

Supplementary Information

**Pressure-assisted solvent- and catalyst-free production
of well-defined poly(1-vinyl-2-pyrrolidone) for biomedical
applications**

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Materials

1-vinyl-2-pyrrolidone (VP, 97%, Sigma-Aldrich) was distilled under reduced pressure. 2,2'-Azobis(2-methylpropionitrile) solution 0.2 M in toluene (AIBN, Sigma-Aldrich), diethyl ether (Chempur, pure for analysis), methanol (Chempur, pure for analysis), PVP K30 (Sigma-Aldrich), PVP K90 (average MW 360000, Sigma-Aldrich) were used as received. Estimated molecular weight and dispersity values of commercially supplied PVP K30 and PVP K90 are $M_{nSEC} \square 38.4$ kg/mol, $\bar{D}=1.89$ and $M_{nSEC}=108.6$ kg/mol, $\bar{D}=1.78$, respectively.

Instruments

Nuclear Magnetic Resonance Spectroscopy

Proton and carbon nuclear magnetic resonance (^1H NMR) spectra were recorded using a Bruker Ascend 600 spectrometer operating at 600 MHz in CDCl_3 as a solvent. Standard experimental conditions and standard Bruker program were used.

The conversion of VP was calculated based on the schemes described previously by some of us¹ and other researchers^{2,3} by comparing the integral areas of the protons of the VP (a, 1H, $\delta=7.11$ ppm) in reference to the methylene protons peaks adjusting to the lactam ring of PVP (c', 2H, $\delta=2.75$ -3.40 ppm). Alternatively, by comparing the integral areas of the protons of the VP (a, 1H, $\delta=7.11$ ppm) to the protons connected to the lactam ring of PVP (a', 1H, $\delta=3.47$ -4.10 ppm) or the vinyl protons of VP (a, 1H, $\delta=7.11$ ppm) to the overlapping resonance between VP (c, 2H, $\delta=3.45$ ppm) and PVP (a', c', 3H, $\delta=2.75$ -4.10 ppm). Note that both calculation ways gave similar results (see Figure 2S).

^1H NMR of PVP (600 MHz, CDCl_3) δ ppm: 1.42-1.84 (2H, $-\text{CH}_2-\text{CH}-$, the main chain); 1.80-2.10 (2H, $-\text{CH}_2-\text{CH}_2-\text{CH}_2-$); 2.10-2.50 (2H, $-\text{CH}_2-\text{C}=\text{O}$); 3.47-4.10 (1H, $-\text{CH}_2-\text{CH}-$, the main chain); 3.00-3.50 (2H, $-\text{CH}_2-\text{N}-$).

^{13}C NMR of PVP (150 MHz, CDCl_3) δ ppm: 175.35 ($-\text{N}-\text{C}=\text{O}$), 41.50-46.43 ($\text{CH}_2-\text{CH}-$, the main chain), 41.77-43.5 ($-\text{CH}_2-\text{N}-\text{CO}-$), 32.3-38.8 ($-\text{CH}_2-\text{CH}-$, the main chain), 30.8-32.3 ($\text{O}=\text{C}-\text{CH}_2-\text{CH}_2-\text{CH}_2-\text{N}-$) 18.41 ($-\text{CH}_2-\text{CH}_2-\text{CH}_2-$).

¹ M. Tarnacka, P. Maksym, A. Zięba, A. Mielańczyk, M. Geppert-Rybczyńska, L. Leon-Boigues, C. Mijangos, K. Kamiński and M. Paluch, *Chem. Commun.*, 2019, **55**, 6441-6444

² A. K. Mishra, V. K. Patel, N. K. Vishwakarma, Ch. S. Biswas, M. Raula, A. Misra, T. K. Mandal and B. Ray, *Macromolecules* 2011, **44**, 8, 2465-2473

³ A. K. Mishra, K. Ramesh, T. K. Paira, D. N. Srivastava, T. K. Mandal, N. Misra and B. Ray, *Polym. Bull.* 2013, **70**, 3201-3220

Size exclusion chromatography

The number-average molecular weight (M_n) and dispersity ($D=M_w/M_n$) of the polymers were determined by Agilent Technologies (Santa Clara, CA, USA) size exclusion chromatography (SEC) equipped with refractive-index and UV detectors using pre-column guard 5 μm (50×7.5 mm) and two columns: PLGel 5 μm MIXED-C (300×7.5 mm) and Malvern Viscotek T6000M (300×8 mm), and it can separate polymers in the molecular weight range from $580 \sim 1.39 \times 10^5$ g/mol. The measurements were carried out in DMF (HPLC grade) as the eluent containing 10 mM LiBr, at 313 K with a flow rate of 0.8 mL/min.

Differential Scanning Calorimetry

Calorimetric measurements of the isothermal reaction were carried out by Mettler-Toledo DSC apparatus equipped with a liquid nitrogen cooling accessory and an HSS8 ceramic sensor (heat flux sensor with 120 thermocouples). Temperature and enthalpy calibrations were performed by using indium and zinc standards. The sample was prepared in an open aluminum crucible (40 μL) outside the DSC apparatus. Samples were scanned at a rate of 10 K/min over a temperature range from 140 K to room temperature.

Rheological measurements

An ARES G2 Rheometer measured viscoelastic properties of synthesized and commercial samples. The instrument was equipped with the aluminum parallel plates geometry (diameter = 8 mm). The gap distance was set to 1 mm. The oscillation frequency sweep tests were conducted at a constant strain (<0.1 s $^{-1}$) within the linear viscoelastic region in a frequency range from 0.1 to 100 rad/s. During the experiment, the temperature was increased from 426 to 452 K with a step of 2 K, from 437 to 449 with a step of 2 K and from 450 to 458 K with a step of 1 K for sample 2c, C1 ($M_n=38.4$ kg/mol), and C2 ($M_n=108.6$ kg/mol), respectively.

High-pressure equipment

High-pressure chamber (LC20T, Unipress), thermostat (Huber KISS K6s), hydraulic press (LCP10, Unipress), high-pressure apparatus devices (see Figure 1S).

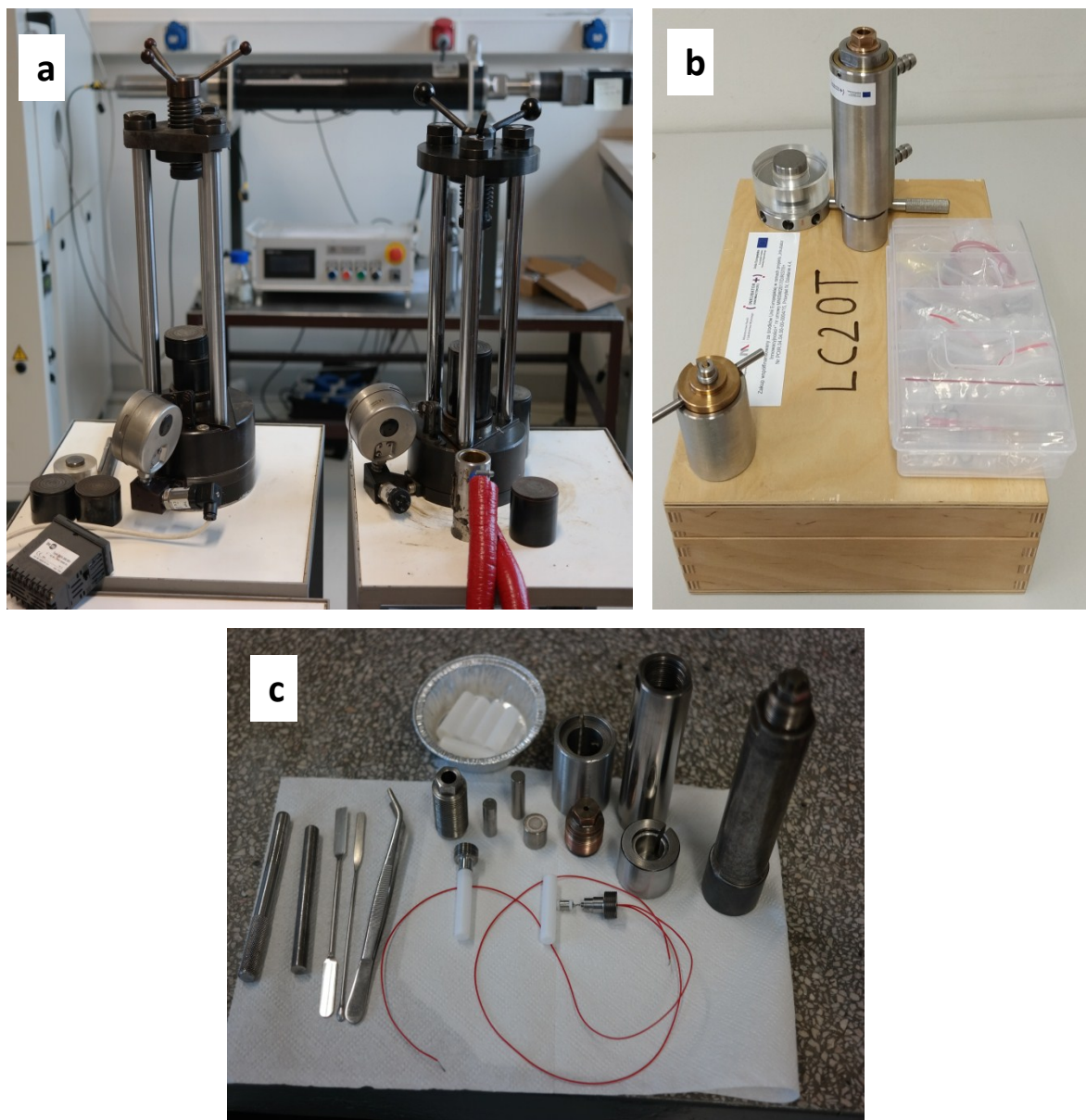


Figure 1S. High-pressure apparatus used in polymerization reactions (a) hydraulic press, (b) high-pressure chamber (c) Teflon ampoules, anti-extrusion rings, stoppers, gaskets.

Procedures

Ambient-pressure free-radical polymerization of VP

VP (1 g, 9 mmol) and AIBN (1.54 μl , 0.008 mmol, 0.15 % wt in respect to VP) were placed in a flask with a magnetic stirring bar. The mixture was purified by three freeze-thaw-pump cycle and purged with nitrogen for 20 min, than the flask was heated to $T = 333 \text{ K}$, for different times. The polymerization was quenched after a predetermined time by cooling and

exposing the reaction mixture to air. The polymer was isolated and purified by ultrafiltration in methanol using a membrane (Millipore, Regenerated Cellulose, YM10, NMWL: 1000), and then precipitated into the cold ether, filtered and dried to constant mass.

High-pressure free-radical polymerization of VP

All high-pressure polymerizations were carried out in 2 mL Teflon ampoules in a high-pressure microreactor purchased from the UniPress. The reactor includes a hydraulic press model LCP20 and a pressure reaction vessel equipped with a temperature controller. VP (1g, 9 mmol) and AIBN (1.54 μ l, 0.008 mmol, 0.15 % wt in respect to VP) were placed in a flask with a magnetic stirring bar. After the vial was purged with nitrogen for 20 min, the flask was immersed in Teflon ampoule. The polymerization was carried out at $T = 333$ K and quenched after a predetermined time by cooling. The polymer was isolated by ultrafiltration in methanol using a membrane (Millipore, Regenerated Cellulose, YM10, NMWL: 1000) then precipitated into the cold ether, filtered and finally dried under vacuum.

Supplemental Figures and Tables

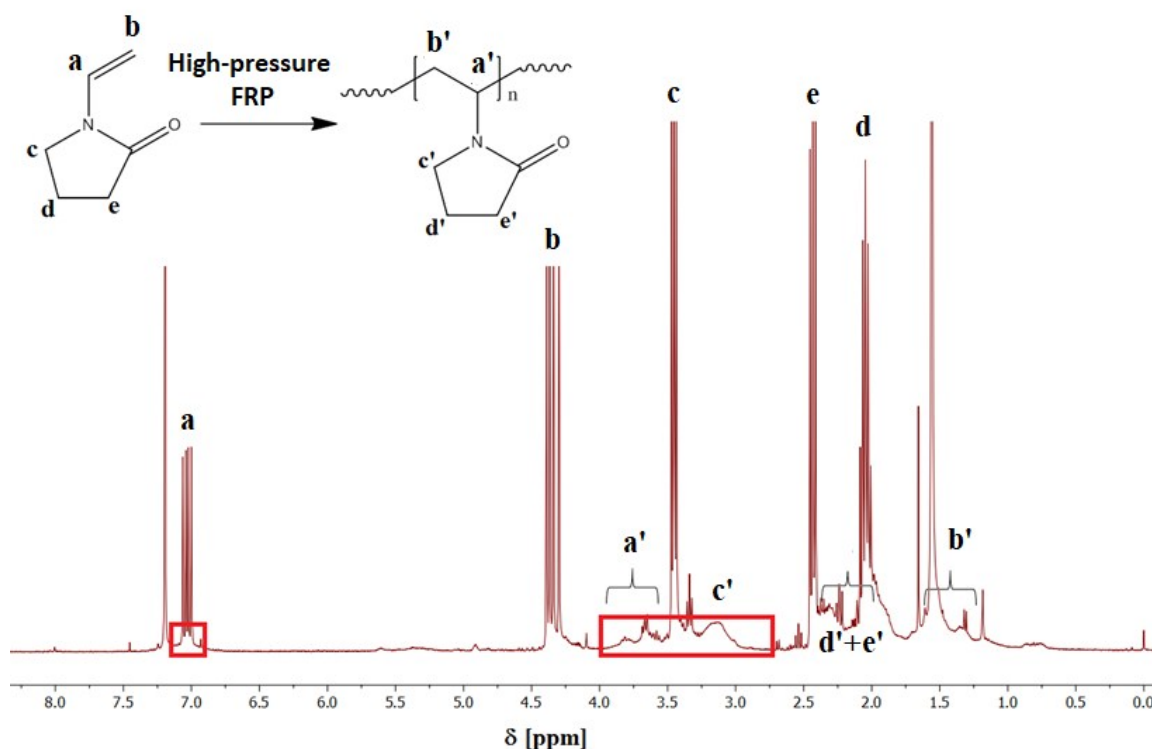


Figure 2S. ^1H NMR spectrum taken from the reaction mixture for VP FRP at high pressure

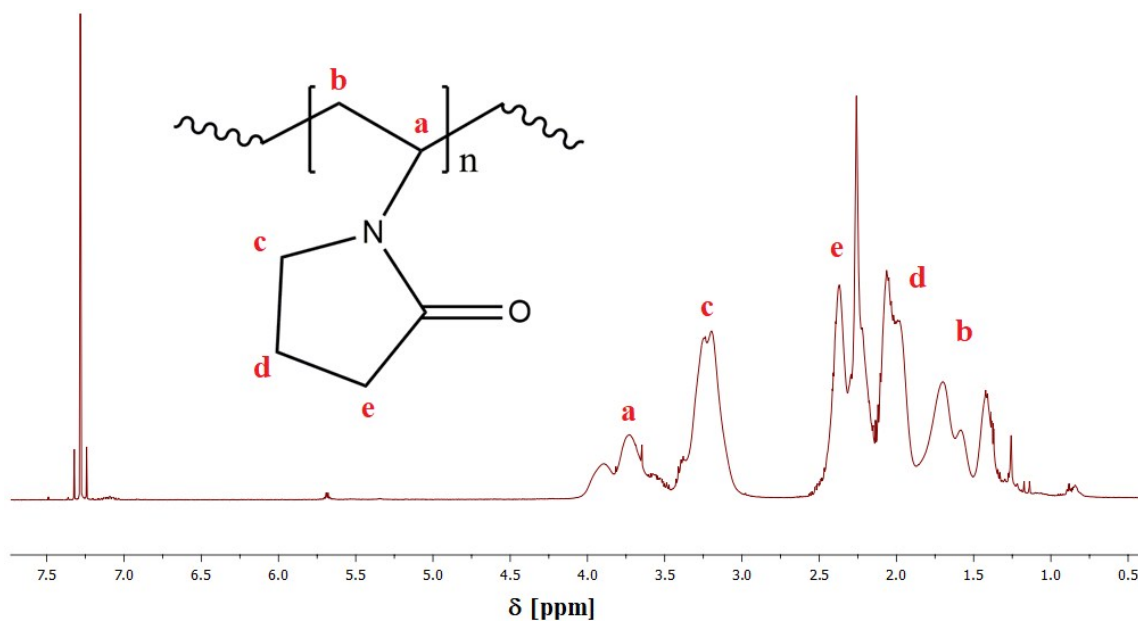


Figure 3S. ^1H NMR spectrum of PVP produced at 250 MPa (sample 2c).

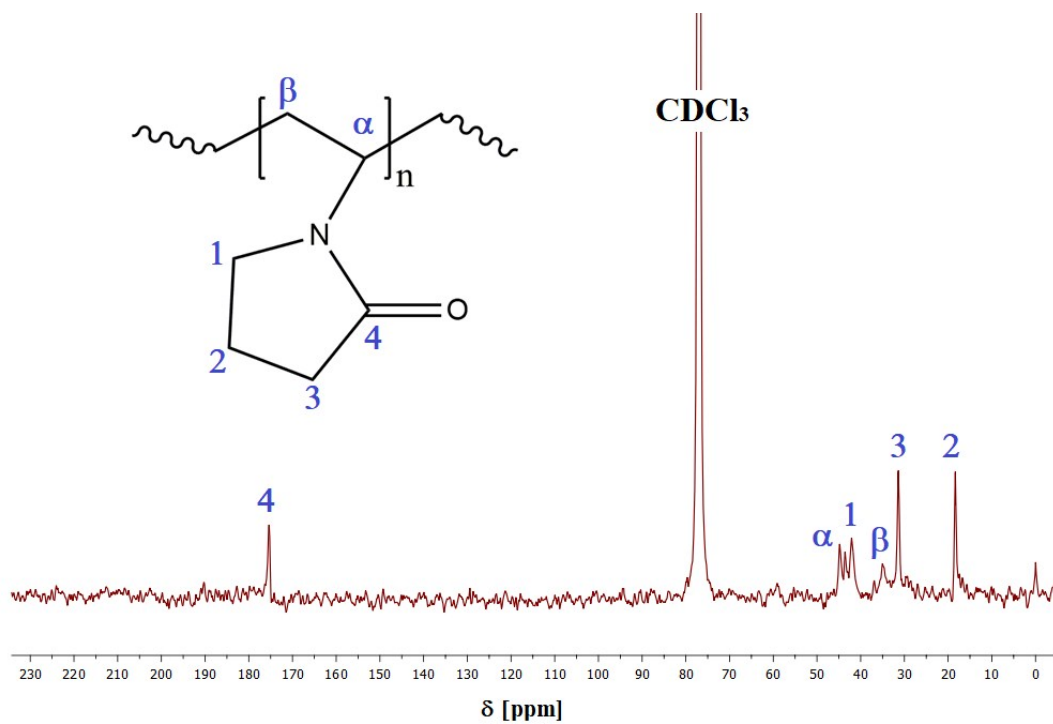


Figure 4S. ^{13}C NMR spectrum of PVP produced at 250 MPa (sample 2c).

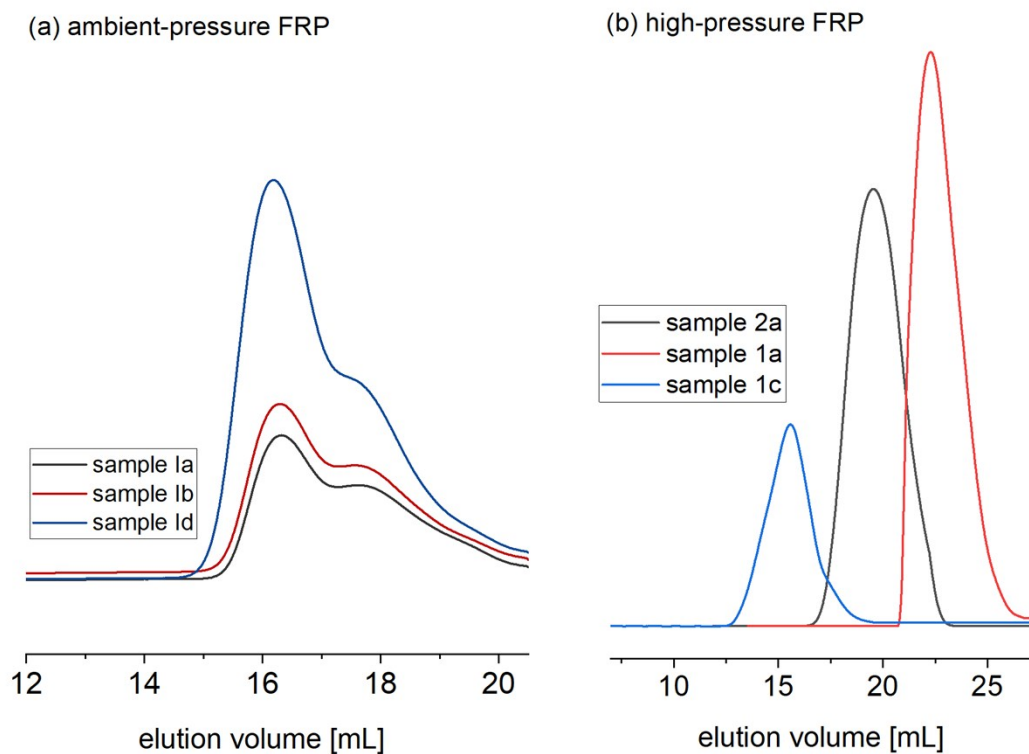


Figure 5S. SEC traces of PVP produced via ambient-pressure FRP (a) and HP FRP $p=250$ MPa (b)

Table 1S. Solubility properties of commercially-supplied and synthesized PVPs

	samples	water	methanol	acetone	chloroform	toluene	ethyl acetate
Commercially-supplied PVP	PVP K30 $M_{nSEC}=38.4$ kg/mol, $\bar{D}=1.89$	+	+	-	+	-	-
	PVP K90 $M_{nSEC}=108.6$ kg/mol, $\bar{D}=1.78$	+	+	-	+	-	-
Synthesized PVP	PVP $M_{nSEC}=16.2-$ 280.5 kg/mol, $\bar{D}=1.27-1.45$	+	+	+	+	-	-