Electronic Supplementary Material (ESI) for Polymer Chemistry.

Electronic Supporting Information

Oxygen Tolerant Photopolymerization for Ultralow Volumes

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EXPERIMENTAL SECTION

Materials

N,N-dimethylacrylamide (DMA, 99%), oligo(ethylene glycol) methyl ether acrylate (OEGA, 480 g/mol) , oligo(ethylene glycol) methyl ether methacrylate (OEGMA, 300 g/mol), *N*-hydroxyethyl acrylate (HEA, 96%,), *N*-hydroxylethyl acrylamide (HEAm, 97%), *N,N'*-methylenebisacrylamide (MBA, 99%) and diacetone acrylamide (DAAm, 99%) were purchased from Sigma Aldrich. *N,N'*-diethylacrylamide (DEA, 97%) was purchased from TCI Chemicals. All liquid monomers (except for HEAm, OEGA and OEGMA) were deinhibited by passing through a column of basic alumina (Ajax Chemical, AR). DAAm and MBA were recrystallized from ethyl acetate and acetone respectively. Eosin Y disodium salt (EY), riboflavin 5'-monophosphate (FMN, 95%), ascorbic acid (AscA, 99%) and 1,4-dioxane (99%) were purchased from Sigma-Aldrich. Methanol (Ajax Finechem, AR) and diethyl ether anhydrous (Merck) were used as received. 4-cyanopentanoic acid dithiobenzoate (CPADB) and 2-(*n*-butyltrithiocarbonate)-propionic acid (BTPA) were synthesized according to literature procedures.[1, 2] Corning 96 well plates (polystyrene, clear) were purchased from Sigma-Aldrich

Instrumentation

All ^{1}H-NMR spectra were recorded using a Bruker 300 or 400 MHz spectrometer. All chemical shifts are reported in ppm (δ) relative to tetramethylsilane, referenced to the chemical shifts of residual solvent resonances. All spectra were acquired in d_6-DMSO unless otherwise stated.

The molecular weight and dispersity of the prepared polymers were measured by GPC. The eluent was DMAc (containing 0.03% w/v LiBr and 0.05% w/v 2,6-dibutyl-4-methylphenol (BHT)) at 50 ^oC (flow rate of 1 mL/min) with a Shimadzu modular system comprising an SIL-10AD auto-injector, a Polymer Laboratories 5.0 μm bead-size guard column (50×7.5 mm^2) followed by four linear PL (Styragel) columns (10^5, 10^4, 10^3 , and 500 Å) and an RID-10A differential refractive-index (RI) detector and UV-Vis detector. The calibration of the system was based on narrow molecular weight distribution of poly(methyl methacrylate) (PMMA) standards with molecular weights of 200–10^6 g mol^{-1}.

DLS measurements were performed using a Malvern Zetasizer Nano Series running DTS software and using a 4 mW He−Ne laser operating at a wavelength of 633 nm and an avalanche photodiode (APD) detector. The scattered light was detected at an angle of 173°.

TEM studies of self-assembled block copolymers were conducted using a Transmission Electron Microscope at an accelerating voltage of 100 kV (JEOL-1400). The polymerization dispersions were diluted with Milli-Q water to a concentration of 0.2 - 0.5 wt% and deposited onto carbon-coated copper grids. Phosphotungstic acid (PTA) staining was applied to all samples.

Synthesis of homopolymers using EY/Asc under green light

A typical synthesis of a PDMA homopolymer ([M]:[RAFT]:[EY]:[AscA] = 200:1:0.009:1) by aqueous RAFT photopolymerization was set up as follows: BTPA (1.8 mg, 7.55 µmol), DMA (150 mg, 1.51 mmol), EY (48.9 µg, 4.9 µL of a 10 mg/mL stock solution), AscA (1.33 mg, 7.55 µmol, 13.3 µL of a 100 mg/mL stock solution) and water (131.8 µL, 50 wt%) were mixed in a vial before 300 µL was pipetted into a single well of a 96 well plate. The cover was secured with rubber bands (to minimize monomer evaporation) and placed under a green LED lamp (λ = 530 nm, 2.65 mW/cm^2) for 2 hours at room temperature. The crude polymer was analyzed by NMR and GPC to determine monomer conversion, number-average molecular weight and molecular weight distribution.

Polymerization kinetics were measured by pipetting 300 µL of a stock solution ([M]:[RAFT]:[EY]:[AscA] = 200:1:0.009:1 at 50 wt% water) into 6 separate wells. The wells were sealed with parafilm to minimize monomer evaporation and oxygen diffusion before being placed under a green LED lamp (λ = 530 nm, 2.65 mW/cm^2). At appropriate time points, a syringe and needle was used to extract samples for analysis by NMR and GPC.

Chain extension of a PDMA macroRAFT in a 96 well plate under green light

To perform in situ chain extension experiments, a PDMA$_{41}$ macro-RAFT agent was first synthesized using the above methodology ([M]:[RAFT]:[EY]:[AscA] = 50:1:0.09:1 at 50 wt% water for 2 hours under green light). The crude PDMA polymer was removed from the well and diluted with 600 µL water. 150 µL of this macroRAFT stock solution was added to a 96 well plate and mixed with additional DMA (95.41 mg, 0.96 mmol, Target DP = 200) and EY (32.7 µg, 3.27 µL of a 10 mg/mL stock solution). Trioxane was added as an internal NMR standard.

Thermal synthesis of PDMA macro-CTA

A typical synthesis of a PDMA macro-CTA by RAFT polymerization was set up as follows: BTPA (144.3 mg, 0.61 mmol), DMA (6.0 g, 0.06 mol), AIBN (4.97 mg, 30.3 μmol) and 1,4-dioxane (25 mL) were added to a 50 mL round bottom flask which was sealed with a rubber septum and purged with nitrogen for 30 min at 0 ^{o}C. The polymerization was carried out for 2 h at 70 ^{o}C before quenching in an ice bath and exposing to air. The resulting polymer was purified by three cycles of precipitation in diethyl ether (after solubilizing in methanol). NMR and GPC characterization data is given in Figure S4. PDMA macroRAFTs synthesized using this approach were designated PDMA-1 (initial [M]:[RAFT] = 50:1]) and PDMA-2 (initial [M]:[RAFT] = 100:1])

Arm first synthesis of star polymers using PDMA macroRAFT arms

A typical synthesis of PDMA stars ([MBA]:[macroRAFT]:[EY]:[AscA] = 5:1:0.019:1) using an arm-first approach was set up as follows: $PDMA_{78}$ macroRAFT (15 mg, 1.88 μmol, PDMA-2), MBA (1.4 mg, 9.4 μmol), EY (24.30 μg, 2.4 μL of a 10 mg/mL stock solution), AscA (0.33 mg, 33.02 μL of a 10 mg/mL stock solution) and water (264.6 μL, 10 wt% macroRAFT) were mixed in a vial before 300 μL was pipetted into a single well of a 96 well plate. The cover was secured with rubber bands and placed under a green LED lamp (λ = 530 nm, 2.65 mW/cm^2) for 8 hours at room temperature. The crude polymer was analyzed by NMR and GPC to determine monomer conversion, number-average molecular weight and molecular weight distribution.

Aqueous dispersion polymerization of DAAm from PDMA macroRAFT

A typical aqueous dispersion polymerization ([DAAm]:[DMA]:[macroRAFT]:[EY]:[AscA] = [160]:[40]:[1]:[0.05]:[1]) at 20 wt% was set up as follows: $PDMA_{41}$ macroRAFT (10 mg, 2.33 μmoles, PDMA-1), DAAm (63.0 mg, 0.37 mmol), DMA (9.22 mg, 0.09 mmol), EY (75.3 μg, 7.5 μL of a 10 mg/mL stock solution), AscA (0.41 mg, 41.0 μL of a 10 mg/mL stock solution) and water (328.8 μL, 80 wt%) were mixed in a vial before 300 μL was pipetted into a single well of a 96 well plate. The cover was secured with rubber bands and placed under a green LED lamp (λ = 530 nm, 2.65 mW/cm^2) for 4 hours at room temperature. The crude polymer was analyzed by NMR and GPC to determine monomer conversion, number-average molecular weight and molecular weight distribution.

Synthesis of homopolymers in a 96 well plate using FMN under blue light

A typical synthesis of a PDMA homopolymer ([M]:[RAFT]:[FMN]:[AscA] = 200:1:0.05:1) by aqueous RAFT photopolymerization was set up as follows: BTPA (1.8 mg, 7.55 μmol), DMA (150 mg, 1.51 mmol), FMN (0.18 mg, 18.06 μL of a 10 mg/mL stock solution), Asc A (1.33 mg, 7.55 μmol,13.3 μL of a 100 mg/mL stock solution) and water (118.6 μL, 50 wt%) were mixed in a vial before 300 μL was pipetted into a single well of a 96 well plate. The cover was secured with rubber bands (to minimize monomer evaporation) and placed under a blue LED lamp (λ_{max} = 460 nm, 2.2 mW/cm^2) for 4 hours at room temperature. The crude polymer was analyzed by NMR and GPC to determine monomer conversion, number-average molecular weight and molecular weight distribution.

Polymerization kinetics were measured by pipetting 300 μL of a stock solution ([M]:[RAFT]:[EY]:[AscA] = 200:1:0.01:1 at 50 wt% water) into 6 separate wells. The wells were irradiated under a blue LED lamp (λ_{max} = 460 nm, 2.2 mW/cm^2). Samples at different time points were analyzed by NMR and GPC.

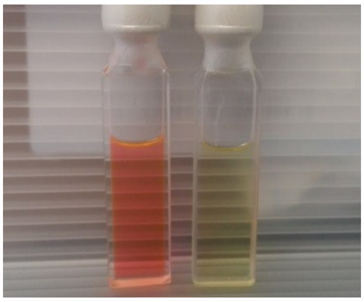


Figure S1. Representative digital photograph of polymerization solution **(left)** before and **(right)** after 60 min green light irradiation. The decrease in EY absorption is due to photoreduction of the dye by ascorbic acid. In the presence of oxygen, hydrogen peroxide is formed which initiates polymerization due to its further reduction by ascorbic acid yielding reactive hydroxyl radicals.

Table S1. Experimental data and characterization of PDMA synthesized using EY/AscA under green light and at variable reaction volumes. Polymerizations were performed in water using [BTPA]:[EY]:[AscA] = 1:0.009:1 at 50 wt% monomer. Control experiments P7, P8 and P9 were performed in the absence of AscA, EY and visible light respectively. n/r = not run

Entry	Volume (μL)	Monomer	Target DP	Irradiation time (h)	Conversion (%)	$M_{n,theo}$ (g/mol)	$M_{n,GPC}$ (g/mol)	Đ
P1	20	DMA	200	2	87	17 500	24 300	1.11
P2	50	DMA	200	2	95	19 100	26 700	1.10
P3	100	DMA	200	2	81	16 300	25 400	1.07
P4	200	DMA	200	2	79	15 900	19 700	1.07
P5	1600	DMA	200	4	85	17 100	21 300	1.06
P6	4400	DMA	200	4	73	14 700	17 800	1.07
P7 (w/o AscA)	1600	DMA	200	4	3	830	n/r	n/r
P8 (w/o EY)	1600	DMA	200	4	1	440	n/r	n/r
P9 (w/o Light)	1600	DMA	200	4	2	630	n/r	n/r
P10	20	DMA	100	2	81	8 300	11 400	1.10
P11	50	DMA	100	2	90	9 200	12 800	1.09
P12	100	DMA	100	2	94	9 600	12 800	1.08
P13	200	DMA	100	2	80	8 200	8 600	1.07
P14	20	DMA	500	2	60	30 000	31 200	1.19
P15	50	DMA	500	2	87	43 400	51 800	1.17
P16	100	DMA	500	2	94	46 800	44 200	1.13
P17	200	DMA	500	2	79	39 400	54 800	1.13
P18	20	DMA	1000	2	43	42 900	48 900	1.41
P19	50	DMA	1000	2	89	88 500	78 000	1.30
P20	100	DMA	1000	2	93	92 400	90 400	1.31
P21	200	DMA	1000	2	87	86 500	86 900	1.22

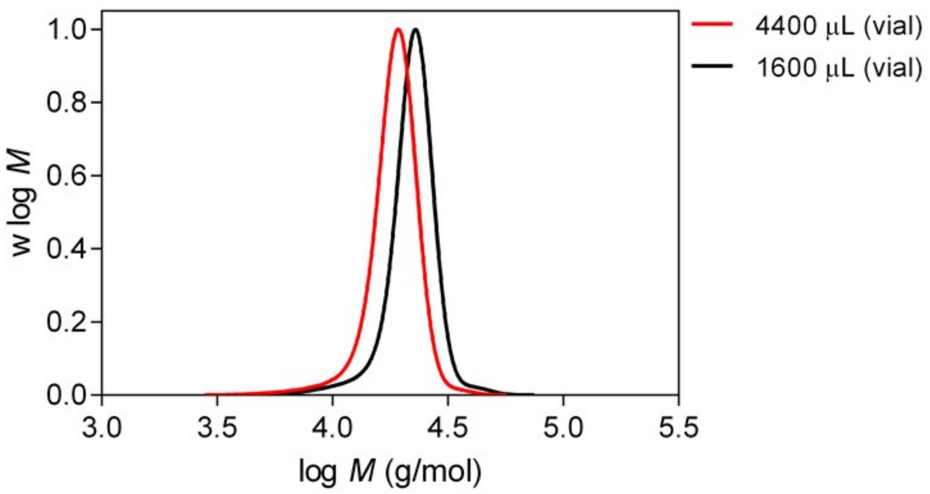
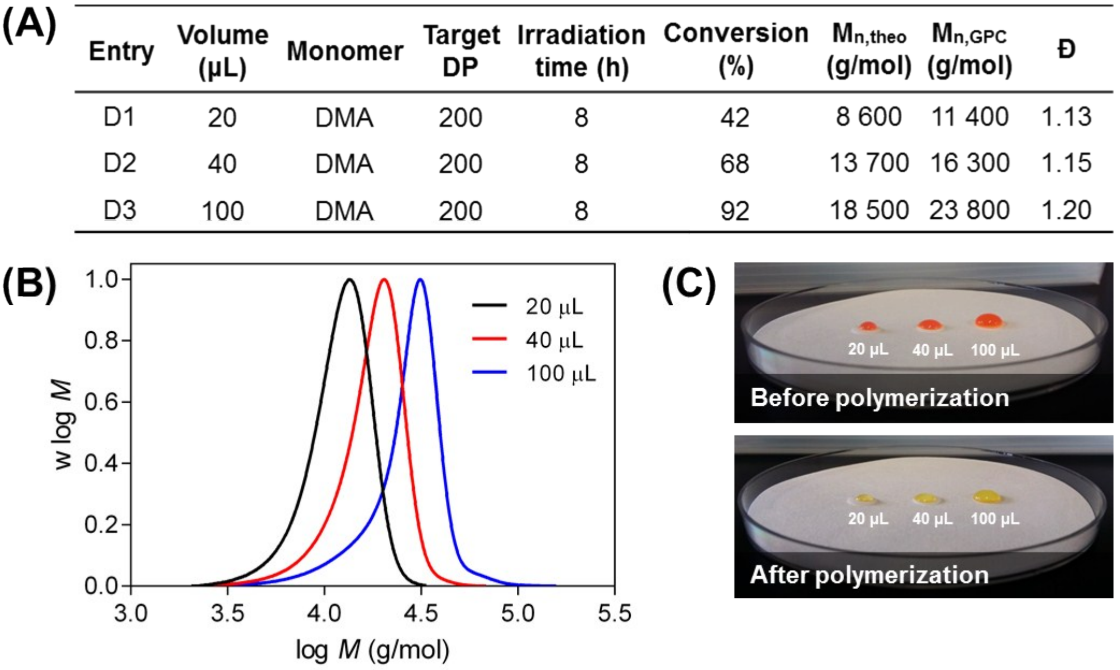


Figure S2. GPC derived molecular weight distributions of PDMA synthesized at DP200 at reaction volumes of 1600 and 4400 μL.



(A)

Entry	Volume (μL)	Monomer	Target DP	Irradiation time (h)	Conversion (%)	$M_{n,theo}$ (g/mol)	$M_{n,GPC}$ (g/mol)	Đ
D1	20	DMA	200	8	42	8 600	11 400	1.13
D2	40	DMA	200	8	68	13 700	16 300	1.15
D3	100	DMA	200	8	92	18 500	23 800	1.20

Figure S3. Experimental details and characterization of PDMA synthesized in discrete droplets (20, 40 and 100 μL) on a polytetrafluoroethylene substrate. **(B)** GPC derived molecular weight distribution of PDMA synthesized in droplets of different volumes. **(C)** Representative digital photographs taken before and after photopolymerization.

Table S2. Experimental data and characterization of PDMA synthesized on a 96-well microtitre plate using EY/AscA under green light. Polymerizations were performed in water using [RAFT]:[EY]:[AscA] = 1:0.009:1 at 50 wt% monomer. The theoretical molecular weight was calculated using the following equation, $M_{n,theo}$ = TargetDP × Conversion × MW^{DMA} + MW^{BTPA}

Entry	**Monomer**	**Irradiation time (h)**	**Target DP**	**Conversion (%)**	**$M_{n,theo}$ (g/mol)**	**$M_{n,GPC}$ (g/mol)**	**Đ**
P22	DMA	2	50	90	4 700	4 900	1.08
P23	DMA	2	75	92	7 100	7 400	1.07
P24	DMA	2	100	94	9 600	9 900	1.07
P25	DMA	2	150	88	13 300	13 200	1.08
P26	DMA	2	200	88	17 700	20 100	1.09

(A)

Entry	Polymer	Target DP	Conversion (%)	$M_{n,theo}$ (g/mol)	$M_{n,GPC}$ (g/mol)	Đ
CE1	$PDMA_{41}$	50	82	4 300	4 400	1.08
CE2	$PDMA_{41}$-*b*-$PDMA_{198}$	200	99	23 900	23 300	1.13
CE3*	$PDMA_{41}$-*b*-$PDMA_{198}$	200	99	23 900	24 700	1.13
CE4	$PDMA_{41}$-*b*-$PDEA_{192}$	200	96	28 700	24 300	1.17

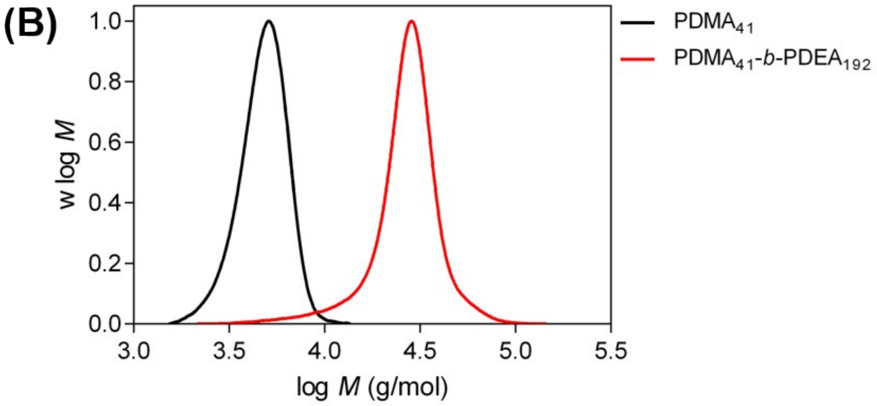
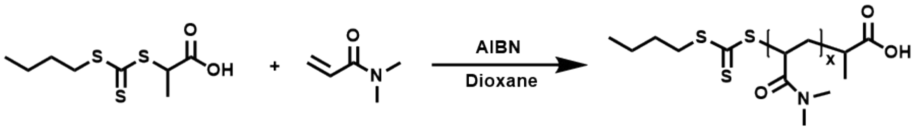


Figure S4. (A) Experimental details and characterization of diblock copolymers synthesized via in situ chain extension (without intermediate purification). **(B)** GPC derived molecular weight distribution of $PDMA_{41}$ macroRAFT (**CE1**) and PDMA-*b*-PDEA (**CE4**) diblock copolymer. ***CE3** chain extension was performed without additional EY (DMA added only).

Table S3. Experimental data and characterization of different polymer families synthesized using EY/AscA under green light. Polymerizations were performed in water using [RAFT]:[EY]:[AscA] = 1:0.009:1 at 50 wt% monomer.

Entry	Monomer	Irradiation time (h)	Target DP	Conversion (%)	$M_{n,theo}$ (g/mol)	$M_{n,GPC}$ (g/mol)	Đ
P27	DEA	2	200	50	13 000	12 500	1.13
P28	HEAm	2	200	53	12 400	18 300	1.12
P29	HEA	1	200	50	11 900	14 500	1.17
P30	OEGA	1	50	80	19 400	16 800	1.16
P31	OEGMA	18	50	57	8 800	9 300	1.15



(A)

Entry	Polymer	[M]:[RAFT]	Conversion (%)	$M_{n,theo}$ (g/mol)	$M_{n,GPC}$ (g/mol)	Đ
PDMA-1	$PDMA_{41}$	50	82	4 300	4 700	1.09
PDMA-2	$PDMA_{78}$	100	78	8 000	8 800	1.07

(B)

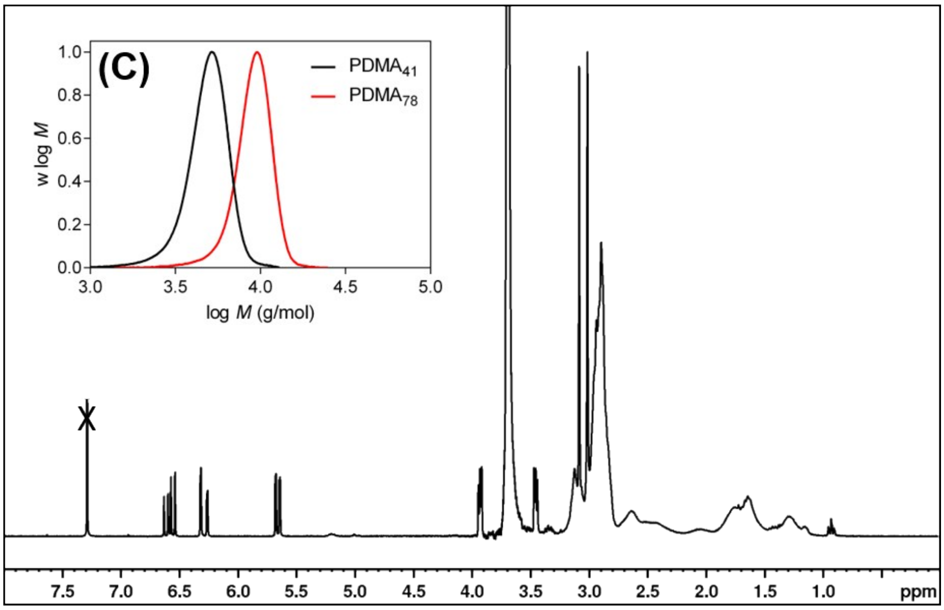


Figure S5. (A) Characterization of PDMA macroRAFT agents prepared by thermally initiated RAFT polymerization. **(B)** NMR spectra of crude PDMA and **(C, Inset)** GPC derived molecular weight distributions of PDMA homopolymers synthesized using thermally initiated RAFT polymerization.

(A)

Sample	Time (h)	Volume (μL)	[MBA]:[macroRAFT]	MBA Conversion (%)	Star Conversion (%)	$M_{n,stars}$ (g/mol)	$Đ_{stars}$	D_h (nm)
PDMA-2	n/a	n/a	n/a	n/a	n/a	n/a	n/a	3.9
CCS-5	8	20	10	18	n/a	n/a	n/a	6.5
CCS-6	8	50	10	78	90	65 800	1.31	8.9
CCS-7	8	100	10	99	96	78 800	1.26	7.6
CCS-8	8	200	10	90	96	69 400	1.21	6.7
CCS-9	14	20	10	45	n/a	n/a	n/a	6.9
CCS-10	14	50	10	94	92	62 800	1.33	11.7

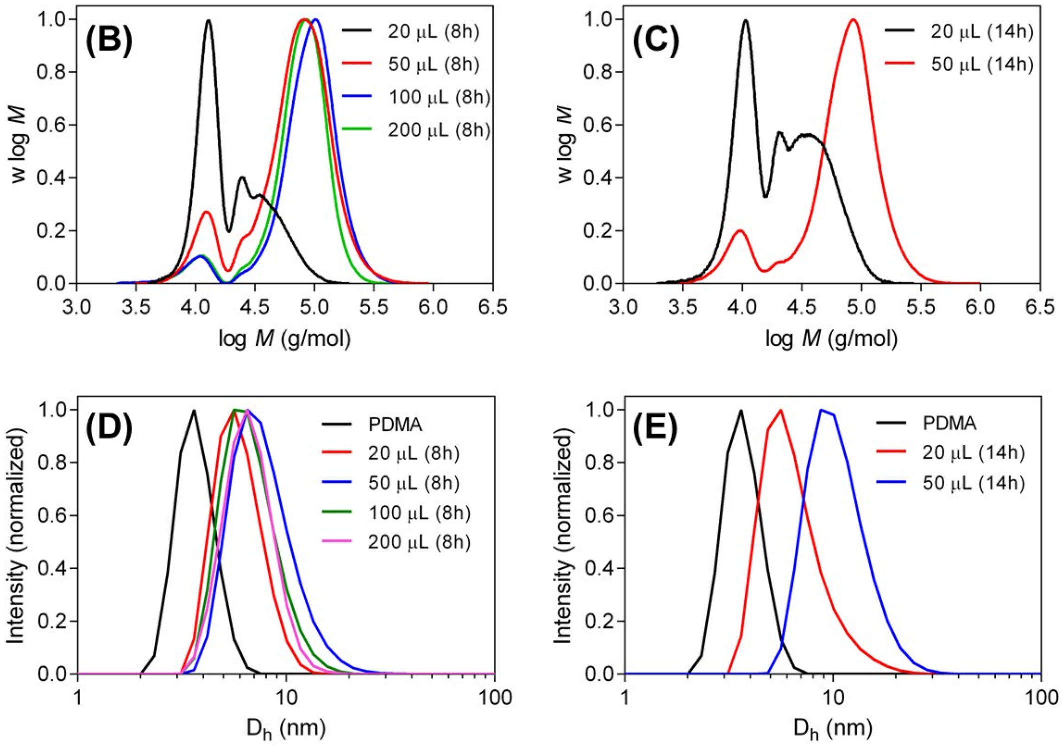


Figure S6. **(A)** Experimental data and characterization of PDMA star polymers synthesized at ultralow volumes (20, 50, 100 and 200 μL) by the arm-first method at a [MBA]:[macroRAFT] ratio of 10:1. **(B, C)** GPC derived molecular weight distributions and **(D, E)** particle size distributions of PDMA star polymers as determined by DLS analysis (volume-based distribution). Star conversions were determined by comparing the integral of the (deconvoluted) peaks associated with the star polymer and residual macroRAFT agent. Polymerizations were irradiated with green light for either **(B, D)** 8 or **(C, E)** 14 h.

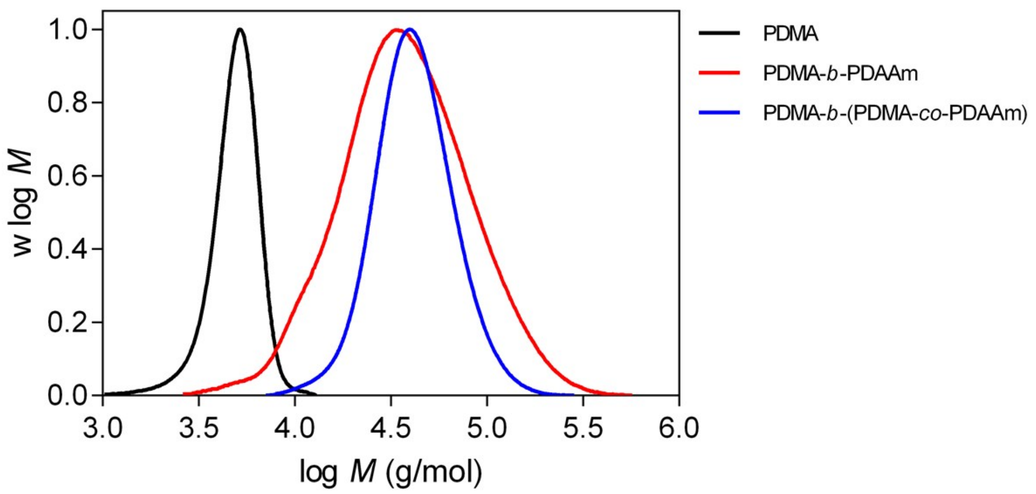


Figure S7. Comparison of GPC derived molecular weight distributions for the aqueous dispersion polymerization of DAAm with (blue line, *Đ* = 1.24) and without DMA (red line, *Đ* = 1.61) as a comonomer.

Table S4. Additional characterization of polymers synthesized using aqueous RAFT dispersion polymerization using a [macroRAFT]:[EY]:[AscA] = 1:0.05:1 and a total solids content of 20 wt%. Theoretical molecular weight was calculated using the following equation: $M_{n,theo} = ([DMA]_0/[macroRAFT]_0 \times \alpha_{DMA} \times MW^{DMA}) + ([DAAm]_0/[macroRAFT]_0 \times \alpha_{DAAm} \times MW^{DAAm}) + M_{n,macroRAFT}$.

Entry	[DAAm]: [macroRAFT]	[DMA]: [macroRAFT]	DAAm conversion (%)	DMA conversion (%)	$M_{n,theo}$ (g/mol)	$M_{n,GPC}$ (g/mol)	Đ
PISA-1	90	10	99	100	20 400	21 100	1.23
PISA-2	180	20	100	100	36 700	35 900	1.24
PISA-3	270	30	99	100	52 500	40 700	1.41
PISA-4	360	40	98	100	68 000	48 800	1.65
PISA-5	80	20	100	100	19 800	18 600	1.14
PISA-6	160	40	100	100	35 300	29 500	1.26
PISA-7	240	60	100	100	50 900	38 900	1.33
PISA-8	320	80	99	100	65 800	50 300	1.44

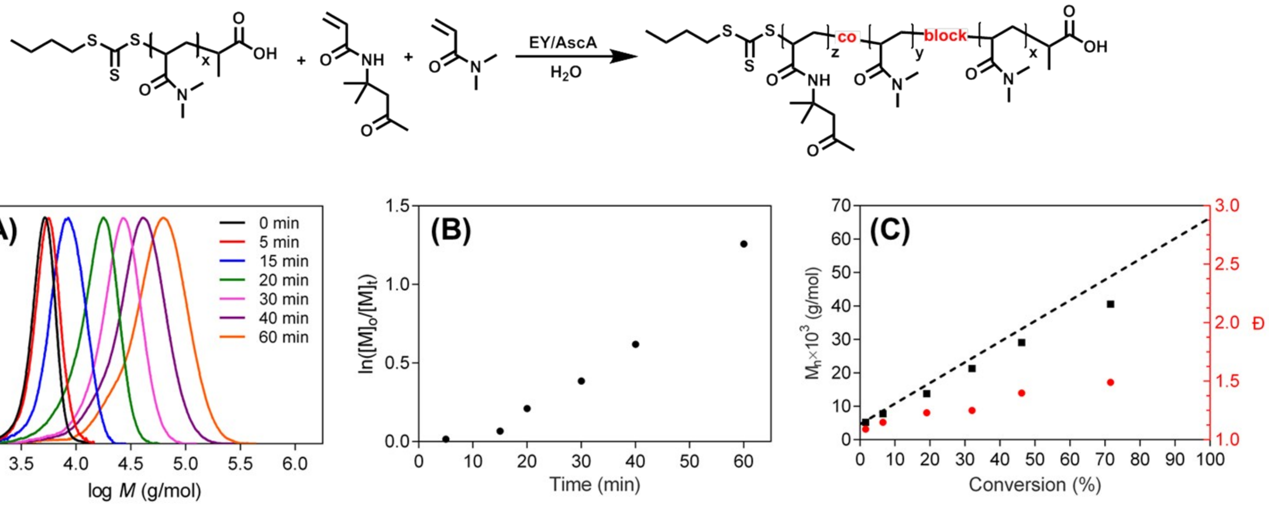


Figure S8. Kinetics of aqueous RAFT dispersion polymerization at a total solids content of 20 wt % and employing [DAAm]:[DMA]:[macroRAFT]:[EY]:[AscA] = 320:80:1:0.05:1. **(A)** GPC derived molecular weight distributions at different irradiation times. Evolution of **(B)** $\mathrm{Ln}([M]_0/[M]_t)$ with irradiation time and **(C)** number average molecular weight (black square) and dispersity (red circle) with monomer conversion.

(A)

Entry	Volume (µL)	DAAm conversion (%)	DMA conversion (%)	$M_{n,theo}$ (g/mol)	$M_{n,GPC}$ (g/mol)	Đ
PISA-9	20	28	13	13 100	20 300	1.34
PISA-10	50	97	99	35 800	41 700	1.18
PISA-11	100	99	99	36 400	42 400	1.17
PISA-12	200	99	99	36 400	42 300	1.16

(B)

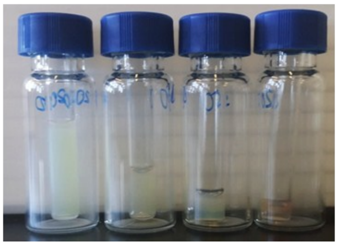
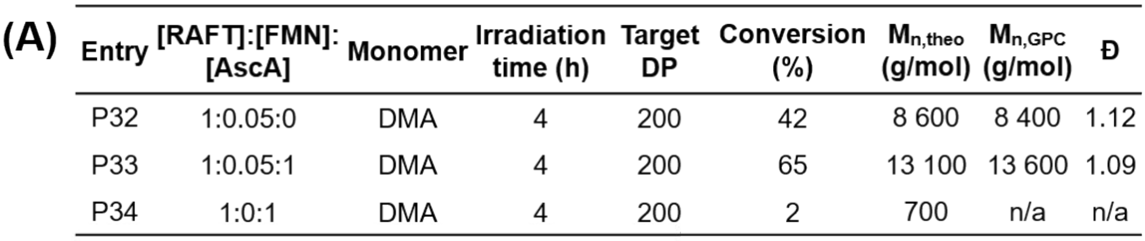


Figure S9. (A) Experimental data, characterization and **(B)** digital photograph of polymers synthesized using aqueous RAFT dispersion polymerization at different solution volumes (20, 50, 100 and 200 µL) using a [DAAm]:[DMA]:[macroRAFT]:[EY]:[AscA] = 180:20:1:0.05:1 and a total solids content of 20 wt%.


(A)

Entry	[RAFT]:[FMN]:[AscA]	Monomer	Irradiation time (h)	Target DP	Conversion (%)	$M_{n,theo}$ (g/mol)	$M_{n,GPC}$ (g/mol)	Đ
P32	1:0.05:0	DMA	4	200	42	8 600	8 400	1.12
P33	1:0.05:1	DMA	4	200	65	13 100	13 600	1.09
P34	1:0:1	DMA	4	200	2	700	n/a	n/a

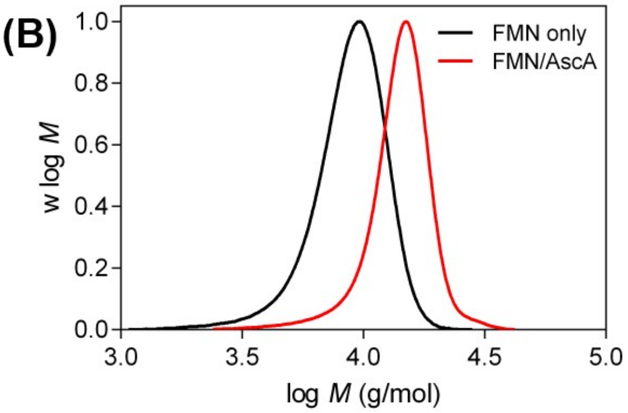


Figure S10. (A) Experimental data and characterization of polymers synthesized using FMN or FMN/AscA. **(B)** GPC derived molecular weight distributions of FMN initiated RAFT polymerization of DMA with and without AscA. Polymerizations were performed using [DMA]:[BTPA]:[FMN] = 200:1:0.05 under blue light irradiation (λ_{max} = 460 nm, 2.2 mW/cm^2) .

Additional References

1. Mitsukami, Y.; Donovan, M. S.; Lowe, A. B.; McCormick, C. L. *Macromolecules* **2001,** 34, (7), 2248-2256.
2. Ferguson, C. J.; Hughes, R. J.; Nguyen, D.; Pham, B. T. T.; Gilbert, R. G.; Serelis, A. K.; Such, C. H.; Hawkett, B. S. *Macromolecules* **2005,** 38, (6), 2191-2204.