

Supporting information for

## RAFT /MADIX polymerization of N-vinylcaprolactam in water-ethanol solvent mixtures

Ine Van Nieuwenhove<sup>a</sup>, Samarendra Maji<sup>b</sup>, Mamoni Dash<sup>a</sup>, Sandra Van Vlierberghe<sup>a\*</sup>, Richard Hoogenboom<sup>b\*</sup> and Peter Dubruel<sup>a\*</sup>

<sup>a.</sup> *Polymer Chemistry and Biomaterials Group - Ghent University, Krijgslaan 281-S4bis, BE-9000 Ghent, e-mail: sandra.vanvlierberghe@ugent.be , peter.dubruel@ugent.be*

<sup>b.</sup> *Supramolecular Chemistry Group - Ghent University, Krijgslaan 281-S4, BE-9000 Ghent, e-mail: Richard.hoogenboom@ugent.be*

† Current address of Dr. Mamoni Dash: National Institute of Science Education and Research, Jatni (Khordha), IN-752050

### A – Experimental Part: materials & instrumentation

#### Materials.

All chemicals were used as received unless specified otherwise. *N*-vinylcaprolactam (NVCL, Sigma Aldrich, 98%) was distilled under reduced pressure and stored in the fridge under inert atmosphere. *L*(+)-Ascorbic Acid (AscAc) , *t*-butylhydroperoxide solution (TBHP, 70 wt% in water), potassium *O*-ethyl xanthate and methyl 2-bromo propionate, chloroform (chromasolv for HPLC grade) and iso-propanol (HPLC grade) were purchased from Sigma Aldrich. Ethanol absolute and acetone, both HPLC grade, and diethyl ether were obtained from Chem-Lab. Diethylene glycol dimethyl ether (diglyme) was received from Avocado Research Chemicals. Deuteroform was purchased from Euriso-top. Triethylamine (HPLC grade) was obtained from Fisher Scientific.

#### Instrumentation.

The monomer conversion was determined via gas chromatography (GC) with a flame ionization detector system (FID). This analysis was performed with an a 7890A Agilent equipped with an Agilent technologies 7693 auto sampler injector and an J&W Advanced Capillary GC column (30 m, 0.320 mm and 0.25mm). Both injector and detector were kept on a constant temperature at respectively 250 and 280°C. Initially, the column was set at 50°C, followed by two heating stages from 50 to 120°C (20°C/min heating rate) and from 100 to 300°C (50°C/min heating rate), and then held at this temperature for 0.5 minutes. The monomer conversions were calculated based on the integration of monomer peak with respect to peak of diglyme as internal standard at different time points of polymerization.

<sup>1</sup>H-NMR spectra were recorded in CDCl<sub>3</sub> with a Bruker Avance 300MHz instrument. The chemical shift was expressed in ppm as a function of the internal standard, tetramethylsilane (TMS).

A Waters GPC Alliance 2965 was used for Size Exclusion Chromatography (SEC) analysis. The device was equipped with a pump, injector, a pre-column and main column, a refractive index detector and an automatic data processing equipment. SEC analysis was performed with an eluent mixture consisting of CHCl<sub>3</sub> (94v%) , triethylamine (4 v%) and iso-propanol (2 v%). Polymer samples (~5 mg) were eluted in 1 ml of this mixture. The measurements were performed at room temperature and at a flow rate of 1 ml/min. Calibration was done with narrow polymethylmethacrylate standards (PMMA) ranging from 5000 to 150,000 g/mol. Furthermore, SEC was also performed on a 1260 series Agilent HPLC system equipped with a diode array, a refractive index, a UV and light scattering detector. Analyses were performed at 50°C in DMA containing 50 mM LiCl as eluent, at a flow rate of 1 ml/min using two mixed-D columns and a mixed-D precolumn in series.

Cloud point temperatures ( $T_{cp}$ ) were determined via turbidimetry on a Crystal16™ parallel crystallizer (Avantium Technologies) which is connected to a recirculation cooler and dry compressed air. Aqueous polymer solutions (5 mg/ml) were heated from 2 to 80 °C with a heating rate of 1.0 °C/min followed by cooling again to 2°C at a cooling rate of 1.0°C/min. This cycle was repeated three times and all polymer samples were measured in duplicate. The  $T_{cp}$ 's are reported as the 50% transmittance temperature in the second heating run.

## B –Methods: Polymer Synthesis and Characterization

### Synthesis of XA1.

O-ethyl-S-(1-methoxycarbonyl)ethyl dithiocarbonate agent (XA1) was synthesized as described in literature.<sup>1</sup> In brief, methyl 2-bromo propionate was dissolved in methanol and cooled to 0°C. Next, potassium O-ethyl xanthate was added and the reaction stirred for 24h. Afterwards, the precipitate was filtered off and the filtrate was diluted with diethyl ether and washed four times with distilled water followed by drying over anhydrous magnesium sulfate. A yellow oil was obtained after evaporation of the diethyl ether. <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>):  $\delta$  = 4.65 (q, 2H), 4.40 (q, 1H), 3.76 (s, 3H), 1.57 (d, 3H), 1.42 (t, 3H).

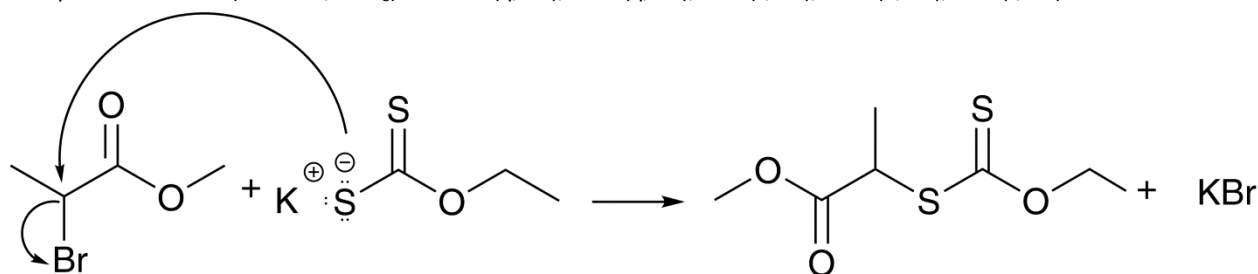


Figure S1 Synthetic scheme for synthesis of O-ethyl-S-(1-methoxycarbonyl)ethyl dithiocarbonate agent (XA1).

### Redox-initiated RAFT/MADIX procedure for polymerization NVCL.

A typical redox-initiated RAFT/MADIX procedure is defined as follows. The NVCL (2 g,  $1.4 \times 10^{-2}$  mol), XA1 (19.95 mg, 0.0956 mmol), TBHP (13.2  $\mu$ l, 0.0956 mmol) and diglyme (0.2 ml) were dissolved in a 1:1 EtOH/H<sub>2</sub>O solvent mixture (3.6 ml) and placed into a 25-ml Schlenk flask. This polymerization mixture was degassed by purging ultra-high purity argon through the solution during 20 - 30 minutes. Subsequently, the Schlenk flask was placed in a thermostated water bath at 25°C. In addition, a stock solution of AscA was made and degassed by purging ultra-high purity argon through the solution. Afterwards, AscA (16.87 mg, 0.0956 mmol) was added to the polymerization mixture under argon to initiate the polymerization. At specific time points, samples were withdrawn from the reaction mixture in order to investigate the polymerization kinetics. The NVCL conversion was determined by GC-FID. After 24h, the reaction was stopped by quenching with liquid nitrogen. The theoretical molecular weight ( $M_{n,theo}$ ) was calculated from this NVCL conversion.

**Table S 1 Overview of the different monomer to CTA ratios applied for RAFT/MADIX polymerization of NVCL.**

[NVCL]/[XA1] ratio	[NVCL]	[XA1]	[TBHP]	[AscA]
300:1	2.5	8.33E-03	8.33E-03	8.33E-03
150:1	2.5	1.67E-02	1.67E-02	1.67E-02
100:1	2.5	2.50E-02	2.50E-02	2.50E-02

**PNVCL purification.**

After polymerization, PNVCL was isolated by diluting the reaction mixture in acetone and precipitating in an excess of cold diethyl ether. The polymer was dried under vacuum at 45°C during 24 h.

**Table S 2 Characteristics of the purified polymers obtained after 24 hours polymerization of *N*-vinylcaprolactam (NVCL) via RAFT/MADIX in different water-ethanol mixtures and in PBS buffer with a [NVCL]:[CTA]:[TBPH/AsCA] ratio of 150:1:1. The results report the mean values with corresponding SD.**

Reaction mixture (v/v %)		Conversion (%) <sup>a</sup>	hydrolysis (%) <sup>a</sup>	DP <sup>b</sup>	M <sub>n,theo</sub> <sup>c</sup> (g/mol)	M <sub>n,SEC</sub> <sup>d</sup> (g/mol)	Đ <sup>d</sup>
EtOH	H <sub>2</sub> O						
100	0	*	*	*	*	*	*
75	25	47 ± 5	1 ± 0	73 ± 9	10100 ± 1300	9100 ± 100	1.14 ± 0.01
50	50	74 ± 4	4 ± 1	112 ± 7	156000 ± 900	9990 ± 800	1.21 ± 0.03
25	75	88 ± 4	8 ± 0	133 ± 7	18600 ± 1000	11700 ± 800	1.20 ± 0.05
0	100	93 ± 3	22 ± 5	141 ± 5	19600 ± 700	12000 ± 1000	1.19 ± 0.04
100 v% PBS		90 ± 2	2 ± 0	135 ± 2	18800 ± 350	6500 ± 450	1.39 ± 0.03

<sup>a</sup> Determined via GC with diglyme as internal standard

<sup>b</sup> Degree of polymerization (DP) calculated from conversion and the applied ratio [NVCL]:[CTA]

<sup>c</sup>  $M_{n,theo} = ([NVCL]:[CTA] \times \text{conversion} \times M_{NVCL}) + MW_{CTA}$

<sup>d</sup> Determined by SEC in CHCl<sub>3</sub> (94 v%) with triethyl amine (4 v%) and iso-propanol (2 v%) at room temperature and with a flow rate of 1 ml/min using PMMA calibration standards.

\* Could not be determined due to the low monomer conversion

**Table S 3 Characteristics of the purified polymers obtained after 24 hours polymerization of *N*-vinylcaprolactam (NVCL) via RAFT/MADIX with three different [NVCL]:[CTA] ratio and [CTA]:[TBPH/AsCA] ratio of 1:1 was applied. The results report the mean values with corresponding SD.**

[NVCL]	[XA1]	Conversion (%) <sup>a</sup>	hydrolysis (%) <sup>a</sup>	DP <sup>b</sup>	M <sub>n,theo</sub> <sup>c</sup> (g/mol)	M <sub>n,SEC</sub> <sup>d</sup> (g/mol)	Đ <sup>d</sup>	T <sub>cp</sub> (°C) <sup>e</sup>
300	1	69 ± 1	3 ± 0.5	205 ± 3	28800 ± 400	16200 ± 2000	1.24 ± 0.05	38.8 ± 0.7
150	1	74 ± 4	4 ± 0.7	112 ± 7	15600 ± 900	10000 ± 800	1.21 ± 0.03	41.6 ± 0.8
100	1	70.2 ± 1	4 ± 0.6	70 ± 1	10000 ± 200	8700 ± 1400	1.15 ± 0.06	42.5 ± 1.1

<sup>a</sup> Determined via GC with diglyme as internal standard

<sup>b</sup> Degree of polymerization (DP) calculated from conversion and the applied ratio [NVCL]:[CTA]

<sup>c</sup>  $M_{n,theo} = ([NVCL]:[CTA] \times \text{conversion} \times M_{NVCL}) + MW_{CTA}$

<sup>d</sup> Determined by SEC in CHCl<sub>3</sub> (94 v%) with triethyl amine (4 v%) and iso-propanol (2 v%) at room temperature and with a flow rate of 1 ml/min using PMMA calibration standards.

<sup>e</sup> Cloud point temperature determined via turbidimetry experiments

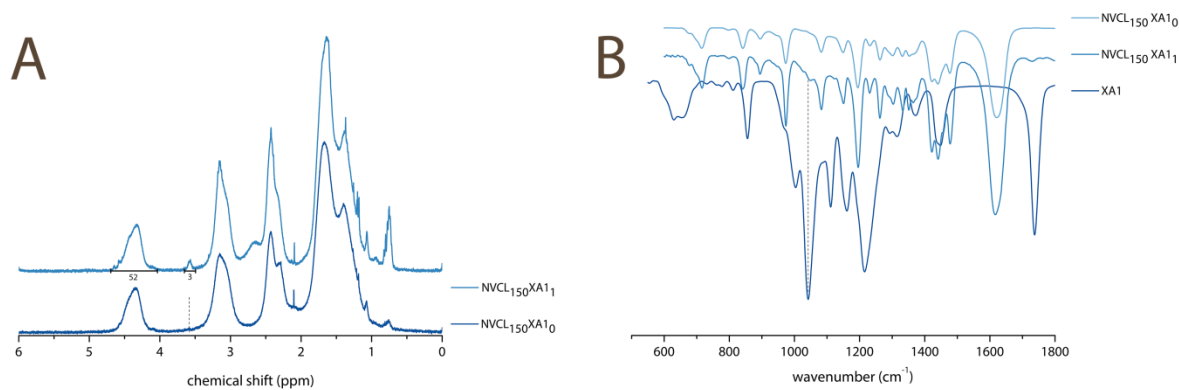


Figure S2 A  $^1\text{H}$  NMR spectra of PNVL polymerized with (top) and without (bottom) chain transfer agent XA1. The dashed line indicates the peak at 3.70 ppm corresponding to the methyl end-group of the xanthate moiety. B IR spectra of PNVL polymerized without (top) and with (middle) chain transfer agent (XA1) in comparison with IR spectrum of XA1 (bottom). The dashed line corresponds with wavenumber of characteristic “CS<sub>2</sub>” stretching.

The  $^1\text{H}$ -NMR spectrum included (bottom) corresponds with a lower molecular weight PNVL polymer:  $M_{n,SEC} = 6200$  g/mol and  $M_{n,theoretical} = 9800$  g/mol (see Figure S2A). The molar mass can be determined via  $^1\text{H}$ -NMR spectroscopy taking into account the resonance at 3.7 ppm corresponding with methyl group from the CTA agent and the peak at 4.44 pm characteristic for a proton from the polymer backbone. Therefore, the following formula can be applied resulting in a  $M_{n,NMR}$  of 7450 g/mol is obtained taking into account the integrations shown in Figure S2A.

$$M_{n,NMR} = \frac{I_{4.4\text{ ppm}}}{I_{3.6\text{ ppm}}/3} \times MW_{NVCL} + MW_{XA1}$$

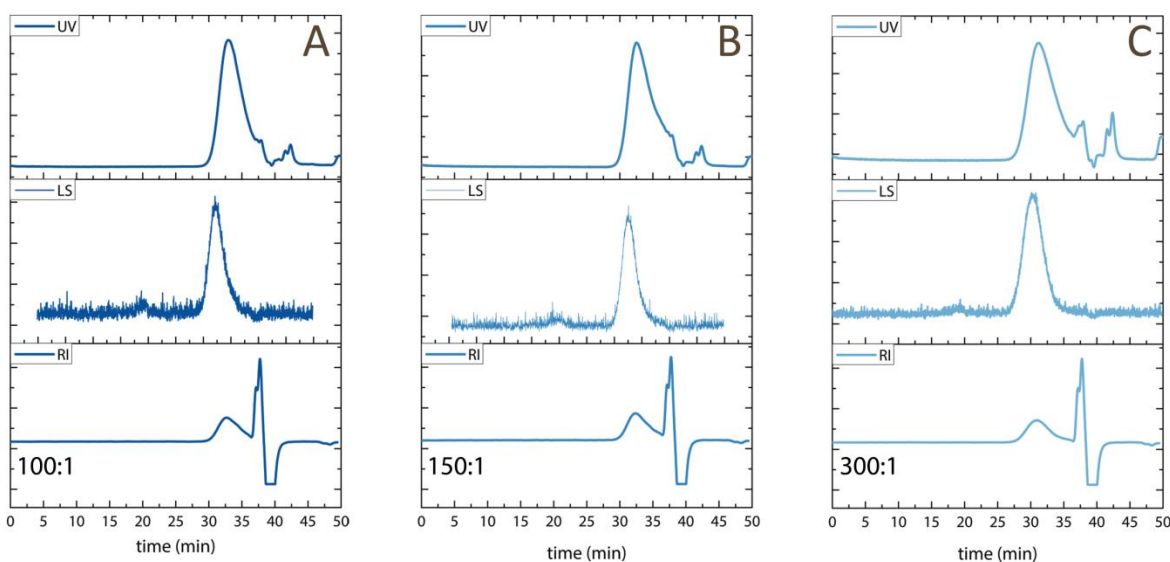


Figure S3 Overview of the SEC chromatograms obtained in SEC-DMA equipped with a UV (at  $\lambda = 290$  nm), LS and RI detector for PNVLs synthesized at 25°C in a 1:1 water ethanol mixture with different [NVCL] to [XA1] ratios applied: A. 100:1, B. 150:1 and C. 300:1 ratio.

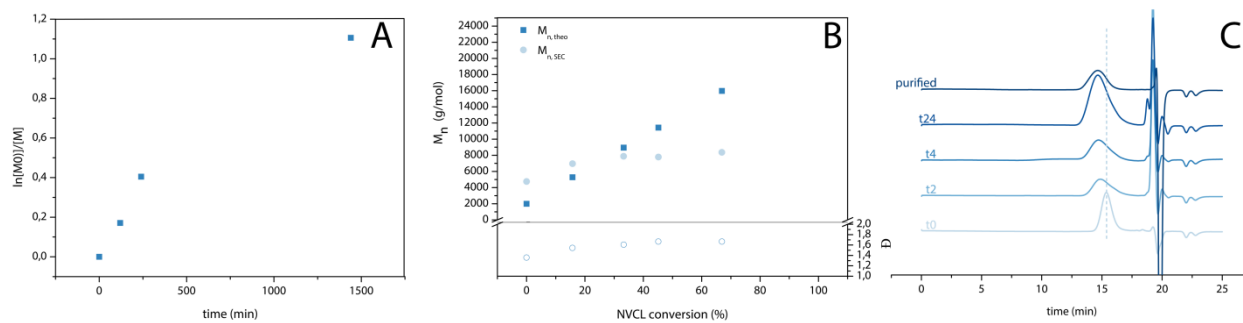


Figure S 4 A. Pseudo first order kinetic plot for chain extension experiment in a 1:1 ethanol-water mixtures, starting from PNVL-CTA with  $M_n = 3100$  g/mol ( $[NVCL]=1.25$  M,  $[NVCL]:[macro-CTA] = 150:1$ ), B. Evolution of the average number molar masses ( $M_n$ ) together with conversion including the dispersities ( $\bar{M}_w/\bar{M}_n$ ), C. Stacked overlay of SEC chromatograms at  $t_0$ ,  $t_2$ ,  $t_4$ ,  $t_{24}$  and after purification obtained in  $CHCl_3:TEA:iPrOH$  (94/4/2 v%).