Supporting Information for:

High-throughput synthesis and screening of rapidly-degrading polyanhydride nanoparticles

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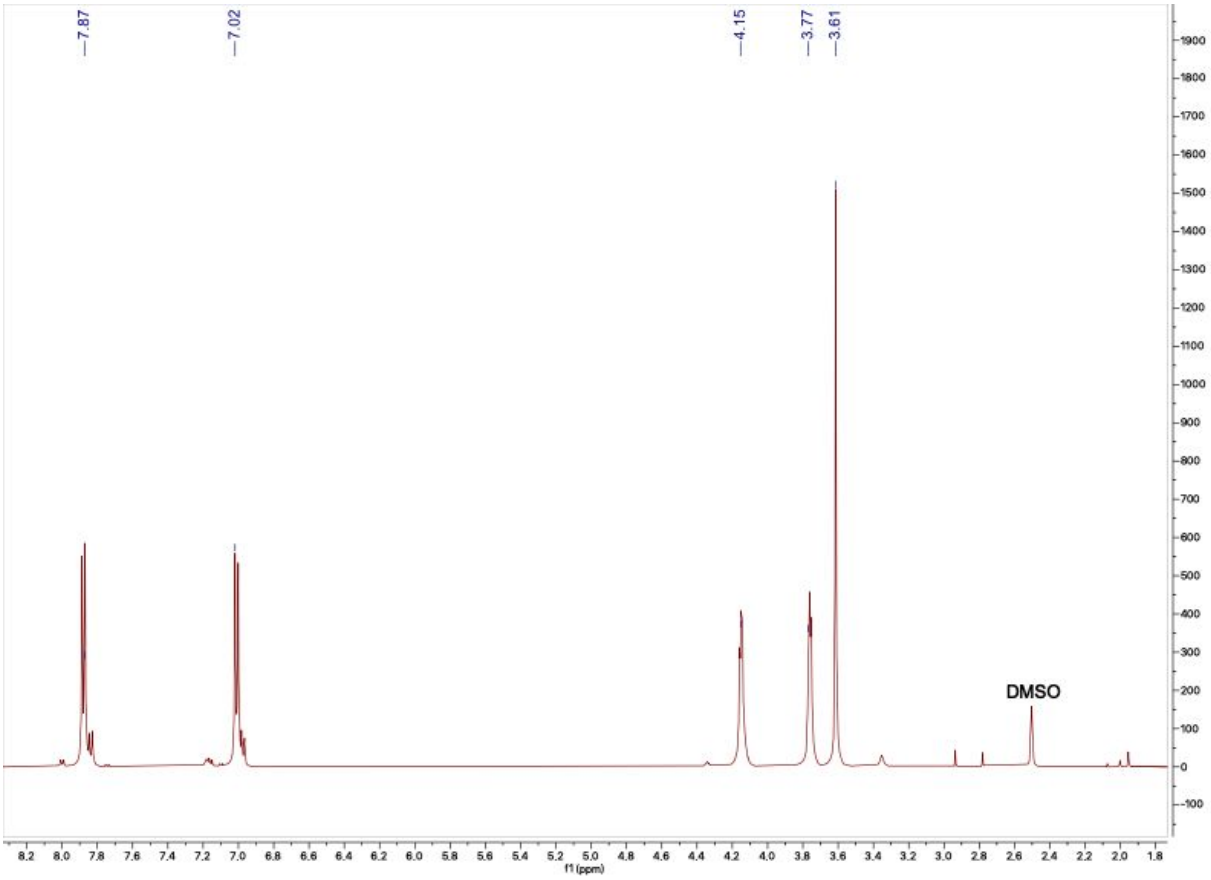


Figure S1. ^{1}H NMR spectrum of CPTEG diacid.

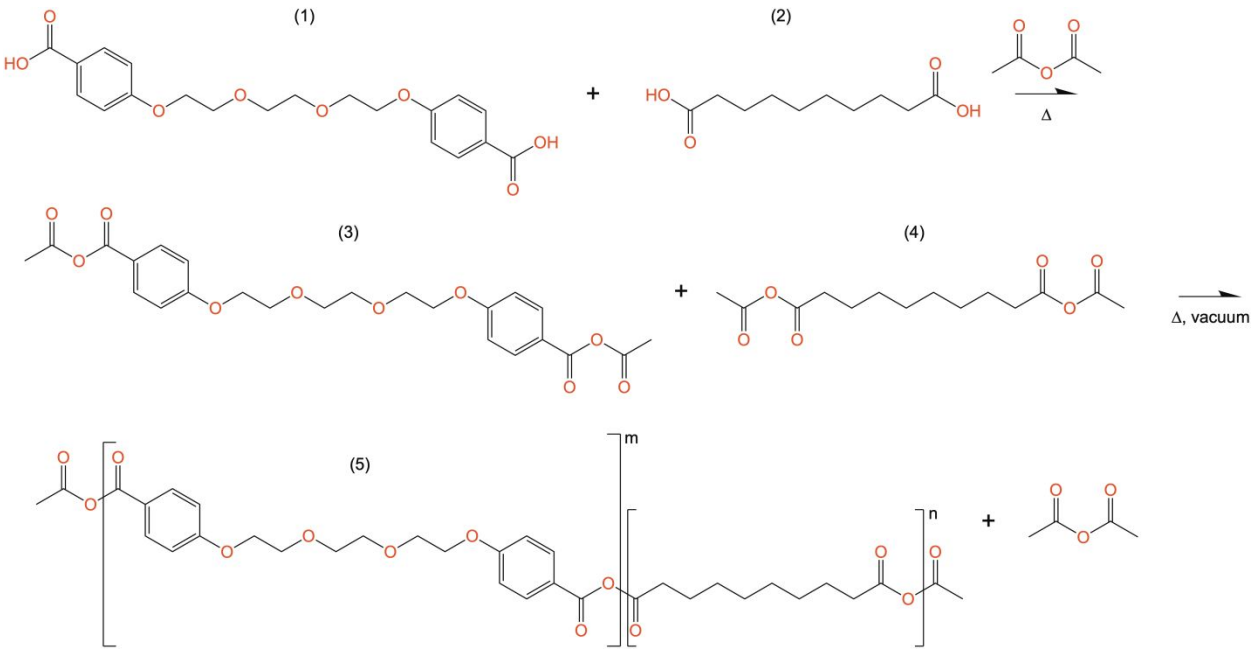
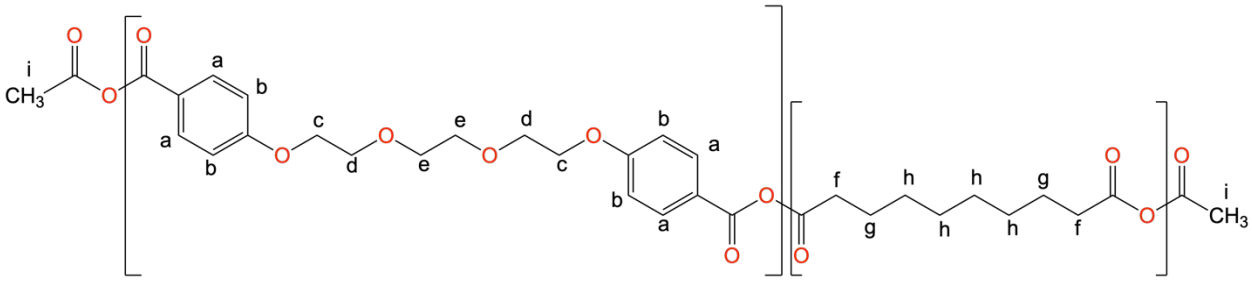
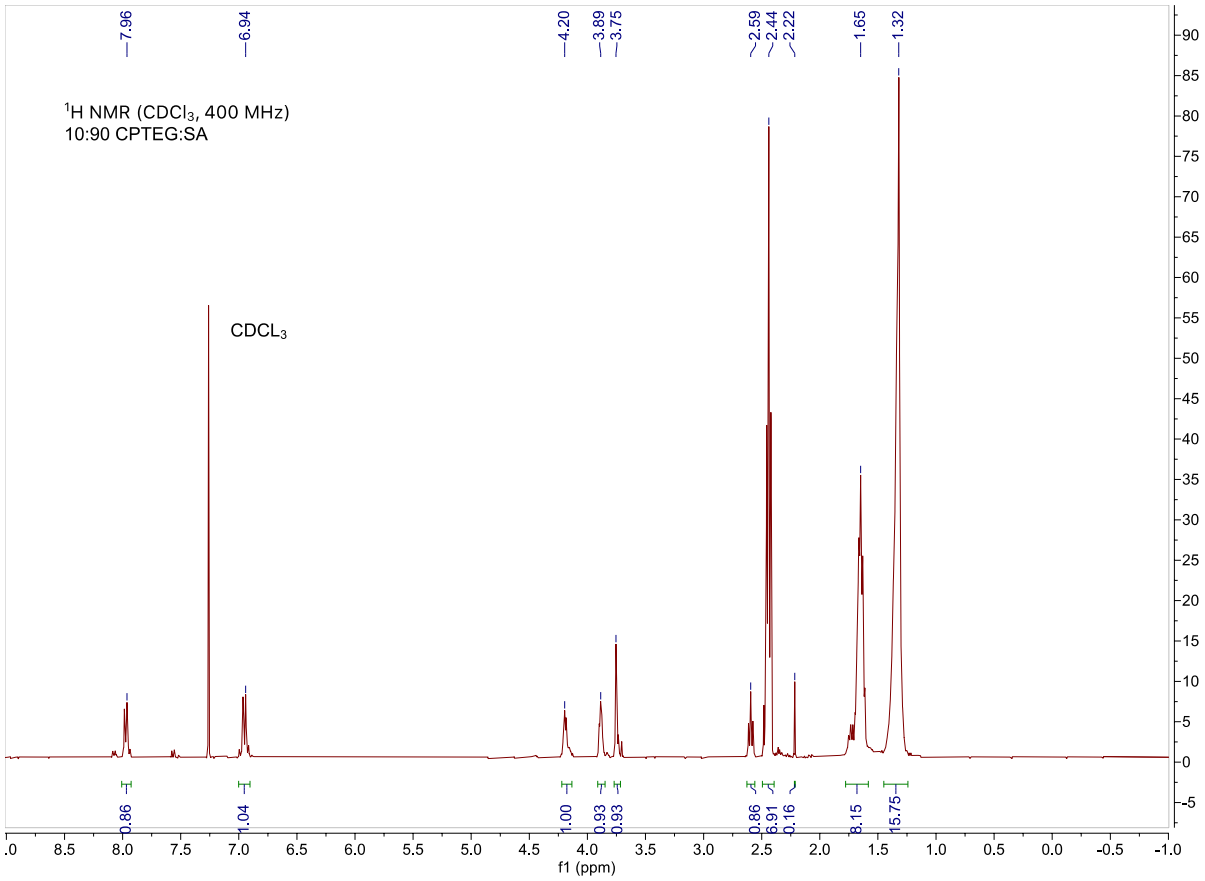
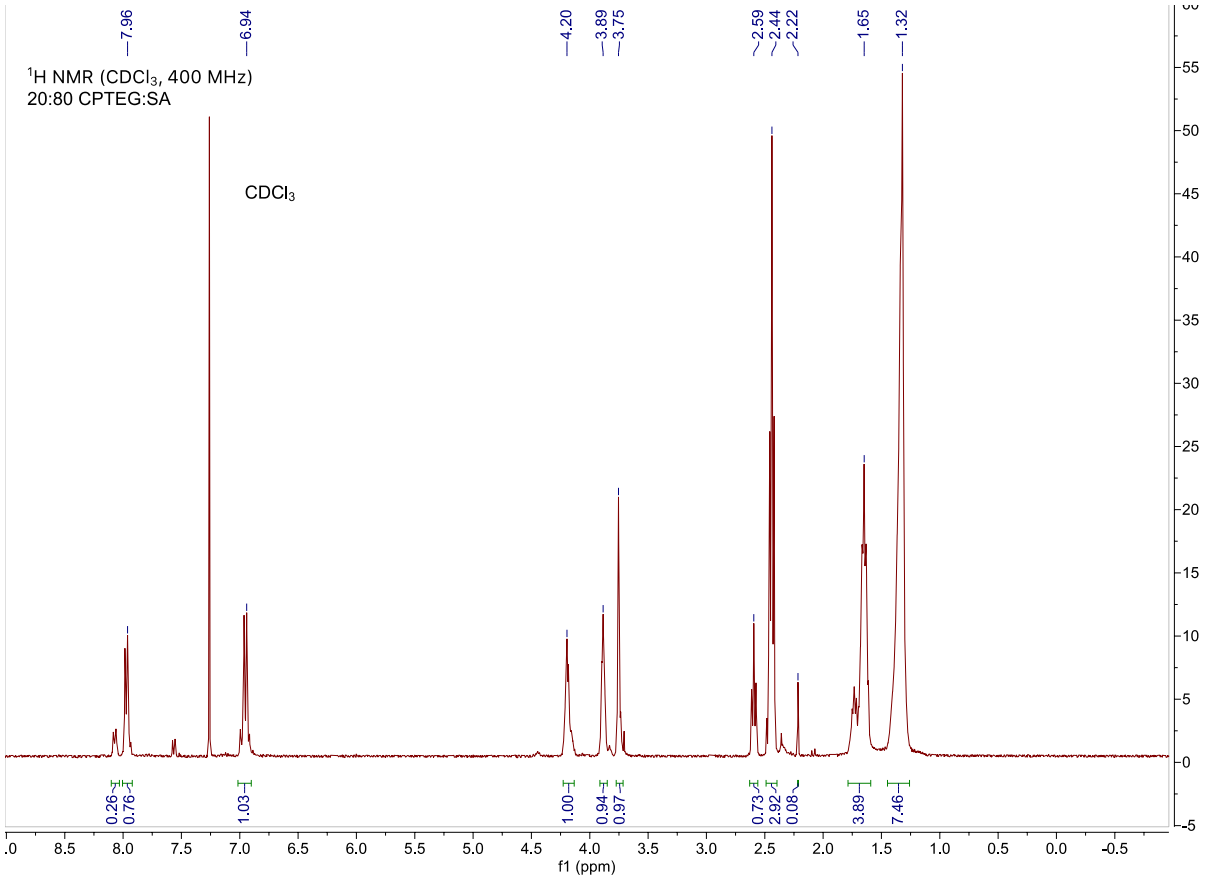


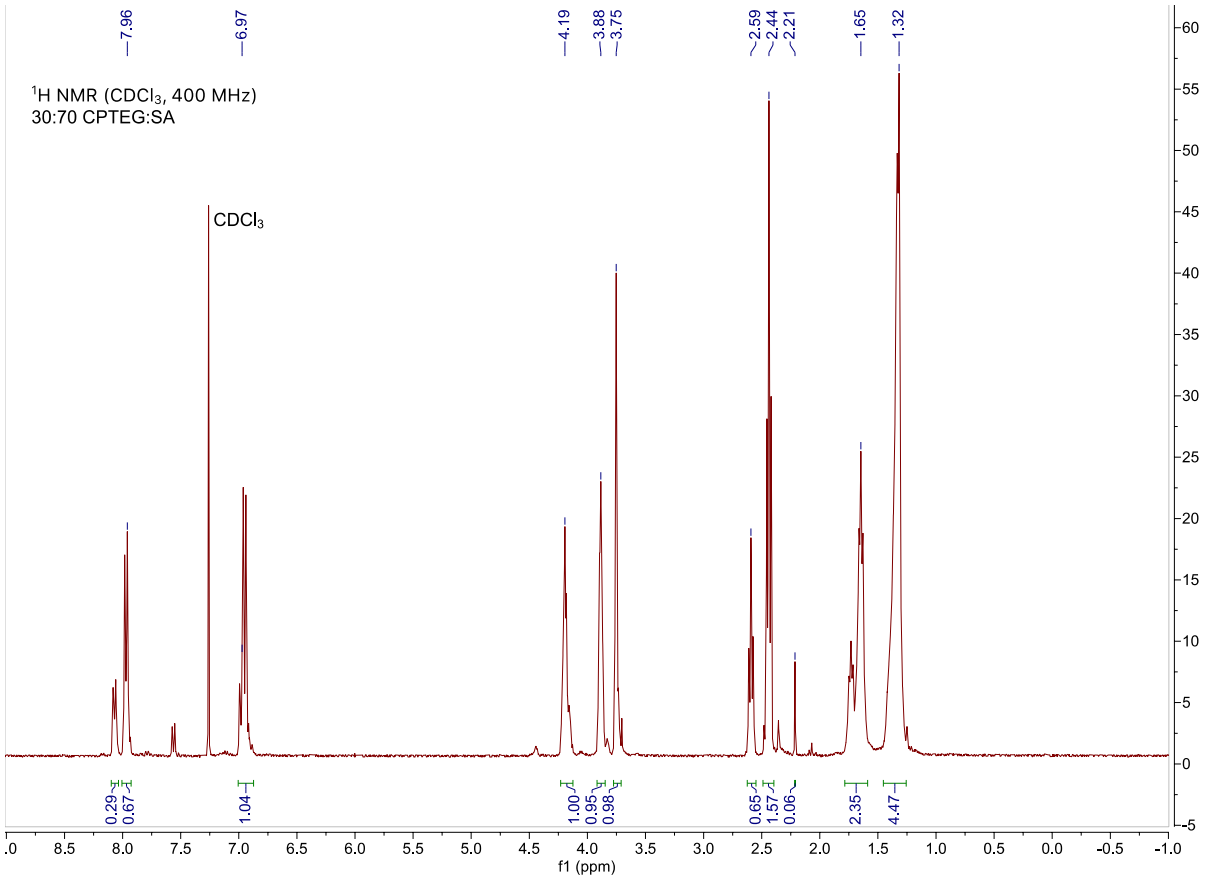
Figure S2. CPTEG:SA copolymerization scheme. CPTEG (1) and SA (2) dicarboxylic acid monomers are acetylated in acetic anhydride, yielding CPTEG (3) and SA (4) prepolymers. Acetic anhydride is removed by rotary evaporation and the remaining prepolymers are reacted under vacuum to yield CPTEG:SA copolymers (5). Polymerization used a melt polycondensation mechanism, where acetic anhydride is produced and continually removed by vacuum.

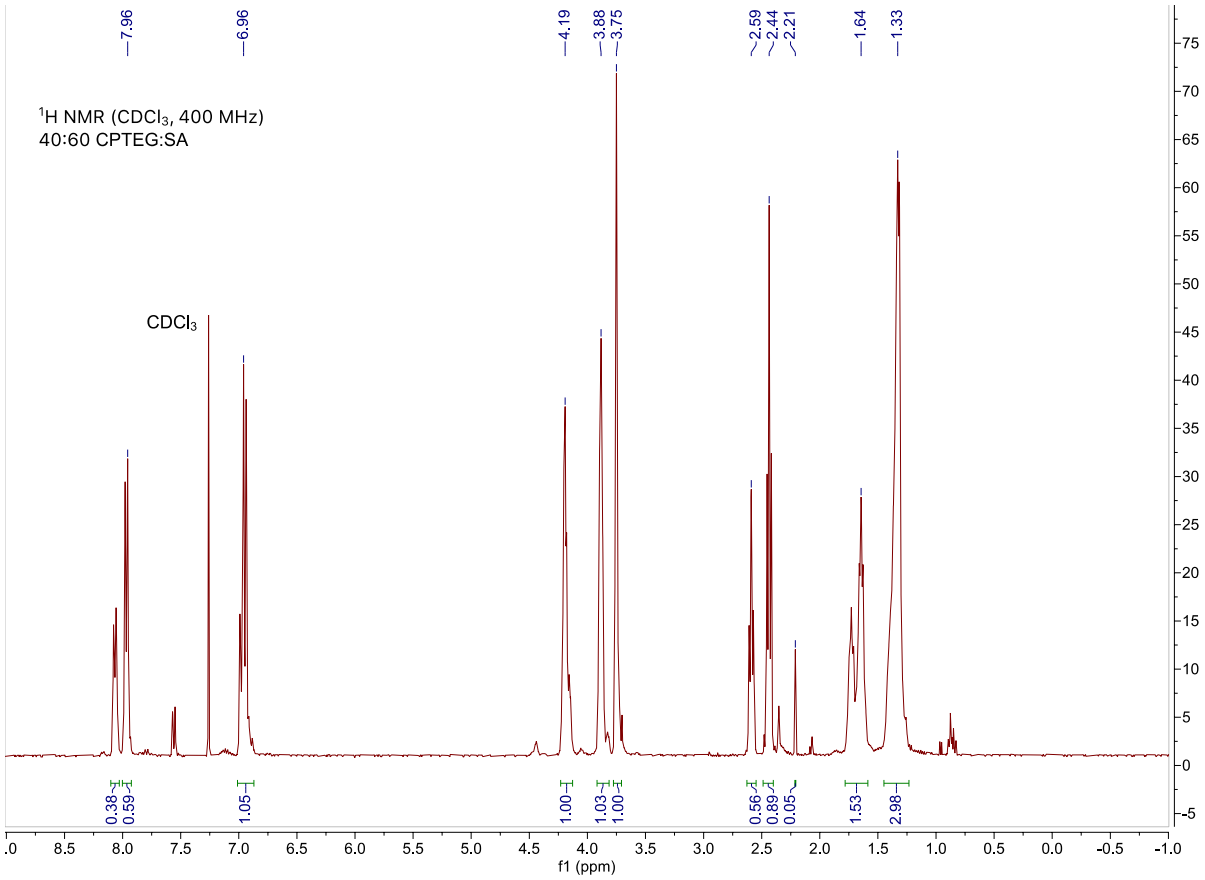


Hydrogen	Shift	# of H	Splitting
a	8.0	4	d
b	7.0	4	d
c	4.2	4	t
d	3.9	4	m
e	3.75	4	m
f	2.6	2	t
f'	2.45	2	t
g	1.65	4	m
h	1.32	8	m
i	2.22	6	s


7.96
6.94
4.20
3.89
3.75
2.59
2.44
2.22
1.65
1.32
^{1}H NMR ($CDCl_3$, 400 MHz)
10:90 CPTEG:SA
$CDCL_3$
0.86
1.04
1.00
0.93
0.93
0.86
6.91
0.16
8.15
15.75
f1 (ppm)


7.96
6.94
4.20
3.89
3.75
2.59
2.44
2.22
1.65
1.32
1H NMR (CDCl3, 400 MHz)
20:80 CPTEG:SA
CDCl3
0.26
0.76
1.03
1.00
0.94
0.97
0.73
2.92
0.08
3.89
7.46
f1 (ppm)


7.96
6.97
4.19
3.88
3.75
2.59
2.44
2.21
1.65
1.32
^{1}H NMR ($CDCl_3$, 400 MHz)
30:70 CPTEG:SA
$CDCl_3$
0.29
0.67
1.04
1.00
0.95
0.98
0.65
1.57
0.06
2.35
4.47
f1 (ppm)


7.96
6.96
4.19
3.88
3.75
2.59
2.44
2.21
1.64
1.33
1H NMR (CDCl3, 400 MHz)
40:60 CPTEG:SA
CDCl3
0.38
0.59
1.05
1.00
1.03
1.00
0.56
0.89
0.05
1.53
2.98
f1 (ppm)

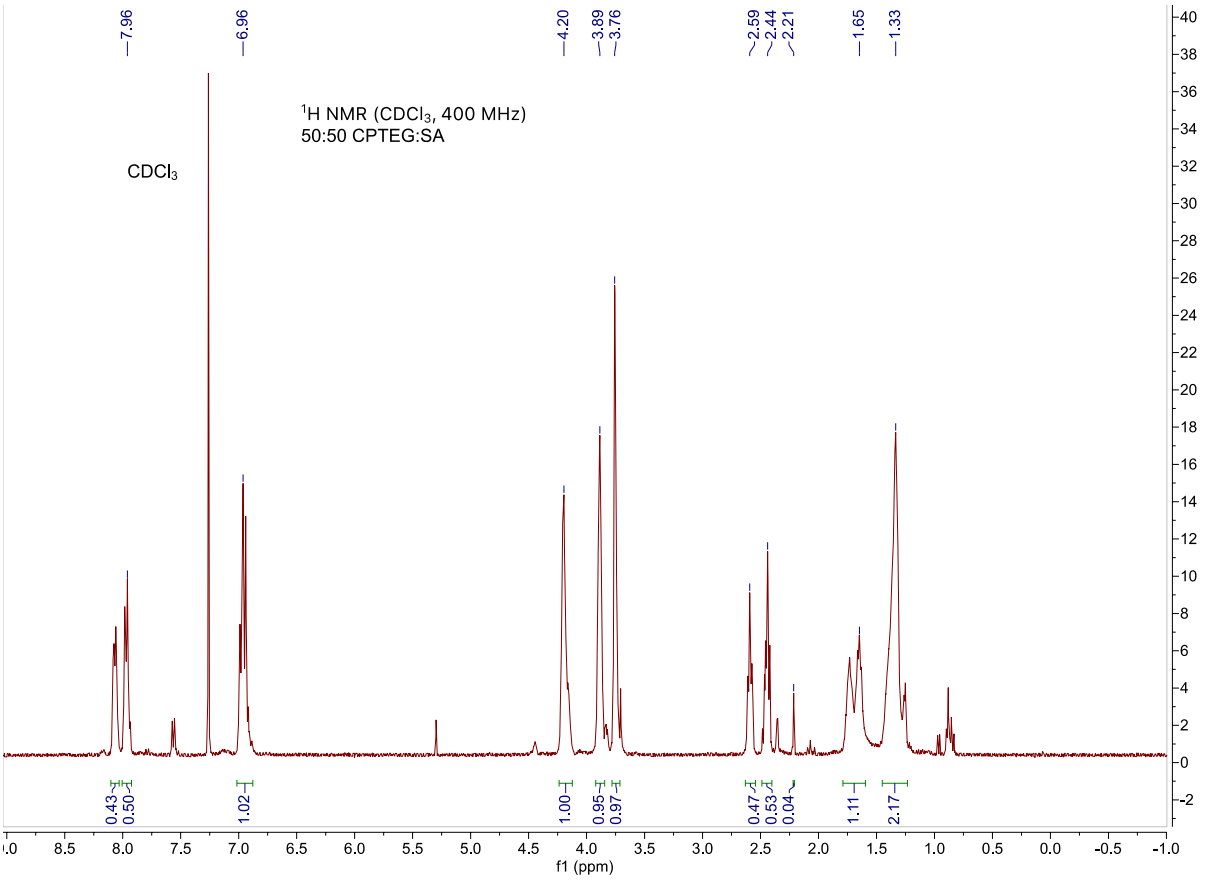


Figure S3. CPTEG:SA ^{1}H NMR peak assignment and labeled spectra of high-throughput polymer library.

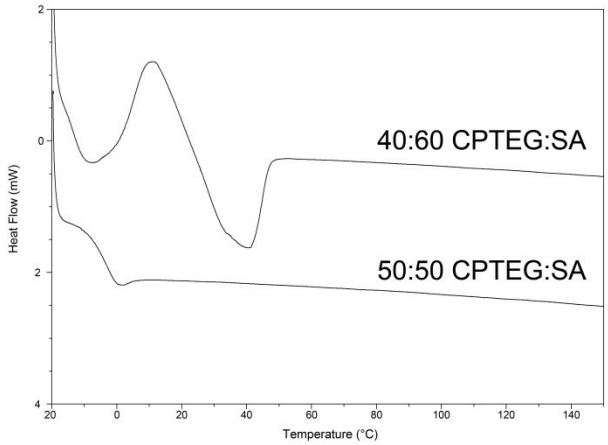


Figure S4. DSC thermograms of CPTEG-rich copolymers. 40:60 CPTEG:SA was thermally unstable and 50:50 CPTEG:SA showed a near-zero °C T_g.

Table S1. Effect of reaction time on copolymer molecular weight and nanoparticle size distribution. Molecular weight was determined by ^{1}H NMR, and nanoparticle diameter was determined by SEM. Cells left blank indicate no nanoparticles were recovered. Size distributions are presented as mean ± standard deviation.

	Reaction time:	**4 hours**	**5 hours**	**6 hours**	**10 hours**
10:90 CPTEG:SA	**Mn (Da)**	14,000	14,800	15,300	27,900
	Diameter (nm)	297 ± 125	291 ± 107	370 nm ± 165	286 ± 98
20:80 CPTEG:SA	**Mn (Da)**	12,000	13,600	14,000	24,300
	Diameter (nm)	445 ± 114	657 ± 257	492 ± 155	355 ± 126
30:70 CPTEG:SA	**Mn (Da)**	11,800	12,200	14,600	24,800
	Diameter (nm)	796 ± 189	868 ± 313	1,054 ± 350	N/A
40:60 CPTEG:SA	**Mn (Da)**	10,600	14,000	14,400	18,400
	Diameter (nm)	295 ± 123	1,505 ± 204	N/A	N/A
50:50 CPTEG:SA	**Mn (Da)**	11,200	12,700	16,500	20,800

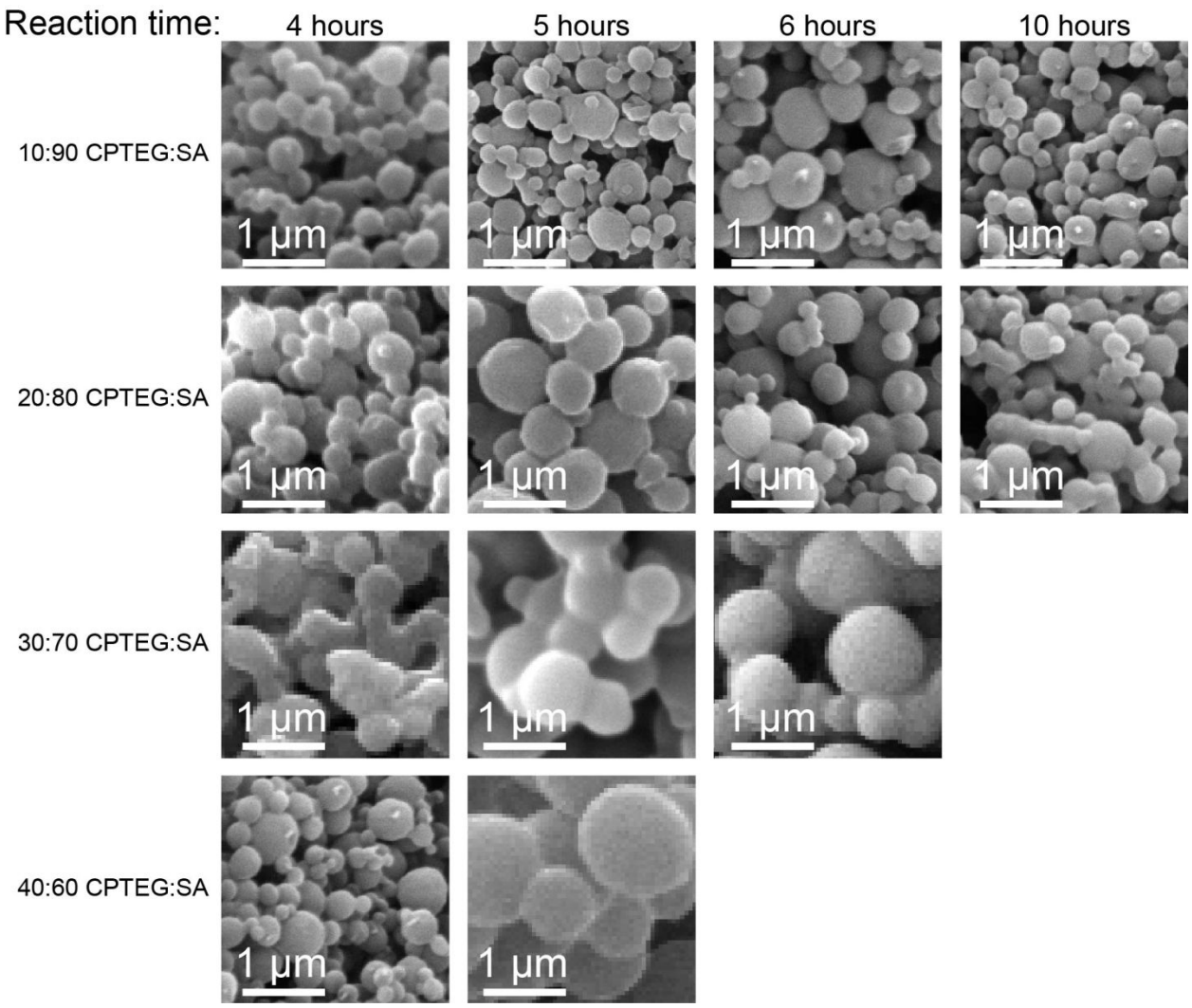


Figure S5. Screening high-throughput CPTEG:SA copolymers for conventional nanoparticles. Size distributions are provided in Table S1. Empty spaces indicate that no particles were able to be recovered due to polymer tackiness. The 5-hour reaction time was selected for subsequent experiments as it produced the most discrete, sub-micron particles with high yield for chemistries with 30 mol % or less CPTEG.

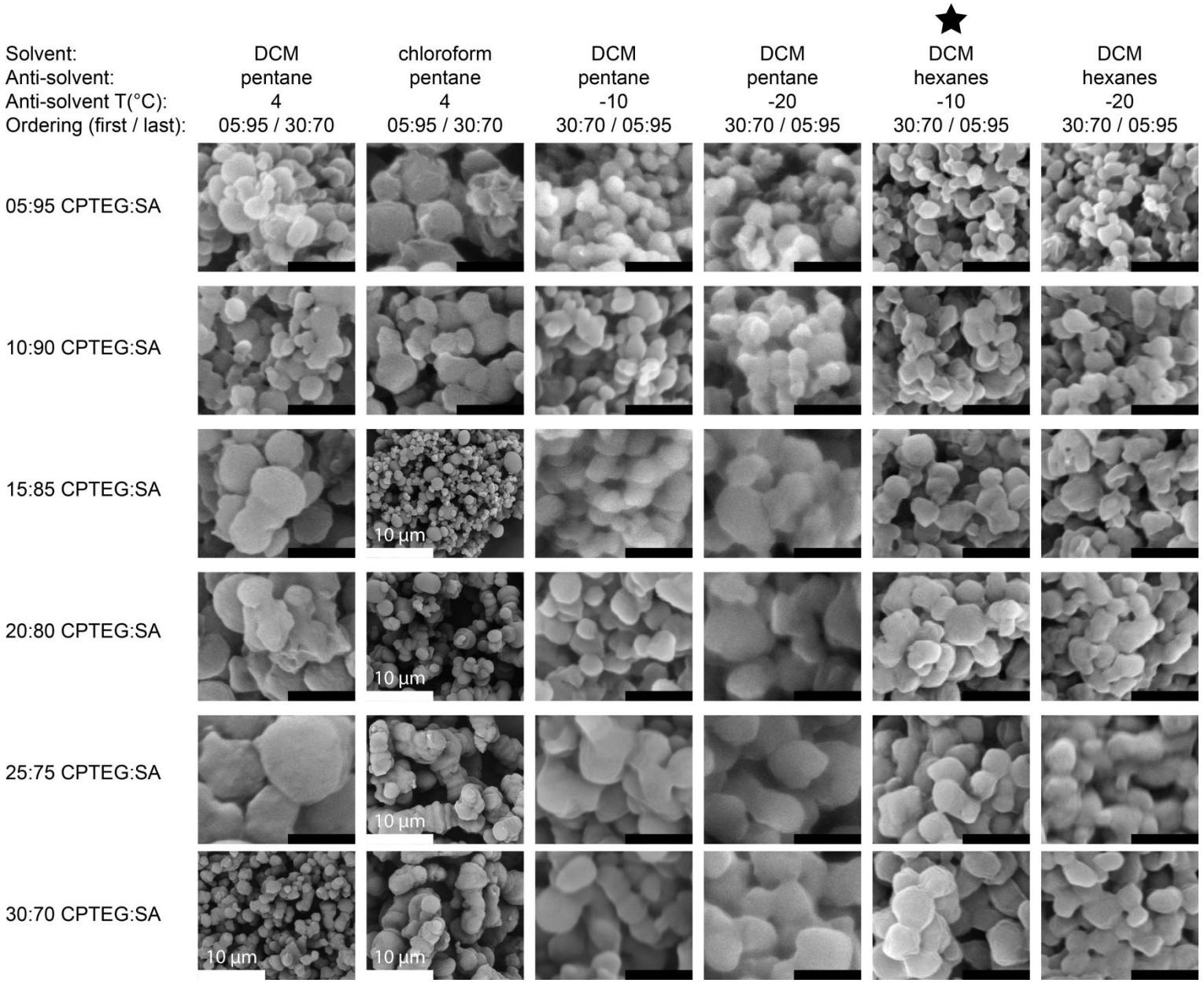

Solvent:
Anti-solvent:
Anti-solvent T(°C):
Ordering (first / last):
DCM
pentane
4
05:95 / 30:70
chloroform
pentane
4
05:95 / 30:70
DCM
pentane
-10
30:70 / 05:95
DCM
pentane
-20
30:70 / 05:95
DCM
hexanes
-10
30:70 / 05:95
DCM
hexanes
-20
30:70 / 05:95
05:95 CPTEG:SA
10:90 CPTEG:SA
15:85 CPTEG:SA
20:80 CPTEG:SA
25:75 CPTEG:SA
30:70 CPTEG:SA
10 µm

Figure S6. Optimization of high-throughput nanoparticle synthesis conditions. Methylene chloride (DCM) and chloroform were tested as solvents, and pentane and hexanes were tested as anti-solvents at 4, –10, and –20°C. For all, polymer concentration in methylene chloride was kept constant at 20 mg//mL and solvent to anti-solvent ratio was kept constant at 1:9. Scale bars represent 1 μm (black), unless noted otherwise (white, 10μm). Star represents the optimal conditions for synthesizing spherical, sub-micron particles, which were used for all other nanoparticle libraries.