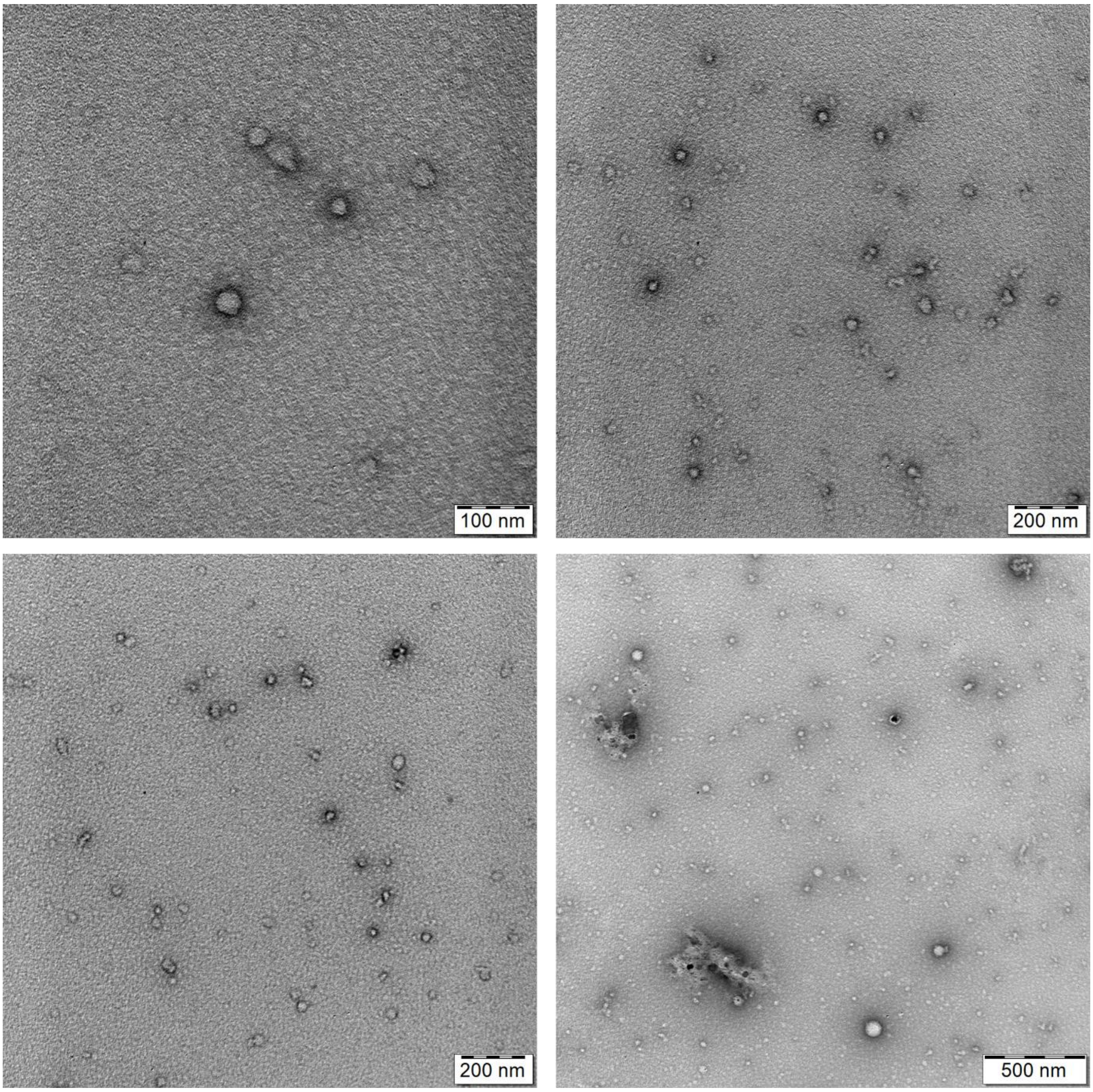

Figure S78. Additional TEM micrographs of **B1** evaluated at 4 °C.

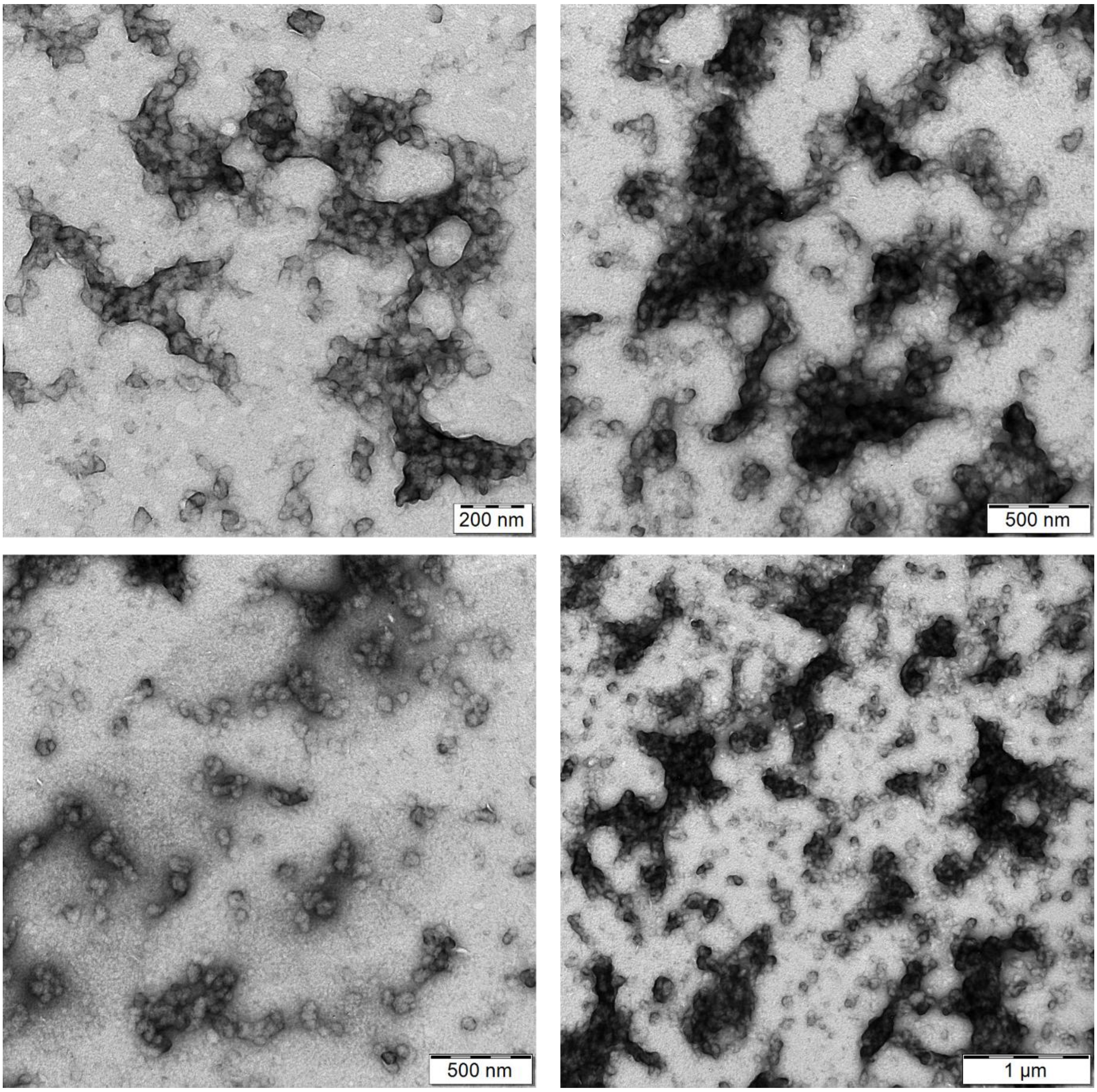

Figure S79. Additional TEM micrographs of **B1** evaluated at 45 °C.

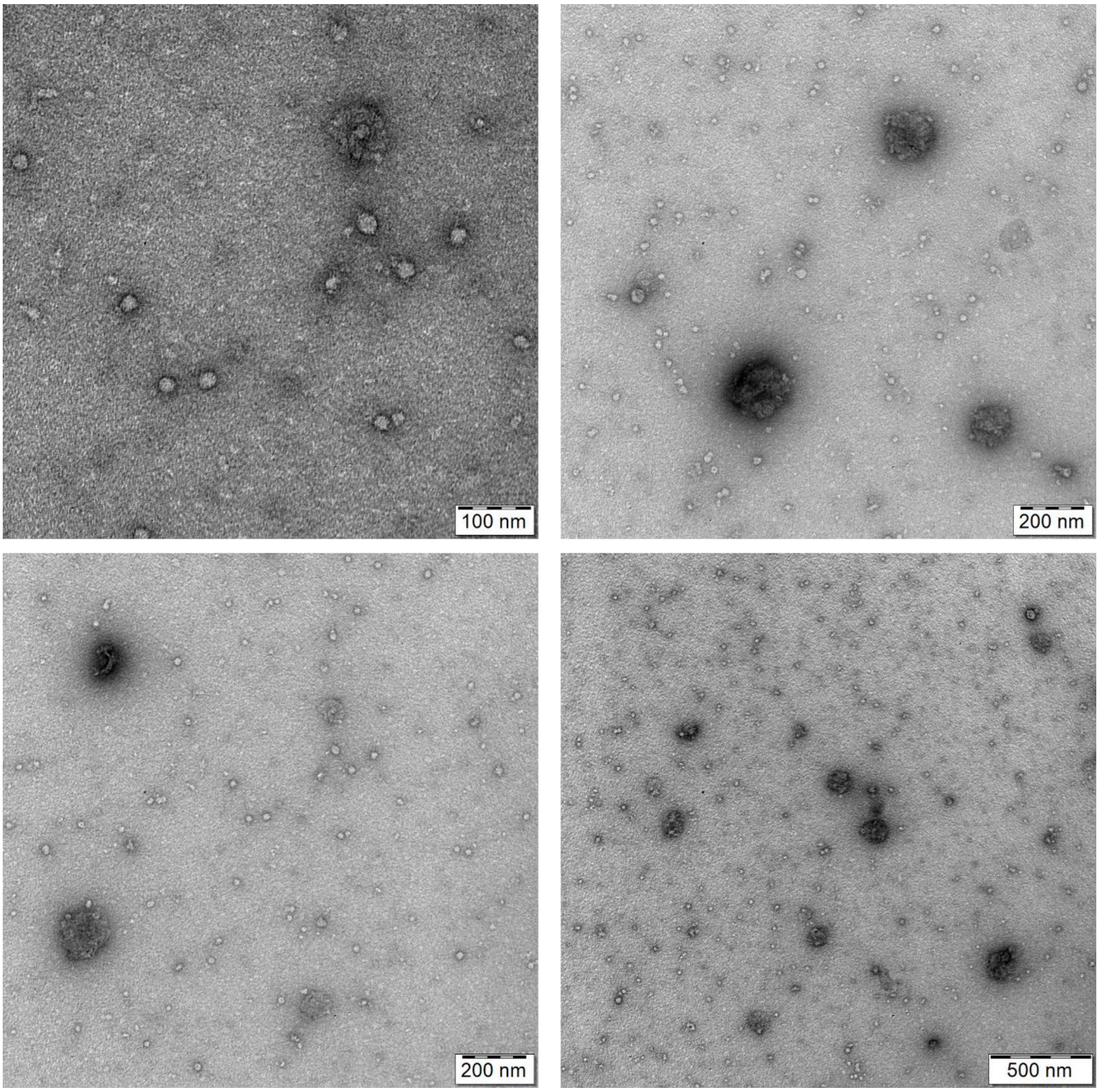

Figure S80. Additional TEM micrographs of **B4** evaluated at 4 °C.

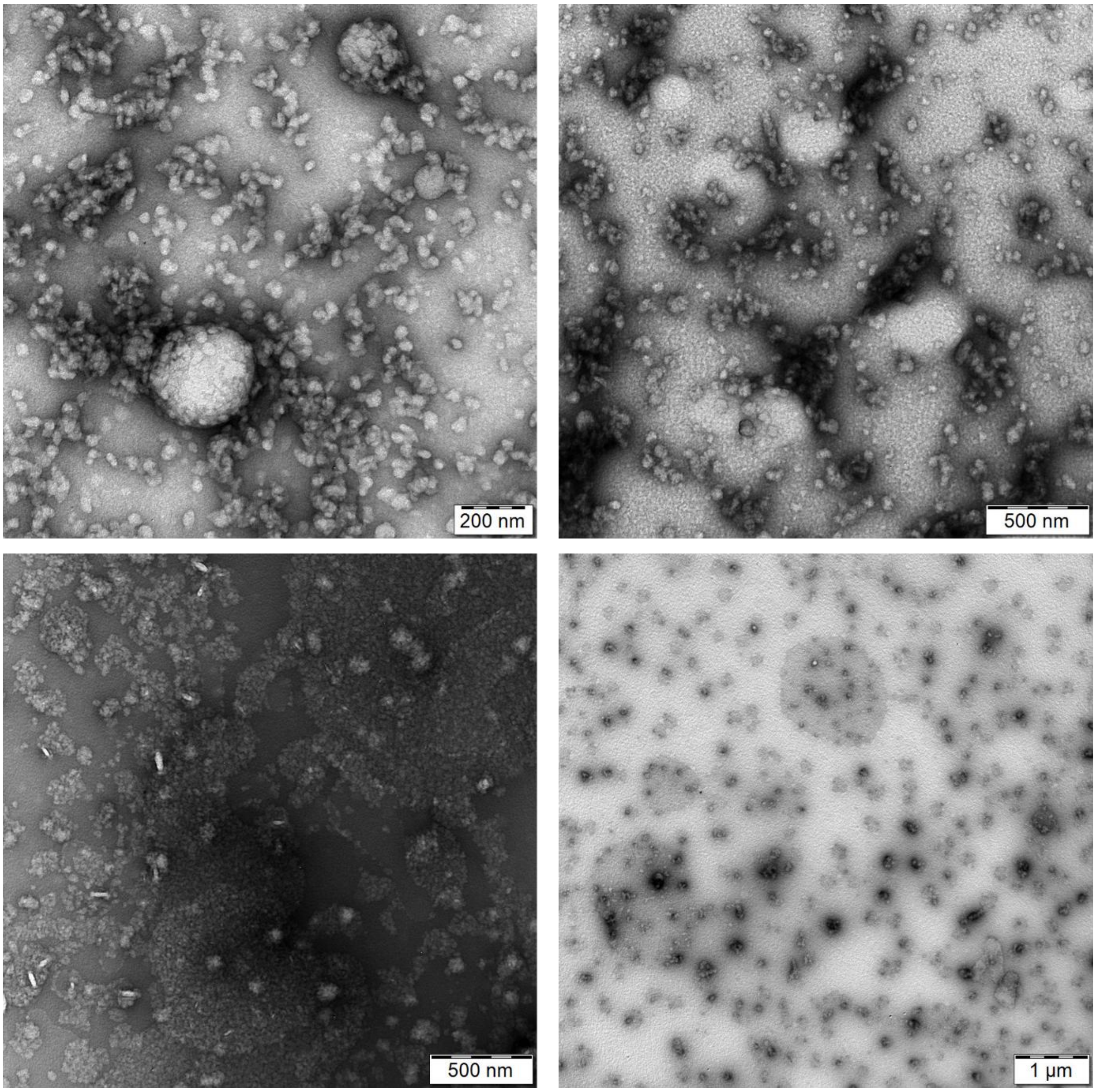

Figure S81. Additional TEM micrographs of **B4** evaluated at 45 °C.

S4. LCST behaviour of statistical copolymers

S4.1. Turbidimetry of S1-S6

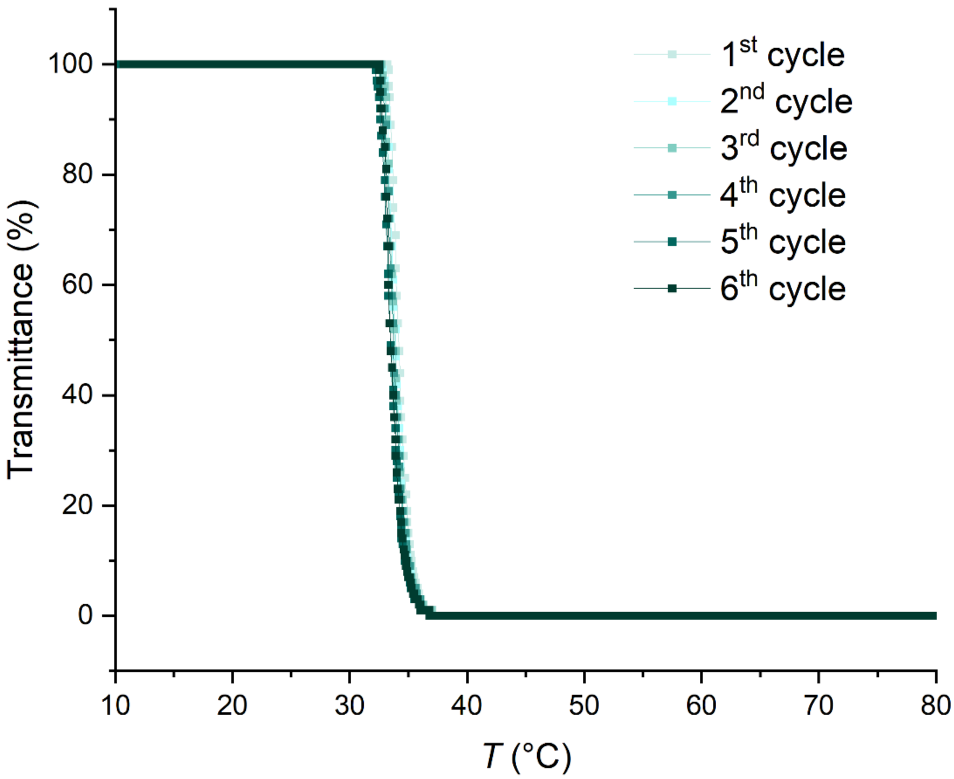

Figure S82. Transmittance of the **S1** solution in PBS, polymer concentration (16.7 *wt* %) as a function of temperature.

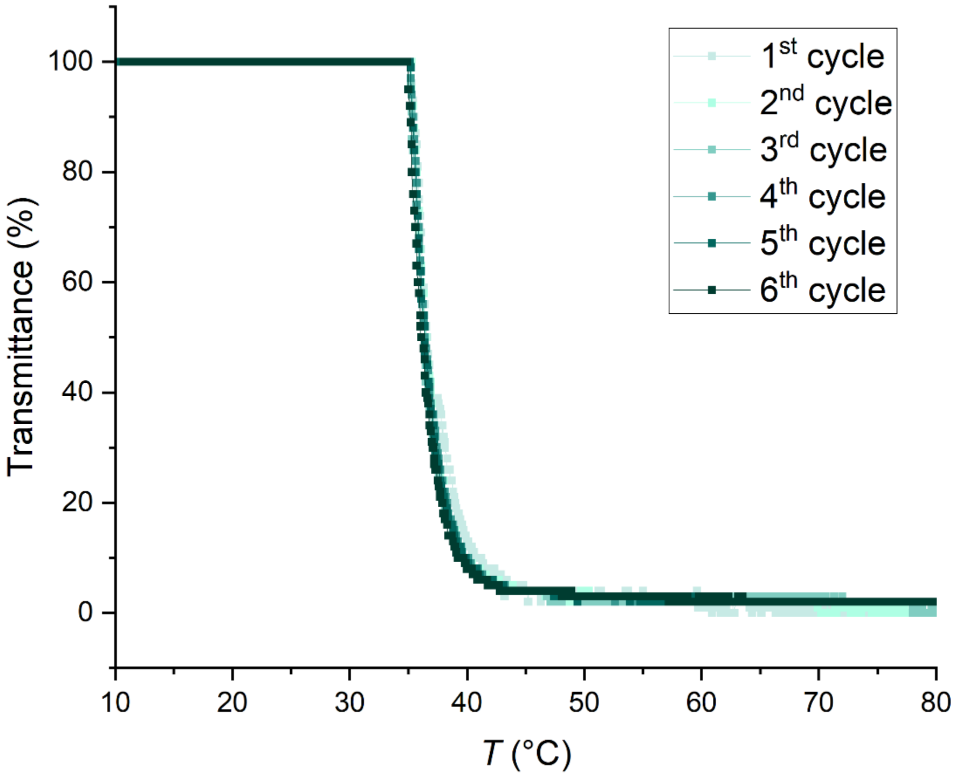

Figure S83. Transmittance of the **S2** solution in PBS, polymer concentration (16.7 *wt* %) as a function of temperature.

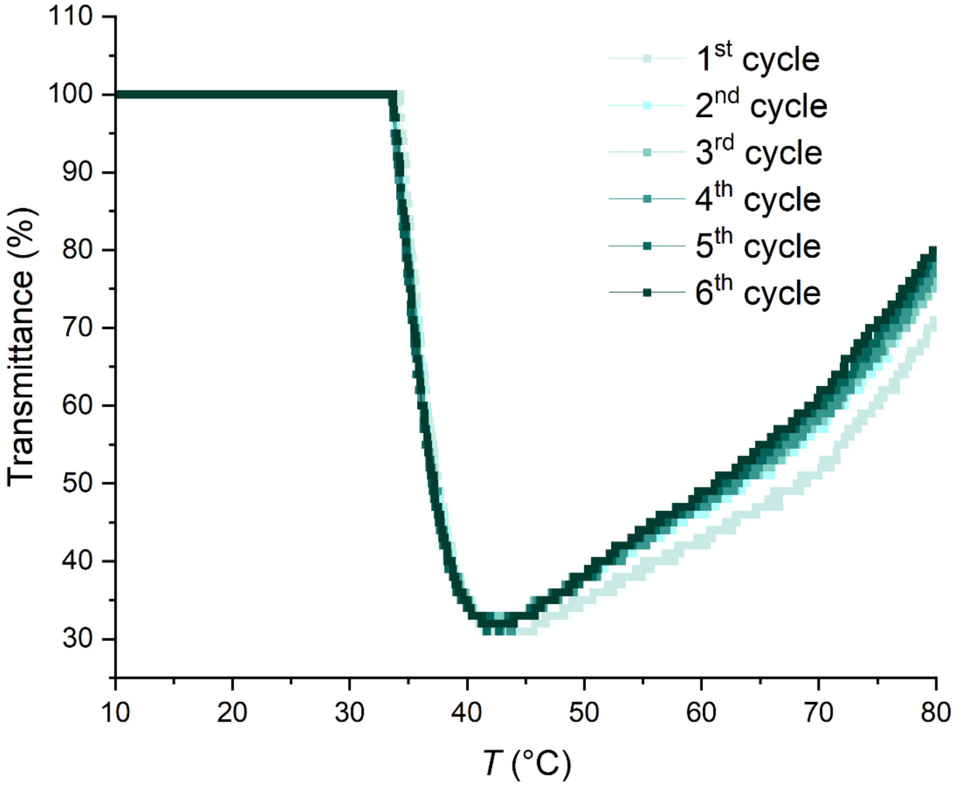

Figure S84. Transmittance of the **S3** solution in PBS, polymer concentration (16.7 *wt* %) as a function of temperature.

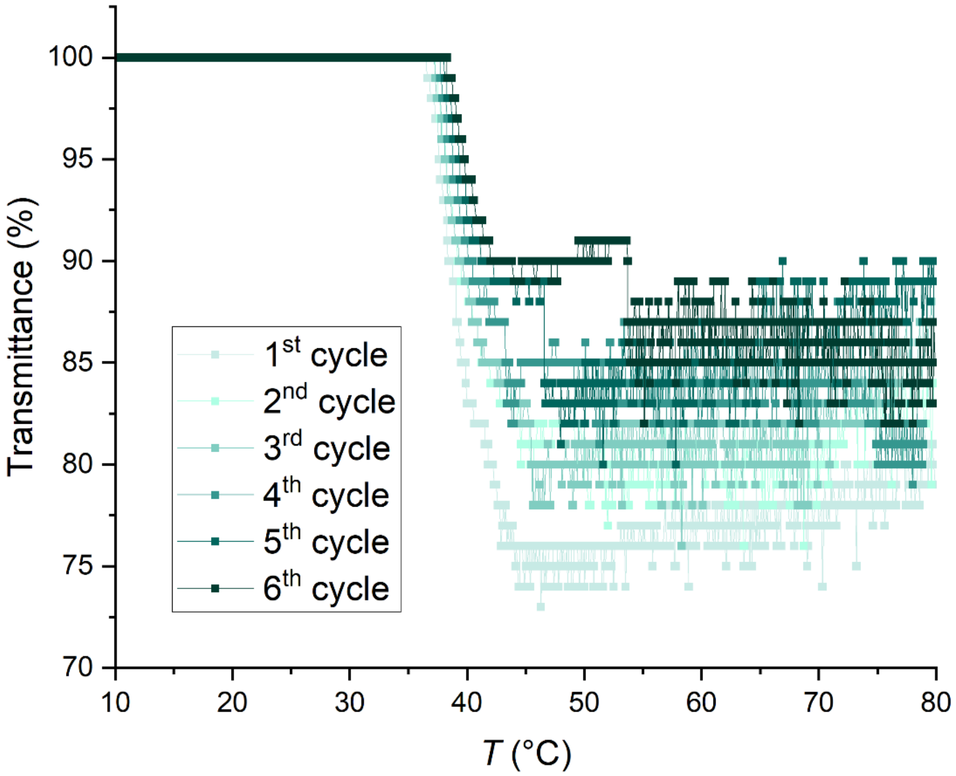

Figure S85. Transmittance of the **S4** solution in PBS, polymer concentration (16.7 *wt* %) as a function of temperature.

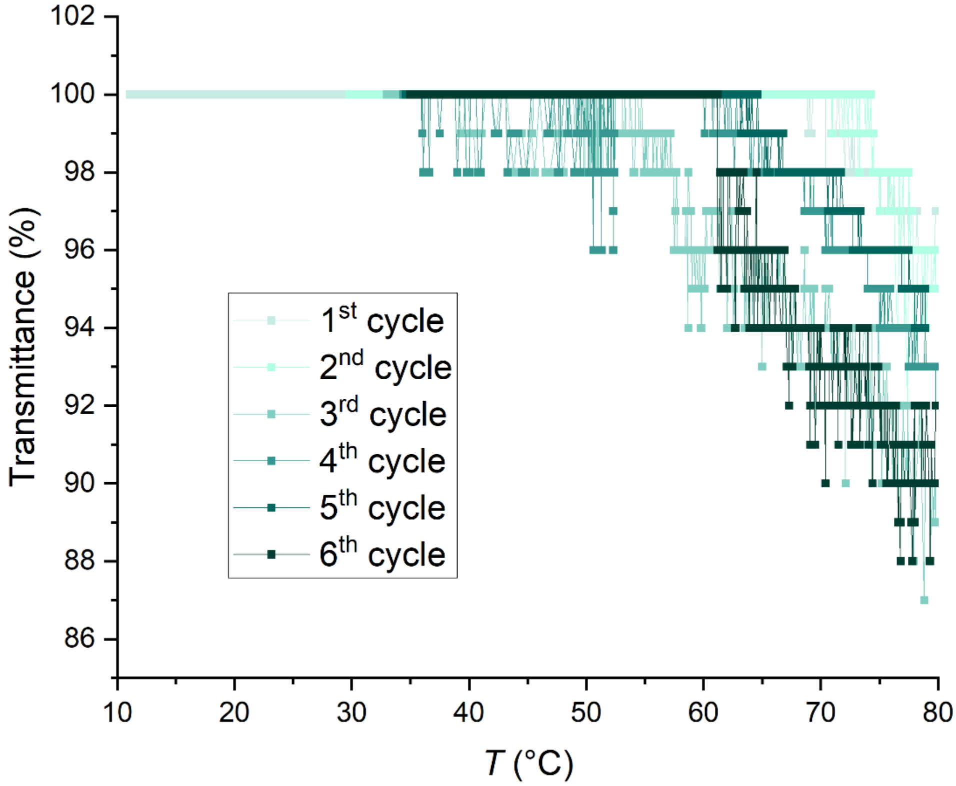

Figure S86. Transmittance of the **S5** solution in PBS, polymer concentration (16.7 *wt* %) as a function of temperature.

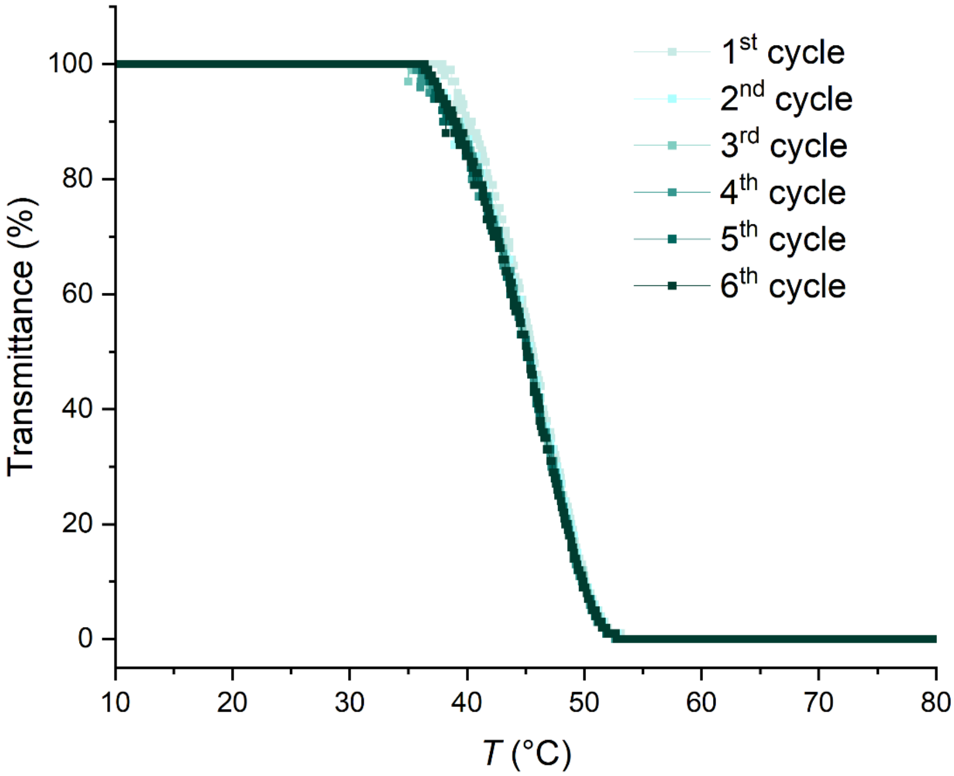

Figure S87. Transmittance of the **S1** solution in PBS, polymer concentration (8.33 *wt* %) as a function of temperature.

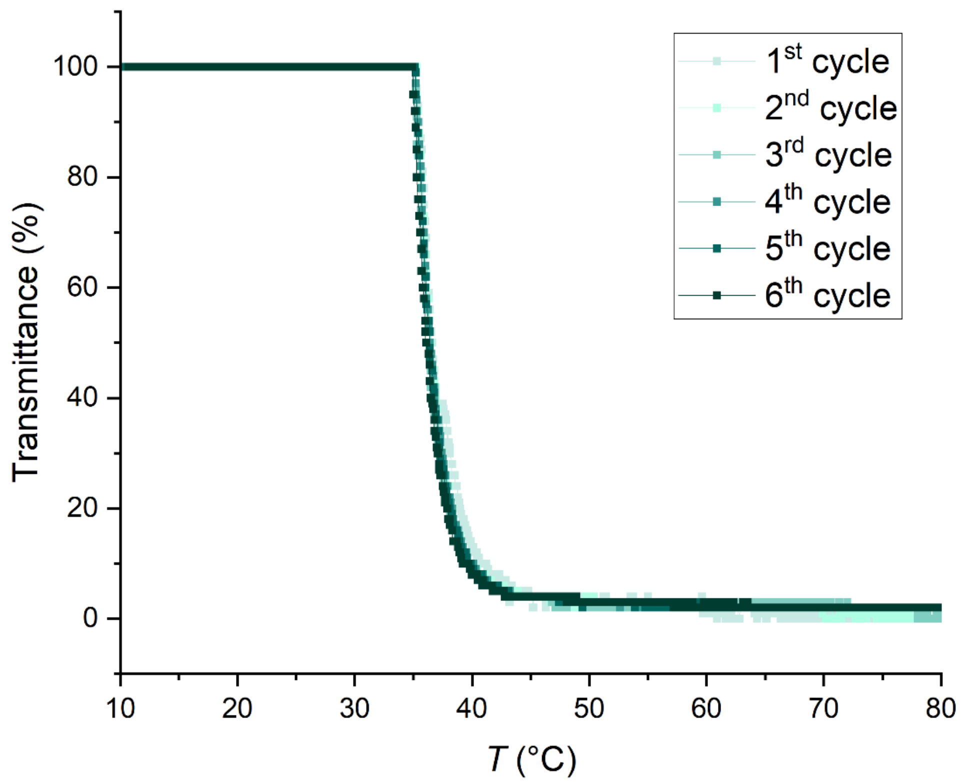

Figure S88. Transmittance of the **S2** solution in PBS, polymer concentration (8.33 *wt* %) as a function of temperature.

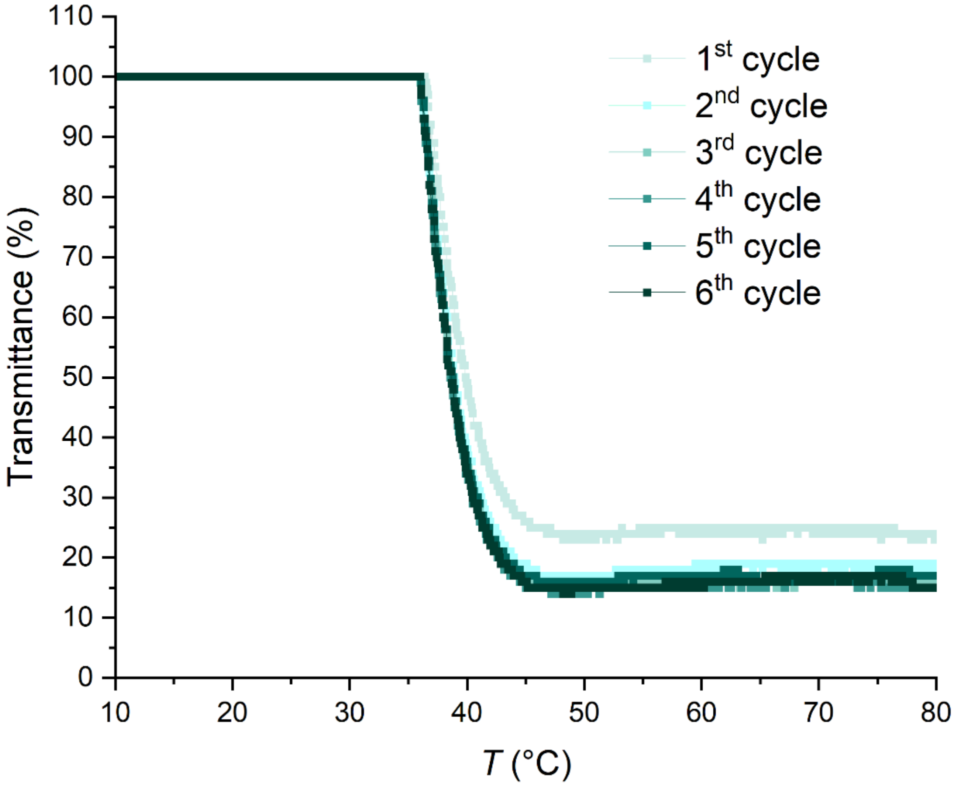

Figure S89. Transmittance of the **S3** solution in PBS, polymer concentration (8.33 *wt* %) as a function of temperature.

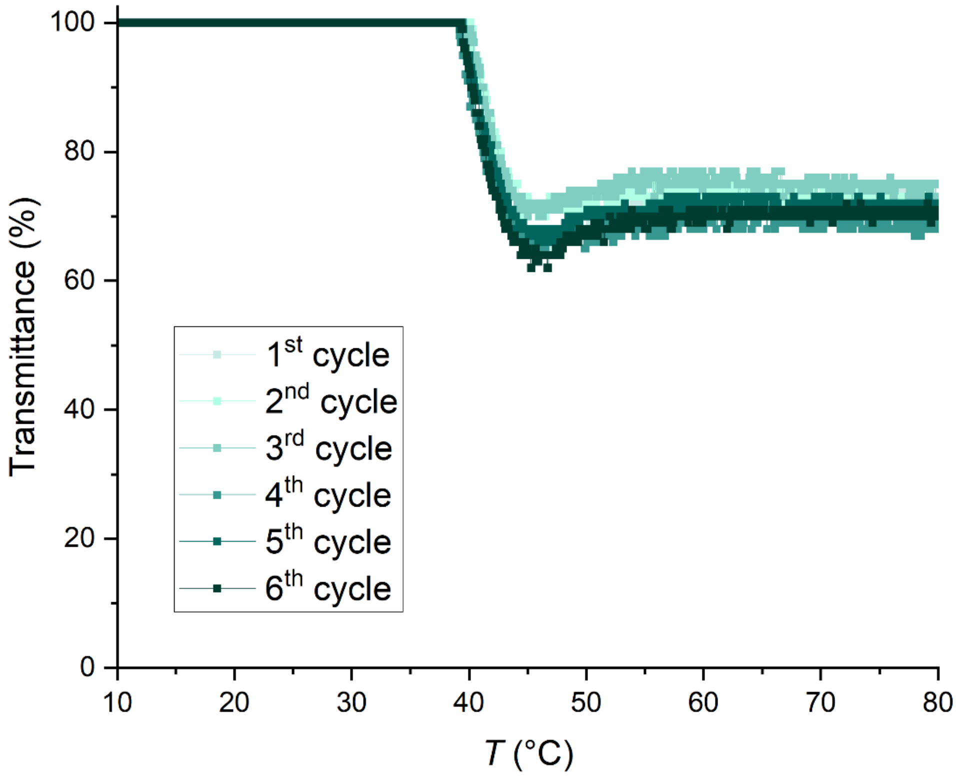

Figure S90. Transmittance of the **S4** solution in PBS, polymer concentration (8.33 *wt* %) as a function of temperature.

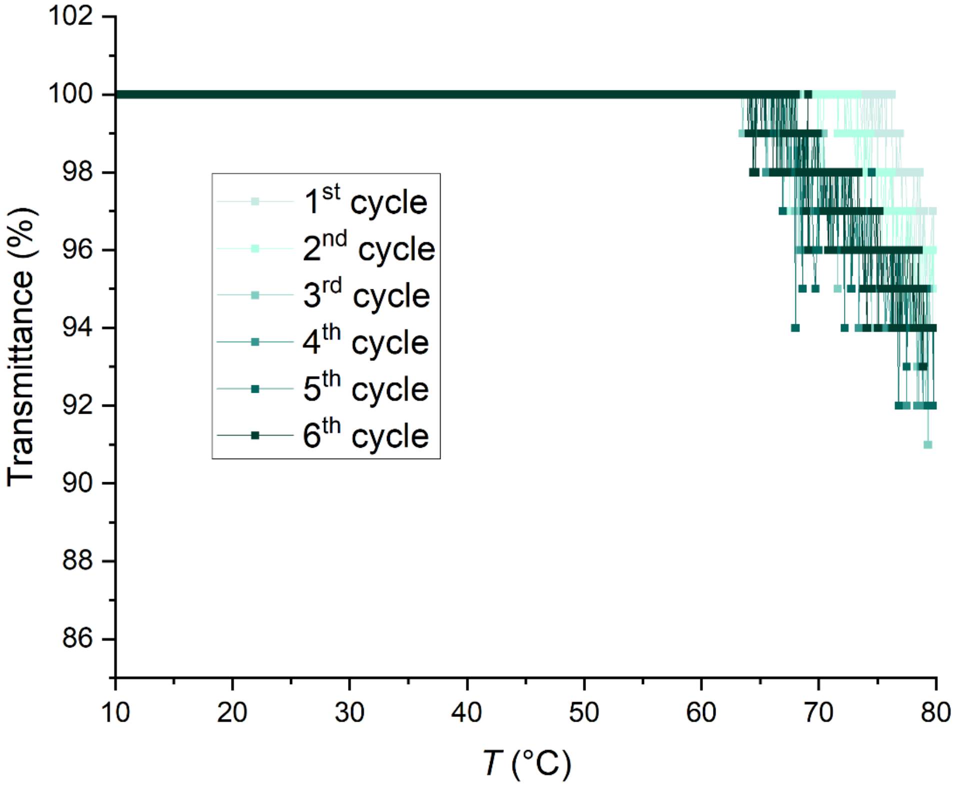

Figure S91. Transmittance of the **S5** solution in PBS, polymer concentration (8.33 *wt* %) as a function of temperature.

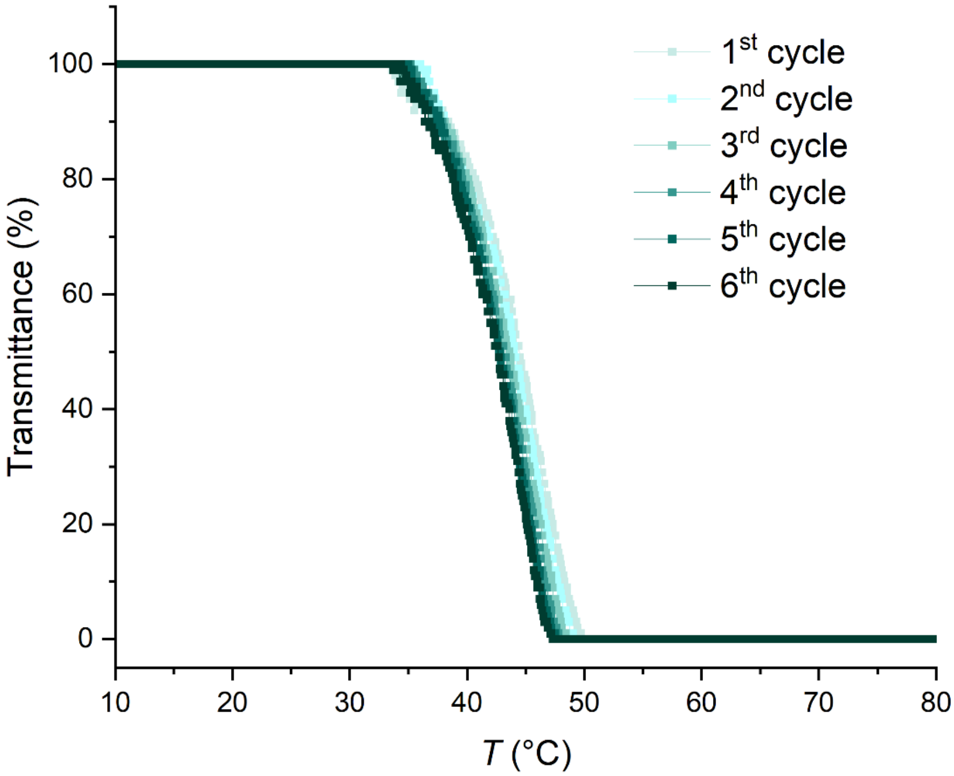

Figure S93. Transmittance of the **S1** solution in PBS, polymer concentration (4.17 *wt* %) as a function of temperature.

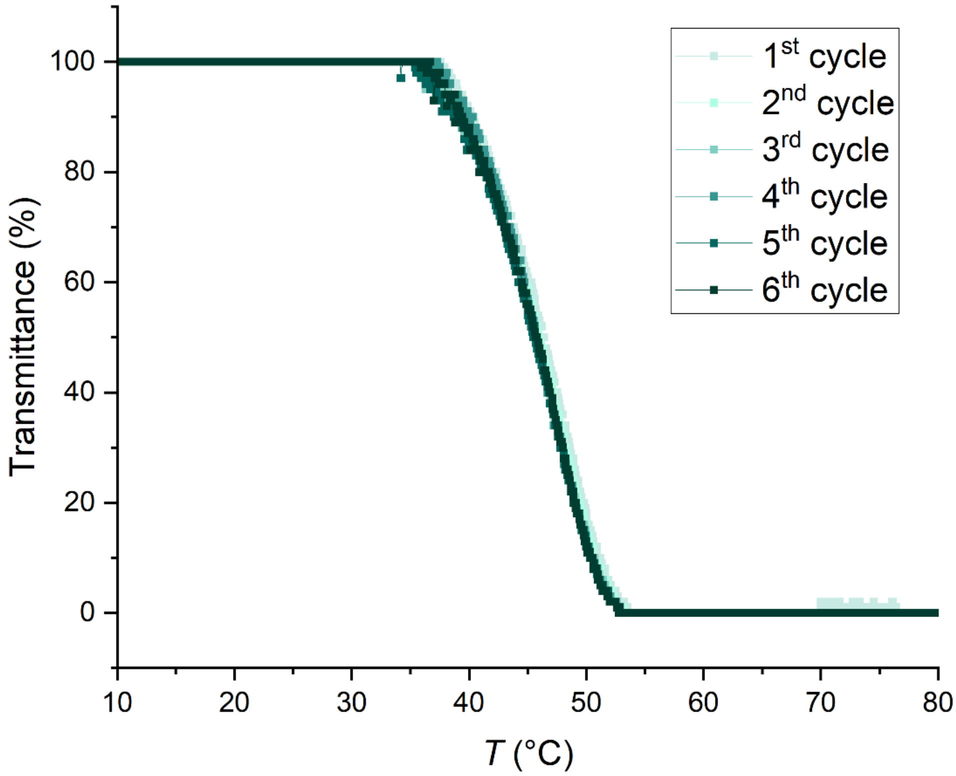

Figure S94. Transmittance of the **S2** solution in PBS, polymer concentration (4.17 *wt* %) as a function of temperature.

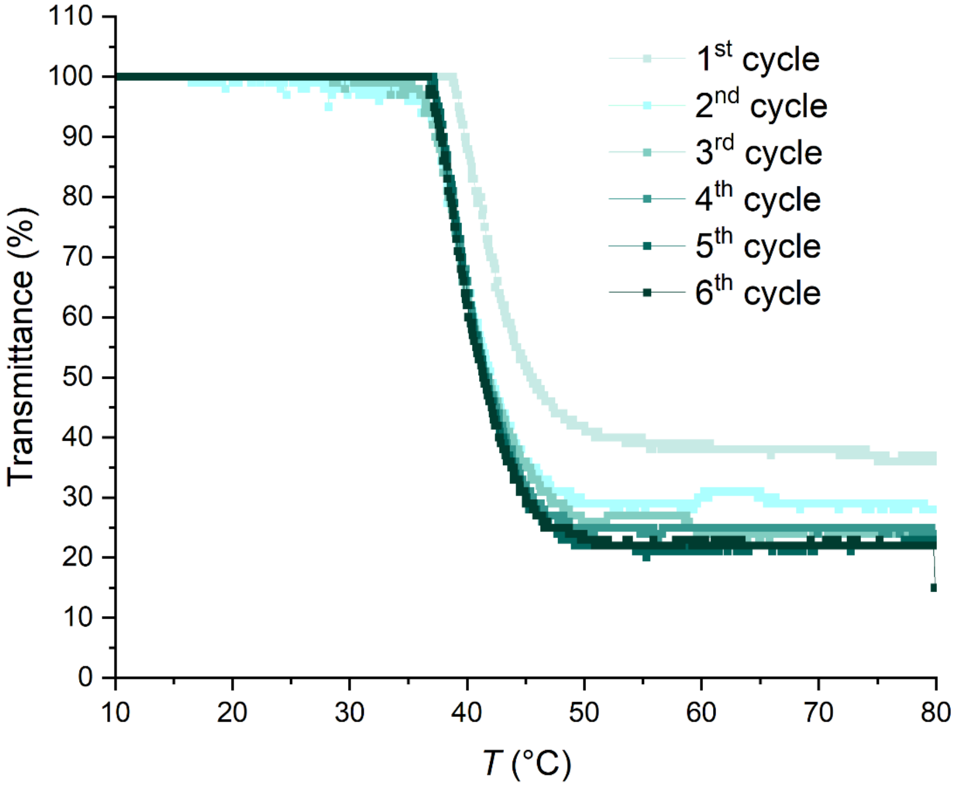

Figure S95. Transmittance of the **S3** solution in PBS, polymer concentration (4.17 *wt* %) as a function of temperature.

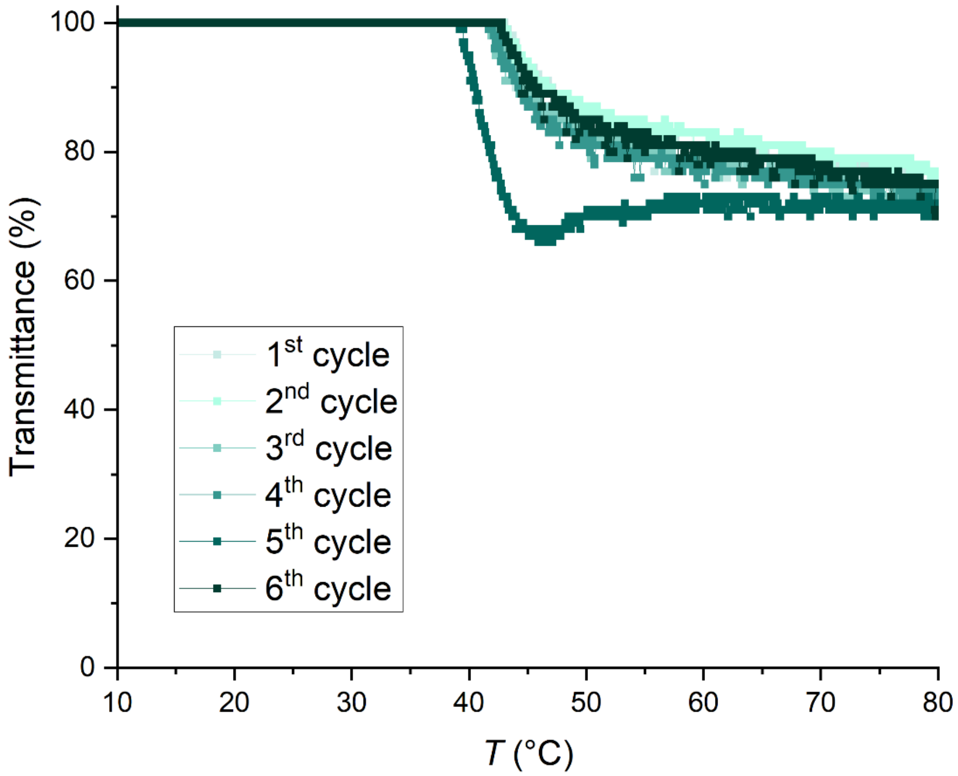

Figure S96. Transmittance of the **S4** solution in PBS, polymer concentration (4.17 *wt* %) as a function of temperature.

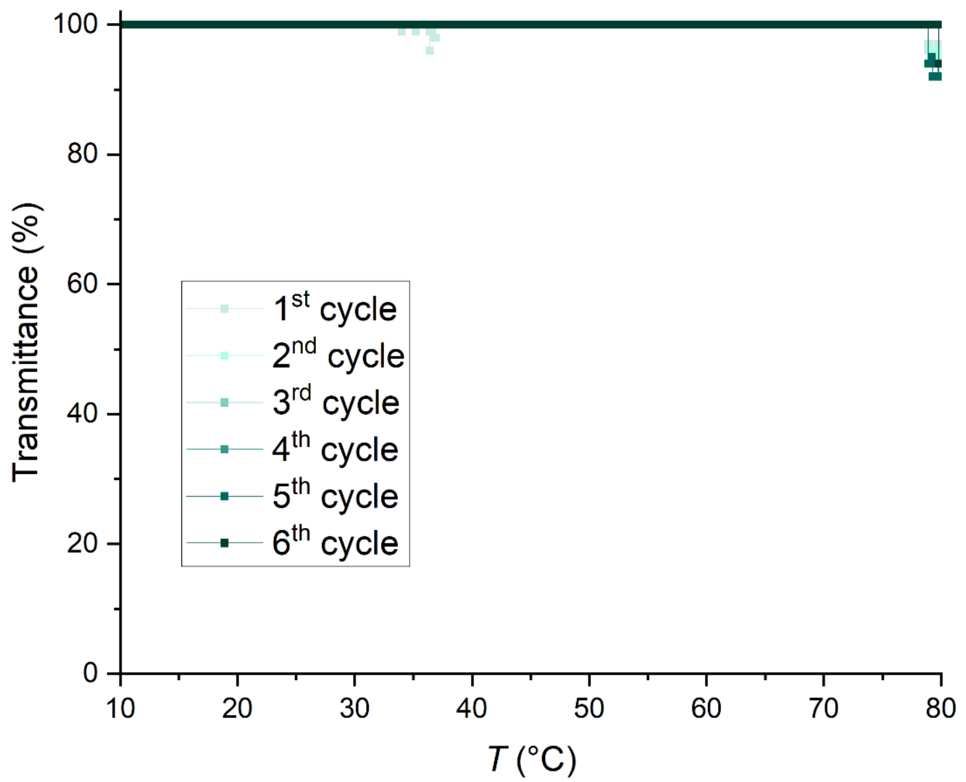

Figure S97. Transmittance of the **S5** solution in PBS, polymer concentration (4.17 *wt* %) as a function of temperature.

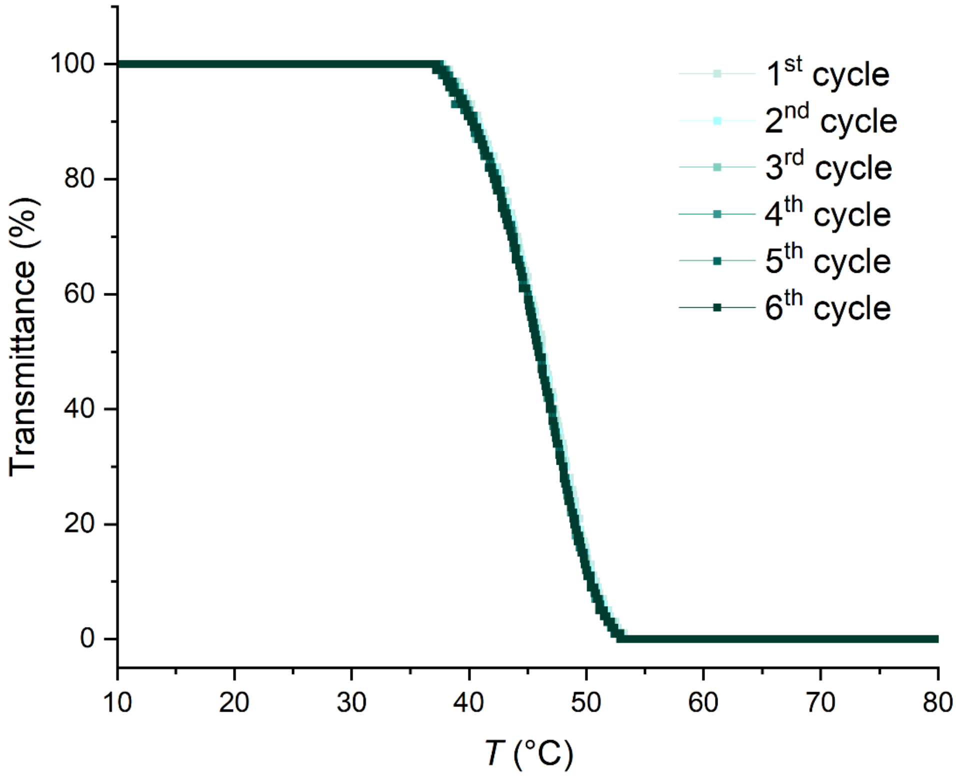

Figure S98. Transmittance of the **S1** solution in PBS, polymer concentration (2.08 *wt* %) as a function of temperature.

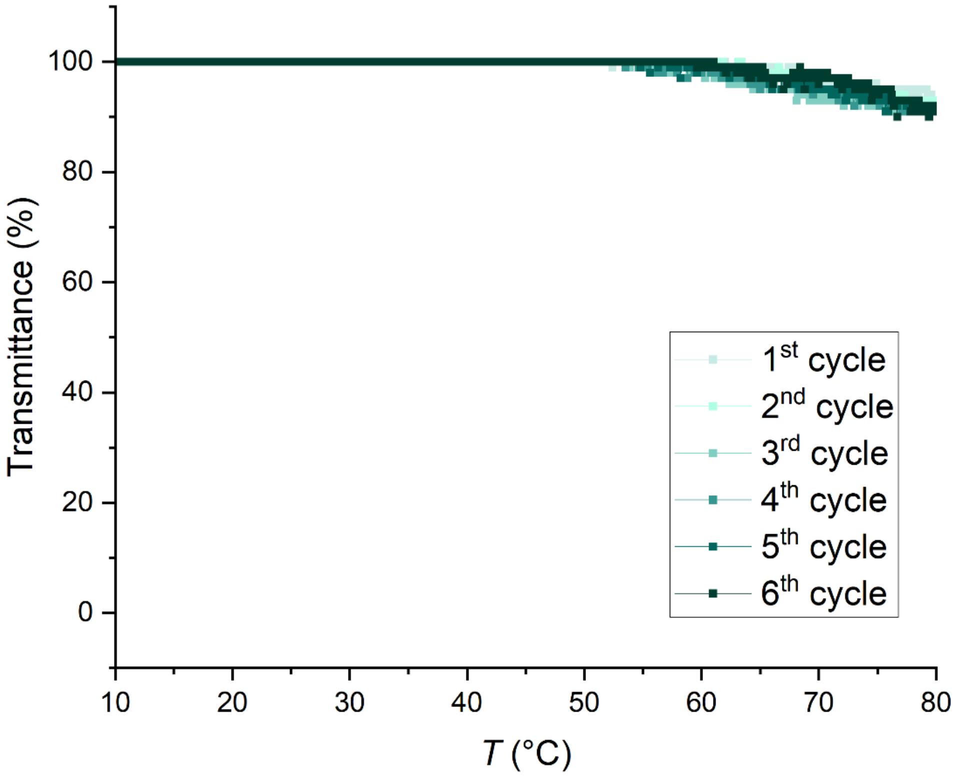

Figure S99. Transmittance of the **S2** solution in PBS, polymer concentration (2.08 *wt* %) as a function of temperature.

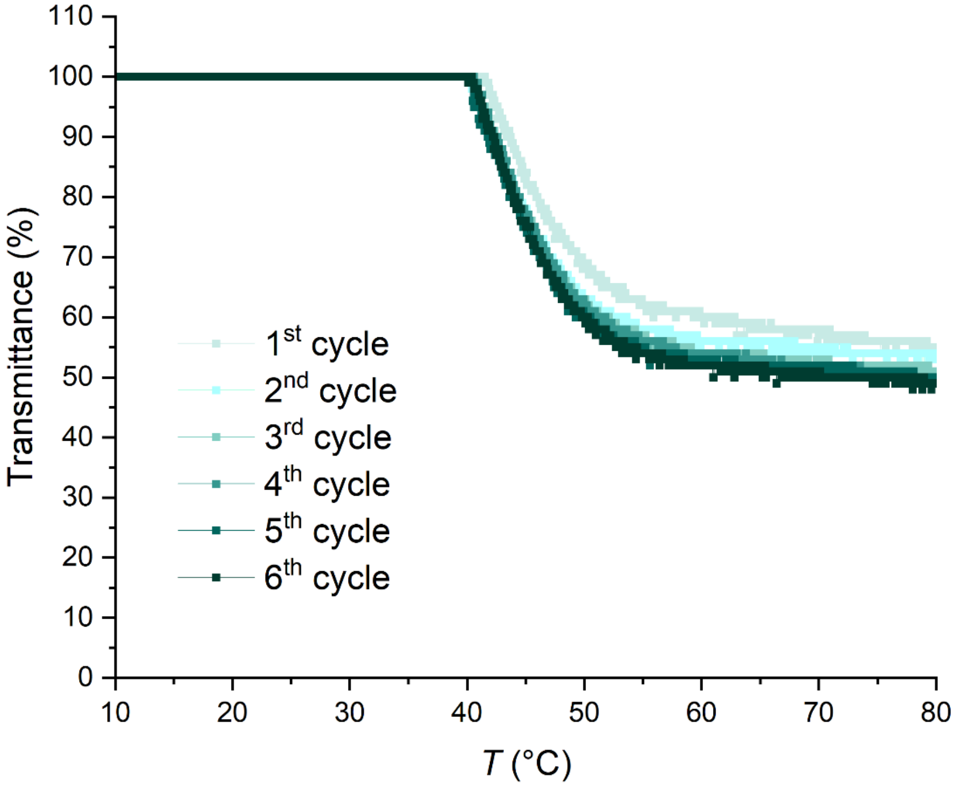

Figure S100. Transmittance of the **S3** solution in PBS, polymer concentration (2.08 *wt* %) as a function of temperature.

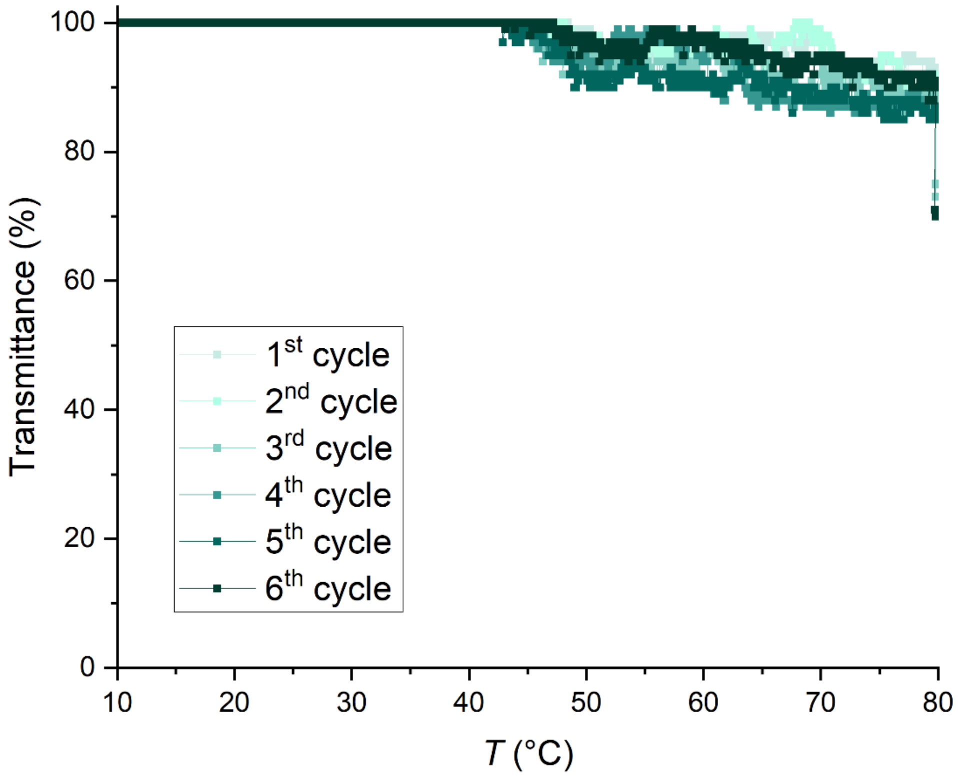

Figure S101. Transmittance of the **S4** solution in PBS, polymer concentration (2.08 *wt* %) as a function of temperature.

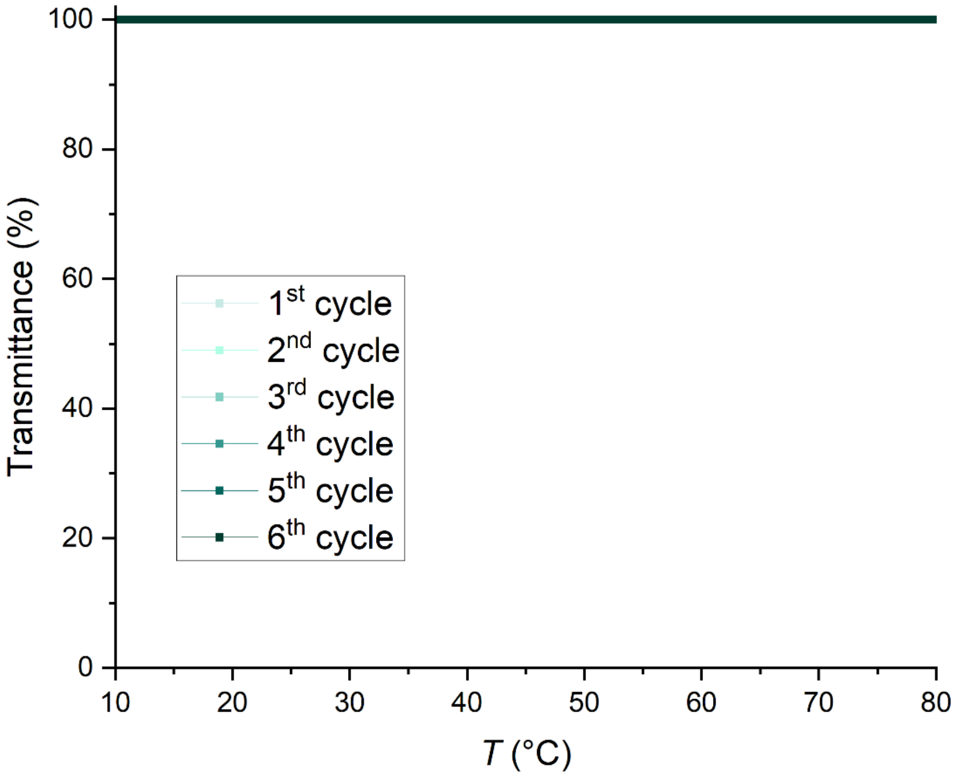

Figure S102. Transmittance of the **S5** solution in PBS, polymer concentration (2.08 *wt* %) as a function of temperature.

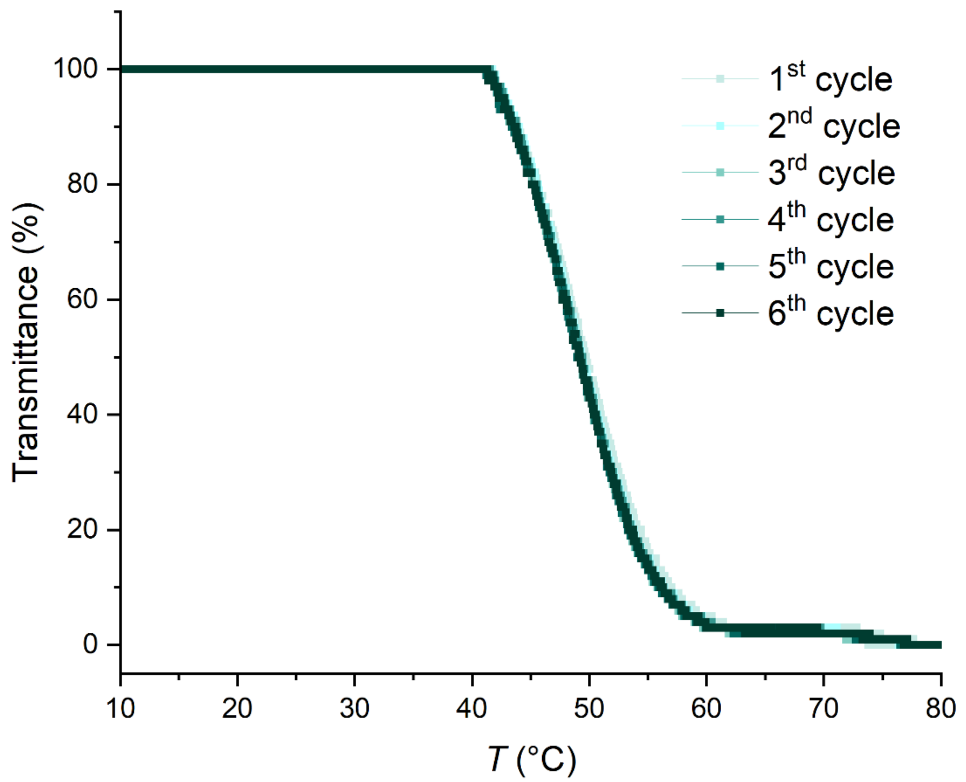

Figure S103. Transmittance of the **S1** solution in PBS, polymer concentration (1.04 *wt* %) as a function of temperature.

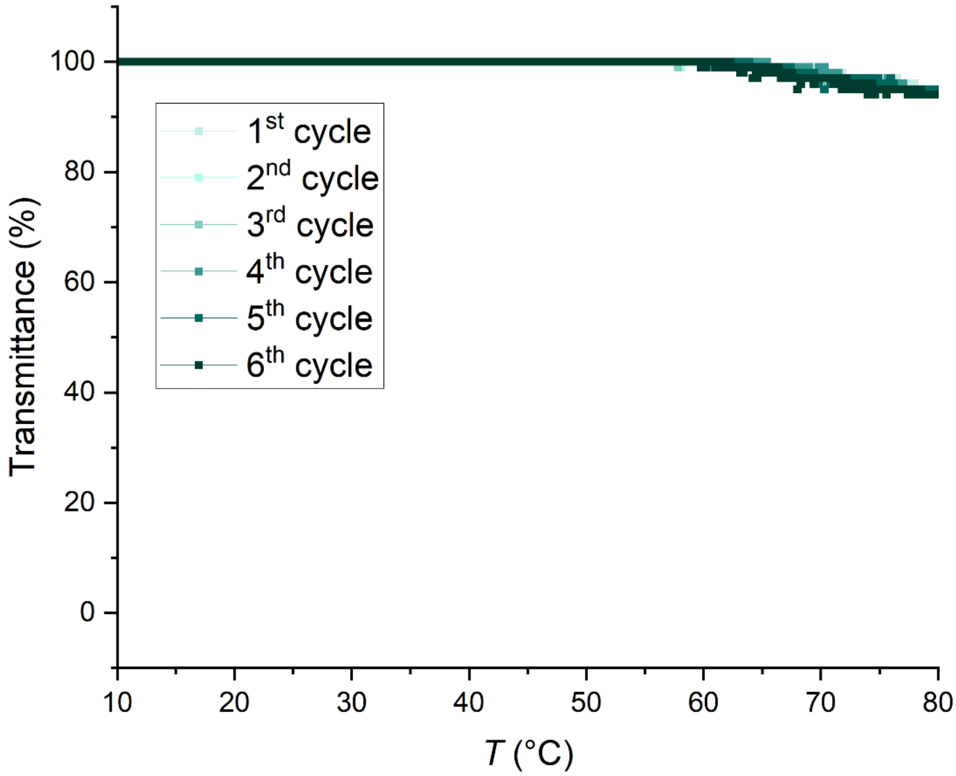

Figure S104. Transmittance of the **S2** solution in PBS, polymer concentration (1.04 *wt* %) as a function of temperature.

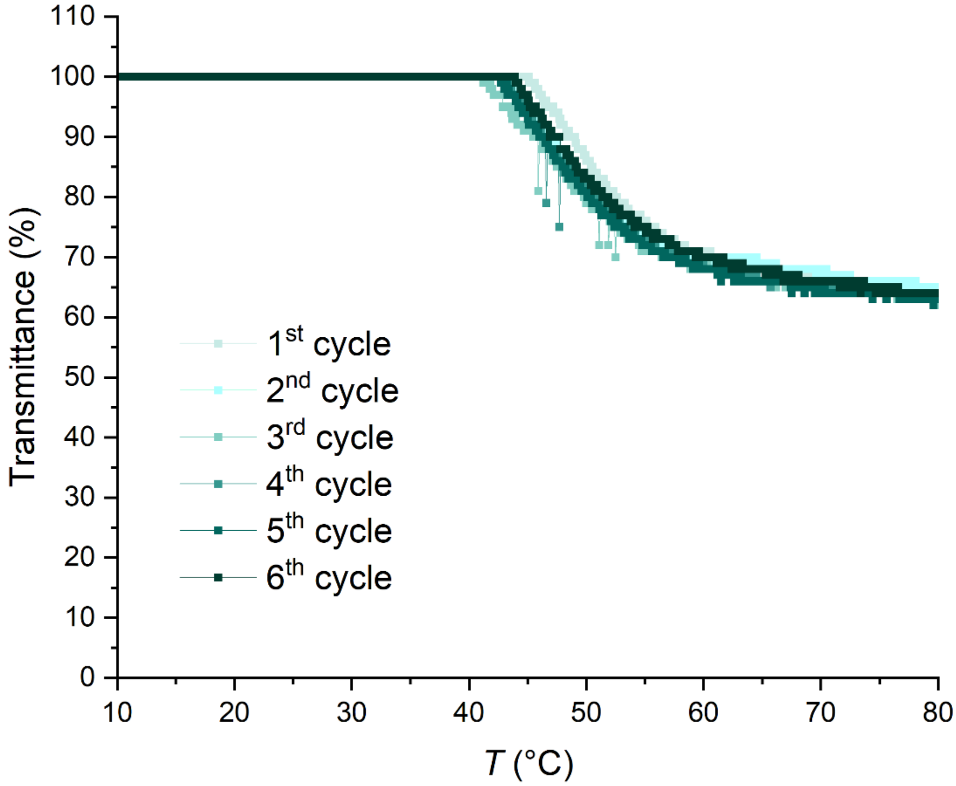

Figure S105. Transmittance of the **S3** solution in PBS, polymer concentration (1.04 *wt* %) as a function of temperature.

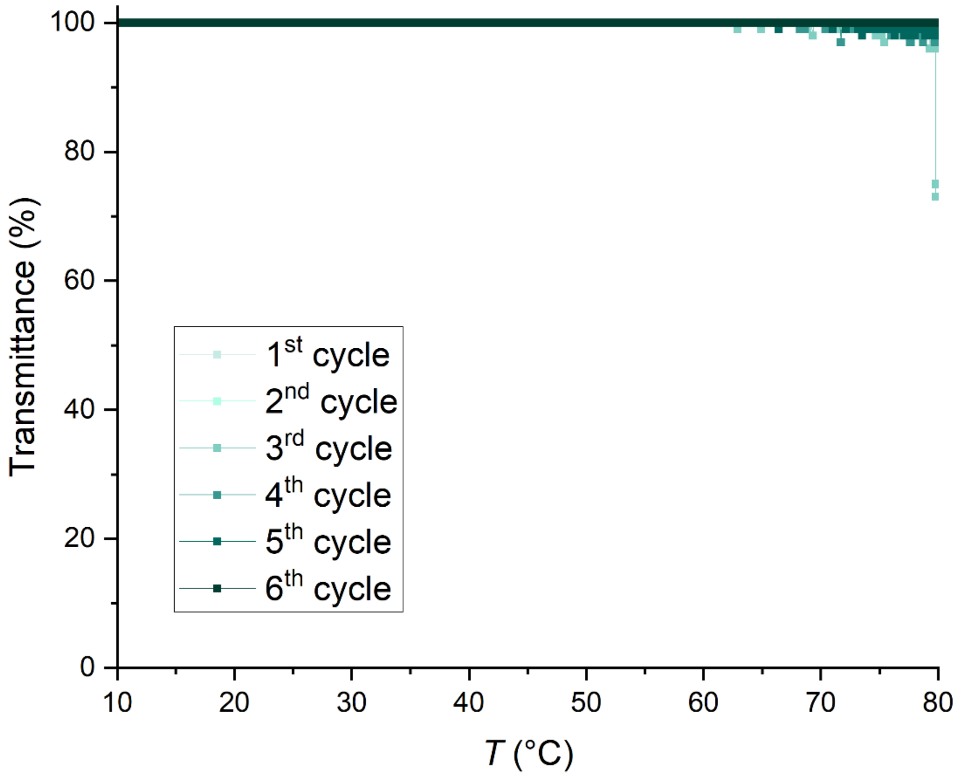

Figure S106. Transmittance of the **S4** solution in PBS, polymer concentration (1.04 *wt* %) as a function of temperature.

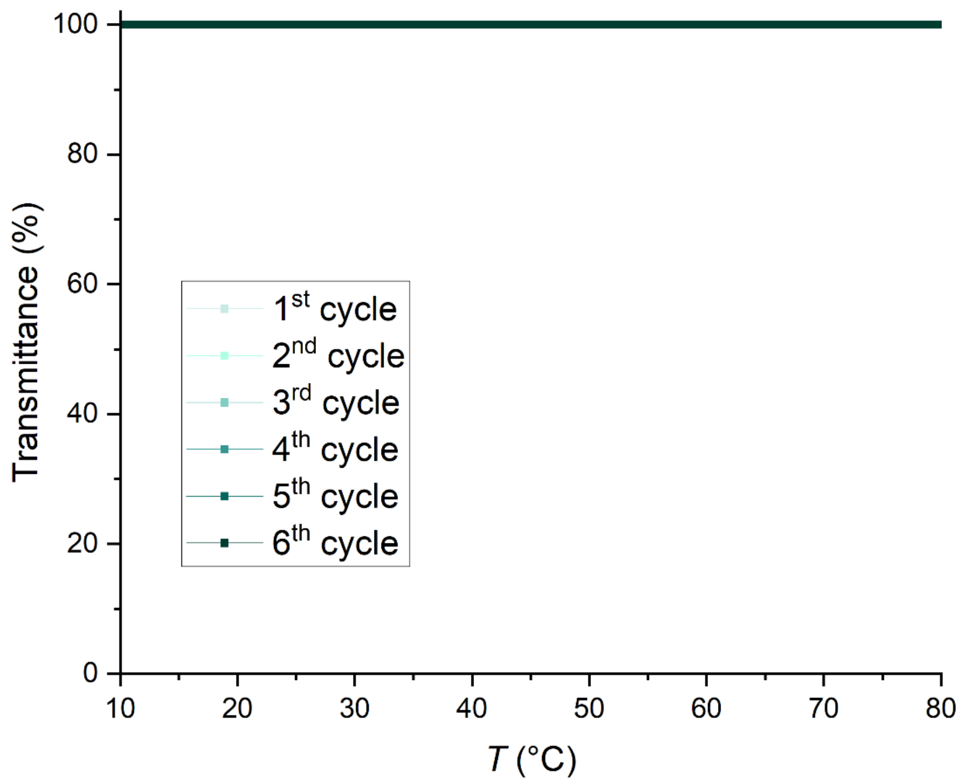

Figure S107. Transmittance of the **S5** solution in PBS, polymer concentration (1.04 *wt* %) as a function of temperature.

S4.1. Turbidimetry of S1m-S6m

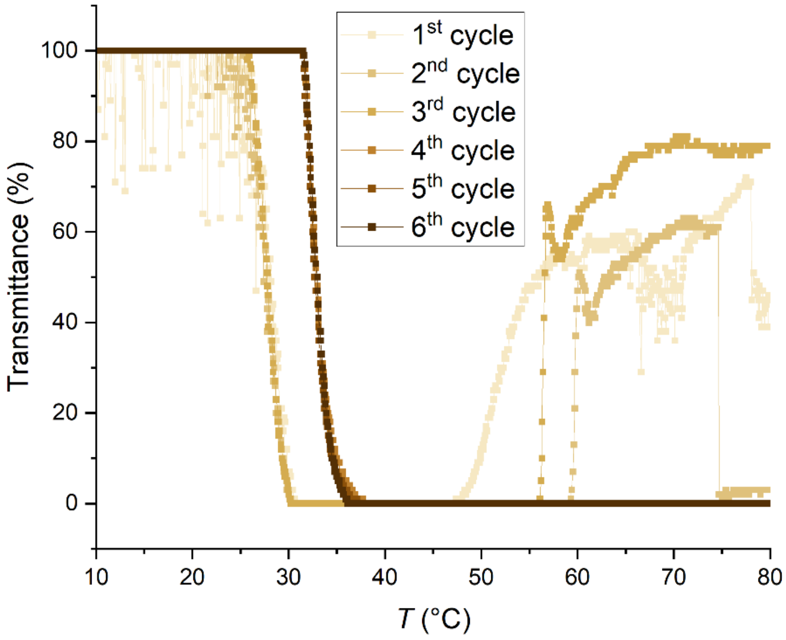

Figure S108. Transmittance of the **S1m** solution in PBS, polymer concentration (1.04 *wt* %) as a function of temperature. After the 3rd cycle, the polymer did not dissolve fully, therefore, the T_{CP} was evaluated from the first 3 cycles.

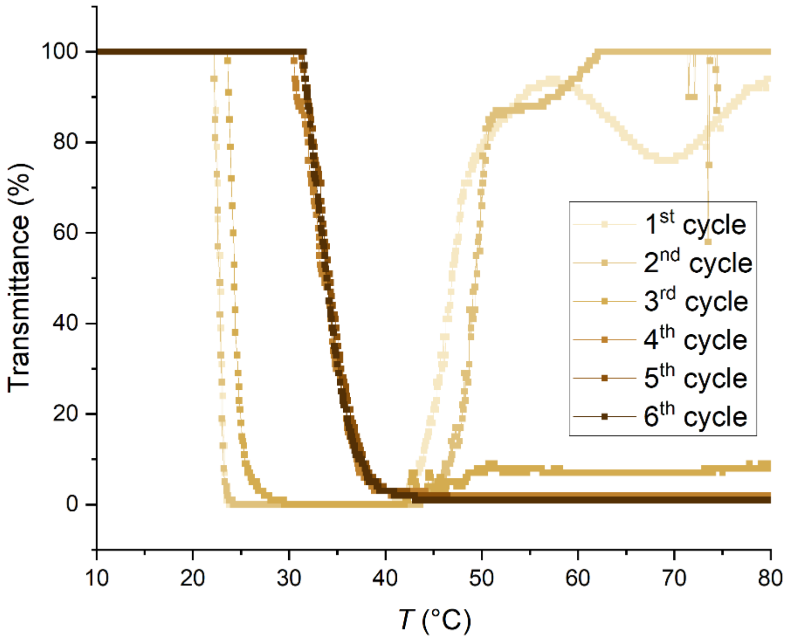

Figure S109. Transmittance of the **S2m** solution in PBS, polymer concentration (1.04 *wt* %) as a function of temperature. After the 3rd cycle, the polymer did not dissolve fully, therefore, the T_{CP} was evaluated from the first 3 cycles.

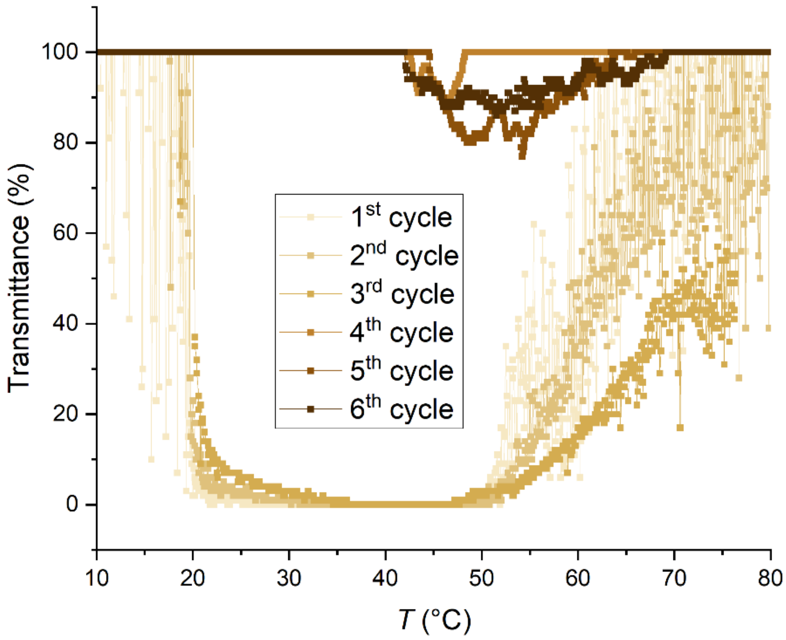

Figure S110. Transmittance of the **S3m** solution in PBS, polymer concentration (1.04 *wt* %) as a function of temperature. After the 3rd cycle, the polymer did not dissolve fully, therefore, the T_{CP} was evaluated from the first 3 cycles.

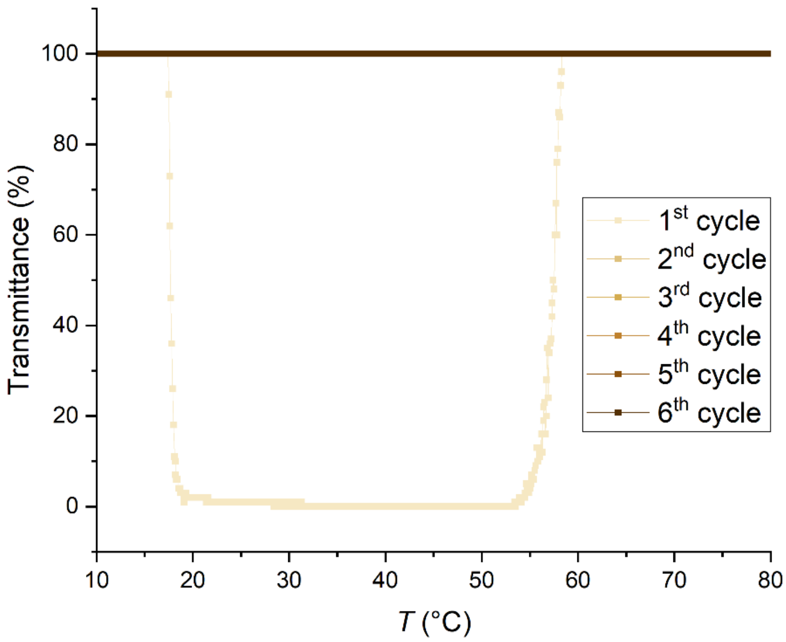

Figure S111. Transmittance of the **S4m** solution in PBS, polymer concentration (1.04 *wt* %) as a function of temperature. After the 1st cycle, the polymer did not dissolve fully, therefore, the T_{CP} was evaluated from the first cycle.

S5. Detection limits of developed polymers determined by µCT

Table S4. Average (RD_{av}) radiodensity, respective standard deviation of the polymer solutions, and minimal (RD_{min}) and maximal detected radiodensity (RD_{max}) of the block copolymers, **B1-B6**.

	B1			**B2**			**B3**		
c_{pol} (wt %)	**RD_{av} (HU) ± SD**	**RD_{min} (HU)**	**RD_{max} (HU)**	**RD_{av} (HU) ± SD**	**RD_{max} (HU)**	**RD_{max} (HU)**	**RD_{av} (HU) ± SD**	**RD_{min} (HU)**	**RD_{max} (HU)**
9.09	903 ± 224	378	1420	1512 ± 293	889	2090	1520 ± 227	959	2114
4.55	412 ± 187	8	954	760 ± 209	405	1270	758 ± 210	314	1151
2.27	151 ± 157	-214	503	308 ± 183	-68	905	358 ± 175	33	809
1.14	63 ± 165	-312	438	151 ± 159	-160	531	155 ± 173	-227	546
0.57	-2 ± 148	-413	383	25 ± 169	-226	476	-18 ± 140	-366	289
0.28	-5 ± 142	-372	382	14 ± 182	-318	433	-21 ± 140	-305	359
	B4			**B5**			**B6**		
c_{pol} (wt %)	**RD_{av} (HU) ± SD**	**RD_{min} (HU)**	**RD_{max} (HU)**	**RD_{av} (HU) ± SD**	**RD_{min} (HU)**	**RD_{max} (HU)**	**RD_{av} (HU) ± SD**	**RD_{min} (HU)**	**RD_{max} (HU)**
9.09	892 ± 207	528	1393	1106 ± 215	598	1568	1548 ± 238	798	2121
4.55	423 ±175	43	788	592 ± 196	297	1162	711 ± 186	270	1307
2.27	204 ± 165	-129	619	257 ± 194	-116	645	320 ± 222	-213	857
1.14	101 ± 154	-186	530	138 ± 185	-223	703	226 ± 190	-189	716
0.57	39 ± 201	-282	465	56 ± 149	-327	489	60 ± 203	-355	611
0.28	15 ± 168	-396	509	52 ± 154	-376	592	-42 ± 156	-251	307

PBS		
RD_{av} (HU) ± SD	**RD_{min} (HU)**	**RD_{max} (HU)**
1 ± 168	-299	399

Table S5. Average (RD_{av}) radiodensity, respective standard deviation of the polymer solutions, and minimal (RD_{min}) and maximal detected radiodensity (RD_{max}) of the block copolymers, **S1-S6**.

	S1			**S2**			**S3**		
c_{pol} (wt %)	**RD_{av} (HU) ± SD**	**RD_{min} (HU)**	**RD_{max} (HU)**	**RD_{av} (HU) ± SD**	**RD_{min} (HU)**	**RD_{max} (HU)**	**RD_{av} (HU) ± SD**	**RD_{min} (HU)**	**RD_{max} (HU)**
9.09	88 ± 160	-303	615	129 ± 162	-223	473	238 ± 167	-105	686
4.55	-4 ± 177	-325	326	44 ± 158	-270	283	161 ± 167	-162	641
2.27	9 ± 186	-325	472	47 ±157	-322	342	53 ± 161	-237	538
1.14	20 ± 98	-169	173	-7 ± 195	-390	344	-10 ± 159	-264	321
0.57	-17 ± 163	-493	387	-41 ± 178	-429	468	0 ± 168	-287	425
0.28	-5 ± 205	-382	560	-41 ± 165	-380	351	1 ± 120	-380	342
	S4			**S5**			**S6**		
c_{pol} (wt %)	**RD_{av} (HU) ± SD**	**RD_{min} (HU)**	**RD_{max} (HU)**	**RD_{av} (HU) ± SD**	**RD_{min} (HU)**	**RD_{max} (HU)**	**RD_{av} (HU) ± SD**	**RD_{min} (HU)**	**RD_{max} (HU)**
9.09	88 ± 160	3	615	129 ± 162	-74	473	238 ± 167	513	686
4.55	-4 ± 177	-231	326	44 ± 158	-53	283	161 ± 167	190	641
2.27	9 ± 186	-296	472	47 ±157	-332	342	53 ± 161	-68	538
1.14	20 ± 98	-320	173	-7 ± 195	-463	344	-10 ± 159	-194	321
0.57	-17 ± 163	-329	387	-41 ± 178	-411	468	0 ± 168	-242	425
0.28	-5 ± 205	-352	560	-41 ± 165	-304	351	1 ± 120	-268	342

Table S6. Parameters of linear fit of resulting RDs of the samples plotted as a function of iodine concentration.

Linear fit	**B1-B6**	**S1-S6**
Slope	541.2	499.5
Y-intercept	-39.24	-38.64
X-intercept	0.07251	0.07735
1/slope	0.001848	0.002002
Std. Error	**B1-B6**	**S1-S6**
Slope	14.9	12.1
Y-intercept	17.01	6.504

S6. Cytotoxicity

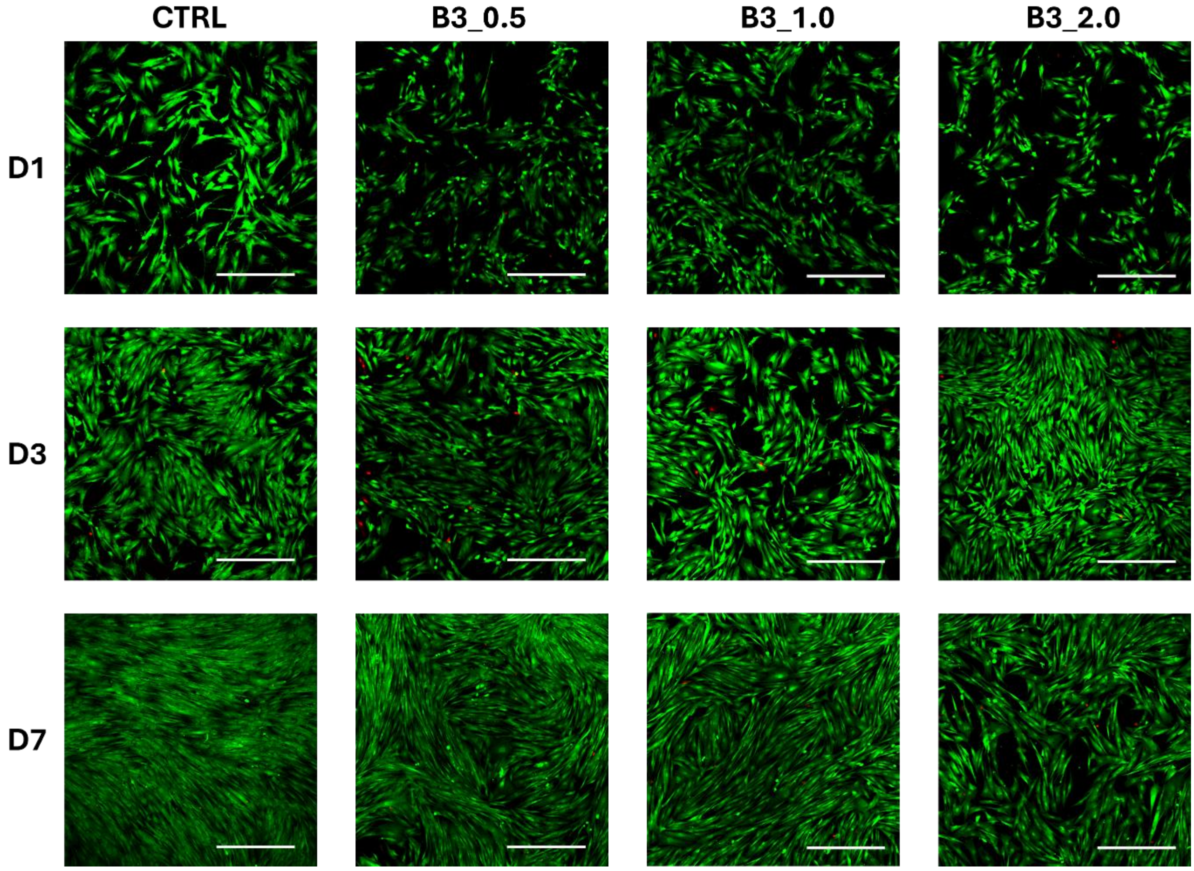

Figure S112. Human foreskin fibroblasts cultivated in the presence of **B3** at 3 different concentrations (0.5, 1.0, and 2.0 mg mL^{-1}) or without (TCP). Live/dead staining was evaluated on days 1, 3, and 7 after seeding. Scale bars represent 200 µm.

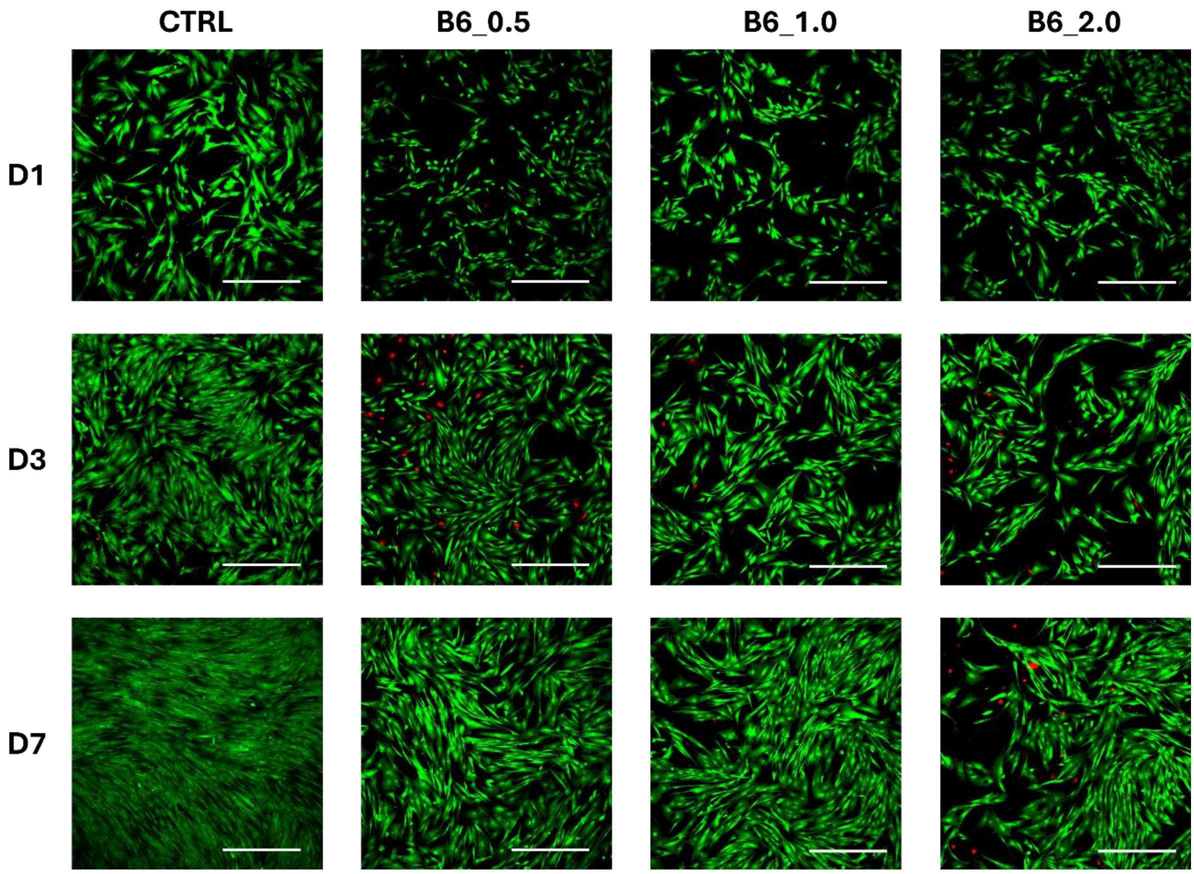

Figure S113. Human foreskin fibroblasts cultivated in the presence of **B6** at 3 different concentrations (0.5, 1.0, and 2.0 mg mL^{-1}) or without (TCP). Live/dead staining was evaluated on days 1, 3, and 7 after seeding. Scale bars represent 200 µm.

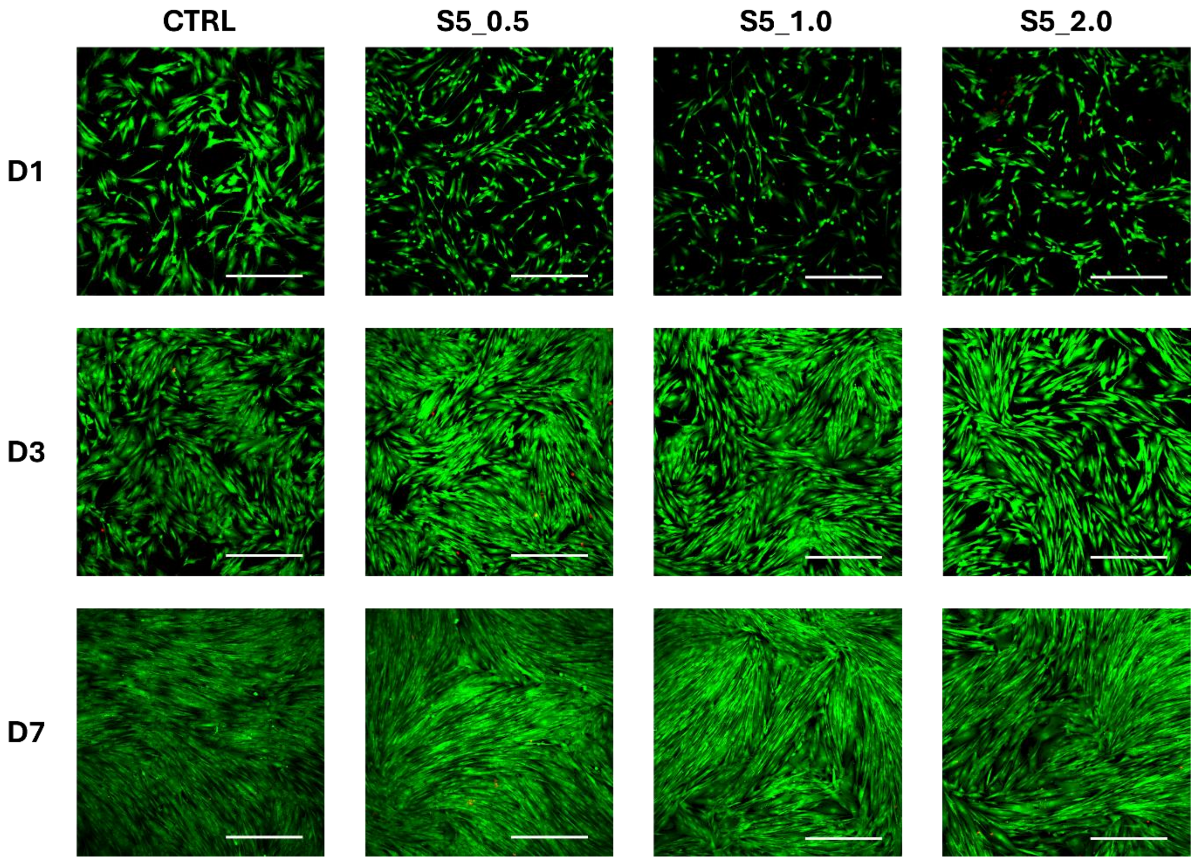

Figure S114. Human foreskin fibroblasts cultivated in the presence of **S5** at 3 different concentrations (0.5, 1.0, and 2.0 mg mL^{-1}) or without (TCP). Live/dead staining was evaluated on days 1, 3, and 7 after seeding. Scale bars represent 200 μm.

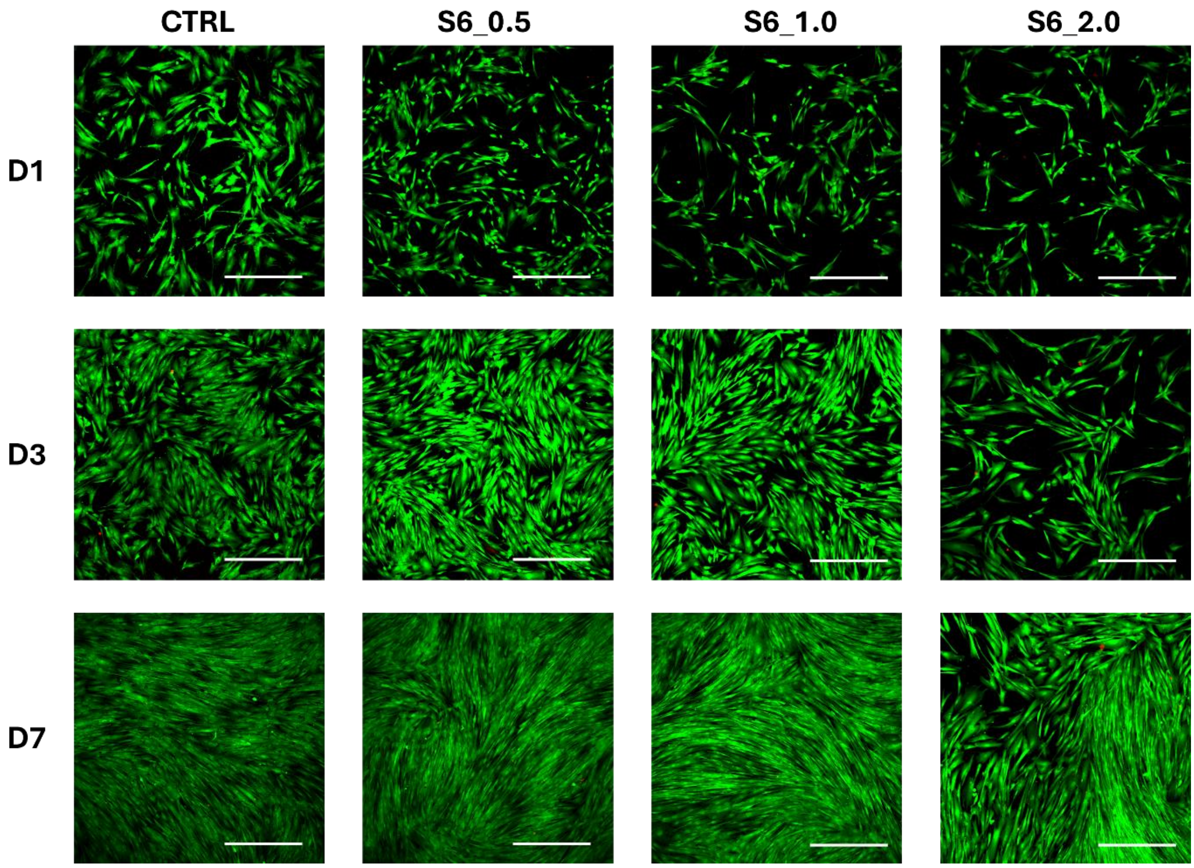

Figure S115. Human foreskin fibroblasts cultivated in the presence of **S6** at 3 different concentrations (0.5, 1.0, and 2.0 mg mL^{-1}) or without (TCP). Live/dead staining was evaluated on days 1, 3, and 7 after seeding. Scale bars represent 200 μm.

S7. Miscellaneous

S7.1. [1]H and SEC analysis of reference polymer PEG-PNIPAM

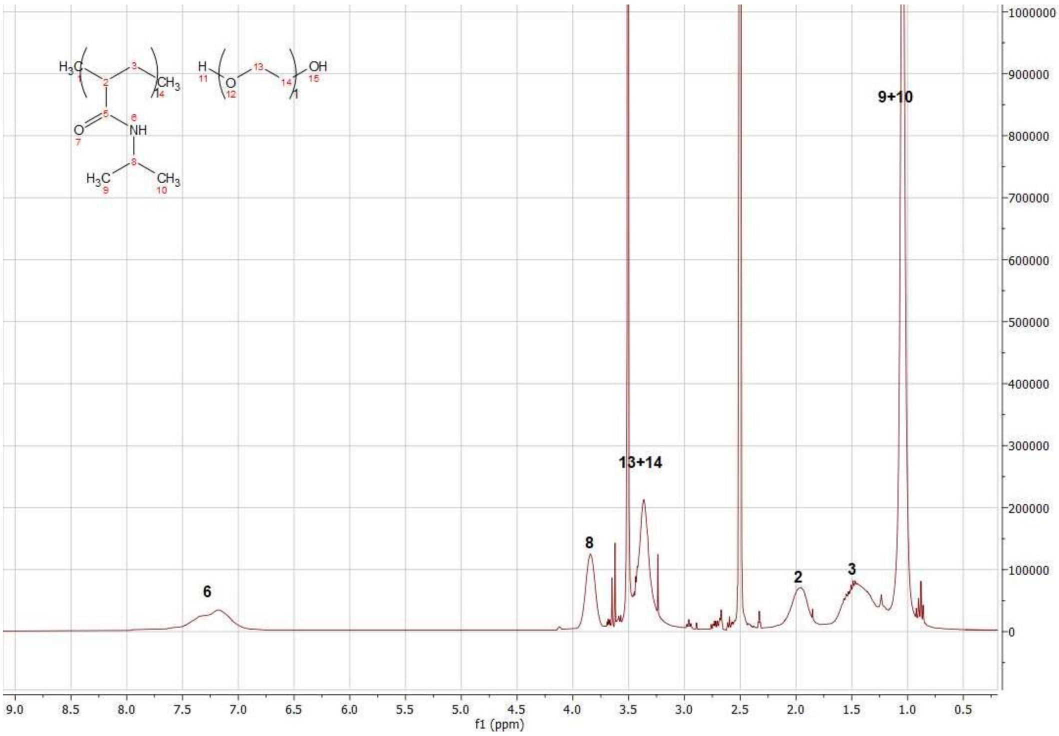

Figure S15. ^{1}H NMR (400 MHz, CD_3OD) spectrum of the PEG-PNIPAM reference polymer.

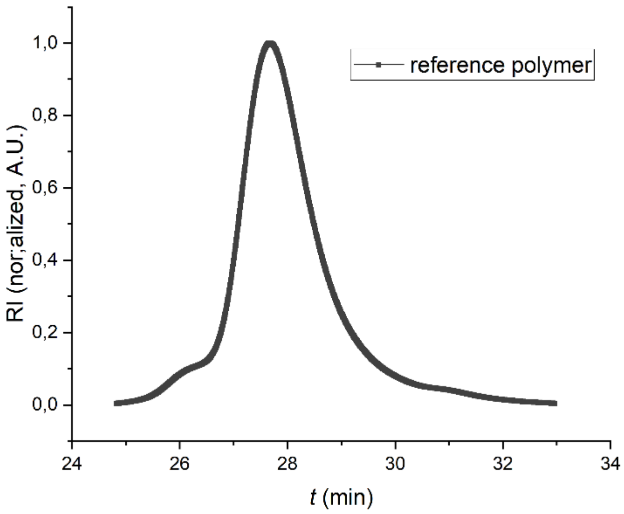

Figure S16. Size exclusion chromatogram of the PEG-PNIPAM reference polymer exploiting as mobile phase DMAc containing 50 mM LiCl at a flow rate of 0.5 mL/min. Molar mass and dispersity values were calculated using PMMA standards. The chromatogram was analysed using Agilent GPC Data Analysis Software (Agilent Technologies, CA). The evaluated M_w of the reference polymer is 46.7 kg/mol, the M_n is 39.0 kg/mol, resulting in a $Đ_M$ of 1.195.

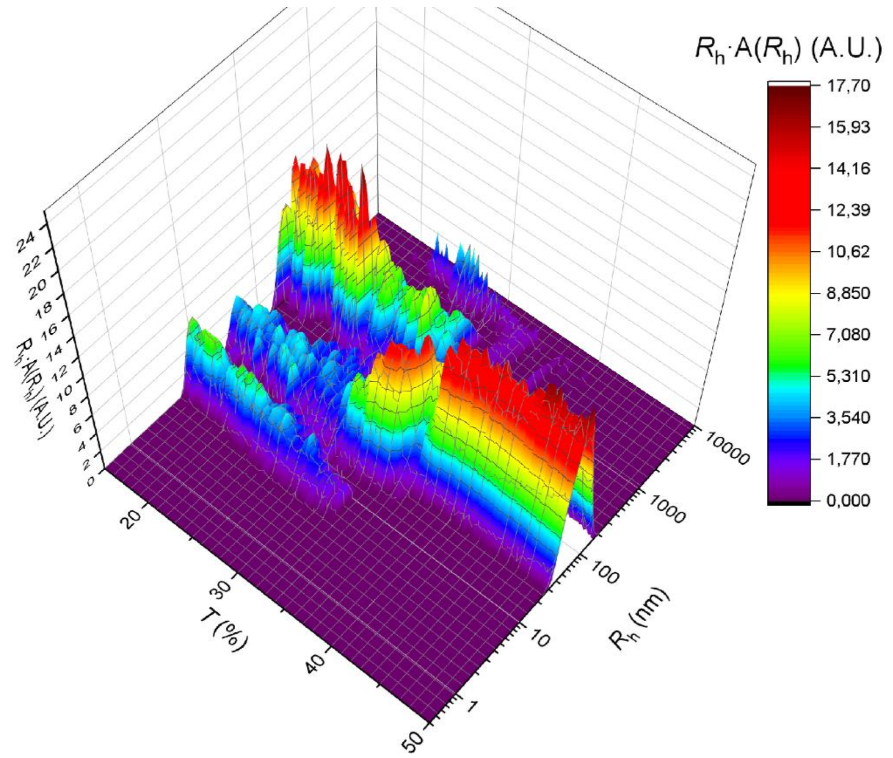

Figure S17. Temperature dependence of the self-assembly of the PEG-PNIPAM reference polymer in PBS measured via DLS. The equal-area representation (the vertical axis shows $R_h \cdot A(R_h)$, where $A(R_h)$ is the intensity distribution function of hydrodynamic radii R_h of particles in the sample).

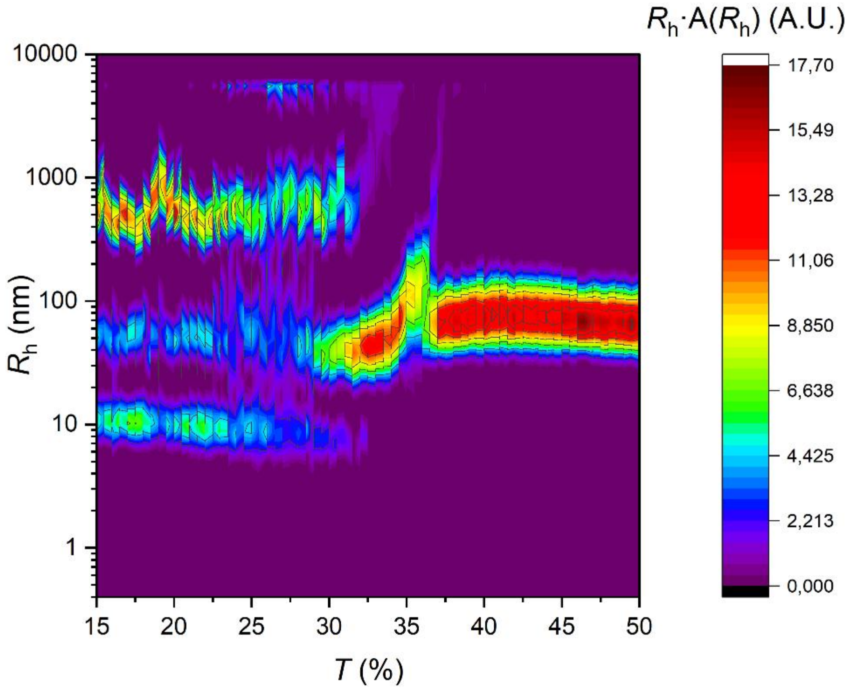

Figure S18. Temperature dependence of the self-assembly of the PEG-PNIPAM reference polymer in PBS measured via DLS. The equal-area representation (the vertical axis shows $R_h \cdot A(R_h)$, where $A(R_h)$ is the intensity distribution function of hydrodynamic radii R_h of particles in the sample).

S7.2. pKa evaluation of PAATIPA

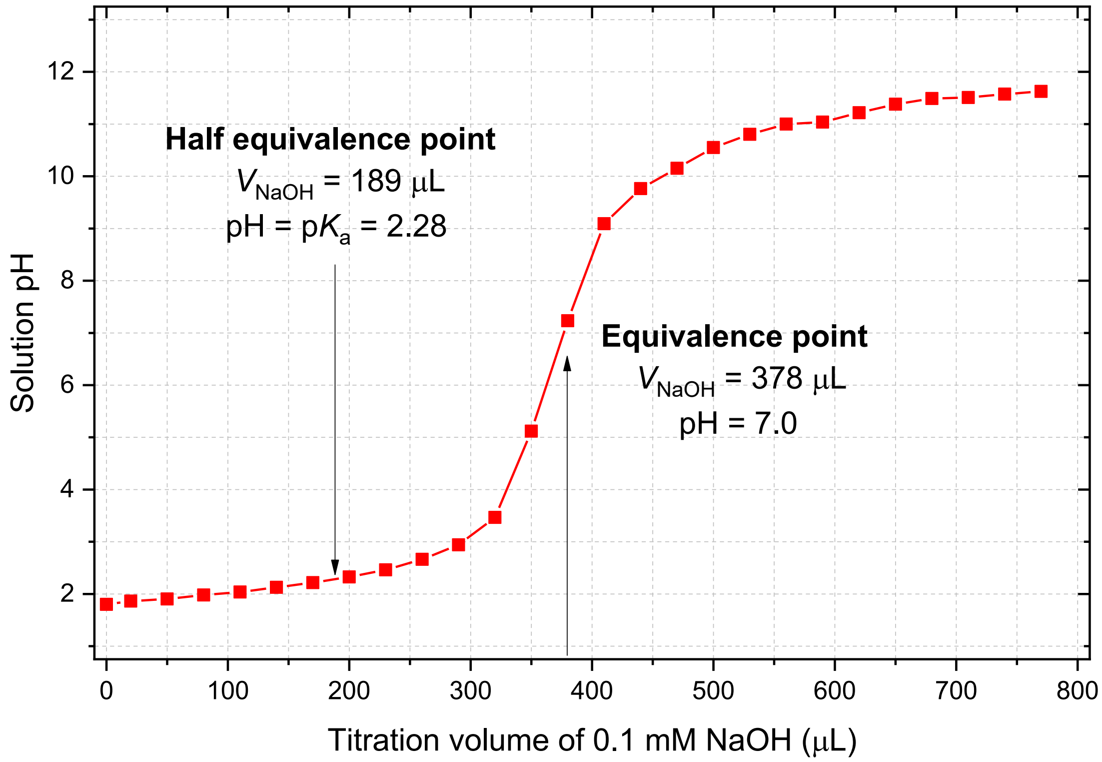

Figure 119. Evaluated pKa of the PAATIPA homopolymer. The polymer was titrated with 0.1 mM NaOH at PAATIPA concentration of 10 mg/mL in ultrapure water.

S7.3. Examples of cationic APIs

Table S6. Examples of cationic drugs and their applications.

Drug	Biomedical applications	Cationic groups
Doxorubicin	Chemotherapy	Primary amine group
Lidocaine	Local anesthetic	Tertiary amine
Benzydamine	Anti-inflammatory	Tertiary amine
Chlorhexidine	Antiseptic	Amine and imine groups
Dimetindene	Antihistaminic	Tertiary amine
Gentamicin	Antibiotic	Multiple amine groups
Tobramycin	Antibiotic	Multiple amine groups
Amikacin	Antibiotic	Multiple amine groups

Table S7. Examples of cationic proteins and their applications.

Peptide	Biomedical applications
LL-37	Human antimicrobial peptide
CXCL	Chemoatractants – immunomodulators
Lysozyme	Antibiotic
Polymyxin B	Antibacterial (enzyme)
Melittin	Animal toxin, supress heamolitic activity

S7.4. Calculations of DPs and PAATIPA and iodine content

S7.2.1. Determination of fractions of PNIPAM and PAATIPA blocks using ^{1}H NMR spectroscopy

The fractions of PNIPAM and PAATIPA blocks were determined from the integrated ^{1}H NMR signals. First, the peak at $\delta = 3.68$ ppm (assigned to proton "8" in PNIPAM) was set as an internal reference and normalized to an integral value of 1. The integrated area corresponding to protons "2+12" and "3+13" in the polymer backbone of PNIPAM sums to 3.055 (experimentally evaluated as average for both PNIPAM macroCTAs). Any excess above 3.055 in that same region is attributed to PAATIPA.

The difference between the observed integral of "2+12" + "3+13" and 3.055 (D) was divided by 3 to determine the contribution per-hydrogen of PAATIPA. To find the fraction of PNIPAM, the reference integral of proton "8" (set to 1) was divided by the sum of itself plus the per-hydrogen PAATIPA contribution. Similarly, the fraction of PAATIPA was obtained by dividing the PAATIPA contribution by that total.

Next, each fraction can be recalculated to molar (*mol* %) and weight percentage (*wt* %).

Related equations:

$$D = I_{\text{“2+12” + “3+13”}} - 3$$

$$f_{PNIPAM} = \frac{I_8}{I_8 + \frac{D}{3}}$$

$$f_{PAATIPA} = \frac{\frac{D}{3}}{I_8 + \frac{D}{3}}$$

S7.2.2. Estimation of DP of diblock copolymers using elemental analysis and SEC measurements

The degree of polymerization (DP) and molar mass, M_n, of the PAATIPA block in diblock copolymers was estimated using elemental analysis. First, the iodine weight percentage (*wt* %) from elemental analysis was obtained for each polymer. The weight percentage of AATIPA was determined by dividing the iodine *wt* % by the fraction of iodine in AATIPA (AATIPA has 62.12 *wt* % of iodine).

Next, the molar mass of the PAATIPA block in diblock copolymers (M_n, PAATIPA) was estimated from the obtained number-weighted molar mass, M_n (evaluated experimentally by SEC), of the respective PNIPAM and PAATIPA weight fractions, (*f*) from elemental analysis. Finally, the degree of polymerization (DP) of the PAATIPA block was obtained by dividing the estimated M_n of PAATIPA by the relative molecular mass of AATIPA (621.8 g/mol). The real DP of the resulting polymer also includes the DP of the respective PNIPAM-based macroCTA.

Related equations:

$$wt\,\%_{\text{PAATIPA}} = \frac{I(\text{wt }\%)}{0.6212}$$

$$wt\,\%_{\text{PNIPAM}} = 100 - \text{wt}\%_{\text{PAATIPA}}$$

$$f_{PAATIPA} = \frac{\text{wt}\%_{\text{PAATIPA}}}{100} \quad f_{PNIPAM} = \frac{\text{wt}\%_{\text{PN}IPAM}}{100}$$

$$M_{n,\text{PAATIPA}} = \frac{M_{n,\text{PNIPAM}}}{f_{PNIPAM}} \times f_{PAATIPA}$$

$$\mathrm{DP_{PAATIPA}} = \frac{M_{n,\mathrm{PAATIPA}}}{M_{\mathrm{r,PAATIPA}}} \quad \mathrm{DP_{PNIPAM}} = \frac{M_{n,\mathrm{PNIPAM}}}{M_{\mathrm{r,PNIPAM}}}$$

$$\mathrm{DP} = \mathrm{DP_{PAATIPA}} + \mathrm{DP_{PNIPAM}}$$

S7.2.2. Estimation of DP of PAATIPA in statistical copolymers using elemental analysis and SEC measurements

The degree of polymerization (DP) of the statistical PNIPAM-*s*-PAATIPA copolymers was estimated using the experimentally obtained M_n of the resulting polymers and elemental analysis in order to determine the ratio between the monomers. First, the iodine weight percentage (*wt* %) from elemental analysis was obtained for each polymer. The weight percentage of AATIPA was determined by dividing the iodine *wt* % by the fraction of iodine in AATIPA (AATIPA has 62.12 *wt* % of iodine).

Related equations:

$$wt\ \%_{\mathrm{PAATIPA}} = \frac{I(\mathrm{wt}\ \%)}{0.6212}$$

$$wt\ \%_{\mathrm{PNIPAM}} = 100 - \mathrm{wt}\%_{\mathrm{PAATIPA}}$$

$$f_{PAATIPA} = \frac{\mathrm{wt}\ \%_{\mathrm{PAATIPA}}}{100} \quad f_{PNIPAM} = \frac{\mathrm{wt}\ \%_{\mathrm{PN}IPAM}}{100}$$

$$\mathrm{DP} = \frac{M_n}{(M_{\mathrm{r,PAATIPA}} \times f_{PAATIPA}) + (M_{\mathrm{r,PNIPAM}} \times f_{\mathrm{PNIPAM}})}$$

S8. Statistical analysis

Table S6. Evaluated data from 2-way ANOVA analysis (mixed model) from MTS assay. Turkey's multiple comparison test, with individual variances computed for each comparison.

Within each row. compare columns (simple effects within rows)					
Number of families	**3**				
Number of comparisons per family	**78**				
Alpha	**0.05**				
Tukey's multiple comparisons test	**Mean Diff.**	**95.00% CI of diff.**	**Significant?**	**Summary**	**Adjusted P Value**
D1					
CTRL vs. B3_0.5	20.63	-2.425 to 43.69	No	ns	0.1261
CTRL vs. B3_1	15.98	-7.075 to 39.04	No	ns	0.4761
CTRL vs. B3_2	17.84	-5.215 to 40.90	No	ns	0.3026
CTRL vs. B6_0.5	28.58	5.519 to 51.63	Yes	**	0.0039
CTRL vs. B6_1	27.34	4.279 to 50.39	Yes	**	0.0073
CTRL vs. B6_2	29	5.942 to 52.06	Yes	**	0.0032
CTRL vs. S5_0.5	13.16	-9.898 to 36.22	No	ns	0.7604
CTRL vs. S5_1	3.073	-19.98 to 26.13	No	ns	>0.9999
CTRL vs. S5_2	1.67	-21.39 to 24.73	No	ns	>0.9999
CTRL vs. S6_0.5	28.22	5.165 to 51.28	Yes	**	0.0047
CTRL vs. S6_1	20.63	-2.428 to 43.69	No	ns	0.1262
CTRL vs. S6_2	13.13	-9.928 to 36.19	No	ns	0.7631
B3_0.5 vs. B3_1	-4.65	-27.71 to 18.41	No	ns	>0.9999
B3_0.5 vs. B3_2	-2.79	-25.85 to 20.27	No	ns	>0.9999
B3_0.5 vs. B6_0.5	7.943	-15.11 to 31.00	No	ns	0.9931
B3_0.5 vs. B6_1	6.703	-16.35 to 29.76	No	ns	0.9986
B3_0.5 vs. B6_2	8.367	-14.69 to 31.42	No	ns	0.9892
B3_0.5 vs. S5_0.5	-7.473	-30.53 to 15.58	No	ns	0.996
B3_0.5 vs. S5_1	-17.56	-40.62 to 5.498	No	ns	0.3265
B3_0.5 vs. S5_2	-18.96	-42.02 to 4.095	No	ns	0.2186
B3_0.5 vs. S6_0.5	7.59	-15.47 to 30.65	No	ns	0.9954
B3_0.5 vs. S6_1	-0.00333	-23.06 to 23.05	No	ns	>0.9999
B3_0.5 vs. S6_2	-7.503	-30.56 to 15.55	No	ns	0.9959
B3_1 vs. B3_2	1.86	-21.20 to 24.92	No	ns	>0.9999
B3_1 vs. B6_0.5	12.59	-10.46 to 35.65	No	ns	0.809
B3_1 vs. B6_1	11.35	-11.70 to 34.41	No	ns	0.8955
B3_1 vs. B6_2	13.02	-10.04 to 36.07	No	ns	0.7731
B3_1 vs. S5_0.5	-2.823	-25.88 to 20.23	No	ns	>0.9999
B3_1 vs. S5_1	-12.91	-35.97 to 10.15	No	ns	0.7824
B3_1 vs. S5_2	-14.31	-37.37 to 8.745	No	ns	0.6488
B3_1 vs. S6_0.5	12.24	-10.82 to 35.30	No	ns	0.8366
B3_1 vs. S6_1	4.647	-18.41 to 27.70	No	ns	>0.9999

B3_1 vs. S6_2	-2.853	-25.91 to 20.20	No	ns	>0.9999
B3_2 vs. B6_0.5	10.73	-12.32 to 33.79	No	ns	0.9275
B3_2 vs. B6_1	9.493	-13.56 to 32.55	No	ns	0.9701
B3_2 vs. B6_2	11.16	-11.90 to 34.21	No	ns	0.9065
B3_2 vs. S5_0.5	-4.683	-27.74 to 18.37	No	ns	>0.9999
B3_2 vs. S5_1	-14.77	-37.83 to 8.288	No	ns	0.6018
B3_2 vs. S5_2	-16.17	-39.23 to 6.885	No	ns	0.4569
B3_2 vs. S6_0.5	10.38	-12.68 to 33.44	No	ns	0.9424
B3_2 vs. S6_1	2.787	-20.27 to 25.84	No	ns	>0.9999
B3_2 vs. S6_2	-4.713	-27.77 to 18.34	No	ns	>0.9999
B6_0.5 vs. B6_1	-1.24	-24.30 to 21.82	No	ns	>0.9999
B6_0.5 vs. B6_2	0.4233	-22.63 to 23.48	No	ns	>0.9999
B6_0.5 vs. S5_0.5	-15.42	-38.47 to 7.641	No	ns	0.5345
B6_0.5 vs. S5_1	-25.5	-48.56 to -2.445	Yes	*	0.0173
B6_0.5 vs. S5_2	-26.91	-49.96 to -3.849	Yes	**	0.009
B6_0.5 vs. S6_0.5	-0.3533	-23.41 to 22.70	No	ns	>0.9999
B6_0.5 vs. S6_1	-7.947	-31.00 to 15.11	No	ns	0.9931
B6_0.5 vs. S6_2	-15.45	-38.50 to 7.611	No	ns	0.5314
B6_1 vs. B6_2	1.663	-21.39 to 24.72	No	ns	>0.9999
B6_1 vs. S5_0.5	-14.18	-37.23 to 8.881	No	ns	0.6627
B6_1 vs. S5_1	-24.26	-47.32 to -1.205	Yes	*	0.0301
B6_1 vs. S5_2	-25.67	-48.72 to -2.609	Yes	*	0.0161
B6_1 vs. S6_0.5	0.8867	-22.17 to 23.94	No	ns	>0.9999
B6_1 vs. S6_1	-6.707	-29.76 to 16.35	No	ns	0.9986
B6_1 vs. S6_2	-14.21	-37.26 to 8.851	No	ns	0.6596
B6_2 vs. S5_0.5	-15.84	-38.90 to 7.218	No	ns	0.4908
B6_2 vs. S5_1	-25.93	-48.98 to -2.869	Yes	*	0.0142
B6_2 vs. S5_2	-27.33	-50.39 to -4.272	Yes	**	0.0073
B6_2 vs. S6_0.5	-0.7767	-23.83 to 22.28	No	ns	>0.9999
B6_2 vs. S6_1	-8.37	-31.43 to 14.69	No	ns	0.9892
B6_2 vs. S6_2	-15.87	-38.93 to 7.188	No	ns	0.4877
S5_0.5 vs. S5_1	-10.09	-33.14 to 12.97	No	ns	0.953
S5_0.5 vs. S5_2	-11.49	-34.55 to 11.57	No	ns	0.8874
S5_0.5 vs. S6_0.5	15.06	-7.995 to 38.12	No	ns	0.5713
S5_0.5 vs. S6_1	7.47	-15.59 to 30.53	No	ns	0.996
S5_0.5 vs. S6_2	-0.03	-23.09 to 23.03	No	ns	>0.9999
S5_1 vs. S5_2	-1.403	-24.46 to 21.65	No	ns	>0.9999
S5_1 vs. S6_0.5	25.15	2.092 to 48.21	Yes	*	0.0203
S5_1 vs. S6_1	17.56	-5.501 to 40.61	No	ns	0.3268
S5_1 vs. S6_2	10.06	-13.00 to 33.11	No	ns	0.954
S5_2 vs. S6_0.5	26.55	3.495 to 49.61	Yes	*	0.0106
S5_2 vs. S6_1	18.96	-4.098 to 42.02	No	ns	0.2189
S5_2 vs. S6_2	11.46	-11.60 to 34.52	No	ns	0.8892
S6_0.5 vs. S6_1	-7.593	-30.65 to 15.46	No	ns	0.9954

S6_0.5 vs. S6_2	-15.09	-38.15 to 7.965	No	ns	0.5681
S6_1 vs. S6_2	-7.5	-30.56 to 15.56	No	ns	0.9959
D3					
CTRL vs. B3_0.5	-5.47	-28.53 to 17.59	No	ns	0.9998
CTRL vs. B3_1	12.12	-10.93 to 35.18	No	ns	0.8452
CTRL vs. B3_2	18.29	-4.771 to 41.34	No	ns	0.2673
CTRL vs. B6_0.5	36.7	13.64 to 59.76	Yes	****	<0.0001
CTRL vs. B6_1	40.65	17.60 to 63.71	Yes	****	<0.0001
CTRL vs. B6_2	52.8	29.75 to 75.86	Yes	****	<0.0001
CTRL vs. S5_0.5	-16.21	-39.27 to 6.848	No	ns	0.4533
CTRL vs. S5_1	-1.65	-24.71 to 21.41	No	ns	>0.9999
CTRL vs. S5_2	-9.733	-32.79 to 13.32	No	ns	0.9639
CTRL vs. S6_0.5	-15.39	-38.45 to 7.665	No	ns	0.5369
CTRL vs. S6_1	-15.76	-38.82 to 7.295	No	ns	0.4986
CTRL vs. S6_2	0.003333	-23.05 to 23.06	No	ns	>0.9999
B3_0.5 vs. B3_1	17.59	-5.465 to 40.65	No	ns	0.3237
B3_0.5 vs. B3_2	23.76	0.6987 to 46.81	Yes	*	0.0374
B3_0.5 vs. B6_0.5	42.17	19.11 to 65.23	Yes	****	<0.0001
B3_0.5 vs. B6_1	46.12	23.07 to 69.18	Yes	****	<0.0001
B3_0.5 vs. B6_2	58.27	35.22 to 81.33	Yes	****	<0.0001
B3_0.5 vs. S5_0.5	-10.74	-33.80 to 12.32	No	ns	0.9272
B3_0.5 vs. S5_1	3.82	-19.24 to 26.88	No	ns	>0.9999
B3_0.5 vs. S5_2	-4.263	-27.32 to 18.79	No	ns	>0.9999
B3_0.5 vs. S6_0.5	-9.923	-32.98 to 13.13	No	ns	0.9583
B3_0.5 vs. S6_1	-10.29	-33.35 to 12.76	No	ns	0.9457
B3_0.5 vs. S6_2	5.473	-17.58 to 28.53	No	ns	0.9998
B3_1 vs. B3_2	6.163	-16.89 to 29.22	No	ns	0.9994
B3_1 vs. B6_0.5	24.58	1.519 to 47.63	Yes	*	0.0262
B3_1 vs. B6_1	28.53	5.472 to 51.59	Yes	**	0.004
B3_1 vs. B6_2	40.68	17.62 to 63.74	Yes	****	<0.0001
B3_1 vs. S5_0.5	-28.33	-51.39 to -5.275	Yes	**	0.0044
B3_1 vs. S5_1	-13.77	-36.83 to 9.285	No	ns	0.7027
B3_1 vs. S5_2	-21.86	-44.91 to 1.201	No	ns	0.0804
B3_1 vs. S6_0.5	-27.52	-50.57 to -4.459	Yes	**	0.0067
B3_1 vs. S6_1	-27.89	-50.94 to -4.829	Yes	**	0.0055
B3_1 vs. S6_2	-12.12	-35.18 to 10.94	No	ns	0.8455
B3_2 vs. B6_0.5	18.41	-4.645 to 41.47	No	ns	0.2577
B3_2 vs. B6_1	22.37	-0.6913 to 45.42	No	ns	0.066
B3_2 vs. B6_2	34.52	11.46 to 57.57	Yes	***	0.0002
B3_2 vs. S5_0.5	-34.5	-57.55 to -11.44	Yes	***	0.0002
B3_2 vs. S5_1	-19.94	-42.99 to 3.121	No	ns	0.1601
B3_2 vs. S5_2	-28.02	-51.08 to -4.962	Yes	**	0.0052
B3_2 vs. S6_0.5	-33.68	-56.74 to -10.62	Yes	***	0.0003

B3_2 vs. S6_1	-34.05	-57.11 to -10.99	Yes	***	0.0002
B3_2 vs. S6_2	-18.28	-41.34 to 4.775	No	ns	0.2675
B6_0.5 vs. B6_1	3.953	-19.10 to 27.01	No	ns	>0.9999
B6_0.5 vs. B6_2	16.1	-6.955 to 39.16	No	ns	0.464
B6_0.5 vs. S5_0.5	-52.91	-75.97 to -29.85	Yes	****	<0.0001
B6_0.5 vs. S5_1	-38.35	-61.41 to -15.29	Yes	****	<0.0001
B6_0.5 vs. S5_2	-46.43	-69.49 to -23.38	Yes	****	<0.0001
B6_0.5 vs. S6_0.5	-52.09	-75.15 to -29.04	Yes	****	<0.0001
B6_0.5 vs. S6_1	-52.46	-75.52 to -29.41	Yes	****	<0.0001
B6_0.5 vs. S6_2	-36.7	-59.75 to -13.64	Yes	****	<0.0001
B6_1 vs. B6_2	12.15	-10.91 to 35.21	No	ns	0.8433
B6_1 vs. S5_0.5	-56.86	-79.92 to -33.81	Yes	****	<0.0001
B6_1 vs. S5_1	-42.3	-65.36 to -19.25	Yes	****	<0.0001
B6_1 vs. S5_2	-50.39	-73.44 to -27.33	Yes	****	<0.0001
B6_1 vs. S6_0.5	-56.05	-79.10 to -32.99	Yes	****	<0.0001
B6_1 vs. S6_1	-56.42	-79.47 to -33.36	Yes	****	<0.0001
B6_1 vs. S6_2	-40.65	-63.71 to -17.59	Yes	****	<0.0001
B6_2 vs. S5_0.5	-69.01	-92.07 to -45.96	Yes	****	<0.0001
B6_2 vs. S5_1	-54.45	-77.51 to -31.40	Yes	****	<0.0001
B6_2 vs. S5_2	-62.54	-85.59 to -39.48	Yes	****	<0.0001
B6_2 vs. S6_0.5	-68.2	-91.25 to -45.14	Yes	****	<0.0001
B6_2 vs. S6_1	-68.57	-91.62 to -45.51	Yes	****	<0.0001
B6_2 vs. S6_2	-52.8	-75.86 to -29.74	Yes	****	<0.0001
S5_0.5 vs. S5_1	14.56	-8.498 to 37.62	No	ns	0.6235
S5_0.5 vs. S5_2	6.477	-16.58 to 29.53	No	ns	0.999
S5_0.5 vs. S6_0.5	0.8167	-22.24 to 23.87	No	ns	>0.9999
S5_0.5 vs. S6_1	0.4467	-22.61 to 23.50	No	ns	>0.9999
S5_0.5 vs. S6_2	16.21	-6.845 to 39.27	No	ns	0.4529
S5_1 vs. S5_2	-8.083	-31.14 to 14.97	No	ns	0.992
S5_1 vs. S6_0.5	-13.74	-36.80 to 9.315	No	ns	0.7056
S5_1 vs. S6_1	-14.11	-37.17 to 8.945	No	ns	0.669
S5_1 vs. S6_2	1.653	-21.40 to 24.71	No	ns	>0.9999
S5_2 vs. S6_0.5	-5.66	-28.72 to 17.40	No	ns	0.9997
S5_2 vs. S6_1	-6.03	-29.09 to 17.03	No	ns	0.9995
S5_2 vs. S6_2	9.737	-13.32 to 32.79	No	ns	0.9638
S6_0.5 vs. S6_1	-0.37	-23.43 to 22.69	No	ns	>0.9999
S6_0.5 vs. S6_2	15.4	-7.661 to 38.45	No	ns	0.5366
S6_1 vs. S6_2	15.77	-7.291 to 38.82	No	ns	0.4983
D7					
CTRL vs. B3_0.5	-12.16	-35.22 to 10.89	No	ns	0.8423
CTRL vs. B3_1	41.94	18.88 to 64.99	Yes	****	<0.0001
CTRL vs. B3_2	63.32	40.27 to 86.38	Yes	****	<0.0001
CTRL vs. B6_0.5	92.62	69.56 to 115.7	Yes	****	<0.0001

CTRL vs. B6_1	110.5	87.44 to 133.6	Yes	****	<0.0001
CTRL vs. B6_2	116.1	93.03 to 139.1	Yes	****	<0.0001
CTRL vs. S5_0.5	-38.9	-61.95 to -15.84	Yes	****	<0.0001
CTRL vs. S5_1	-25.66	-48.71 to -2.599	Yes	*	0.0161
CTRL vs. S5_2	-14.23	-37.29 to 8.825	No	ns	0.6569
CTRL vs. S6_0.5	-23.69	-46.75 to -0.6354	Yes	*	0.0384
CTRL vs. S6_1	-40.25	-63.31 to -17.19	Yes	****	<0.0001
CTRL vs. S6_2	-18.23	-41.29 to 4.828	No	ns	0.2716
B3_0.5 vs. B3_1	54.1	31.04 to 77.16	Yes	****	<0.0001
B3_0.5 vs. B3_2	75.49	52.43 to 98.54	Yes	****	<0.0001
B3_0.5 vs. B6_0.5	104.8	81.72 to 127.8	Yes	****	<0.0001
B3_0.5 vs. B6_1	122.7	99.61 to 145.7	Yes	****	<0.0001
B3_0.5 vs. B6_2	128.3	105.2 to 151.3	Yes	****	<0.0001
B3_0.5 vs. S5_0.5	-26.73	-49.79 to -3.675	Yes	**	0.0097
B3_0.5 vs. S5_1	-13.49	-36.55 to 9.565	No	ns	0.7296
B3_0.5 vs. S5_2	-2.07	-25.13 to 20.99	No	ns	>0.9999
B3_0.5 vs. S6_0.5	-11.53	-34.59 to 11.53	No	ns	0.885
B3_0.5 vs. S6_1	-28.09	-51.14 to -5.029	Yes	**	0.005
B3_0.5 vs. S6_2	-6.067	-29.12 to 16.99	No	ns	0.9995
B3_1 vs. B3_2	21.39	-1.671 to 44.44	No	ns	0.096
B3_1 vs. B6_0.5	50.68	27.62 to 73.74	Yes	****	<0.0001
B3_1 vs. B6_1	68.56	45.51 to 91.62	Yes	****	<0.0001
B3_1 vs. B6_2	74.15	51.10 to 97.21	Yes	****	<0.0001
B3_1 vs. S5_0.5	-80.83	-103.9 to -57.78	Yes	****	<0.0001
B3_1 vs. S5_1	-67.59	-90.65 to -44.54	Yes	****	<0.0001
B3_1 vs. S5_2	-56.17	-79.23 to -33.11	Yes	****	<0.0001
B3_1 vs. S6_0.5	-65.63	-88.69 to -42.57	Yes	****	<0.0001
B3_1 vs. S6_1	-82.19	-105.2 to -59.13	Yes	****	<0.0001
B3_1 vs. S6_2	-60.17	-83.22 to -37.11	Yes	****	<0.0001
B3_2 vs. B6_0.5	29.29	6.235 to 52.35	Yes	**	0.0027
B3_2 vs. B6_1	47.18	24.12 to 70.23	Yes	****	<0.0001
B3_2 vs. B6_2	52.77	29.71 to 75.82	Yes	****	<0.0001
B3_2 vs. S5_0.5	-102.2	-125.3 to -79.16	Yes	****	<0.0001
B3_2 vs. S5_1	-88.98	-112.0 to -65.92	Yes	****	<0.0001
B3_2 vs. S5_2	-77.56	-100.6 to -54.50	Yes	****	<0.0001
B3_2 vs. S6_0.5	-87.02	-110.1 to -63.96	Yes	****	<0.0001
B3_2 vs. S6_1	-103.6	-126.6 to -80.52	Yes	****	<0.0001
B3_2 vs. S6_2	-81.55	-104.6 to -58.50	Yes	****	<0.0001
B6_0.5 vs. B6_1	17.88	-5.175 to 40.94	No	ns	0.2993
B6_0.5 vs. B6_2	23.47	0.4154 to 46.53	Yes	*	0.0421
B6_0.5 vs. S5_0.5	-131.5	-154.6 to -108.5	Yes	****	<0.0001
B6_0.5 vs. S5_1	-118.3	-141.3 to -95.22	Yes	****	<0.0001
B6_0.5 vs. S5_2	-106.9	-129.9 to -83.79	Yes	****	<0.0001
B6_0.5 vs. S6_0.5	-116.3	-139.4 to -93.25	Yes	****	<0.0001

B6_0.5 vs. S6_1	-132.9	-155.9 to -109.8	Yes	****	<0.0001
B6_0.5 vs. S6_2	-110.8	-133.9 to -87.79	Yes	****	<0.0001
B6_1 vs. B6_2	5.59	-17.47 to 28.65	No	ns	0.9998
B6_1 vs. S5_0.5	-149.4	-172.5 to -126.3	Yes	****	<0.0001
B6_1 vs. S5_1	-136.2	-159.2 to -113.1	Yes	****	<0.0001
B6_1 vs. S5_2	-124.7	-147.8 to -101.7	Yes	****	<0.0001
B6_1 vs. S6_0.5	-134.2	-157.3 to -111.1	Yes	****	<0.0001
B6_1 vs. S6_1	-150.8	-173.8 to -127.7	Yes	****	<0.0001
B6_1 vs. S6_2	-128.7	-151.8 to -105.7	Yes	****	<0.0001
B6_2 vs. S5_0.5	-155	-178.0 to -131.9	Yes	****	<0.0001
B6_2 vs. S5_1	-141.7	-164.8 to -118.7	Yes	****	<0.0001
B6_2 vs. S5_2	-130.3	-153.4 to -107.3	Yes	****	<0.0001
B6_2 vs. S6_0.5	-139.8	-162.8 to -116.7	Yes	****	<0.0001
B6_2 vs. S6_1	-156.3	-179.4 to -133.3	Yes	****	<0.0001
B6_2 vs. S6_2	-134.3	-157.4 to -111.3	Yes	****	<0.0001
S5_0.5 vs. S5_1	13.24	-9.818 to 36.30	No	ns	0.7531
S5_0.5 vs. S5_2	24.66	1.605 to 47.72	Yes	*	0.0252
S5_0.5 vs. S6_0.5	15.2	-7.855 to 38.26	No	ns	0.5567
S5_0.5 vs. S6_1	-1.353	-24.41 to 21.70	No	ns	>0.9999
S5_0.5 vs. S6_2	20.67	-2.391 to 43.72	No	ns	0.1246
S5_1 vs. S5_2	11.42	-11.63 to 34.48	No	ns	0.8914
S5_1 vs. S6_0.5	1.963	-21.09 to 25.02	No	ns	>0.9999
S5_1 vs. S6_1	-14.59	-37.65 to 8.465	No	ns	0.6201
S5_1 vs. S6_2	7.427	-15.63 to 30.48	No	ns	0.9962
S5_2 vs. S6_0.5	-9.46	-32.52 to 13.60	No	ns	0.9709
S5_2 vs. S6_1	-26.02	-49.07 to -2.959	Yes	*	0.0137
S5_2 vs. S6_2	-3.997	-27.05 to 19.06	No	ns	>0.9999
S6_0.5 vs. S6_1	-16.56	-39.61 to 6.501	No	ns	0.419
S6_0.5 vs. S6_2	5.463	-17.59 to 28.52	No	ns	0.9998
S6_1 vs. S6_2	22.02	-1.038 to 45.08	No	ns	0.0756
Test details	**Mean 1**	**Mean 2**	**Mean Diff.**	**SE of diff.**	**N1**
D1					
CTRL vs. B3_0.5	100	79.37	20.63	6.747	3
CTRL vs. B3_1	100	84.02	15.98	6.747	3
CTRL vs. B3_2	100	82.16	17.84	6.747	3
CTRL vs. B6_0.5	100	71.42	28.58	6.747	3
CTRL vs. B6_1	100	72.66	27.34	6.747	3
CTRL vs. B6_2	100	71	29	6.747	3
CTRL vs. S5_0.5	100	86.84	13.16	6.747	3
CTRL vs. S5_1	100	96.93	3.073	6.747	3
CTRL vs. S5_2	100	98.33	1.67	6.747	3

CTRL vs. S6_0.5	100	71.78	28.22	6.747	3
CTRL vs. S6_1	100	79.37	20.63	6.747	3
CTRL vs. S6_2	100	86.87	13.13	6.747	3
B3_0.5 vs. B3_1	79.37	84.02	-4.65	6.747	3
B3_0.5 vs. B3_2	79.37	82.16	-2.79	6.747	3
B3_0.5 vs. B6_0.5	79.37	71.42	7.943	6.747	3
B3_0.5 vs. B6_1	79.37	72.66	6.703	6.747	3
B3_0.5 vs. B6_2	79.37	71	8.367	6.747	3
B3_0.5 vs. S5_0.5	79.37	86.84	-7.473	6.747	3
B3_0.5 vs. S5_1	79.37	96.93	-17.56	6.747	3
B3_0.5 vs. S5_2	79.37	98.33	-18.96	6.747	3
B3_0.5 vs. S6_0.5	79.37	71.78	7.59	6.747	3
B3_0.5 vs. S6_1	79.37	79.37	-0.00333	6.747	3
B3_0.5 vs. S6_2	79.37	86.87	-7.503	6.747	3
B3_1 vs. B3_2	84.02	82.16	1.86	6.747	3
B3_1 vs. B6_0.5	84.02	71.42	12.59	6.747	3
B3_1 vs. B6_1	84.02	72.66	11.35	6.747	3
B3_1 vs. B6_2	84.02	71	13.02	6.747	3
B3_1 vs. S5_0.5	84.02	86.84	-2.823	6.747	3
B3_1 vs. S5_1	84.02	96.93	-12.91	6.747	3
B3_1 vs. S5_2	84.02	98.33	-14.31	6.747	3
B3_1 vs. S6_0.5	84.02	71.78	12.24	6.747	3
B3_1 vs. S6_1	84.02	79.37	4.647	6.747	3
B3_1 vs. S6_2	84.02	86.87	-2.853	6.747	3
B3_2 vs. B6_0.5	82.16	71.42	10.73	6.747	3
B3_2 vs. B6_1	82.16	72.66	9.493	6.747	3
B3_2 vs. B6_2	82.16	71	11.16	6.747	3
B3_2 vs. S5_0.5	82.16	86.84	-4.683	6.747	3
B3_2 vs. S5_1	82.16	96.93	-14.77	6.747	3
B3_2 vs. S5_2	82.16	98.33	-16.17	6.747	3
B3_2 vs. S6_0.5	82.16	71.78	10.38	6.747	3
B3_2 vs. S6_1	82.16	79.37	2.787	6.747	3
B3_2 vs. S6_2	82.16	86.87	-4.713	6.747	3
B6_0.5 vs. B6_1	71.42	72.66	-1.24	6.747	3
B6_0.5 vs. B6_2	71.42	71	0.4233	6.747	3
B6_0.5 vs. S5_0.5	71.42	86.84	-15.42	6.747	3
B6_0.5 vs. S5_1	71.42	96.93	-25.5	6.747	3
B6_0.5 vs. S5_2	71.42	98.33	-26.91	6.747	3
B6_0.5 vs. S6_0.5	71.42	71.78	-0.3533	6.747	3
B6_0.5 vs. S6_1	71.42	79.37	-7.947	6.747	3
B6_0.5 vs. S6_2	71.42	86.87	-15.45	6.747	3
B6_1 vs. B6_2	72.66	71	1.663	6.747	3
B6_1 vs. S5_0.5	72.66	86.84	-14.18	6.747	3
B6_1 vs. S5_1	72.66	96.93	-24.26	6.747	3

B6_1 vs. S5_2	72.66	98.33	-25.67	6.747	3
B6_1 vs. S6_0.5	72.66	71.78	0.8867	6.747	3
B6_1 vs. S6_1	72.66	79.37	-6.707	6.747	3
B6_1 vs. S6_2	72.66	86.87	-14.21	6.747	3
B6_2 vs. S5_0.5	71	86.84	-15.84	6.747	3
B6_2 vs. S5_1	71	96.93	-25.93	6.747	3
B6_2 vs. S5_2	71	98.33	-27.33	6.747	3
B6_2 vs. S6_0.5	71	71.78	-0.7767	6.747	3
B6_2 vs. S6_1	71	79.37	-8.37	6.747	3
B6_2 vs. S6_2	71	86.87	-15.87	6.747	3
S5_0.5 vs. S5_1	86.84	96.93	-10.09	6.747	3
S5_0.5 vs. S5_2	86.84	98.33	-11.49	6.747	3
S5_0.5 vs. S6_0.5	86.84	71.78	15.06	6.747	3
S5_0.5 vs. S6_1	86.84	79.37	7.47	6.747	3
S5_0.5 vs. S6_2	86.84	86.87	-0.03	6.747	3
S5_1 vs. S5_2	96.93	98.33	-1.403	6.747	3
S5_1 vs. S6_0.5	96.93	71.78	25.15	6.747	3
S5_1 vs. S6_1	96.93	79.37	17.56	6.747	3
S5_1 vs. S6_2	96.93	86.87	10.06	6.747	3
S5_2 vs. S6_0.5	98.33	71.78	26.55	6.747	3
S5_2 vs. S6_1	98.33	79.37	18.96	6.747	3
S5_2 vs. S6_2	98.33	86.87	11.46	6.747	3
S6_0.5 vs. S6_1	71.78	79.37	-7.593	6.747	3
S6_0.5 vs. S6_2	71.78	86.87	-15.09	6.747	3
S6_1 vs. S6_2	79.37	86.87	-7.5	6.747	3
D3					
CTRL vs. B3_0.5	156.7	162.2	-5.47	6.747	3
CTRL vs. B3_1	156.7	144.6	12.12	6.747	3
CTRL vs. B3_2	156.7	138.4	18.29	6.747	3
CTRL vs. B6_0.5	156.7	120	36.7	6.747	3
CTRL vs. B6_1	156.7	116.1	40.65	6.747	3
CTRL vs. B6_2	156.7	103.9	52.8	6.747	3
CTRL vs. S5_0.5	156.7	172.9	-16.21	6.747	3
CTRL vs. S5_1	156.7	158.4	-1.65	6.747	3
CTRL vs. S5_2	156.7	166.4	-9.733	6.747	3
CTRL vs. S6_0.5	156.7	172.1	-15.39	6.747	3
CTRL vs. S6_1	156.7	172.5	-15.76	6.747	3
CTRL vs. S6_2	156.7	156.7	0.003333	6.747	3
B3_0.5 vs. B3_1	162.2	144.6	17.59	6.747	3
B3_0.5 vs. B3_2	162.2	138.4	23.76	6.747	3
B3_0.5 vs. B6_0.5	162.2	120	42.17	6.747	3
B3_0.5 vs. B6_1	162.2	116.1	46.12	6.747	3
B3_0.5 vs. B6_2	162.2	103.9	58.27	6.747	3

B3_0.5 vs. S5_0.5	162.2	172.9	-10.74	6.747	3
B3_0.5 vs. S5_1	162.2	158.4	3.82	6.747	3
B3_0.5 vs. S5_2	162.2	166.4	-4.263	6.747	3
B3_0.5 vs. S6_0.5	162.2	172.1	-9.923	6.747	3
B3_0.5 vs. S6_1	162.2	172.5	-10.29	6.747	3
B3_0.5 vs. S6_2	162.2	156.7	5.473	6.747	3
B3_1 vs. B3_2	144.6	138.4	6.163	6.747	3
B3_1 vs. B6_0.5	144.6	120	24.58	6.747	3
B3_1 vs. B6_1	144.6	116.1	28.53	6.747	3
B3_1 vs. B6_2	144.6	103.9	40.68	6.747	3
B3_1 vs. S5_0.5	144.6	172.9	-28.33	6.747	3
B3_1 vs. S5_1	144.6	158.4	-13.77	6.747	3
B3_1 vs. S5_2	144.6	166.4	-21.86	6.747	3
B3_1 vs. S6_0.5	144.6	172.1	-27.52	6.747	3
B3_1 vs. S6_1	144.6	172.5	-27.89	6.747	3
B3_1 vs. S6_2	144.6	156.7	-12.12	6.747	3
B3_2 vs. B6_0.5	138.4	120	18.41	6.747	3
B3_2 vs. B6_1	138.4	116.1	22.37	6.747	3
B3_2 vs. B6_2	138.4	103.9	34.52	6.747	3
B3_2 vs. S5_0.5	138.4	172.9	-34.5	6.747	3
B3_2 vs. S5_1	138.4	158.4	-19.94	6.747	3
B3_2 vs. S5_2	138.4	166.4	-28.02	6.747	3
B3_2 vs. S6_0.5	138.4	172.1	-33.68	6.747	3
B3_2 vs. S6_1	138.4	172.5	-34.05	6.747	3
B3_2 vs. S6_2	138.4	156.7	-18.28	6.747	3
B6_0.5 vs. B6_1	120	116.1	3.953	6.747	3
B6_0.5 vs. B6_2	120	103.9	16.1	6.747	3
B6_0.5 vs. S5_0.5	120	172.9	-52.91	6.747	3
B6_0.5 vs. S5_1	120	158.4	-38.35	6.747	3
B6_0.5 vs. S5_2	120	166.4	-46.43	6.747	3
B6_0.5 vs. S6_0.5	120	172.1	-52.09	6.747	3
B6_0.5 vs. S6_1	120	172.5	-52.46	6.747	3
B6_0.5 vs. S6_2	120	156.7	-36.7	6.747	3
B6_1 vs. B6_2	116.1	103.9	12.15	6.747	3
B6_1 vs. S5_0.5	116.1	172.9	-56.86	6.747	3
B6_1 vs. S5_1	116.1	158.4	-42.3	6.747	3
B6_1 vs. S5_2	116.1	166.4	-50.39	6.747	3
B6_1 vs. S6_0.5	116.1	172.1	-56.05	6.747	3
B6_1 vs. S6_1	116.1	172.5	-56.42	6.747	3
B6_1 vs. S6_2	116.1	156.7	-40.65	6.747	3
B6_2 vs. S5_0.5	103.9	172.9	-69.01	6.747	3
B6_2 vs. S5_1	103.9	158.4	-54.45	6.747	3
B6_2 vs. S5_2	103.9	166.4	-62.54	6.747	3
B6_2 vs. S6_0.5	103.9	172.1	-68.2	6.747	3

B6_2 vs. S6_1	103.9	172.5	-68.57	6.747	3
B6_2 vs. S6_2	103.9	156.7	-52.8	6.747	3
S5_0.5 vs. S5_1	172.9	158.4	14.56	6.747	3
S5_0.5 vs. S5_2	172.9	166.4	6.477	6.747	3
S5_0.5 vs. S6_0.5	172.9	172.1	0.8167	6.747	3
S5_0.5 vs. S6_1	172.9	172.5	0.4467	6.747	3
S5_0.5 vs. S6_2	172.9	156.7	16.21	6.747	3
S5_1 vs. S5_2	158.4	166.4	-8.083	6.747	3
S5_1 vs. S6_0.5	158.4	172.1	-13.74	6.747	3
S5_1 vs. S6_1	158.4	172.5	-14.11	6.747	3
S5_1 vs. S6_2	158.4	156.7	1.653	6.747	3
S5_2 vs. S6_0.5	166.4	172.1	-5.66	6.747	3
S5_2 vs. S6_1	166.4	172.5	-6.03	6.747	3
S5_2 vs. S6_2	166.4	156.7	9.737	6.747	3
S6_0.5 vs. S6_1	172.1	172.5	-0.37	6.747	3
S6_0.5 vs. S6_2	172.1	156.7	15.4	6.747	3
S6_1 vs. S6_2	172.5	156.7	15.77	6.747	3
D7					
CTRL vs. B3_0.5	223.7	235.9	-12.16	6.747	3
CTRL vs. B3_1	223.7	181.8	41.94	6.747	3
CTRL vs. B3_2	223.7	160.4	63.32	6.747	3
CTRL vs. B6_0.5	223.7	131.1	92.62	6.747	3
CTRL vs. B6_1	223.7	113.2	110.5	6.747	3
CTRL vs. B6_2	223.7	107.6	116.1	6.747	3
CTRL vs. S5_0.5	223.7	262.6	-38.9	6.747	3
CTRL vs. S5_1	223.7	249.4	-25.66	6.747	3
CTRL vs. S5_2	223.7	238	-14.23	6.747	3
CTRL vs. S6_0.5	223.7	247.4	-23.69	6.747	3
CTRL vs. S6_1	223.7	264	-40.25	6.747	3
CTRL vs. S6_2	223.7	242	-18.23	6.747	3
B3_0.5 vs. B3_1	235.9	181.8	54.1	6.747	3
B3_0.5 vs. B3_2	235.9	160.4	75.49	6.747	3
B3_0.5 vs. B6_0.5	235.9	131.1	104.8	6.747	3
B3_0.5 vs. B6_1	235.9	113.2	122.7	6.747	3
B3_0.5 vs. B6_2	235.9	107.6	128.3	6.747	3
B3_0.5 vs. S5_0.5	235.9	262.6	-26.73	6.747	3
B3_0.5 vs. S5_1	235.9	249.4	-13.49	6.747	3
B3_0.5 vs. S5_2	235.9	238	-2.07	6.747	3
B3_0.5 vs. S6_0.5	235.9	247.4	-11.53	6.747	3
B3_0.5 vs. S6_1	235.9	264	-28.09	6.747	3
B3_0.5 vs. S6_2	235.9	242	-6.067	6.747	3
B3_1 vs. B3_2	181.8	160.4	21.39	6.747	3
B3_1 vs. B6_0.5	181.8	131.1	50.68	6.747	3

B3_1 vs. B6_1	181.8	113.2	68.56	6.747	3
B3_1 vs. B6_2	181.8	107.6	74.15	6.747	3
B3_1 vs. S5_0.5	181.8	262.6	-80.83	6.747	3
B3_1 vs. S5_1	181.8	249.4	-67.59	6.747	3
B3_1 vs. S5_2	181.8	238	-56.17	6.747	3
B3_1 vs. S6_0.5	181.8	247.4	-65.63	6.747	3
B3_1 vs. S6_1	181.8	264	-82.19	6.747	3
B3_1 vs. S6_2	181.8	242	-60.17	6.747	3
B3_2 vs. B6_0.5	160.4	131.1	29.29	6.747	3
B3_2 vs. B6_1	160.4	113.2	47.18	6.747	3
B3_2 vs. B6_2	160.4	107.6	52.77	6.747	3
B3_2 vs. S5_0.5	160.4	262.6	-102.2	6.747	3
B3_2 vs. S5_1	160.4	249.4	-88.98	6.747	3
B3_2 vs. S5_2	160.4	238	-77.56	6.747	3
B3_2 vs. S6_0.5	160.4	247.4	-87.02	6.747	3
B3_2 vs. S6_1	160.4	264	-103.6	6.747	3
B3_2 vs. S6_2	160.4	242	-81.55	6.747	3
B6_0.5 vs. B6_1	131.1	113.2	17.88	6.747	3
B6_0.5 vs. B6_2	131.1	107.6	23.47	6.747	3
B6_0.5 vs. S5_0.5	131.1	262.6	-131.5	6.747	3
B6_0.5 vs. S5_1	131.1	249.4	-118.3	6.747	3
B6_0.5 vs. S5_2	131.1	238	-106.9	6.747	3
B6_0.5 vs. S6_0.5	131.1	247.4	-116.3	6.747	3
B6_0.5 vs. S6_1	131.1	264	-132.9	6.747	3
B6_0.5 vs. S6_2	131.1	242	-110.8	6.747	3
B6_1 vs. B6_2	113.2	107.6	5.59	6.747	3
B6_1 vs. S5_0.5	113.2	262.6	-149.4	6.747	3
B6_1 vs. S5_1	113.2	249.4	-136.2	6.747	3
B6_1 vs. S5_2	113.2	238	-124.7	6.747	3
B6_1 vs. S6_0.5	113.2	247.4	-134.2	6.747	3
B6_1 vs. S6_1	113.2	264	-150.8	6.747	3
B6_1 vs. S6_2	113.2	242	-128.7	6.747	3
B6_2 vs. S5_0.5	107.6	262.6	-155	6.747	3
B6_2 vs. S5_1	107.6	249.4	-141.7	6.747	3
B6_2 vs. S5_2	107.6	238	-130.3	6.747	3
B6_2 vs. S6_0.5	107.6	247.4	-139.8	6.747	3
B6_2 vs. S6_1	107.6	264	-156.3	6.747	3
B6_2 vs. S6_2	107.6	242	-134.3	6.747	3
S5_0.5 vs. S5_1	262.6	249.4	13.24	6.747	3
S5_0.5 vs. S5_2	262.6	238	24.66	6.747	3
S5_0.5 vs. S6_0.5	262.6	247.4	15.2	6.747	3
S5_0.5 vs. S6_1	262.6	264	-1.353	6.747	3
S5_0.5 vs. S6_2	262.6	242	20.67	6.747	3
S5_1 vs. S5_2	249.4	238	11.42	6.747	3

S5_1 vs. S6_0.5	249.4	247.4	1.963	6.747	3
S5_1 vs. S6_1	249.4	264	-14.59	6.747	3
S5_1 vs. S6_2	249.4	242	7.427	6.747	3
S5_2 vs. S6_0.5	238	247.4	-9.46	6.747	3
S5_2 vs. S6_1	238	264	-26.02	6.747	3
S5_2 vs. S6_2	238	242	-3.997	6.747	3
S6_0.5 vs. S6_1	247.4	264	-16.56	6.747	3
S6_0.5 vs. S6_2	247.4	242	5.463	6.747	3
S6_1 vs. S6_2	264	242	22.02	6.747	3

Table S8. Evaluated data from 2-way ANOVA analysis (mixed model) from the drug encapsulation results of **B6** at different concentrations. Turkey's multiple comparison test, with individual variances computed for each comparison.

Compare column means (main column effect)								
Number of families	**1**							
Number of comparisons per family	**10**							
Alpha	**0.05**							
Tukey's multiple comparisons test	**Mean Diff.**	**95.00% CI of diff.**	**Significant?**	**Summary**	**Adjusted P Value**			
Control vs. B6 (EE)	-47.33	-50.44 to -44.23	Yes	****	<0.0001			
Control vs. B6 (DL)	23.28	20.17 to 26.38	Yes	****	<0.0001			
Control vs. Reference (EE)	34.33	31.23 to 37.44	Yes	****	<0.0001			
Control vs. Reference (DL)	37.08	33.98 to 40.19	Yes	****	<0.0001			
B6 (EE) vs. B6 (DL)	70.61	67.51 to 73.72	Yes	****	<0.0001			
B6 (EE) vs. Reference (EE)	81.67	78.56 to 84.77	Yes	****	<0.0001			
B6 (EE) vs. Reference (DL)	84.42	81.31 to 87.52	Yes	****	<0.0001			
B6 (DL) vs. Reference (EE)	11.06	7.952 to 14.16	Yes	****	<0.0001			
B6 (DL) vs. Reference (DL)	13.81	10.70 to 16.91	Yes	****	<0.0001			
Reference (EE) vs. Reference (DL)	2.751	-0.3533 to 5.855	No	ns	0.1039			
Test details	**Mean 1**	**Mean 2**	**Mean Diff.**	**SE of diff.**	**N1**	**N2**	**q**	**DF**
Control vs. B6 (EE)	37.39	84.72	-47.33	1.087	12	12	61.59	40
Control vs. B6 (DL)	37.39	14.11	23.28	1.087	12	12	30.29	40
Control vs. Reference (EE)	37.39	3.056	34.33	1.087	12	12	44.68	40
Control vs. Reference (DL)	37.39	0.3056	37.08	1.087	12	12	48.25	40
B6 (EE) vs. B6 (DL)	84.72	14.11	70.61	1.087	12	12	91.88	40
B6 (EE) vs. Reference (EE)	84.72	3.056	81.67	1.087	12	12	106.3	40
B6 (EE) vs. Reference (DL)	84.72	0.3056	84.42	1.087	12	12	109.8	40
B6 (DL) vs. Reference (EE)	14.11	3.056	11.06	1.087	12	12	14.39	40

B6 (DL) vs. Reference (DL)	14.11	0.3056	13.81	1.087	12	12	17.97	40
Reference (EE) vs. Reference (DL)	3.056	0.3056	2.751	1.087	12	12	3.579	40

Table S9. Evaluated data from 2-way ANOVA analysis (mixed model) from the drug encapsulation results of **B6** at different concentrations. Turkey's multiple comparison test, with individual variances computed for each comparison.

Compare row means (main row effect)								
Number of families	**1**							
Number of comparisons per family	**6**							
Alpha	**0.05**							
Tukey's multiple comparisons test	**Mean Diff,**	**95,00% CI of diff,**	**Significant?**	**Summary**	**Adjusted P Value**			
35 vs. 20	5.269	3,470 to 7,069	Yes	****	<0,0001			
35 vs. 10	0.186	-1,613 to 1,986	No	ns	0.9906			
35 vs. 5	-1.584	-3,383 to 0,2155	No	ns	0.0948			
20 vs. 10	-5.083	-6,883 to -3,284	Yes	****	<0,0001			
20 vs. 5	-6.853	-8,653 to -5,054	Yes	****	<0,0001			
10 vs. 5	-1.77	-3,570 to 0,02946	No	ns	0.0547			
Test details	**Mean 1**	**Mean 2**	**Mean Diff,**	**SE of diff,**	**N1**	**N2**	**q**	**DF**
35 vs. 20	50.39	45.12	5.269	0.629	6	6	11.85	16
35 vs. 10	50.39	50.2	0.186	0.629	6	6	0.4183	16
35 vs. 5	50.39	51.97	-1.584	0.629	6	6	3.562	16
20 vs. 10	45.12	50.2	-5.083	0.629	6	6	11.43	16
20 vs. 5	45.12	51.97	-6.853	0.629	6	6	15.41	16
10 vs. 5	50.2	51.97	-1.77	0.629	6	6	3.98	16

Table S10. Evaluated data from 2-way ANOVA analysis (mixed model) from the drug encapsulation results of **B1-B6**. Turkey's multiple comparison test, with individual variances computed for each comparison.

Within each column, compare rows (simple effects within columns)					
Number of families	**2**				
Number of comparisons per family	**15**				
Alpha	**0.05**				
Tukey's multiple comparisons test	**Mean Diff,**	**95,00% CI of diff,**	**Significant?**	**Summary**	**Adjusted P Value**
EE					

B1 vs. B2	-22.24	-27,20 to -17,29	Yes	****	<0,0001
B1 vs. B3	-27.74	-32,70 to -22,78	Yes	****	<0,0001
B1 vs. B4	6.157	1,200 to 11,11	Yes	**	0.0091
B1 vs. B5	6.157	1,200 to 11,11	Yes	**	0.0091
B1 vs. B6	-7.993	-12,95 to -3,036	Yes	***	0.0006
B2 vs. B3	-5.494	-10,45 to -0,5372	Yes	*	0.0238
B2 vs. B4	28.4	23,45 to 33,36	Yes	****	<0,0001
B2 vs. B5	28.4	23,45 to 33,36	Yes	****	<0,0001
B2 vs. B6	14.25	9,295 to 19,21	Yes	****	<0,0001
B3 vs. B4	33.9	28,94 to 38,85	Yes	****	<0,0001
B3 vs. B5	33.9	28,94 to 38,85	Yes	****	<0,0001
B3 vs. B6	19.75	14,79 to 24,70	Yes	****	<0,0001
B4 vs. B5	0	-4,957 to 4,957	No	ns	>0,9999
B4 vs. B6	-14.15	-19,11 to -9,193	Yes	****	<0,0001
B5 vs. B6	-14.15	-19,11 to -9,193	Yes	****	<0,0001
DL					
B1 vs. B2	-7.786	-12,74 to -2,829	Yes	***	0.0008
B1 vs. B3	-9.709	-14,67 to -4,752	Yes	****	<0,0001
B1 vs. B4	2.155	-2,802 to 7,112	No	ns	0.7582
B1 vs. B5	1.268	-3,689 to 6,225	No	ns	0.9664
B1 vs. B6	-2.797	-7,754 to 2,160	No	ns	0.5174
B2 vs. B3	-1.923	-6,880 to 3,034	No	ns	0.8328
B2 vs. B4	9.941	4,984 to 14,90	Yes	****	<0,0001
B2 vs. B5	9.054	4,097 to 14,01	Yes	***	0.0001
B2 vs. B6	4.988	0,03133 to 9,945	Yes	*	0.0479
B3 vs. B4	11.86	6,907 to 16,82	Yes	****	<0,0001
B3 vs. B5	10.98	6,020 to 15,93	Yes	****	<0,0001
B3 vs. B6	6.911	1,954 to 11,87	Yes	**	0.0029
B4 vs. B5	-0.8868	-5,844 to 4,070	No	ns	0.9931
B4 vs. B6	-4.952	-9,909 to 0,004541	No	ns	0.0503
B5 vs. B6	-4.066	-9,023 to 0,8914	No	ns	0.1532
Test details	**Mean 1**	**Mean 2**	**Mean Diff,**	**SE of diff,**	**N1**
EE					
B1 vs. B2	66.65	88.9	-22.24	1.603	3
B1 vs. B3	66.65	94.39	-27.74	1.603	3
B1 vs. B4	66.65	60.5	6.157	1.603	3
B1 vs. B5	66.65	60.5	6.157	1.603	3
B1 vs. B6	66.65	74.65	-7.993	1.603	3
B2 vs. B3	88.9	94.39	-5.494	1.603	3
B2 vs. B4	88.9	60.5	28.4	1.603	3

B2 vs. B5	88.9	60.5	28.4	1.603	3
B2 vs. B6	88.9	74.65	14.25	1.603	3
B3 vs. B4	94.39	60.5	33.9	1.603	3
B3 vs. B5	94.39	60.5	33.9	1.603	3
B3 vs. B6	94.39	74.65	19.75	1.603	3
B4 vs. B5	60.5	60.5	0	1.603	3
B4 vs. B6	60.5	74.65	-14.15	1.603	3
B5 vs. B6	60.5	74.65	-14.15	1.603	3
DL					
B1 vs. B2	23.33	31.11	-7.786	1.603	3
B1 vs. B3	23.33	33.04	-9.709	1.603	3
B1 vs. B4	23.33	21.17	2.155	1.603	3
B1 vs. B5	23.33	22.06	1.268	1.603	3
B1 vs. B6	23.33	26.13	-2.797	1.603	3
B2 vs. B3	31.11	33.04	-1.923	1.603	3
B2 vs. B4	31.11	21.17	9.941	1.603	3
B2 vs. B5	31.11	22.06	9.054	1.603	3
B2 vs. B6	31.11	26.13	4.988	1.603	3
B3 vs. B4	33.04	21.17	11.86	1.603	3
B3 vs. B5	33.04	22.06	10.98	1.603	3
B3 vs. B6	33.04	26.13	6.911	1.603	3
B4 vs. B5	21.17	22.06	-0.8868	1.603	3
B4 vs. B6	21.17	26.13	-4.952	1.603	3
B5 vs. B6	22.06	26.13	-4.066	1.603	3