Supporting Information

Experimental

Materials

Carbon disulfide, butyl mercaptan, n-dodecyl mercaptan, trimethylsilyl diazomethane, deuterated chloroform, deuterated DMSO, 2-bromopropionic acid, 2-bromo-2-methylpropionic acid, triethylborane (Et_3B), tribasic potassium phosphate, alpha-lipoic acid, and N-isopropylacrylamide (NiPam) were purchased from Adamas. Acetone, chloroform, n-hexane, dichloromethane, HCl, toluene, ethyl acetate, and petroleum ether were purchased from Shaanxi Guoyao Company. Tetrabutylammonium sulfate was purchased from Energy Chemical. Sodium hydroxide and anhydrous sodium sulfate were purchased from Aladdin Company. 4-Methyloxypyridine (MeOPy) and 4-(Dimethylamino)pyridine (DMAP) were purchased from Bide Pharmatech. N-Phenylmethylamine and acryloyl chloride were purchased from Rhawn.

Characterization

The ^1H NMR characterization of chain transfer agents, initiators, and N-methyl -N-phenylacrylamide monomers was performed using a Bruker Avance Neo 500 MHz NMR spectrometer at 25℃. Each test sample weighed 1 mg, with 0.6 mL of deuterated reagent. The molecular weight (M_n) molecular weight distribution (M_w/M_n) of the ball-milled polymers were determined using an Agilent 1260 HPLC system equipped with G7110B pump and a G7162A refractive index detector. Apparent molecular weight was measured on a single PL gel MIXED-C column using a linear polymethyl methacrylate standard. The polymers prepared in this experiment required pretreatment prior to testing. The synthesized TA copolymers were dissolved in HPLC-grade tetrahydrofuran (THF) solution and subjected to methylation with trimethylsilyl diazomethane for 2–3 hours. The solution was then filtered through a 0.22 μm nylon membrane filter head and injected into a 1.5 mL chromatographic vial for subsequent testing. For the solid-state ball-milling copolymerization, a 25 mL stainless steel ball milling jar was used with 10 mm × 2 stainless steel grinding balls. The ball milling apparatus employed a German Retsch MM400 ball mill operating at a maximum frequency of 30 Hz.

Synthesis of 2,2'-(thiocarbonylbis(sulfanediyl))bis(2-methylpropanoic acid)(ATTC)

The synthesis of ATTC was performed according to the literature.[1] A 500 mL round-bottom flask was mixed with 11.4 g acetone, 24 g chloroform, and 26 mL n-hexane. After stirring, the flask was placed in an ice bath. Once the mixture cooled to 0 °C, 0.52 g tetrabutylammonium sulfate was

added, followed by stirring for 30 min. Slowly add 6.0 g of carbon disulfide dropwise. After completion of the addition, slowly add 50 mL of 50% NaOH solution while maintaining the temperature below 10 °C. After completion of the addition, stir the reaction mixture at room temperature for 12 hours. An orange-yellow solid will precipitate during the reaction. Upon completion, add 100 mL of deionized water to dissolve the precipitate. Add 10 M HCl to adjust the solution pH to < 4. Continue stirring for 30 minutes to allow the product to precipitate. Filter the solid product and wash with water. Vacuum dry to obtain an orange-yellow crude product. Wash the crude product with a toluene/acetone mixture (4:1) for 30 min. Filter to collect a yellow powder. Vacuum dry to obtain purified ATTC with a yield of 78%. ^{1}H NMR (500 MHz, Chloroform-*d*) δ 1.70 (s, 12H) (Fig. S1).

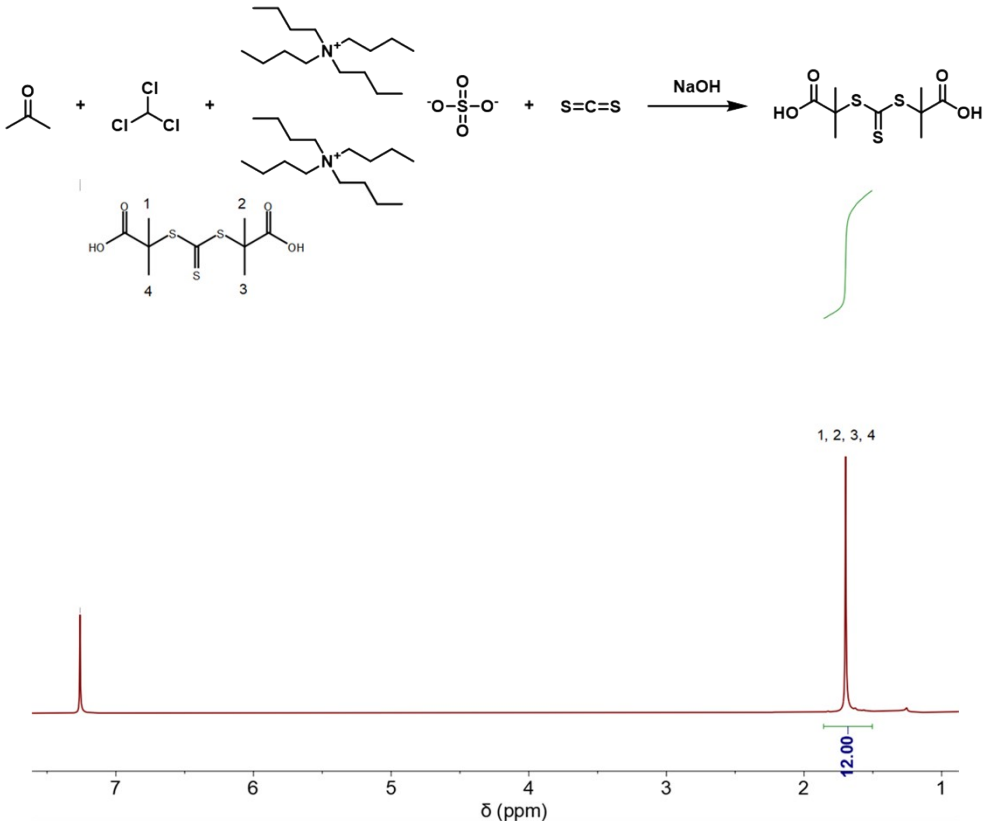


Fig. S1. Synthesis procedure and ^{1}H NMR of ATTC chain transfer agent

Synthesis of 2-butylsulfanyl-thiocarbonylsulfanyl-propionic acid(BTPA)

The synthesis of BTPA was performed according to the literature.[2] A mixture of 200 mmol butyl mercaptan and water was added to a 250 mL round-bottom flask. Sodium hydroxide (200 mmol) was dissolved in water to form a 50% w/w aqueous solution, which was then slowly added dropwise to the mixture after being cooled to room temperature. Subsequently, 10 mL acetone was added to the reaction mixture and stirred until the solution became clear. The resulting clear solution

was stirred for 30 minutes and cooled to room temperature. Subsequently, 225 mmol of carbon disulfide was added to the reaction mixture and stirred for 30 minutes. The reaction mixture was then cooled to 0°C in an ice bath. Next, 205 mmol of 2-bromopropionic acid was added dropwise, followed by 16.4 mL of 50% sodium hydroxide aqueous solution, maintaining the ice bath throughout to control the temperature. After the exothermic reaction ceases, add 30 mL water and react at room temperature for 24 hours. Upon completion, dilute the mixture with 50 mL water and cool the reaction mixture on an ice bath to 0°C. Add 60 mL of 10 M HCl dropwise until a yellow oily substance separates. Stir under ice bath conditions for 30 minutes. After the yellow product precipitates, filter and collect the solid. Wash the product with cold water and dry it. Recrystallize from n-hexane to obtain a yellow crystalline product in 87% yield. ^{1}H NMR (500 MHz, Chloroform-*d*) δ 4.86 (q, *J* = 7.4 Hz, 1H), 3.45 – 3.30 (m, 2H), 1.80 – 1.56 (m, 5H), 1.44 (h, *J* = 7.4 Hz, 2H), 0.94 (t, *J* = 7.4 Hz, 3H) (Fig. S2).

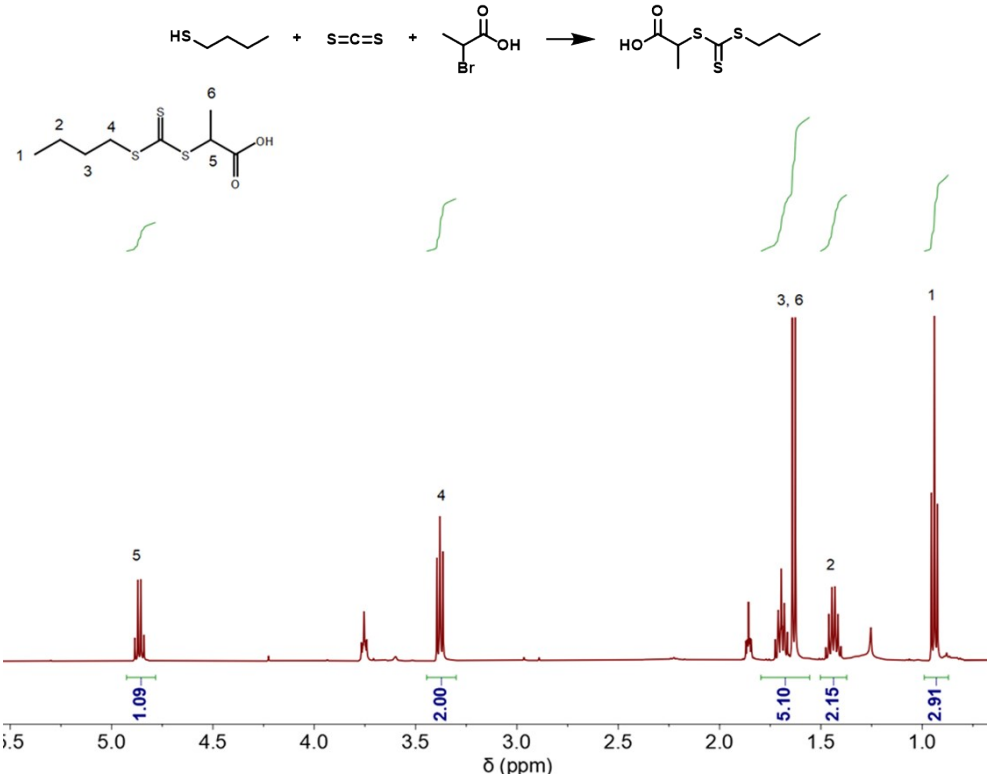


Fig. S2. Synthesis procedure and ^{1}H NMR of BTPA chain transfer agent

Synthesis of 2-(dodecylthiocarbonothioylthio)-2-methylpropionic acid(DDMAT)

The synthesis of DDMAT was performed according to the literature.[3] Add 60 mL acetone to a 250 mL round-bottom flask, followed by 3.5 g K_3PO_4 and 5 mL n-dodecyl mercaptan. Stir the mixture at room temperature for 20 min. Slowly add 2.72 mL carbon disulfide to the mixture. Continue stirring the mixture at room temperature for 20 min. After the reaction, add 2.505 g of 2-

bromo-2-methylpropanoic acid to the mixture and stir at room temperature for 12 h. Upon completion, add 200 mL of 1 M HCl to the mixture. After reacting for a period, extract the mixture with dichloromethane. Wash the organic layer with deionized water and saturated NaCl solution, then dry it over anhydrous sodium sulfate. Remove the solvent by rotary evaporation to obtain a yellow crude product. Recrystallize from n-hexane to yield a pale yellow solid product in 74% yield. ^{1}H NMR (500 MHz, Chloroform-*d*) δ 3.36 – 3.18 (m, 2H), 1.86 – 1.54 (m, 8H), 1.42 – 1.24 (m, 18H), 0.88 (t, *J* = 6.9 Hz, 3H) (Fig. S3).

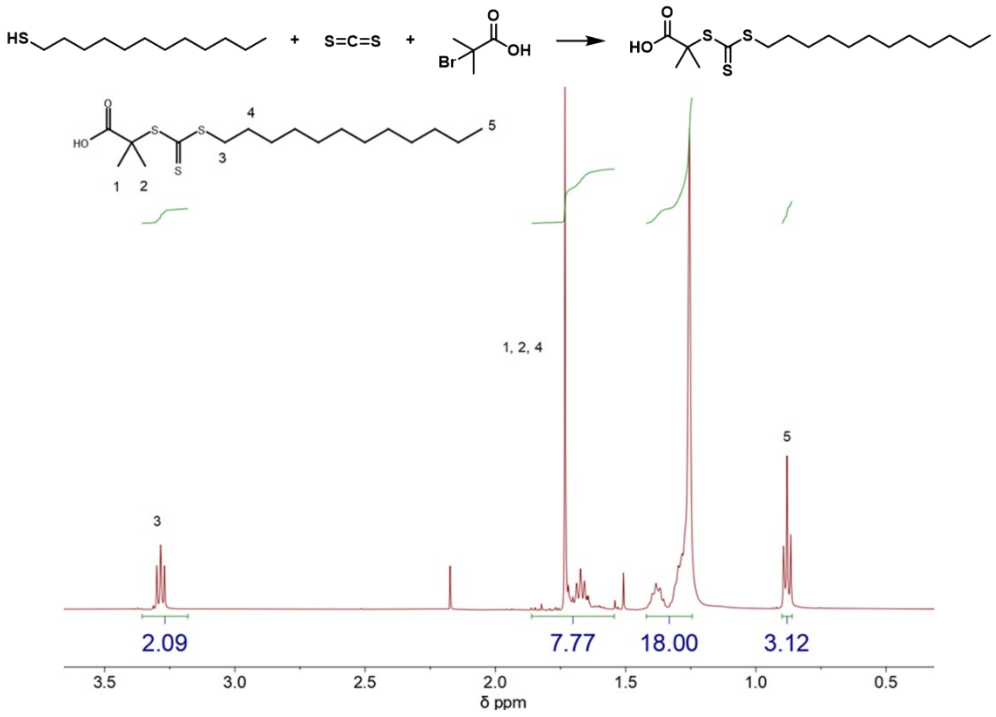


Fig. S3. Synthesis procedure and ^{1}H NMR of DDMAT chain transfer agent

Synthesis of 4-cyano-4-(((dodecylthio)carbonothioyl)thio)pentanoic acid(CDTPA)

The synthesis of CDTPA was performed according to the literature.[4] At 0°C, dodecyl mercaptan (15.4 g, 76 mmol) was slowly added to a solution of sodium hydride (3.15 g, 79 mmol) in anhydrous diethyl ether (150 mL). The reaction proceeded rapidly, releasing gas and forming a white, viscous paste of sodium dodecyl mercaptide. The mixture was then cooled to 0°C, and carbon disulfide (6.0 g, 79 mmol) was slowly added dropwise. The solution gradually formed a yellow precipitate of sodium S-dodecyl trithiocarbonate. The resulting sodium S-dodecyl trithiocarbonate was dissolved in anhydrous diethyl ether (100 mL). Solid iodine (6.3 g, 25 mmol) was added in portions under stirring. The mixture was stirred continuously at room temperature for 1 h. After the reaction, the solid sodium iodide was washed with diethyl ether and filtered off. The yellow-brown filtrate was further washed with sodium thiosulfate aqueous solution to remove residual iodine. The

organic phase was dried over anhydrous magnesium sulfate, and the solvent was removed by rotary evaporation to afford bis(dodecylthioylcarbonyl) disulfide. 4,4'-Azobis(4-cyanopentanoic acid) (3.15 g, 11.25 mmol) and the previously synthesized bis(dodecanethiolylthioyl) disulfide (4.16 g, 7.5 mmol) were dissolved together in ethyl acetate (75 mL). The reaction mixture was refluxed under nitrogen protection with continuous stirring for 18 h. After completion, the mixture was cooled to room temperature. The resulting solution was extracted multiple times with deionized water (3 × 500 mL) to remove water-soluble byproducts and unreacted starting materials. The organic layer was dried over anhydrous magnesium sulfate and the solvent was removed by vacuum distillation, yielding a pale yellow oily crude product. To further enhance product purity, recrystallization was performed twice using n-hexane as the solvent. This yielded high-purity chain transfer agent 4-cyano-4-[(dodecylthioylthiocarbonyl)thioyl]pentanoic acid (CDTPA), a pale yellow solid, in 76% yield. ^{1}H NMR (500 MHz,) δ 3.33 (t, *J* = 7.5 Hz, 2H), 2.69 (ddd, *J* = 8.6, 6.6, 1.8 Hz, 2H), 2.59 – 2.49 (m, 1H), 2.39 (ddd, *J* = 14.3, 9.5, 6.8 Hz, 1H), 1.89 (s, 3H), 1.72 – 1.66 (m, 2H), 1.44 – 1.35 (m, 2H), 1.26 (s, 16H), 0.88 (t, *J* = 6.8 Hz, 3H) (Fig. S4).

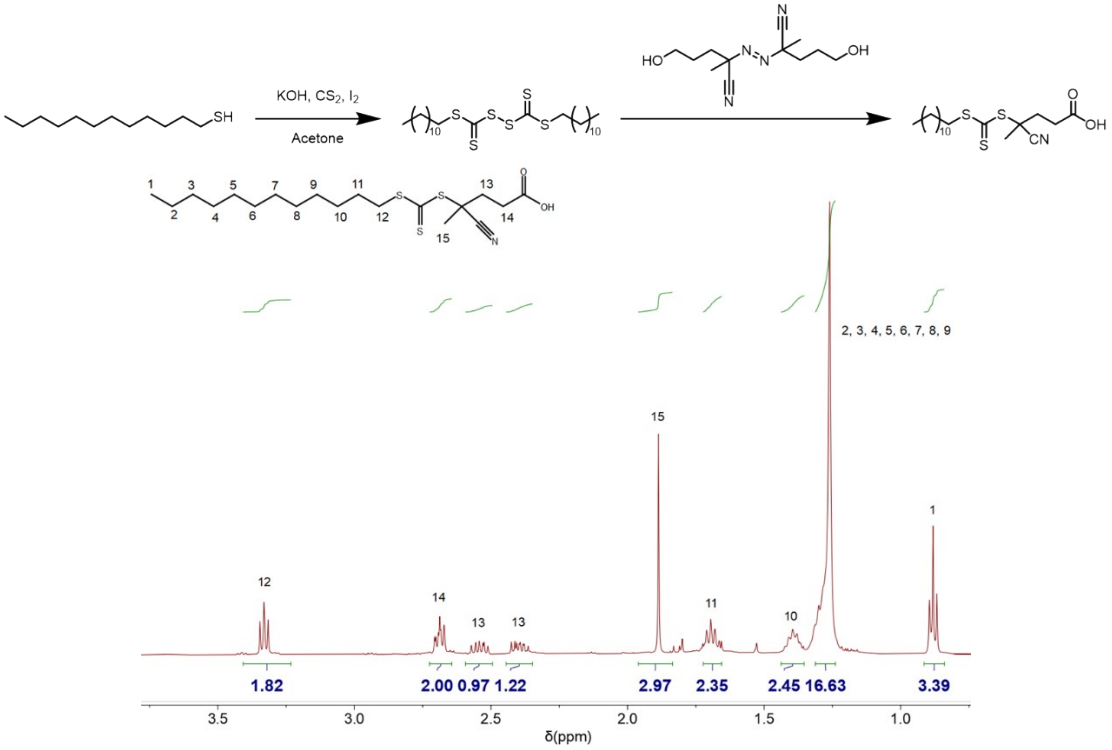


Fig. S4. Synthesis procedure and ^{1}H NMR of CDTPA chain transfer agent

Synthesis of amine-coordinated triethylborane(Et_3B-amine) complex initiator

The synthesis steps for the amine-coordinated alkylboron complex initiator were performed according to the literature.[5, 6] Add anhydrous THF to a 50 mL three-neck flask, then dissolve 20 mmol of amine ligand in the THF. Place the round-bottom flask in an ice bath and purge with dry

nitrogen for 15 min. Slowly add 20 mL of 1 M triethylboron THF solution. Stir for 1 hour, then remove the THF solution by rotary evaporation to obtain the amine-coordinated Et_3B complex (Fig. S5).

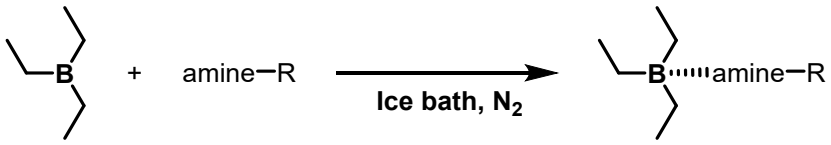


Fig. S5. Synthesis procedure of amino-coordinated alkylboron complex initiators

Triethylborane-4-methoxypyridine (Et_3B-MeOPy): Pale yellow transparent solution, yield 91%. ^{1}H NMR (500 MHz, Chloroform-*d*) δ 8.39 – 8.20 (m, 2H), 6.96 – 6.76 (m, 2H), 3.86 (s, 3H), 0.51 (t, *J* = 7.7 Hz, 9H), 0.32 (q, *J* = 7.4 Hz, 6H) (Fig. S6).

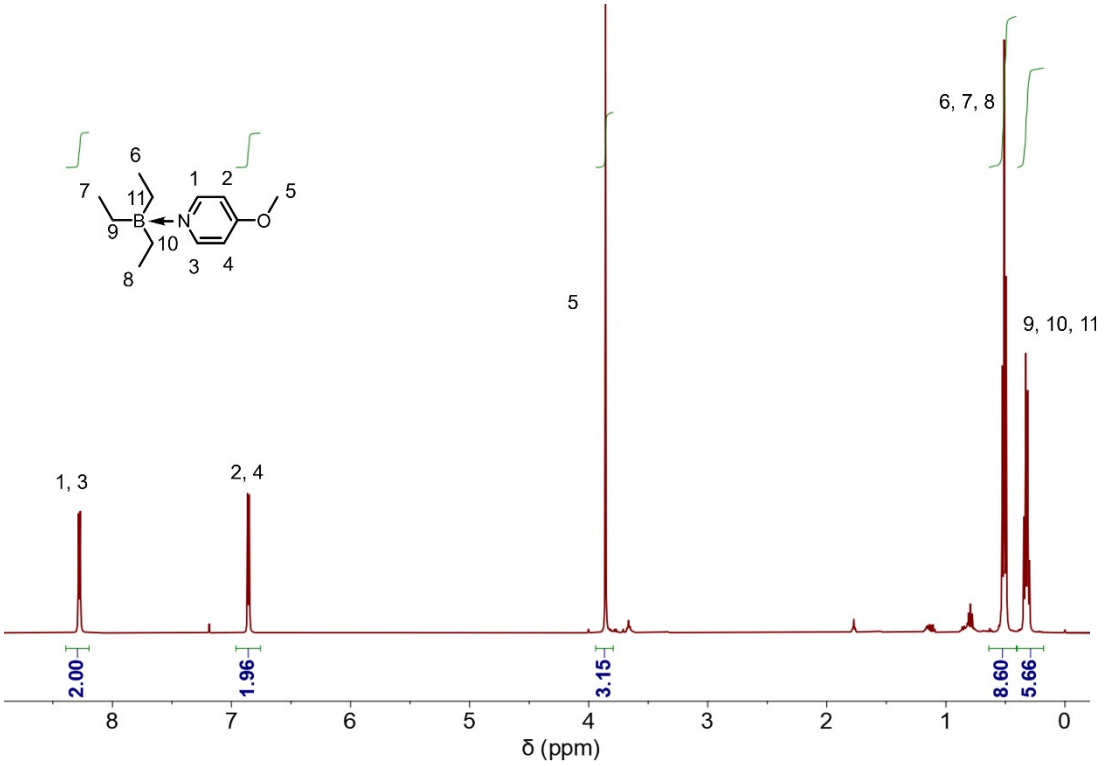


Fig. S6. ^{1}H NMR of Et_3B-MeOPy initiator

Triethylborane-4-(dimethylamino)pyridine (Et_3B-DMAP): After rotary evaporation, a pale yellow solid was obtained. Upon washing with anhydrous hexane, a white solid powder was yielded with a 97% yield. ^{1}H NMR (500 MHz, Chloroform-*d*) δ 8.14 (d, *J* = 49.4 Hz, 2H), 6.56 (d, *J* = 6.5 Hz, 2H), 3.11 (s, 6H), 0.61 (t, *J* = 7.6 Hz, 5H), 0.37 (q, *J* = 7.7 Hz, 3H) (Fig. S7).

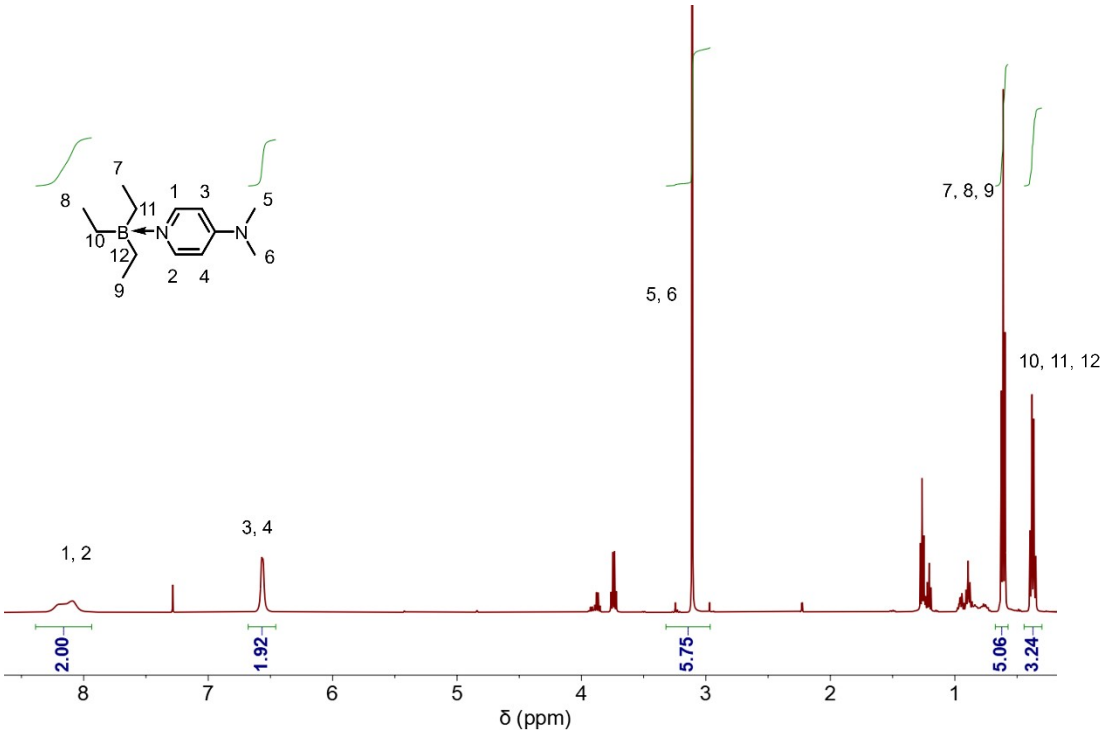


Fig. S7. ^{1}H NMR of Et_3B-DMAP initiator

Synthesis of N-methyl-N-phenylacrylamide(NNPAM)

The synthesis process was referred to the steps of literature.[7] 110 mmol triethylamine and 100 mmol N-phenylmethylamine were dissolved in dichloromethane and stirred under ice bath for 15 min, after that 110 mmol acryloyl chloride was dissolved in dichloromethane and added drop by drop, the dropwise acceleration of acryloyl chloride was controlled to finish the dropwise acceleration within 40 min-1h, avoiding the dropwise acceleration, and keeping the ice bath condition all the time in the process of dropwise acceleration. After the dropwise addition was completed, the reaction was continued to stir under the ice bath condition for 15 min, after which the reaction was carried out at room temperature overnight. At the end of the reaction water was added to the reaction vessel to burst the reaction and stirred for 15 min. after which the reaction mixture was diluted with dichloromethane. The reaction solution was washed with 1M HCl and saturated NaCl. The organic layer was separated and dried with anhydrous sodium sulfate, followed by filtration and spinning to obtain the crude product. Purification of the product by column chromatography (EA:PE=1:1) gave a pale yellow crystalline solid. ^{1}H NMR (500 MHz, Chloroform-*d*) δ 7.41 (t, J = 7.6 Hz, 2H), 7.33 (t, J = 7.3 Hz, 1H), 7.22 – 7.12 (m, 2H), 6.37 (dd, J = 16.8, 2.1 Hz, 1H), 6.07 (dd, J = 16.8, 10.4 Hz, 1H), 5.51 (dd, J = 10.4, 2.1 Hz, 1H), 3.36 (s, 3H) (Fig. S8).

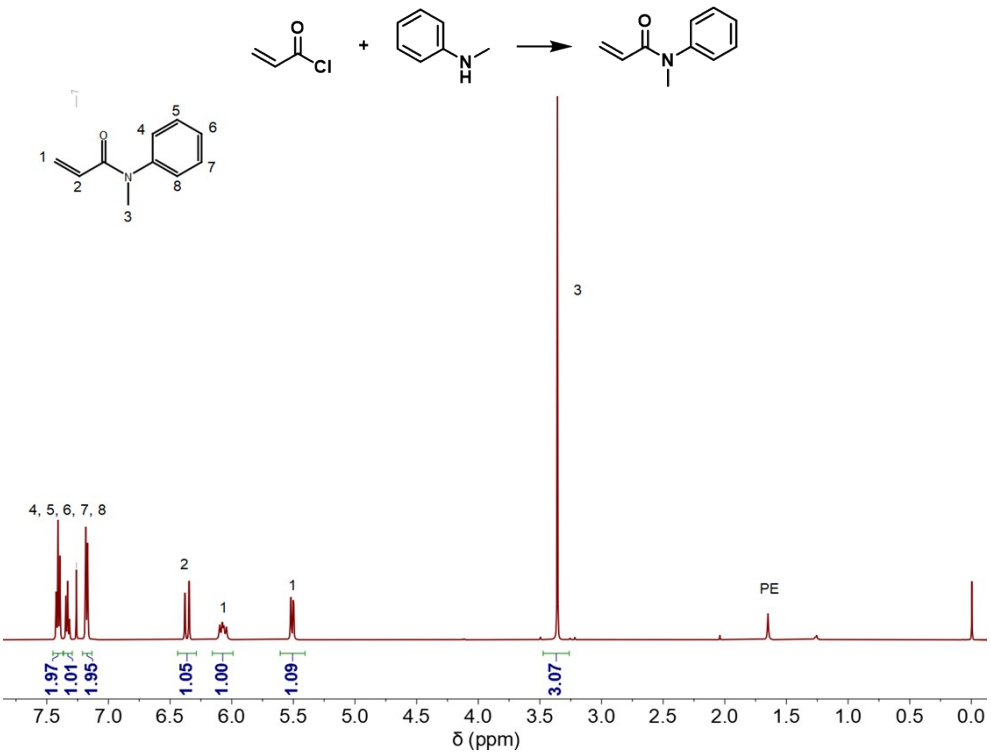


Fig. S8. Synthesis procedure and ^{1}H NMR of NNPAM monomer

General Procedure for the Mechanochemical Ball Milling Copolymerization of Lipoic Acid Copolymers

NIPam was purified to remove inhibitors by recrystallization in methanol. In a typical procedure, a 25 mL stainless steel ball milling jar was charged with two 10 mm stainless steel grinding balls, followed by NiPam (1 g, 8.84 mmol, 70 eq.), TA (0.781 g, 3.79 mmol, 30 eq.), ATTC (35.6 mg, 0.126 mmol, 1 eq.), and Et_3B-DMAP (0.138 g, 0.631 mmol, 5 eq.) to achieve a target degree of polymerization of 100, and the reaction mixture was ball-milled at 30 Hz for 1 hour with the ambient temperature maintained at 26 ± 6 °C , after which the resulting copolymer was purified by dialysis (34 mm, 1 kDa molecular weight cutoff) in acetone (1 L × 3).

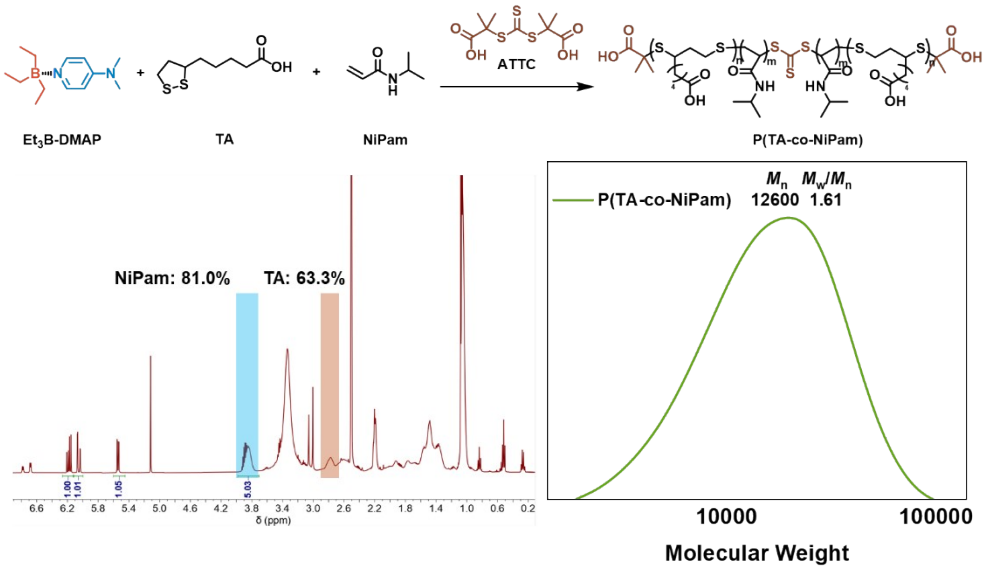


Fig. S9.[1]H NMR and GPC curves of P(TA-co-NiPam) prepared by mechanochemical solid-state ball milling

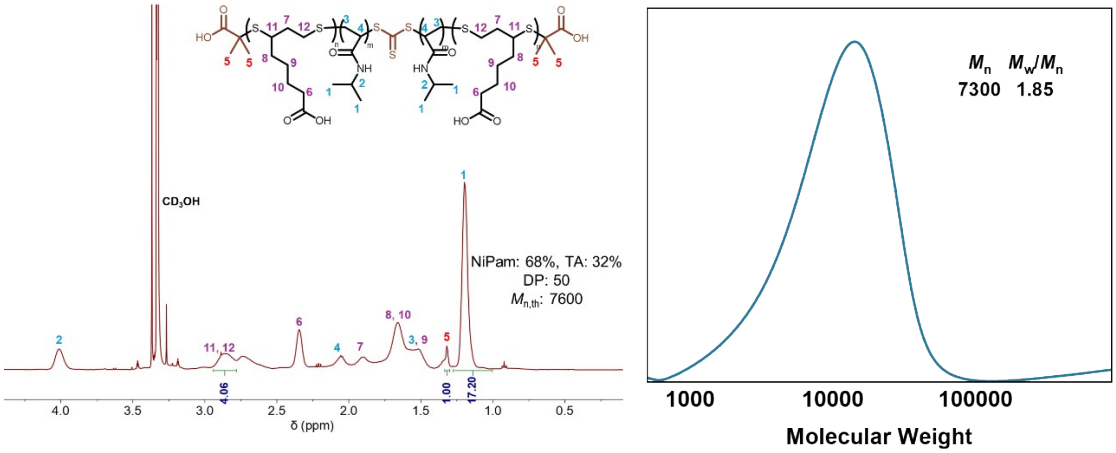


Fig S10. [1]H NMR analysis and GPC curves of the purified copolymer

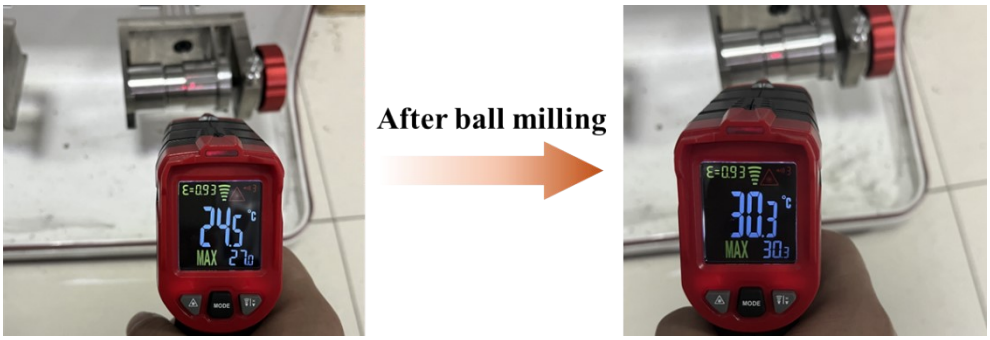


Fig. S11. Temperature changes in the ball milling jar before and after ball milling

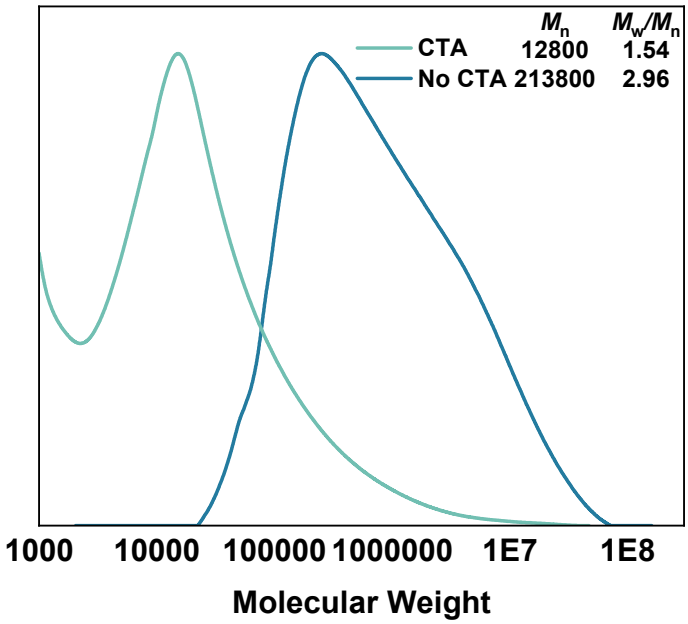


Fig. S12. GPC curves for the CTA-added and CTA-free control experiments. 30 Hz, 30 min.

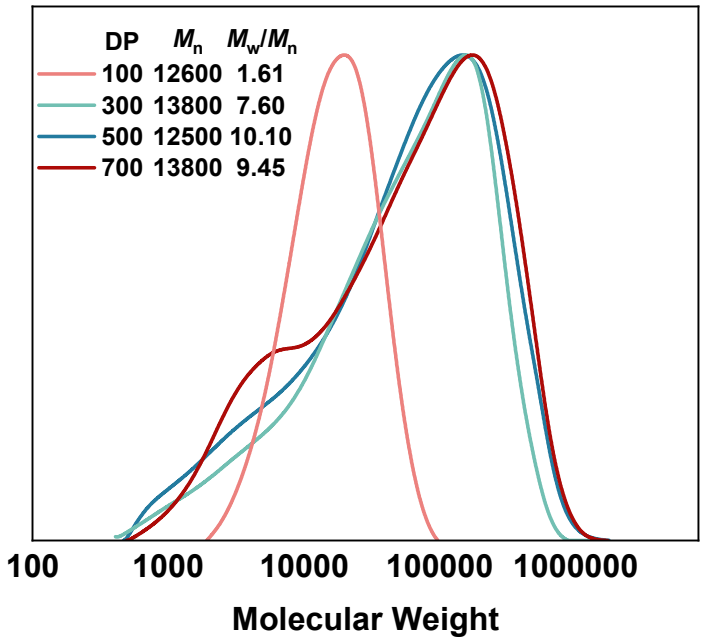


Fig. S13. GPC Curves of Lipoic Acid Copolymers with Different Targets

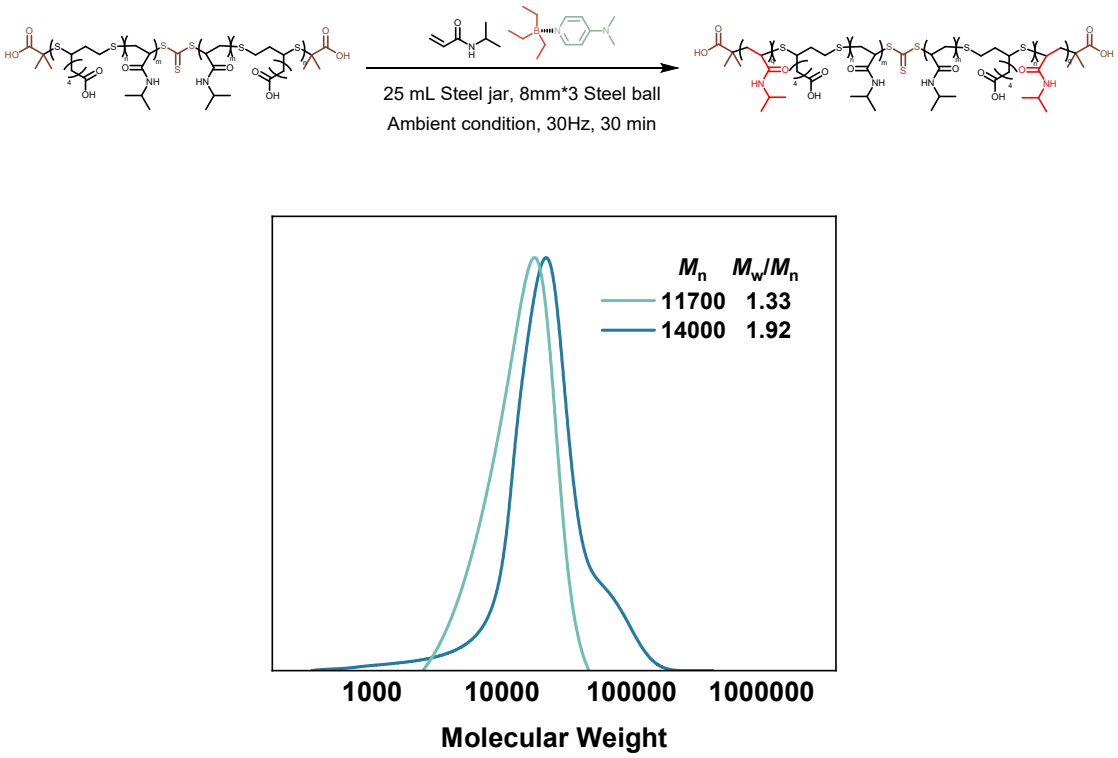


Fig S14. Chain extension experiments on purified polymers. GPC curves for the P(NiPam-co-TA) chain extension experiment. Green represents the copolymer before chain extension, blue represents the copolymer after chain extension. [NiPam]:[Macro-CTA]:[Et_3B-DMAP]=50:1:5.

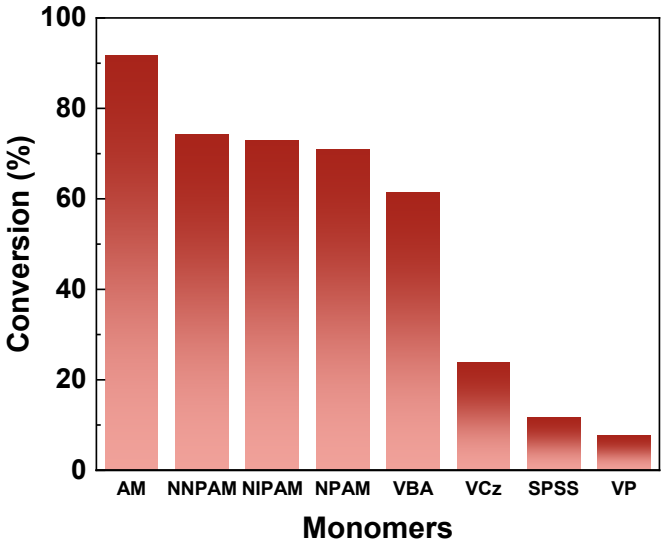
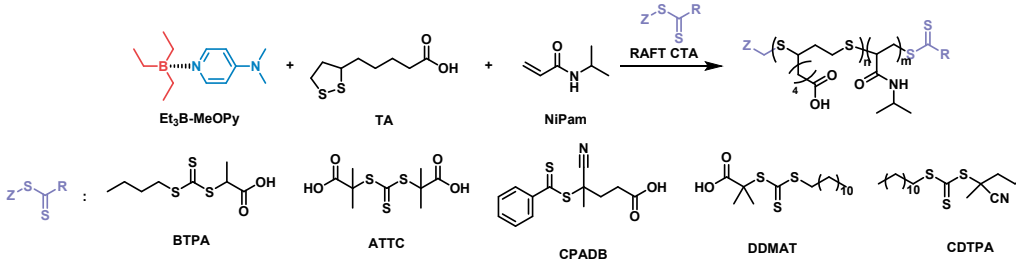


Fig. S15. Monomers conversion rates in ball milling copolymerization of different solid monomers with lipoic acid

Table S1. Effect of different RAFT chain transfer agents on the mechanochemical solid-state ball milling copolymerization of lipoic acid



Entry[a]	CTA	Conversion (%)[b]	mol %$_{NiPam}$: mol %$_{TA}$	$M_{n,th}$[c]	$M_{n,GPC}$[d]	M_w/M_n[d]
1	BTPA	TA:51.7, NiPam:49.7	79.8:20.2	7300	13100	2.09
2	ATTC	TA:63.3, NiPam:81.0	63.6:36.4	10600	12600	1.61
3	CPADB	TA:34.5, NiPam:34.2	87.7:12.3	5100	10500	4.21
4	DDMAT	TA:61.4, NiPam:67.0	74.6:25.4	12000	13900	1.82
5	CDTPA	TA:61.4, NiPam:59.2	55.9:44.1	11400	22800	1.94

[a]Target DP=100. [TA]$_0$:[NiPam]$_0$:[RAFT agent]$_0$:[Et_3B-DMAP]$_0$=30:70:1:5. [b]Conversion was determined by ^{1}H NMR spectroscopy. [c]$M_{n,th}$ was calculated based on the conversion (i.e., $M_{n,th} = M_{CTA} + M_{NiPam} \times \text{Conversion}_{NiPam}\,\% \times 70 + M_{TA} \times \text{Conversion}_{TA}\,\% \times 30$) [d]$M_{n,GPC}$ and M_w/M_n were determined by GPC in THF, base on linear PMMA calibration standards.

Table S2. Control experiments of ball-milled copolymerization of TA and NiPam with different coordination strength initiators with and without ball-milling

Entry[a]	Intiator	Condition	Conversion (%)[c]
1	Et_3B-MeOPy	Without ball milling	TA:17.2, NiPam:23.1
2	Et_3B-DMAP	Without ball milling	TA:13.3, NiPam:11.6
3[b]	Et_3B-MeOPy	Standard reaction	TA:50.8, NiPam:36.3
4[b]	Et_3B-DMAP	Standard reaction	TA:52.2, NiPam:83.8

[a]Target DP=100. [TA]$_0$:[NiPam]$_0$:[ATTC]$_0$:[Intiator]$_0$=30:70:1:5. Reaction time 30 min. [b]25 mL stainless steel jar, 10 mm*2 stainless steel grinding ball, ball milling frequency is 30 Hz. [c] Conversion was determined by ^{1}H NMR spectroscopy.

Table S3. Effect of different ball milling frequencies in the solid nonhomogeneous regime

Entry[a]	Frequence (Hz)	Conversion (%)[b]	mol %$_{NiPam}$: mol %$_{TA}$	$M_{n,th}$[c]	$M_{n,GPC}$[d]	M_w/M_n[d]
1	10	TA:42.0, NiPam:41.5	58.8:41.2	5800	12100	1.85

2	30	TA:63.3, NiPam:81.0	63.6:36.4	10600	12600	1.61

[a]Target DP=100. $[TA]_0$:$[NiPam]_0$:$[ATTC]_0$:$[Et_3B\text{-}DMAP]_0$=30:70:1:5. 25 mL stainless steel jar, 10 mm*2 stainless steel grinding ball, reaction time is 30 min. [b]Conversion was determined by ^1H NMR spectroscopy. [c]$M_{n,th}$ was calculated based on the conversion (i.e., $M_{n,th} = M_{CTA} + M_{NiPam} \times Conversion_{NiPam}\ \% \times 70 + M_{TA} \times Conversion_{TA}\ \% \times 30$) [d]$M_{n,GPC}$ and M_w/M_n were determined by GPC in THF, base on linear PMMA calibration standards.

Table S4. Monomer conversion and molecular weight characteristics of copolymerization of different types of solid monomers with lipoic acid

Entry[a]	Soild Monomer	Conversion (%)[b]	mol %$_M$: mol %$_{TA}$	$M_{n,th}$[c]	$M_{n,GPC}$[d]	M_w/M_n[d]
1[e]	AM	AM:91.8%, TA:56.4%	61.9:38.1	8000	8300[e]	1.61[e]
2	NiPam	NiPam:81.0%, TA:63.3%	63.6:36.4	9900	12600	1.61
3	NPAM	NPAM:70.9%, TA:75.5%	58.4:41.6	11900	15300	1.80
4	NNPAM	NNPAM:74.2%, TA:50.7%	69.5:30.5	11500	12300	1.97
5	VP	VP:7.7%, TA:11.5%	35.9:64.1	1500	5000	1.62
6	VBA	VBA:61.3%, TA:44.2%	58.2:41.8	9100	9600	1.39
7	SPSS	SPSS:11.7%, TA:10.2%	49.5:50.5	2300	5800	2.24
8	VCz	VCz:23.9%, TA:13.2%	64.4:35.6	4000	6300	2.10

[a]Target DP=100. $[TA]_0$:[Soild Monomer]$_0$:$[ATTC]_0$:$[Et_3B\text{-}DMAP]_0$=30:70:1:5. Reaction condition: 25 mL stainless steel jar and 10 mm*2 stainless steel grinding ball. Ball milling frequency is 30 Hz and reaction time is 30 Hz. [b]Conversion was determined by ^1H NMR spectroscopy. [c]$M_{n,th}$ was calculated based on the conversion (i.e., $M_{n,th} = M_{CTA} + M_{mononer} \times Conversion_{monomer}\ \% \times 70 + M_{TA} \times Conversion_{TA}\ \% \times 30$) [d]$M_{n,GPC}$ and M_w/M_n were determined by GPC in THF, base on linear PMMA calibration standards. [e]$M_{n,GPC}$ and M_w/M_n of P(AM-co-TA) were determined by GPC in DMF, base on linear PS calibration standards.

Table S5. Mechanochemical Ball Milling Copolymerization at Different Degrees of Polymerization

Entry[a]	DP	Conversion (%)	$M_{n,th}$	$M_{n,GPC}$	M_w/M_n
1	100	TA: 63.3, NiPam: 81.0	10800	12600	1.61
2	300	TA: 69.6, NiPam: 79.1	43600	13800	7.60
3	600	TA: 50.3, NiPam: 84.8	60000	12500	10.10
4	800	TA: 49.1, NiPam: 77.4	74600	13800	9.45

[a] 25 mL stainless steel grinding jar, 4*10 mm stainless steel grinding balls, 30 Hz, 30 min. Initial feed TA content is 30%.

Reference

1. P. Chakma, S. M. Zeitler, F. Baum, J. Yu, W. Shindy, L. D. Pozzo and M. R. Golder, *Angewandte Chemie*, 2023, **135**, e202215733.
2. S. Shanmugam, J. Cuthbert, T. Kowalewski, C. Boyer and K. Matyjaszewski, *Macromolecules*, 2018, **51**, 7776-7784.
3. T. Nwoko, N. D. A. Watuthanthrige, B. Parnitzke, K. Yehl and D. Konkolewicz, *Polymer Chemistry*, 2021, **12**, 6761-6770.
4. S. Wang, L. Li, Q. Liu and M. W. Urban, *Macromolecules*, 2022, **55**, 4703-4709.
5. Z. Chen, Y. Du, X. Li and X. Pan, *Macromolecules*, 2024, **57**, 4192-4198.
6. H. Feng, Z. Chen, L. Li, X. Shao, W. Fan, C. Wang, L. Song, K. Matyjaszewski, X. Pan and Z. Wang, *Nature Communications*, 2024, **15**, 6179.
7. W. Li, L. Tan, Y. Chen, R. Liu, Z. Qi, S. Yuan, Z. Huang, S. Wei, X. Du and D. Yi, *Chinese Journal of Chemistry*, 2024, **42**, 157-163.