Supporting Information

Synthesis of polysarcosine from air and moisture stable *N*-phenoxycarbonyl-*N*-methylglycine assisted by tertiary amine base

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Analytical instrumentation and methods

Nuclear magnetic resonance (NMR) spectroscopy. ^{1}H NMR spectra of polymer samples were recorded on a Bruker Avance III 600 MHz spectrometer in D_2O (δ 4.79 ppm); the number of scans was 128. ^{1}H and ^{13}C NMR spectra of all other materials were recorded on a Bruker Avance 300 MHz Spectrometer in DMSO-d_6 (δ 2.50 ppm (^{1}H), 39.5 ppm (^{13}C)) and $CDCl_3$ (δ 7.26 ppm (^{1}H), 77.0 ppm (^{13}C)). Unless otherwise mentioned, the number of scans was 128 (^{1}H) and 1024 (^{13}C).

Fourier transformation infrared (FT-IR) spectroscopy was performed on a Bruker Vertex 70 fitted with a PLATINUM ATR. Liquid samples were placed directly on the ATR diamond under an argon flow. The spectra were acquired and processed with the OPUS 7.0 software. The number of scans was 32, the built-in atmospheric correction function was turned on, and the background was automatically subtracted; in the case of liquid samples, the background was generated using the very same solvent as the one used for the sample.

Matrix-assisted laser desorption/ionization–time of flight mass spectrometry (MALDI-TOF MS). Mass spectra were acquired with an Autoflex III MALDI-TOF mass spectrometer (Bruker Daltonics, Bremen, Germany) which is equipped with a frequency tripled Nd:YAG laser (λ = 355 nm); spectra were recorded in linear mode. Samples were prepared by mixing matrix (trans-2-[3-(4-*tert*-butylphenyl)-2-methyl-2-propenylidene]malononitrile), DCTB) and analyte solutions (10 mg mL^{-1} in THF) in a ratio 10:1 (v/v) and spotting a volume of 0.5 µL of this mixture on the target using an Eppendorf pipette (dried-droplet method). Spectra were recorded without addition of salt or with addition of 0.5 µL potassium trifluoroacetate (2 mg mL^{-1} in THF) as dopant. Calibration was done with a mixture of two poly(ethylene glycol) standards (M_n = 1400 and 6000 g mol^{-1}).

Size exclusion chromatography (SEC). Measurements were performed with (*i*) eluent: 0.058 M LiBr in NMP at 60 °C, flow rate 0.5 mL min^{-1}, stationary phase: 300 × 8 mm^2 PSS-GRAM 7µ analytical linear or (*ii*) eluent: 0.1 N aqueous $NaNO_3$ at 25 °C, flow rate 1.0 mL min^{-1}, stationary phase: 300 × 8 mm^2 PSS-Suprema 10µ 30 + 300 Å; detectors: UV (λ = 270 nm or 265 nm) and RI. Solutions containing ~0.1-0.15 wt % polymer were filtered through 0.45 µm filters; the injected volume was 100 µL. Calibration curves were recorded with polystyrene or poly(ethylene oxide) standards, respectively. Data analysis was done with the PSS WinGPC UniChrom software (PSS GmbH, Mainz, Germany).

Chemicals

Sarcosine (Sar, 98%) and *tert*-butylammonium hydroxide (40% w/w in methanol) were purchased from Alfa Aesar. Dimethyl sulfoxide (DMSO, 99.7+%, extra dry, AcroSeal), methanol (MeOH, 99.8%, extra dry, AcroSeal), acetonitrile (99.9%, extra dry, over molecular sieves, AcroSeal), diphenyl carbonate (DPC, 99.5%), triethylamine (TEA, 99%, pure), were purchased from ACROS Organics. *N*,*N*-Diisopropyl-ethylamine (DIPEA, ≥99%, for synthesis) and lithium chloride (≥99%) were purchased from Roth. Potassium hydroxide (puriss. p.a., Reag. Ph. Eur., ≥85%, pellets) was purchased from Sigma-Aldrich. Benzylamine (for synthesis, dried with molecular sieves) was purchased from Merck KGaA. Ethyl acetate (EtOAc), heptanes (Heptan Isomerengemisch), tetrahydrofuran (THF), and acetone were of technical grade quality from VWR. Standard Silica 60 M (0.04-0.063 mm, particle size 230-400 mesh) was purchased from Macherey-Nagel.

Synthesis of *N*-phenoxycarbonyl-*N*-sarcosine (Poc-Sar)

Method A (adapted from S. Yamada et al. *J. Polym. Sci. Part A: Polym. Chem.* **2012**, *50*, 2527). Sarcosine (5.0 g, 56.1 mmol, 1 equiv) was suspended in 31 mL of MeOH, and then 56.1 mL of 40% solution of tetrabutylammonium hydroxide in MeOH (1 equiv) was added dropwise. After 1 h the MeOH was evaporated and 15.5 mL of acetonitrile was added. To this solution, a solution of 12.02 g of DPC (56.1 mmol, 1 equiv) in 15.5 mL of acetonitrile (solution II) was added dropwise. The reaction was left to proceed overnight at room temperature, and then the solvent was evaporated. The product (Poc-Sar) was purified either by double extraction (initially pH around 9 and washing with EtOAc, then pH around 3 and extraction with EtOAc) or by extraction (after decrease of the pH to 3-4) with EtOAc and then column chromatography (silica) with a mixture of heptanes:EtOAc 7:3 (v/v). Yield: 49%.

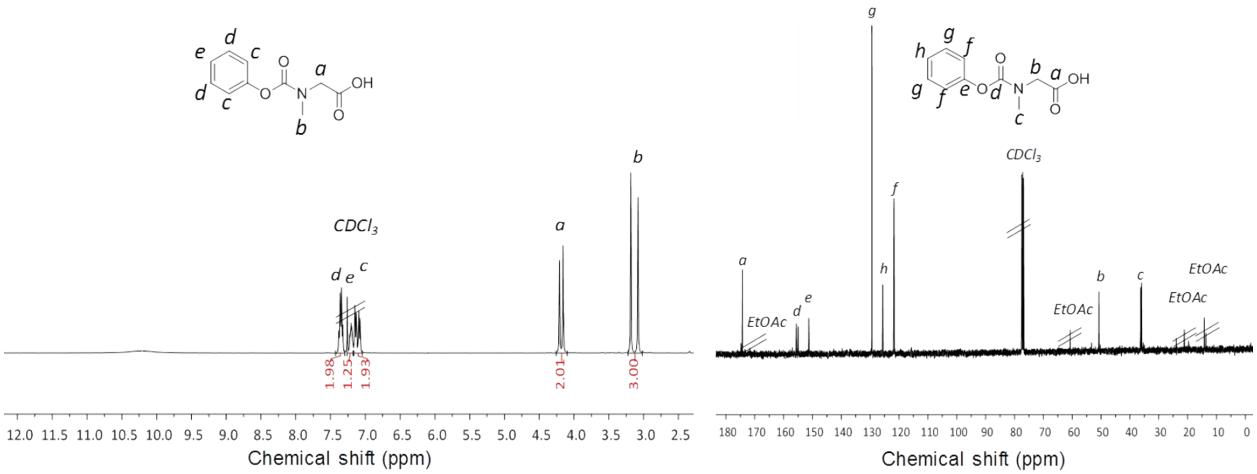

Figure S1. ^{1}H (left) and ^{13}C (right) NMR spectra of Poc-Sar prepared by method A.

Method B (this work, B. Thongrom). Sarcosine (1.0 g, 11.2 mmol, 1 equiv) was suspended in 20 ml of MeOH, to which KOH (0.63 g, 1 equiv) and LiCl (0.27 g, 1 equiv) were added. The opaque solution was combined with a solution of 2.4 g DCP (11.2 mmol, 1 equiv) in 20 mL of THF, and the reaction was left to proceed overnight at room temperature. The non-dissolved salts were filtered off and the solvents were evaporated. Water (~20 mL) was added to the flask and the pH was adjusted to 3-4 with 0.1 N aqueous HCl. The water was evaporated and the product (Poc-Sar) was purified by column chromatography (silica) with a mixture of heptanes:EtOAc 7:3 (v/v). Yield: 52%.

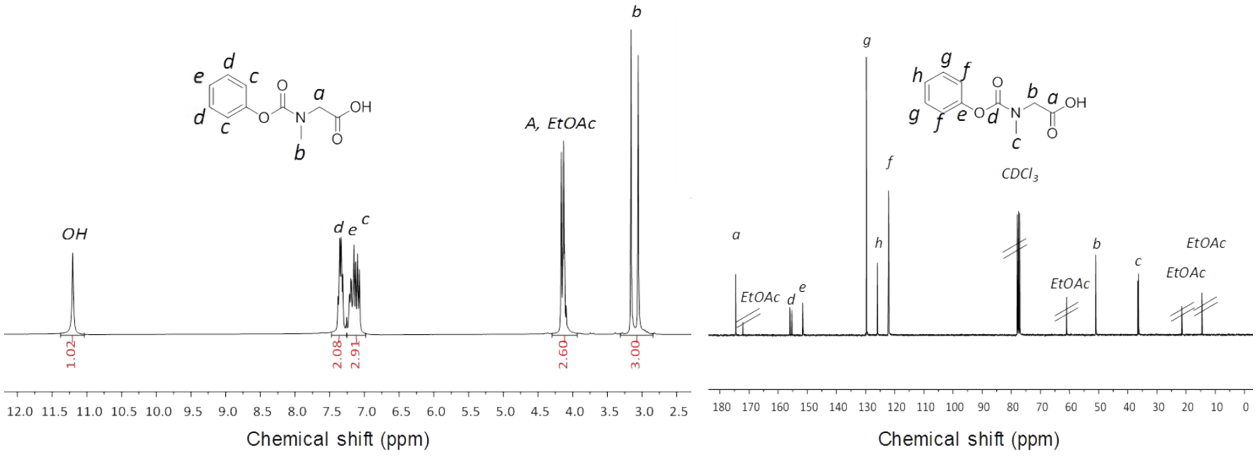

Figure S2. ^{1}H (left) and ^{13}C (right) NMR spectra of Poc-Sar prepared by method B.

Intramolecular condensation of *N*-phenoxycarbonyl-*N*-sarcosine into sarcosine-NCA

Poc-Sar (250 mg, 1.076 mmol, 1 equiv) was dried in high vacuum and flushed with nitrogen 5 times, and then DMSO (1.55 mL) and TEA (0, 0.5, 1.0, or 2 equiv) were added. The reaction vials were heated to 60 °C, and when the oil bath reached this temperature was set as t = 0 min. Aliquot samples were taken under nitrogen flow after 15 min, 30 min, 1 h, 2 h, 4 h, and 24 h and analyzed by FT-IR spectroscopy (Figure S3) and ^{1}H NMR spectroscopy (~0.01 mL samples diluted with ~0.5 mL $CDCl_3$) (Figure S4).

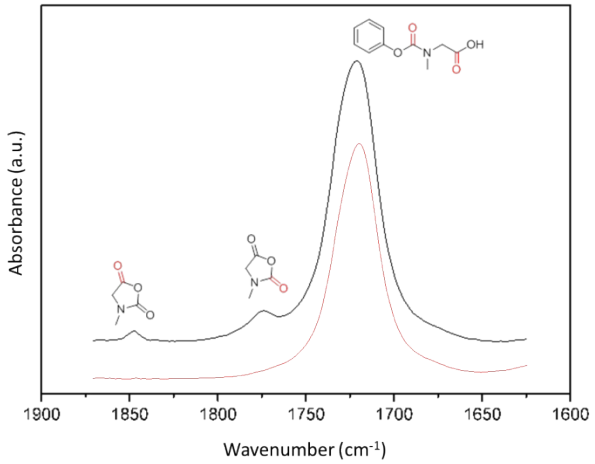

Figure S3. Exemplary FT-IR spectra of the mixture of Poc-Sar/0.5 equiv TEA/DMSO after reaction time of 0 min (red) and 15 min (black) at 60 °C.

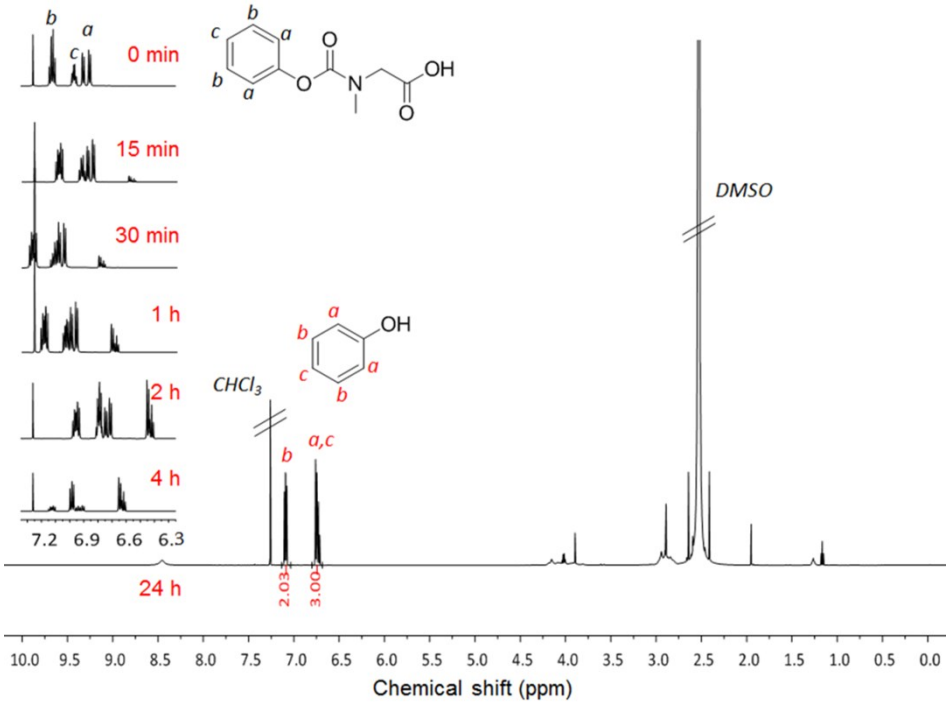

Figure S4. Exemplary ^{1}H NMR spectra of the mixture of Poc-Sar/0.5 equiv TEA/DMSO (in $CDCl_3$) for different reaction times (at 60 °C). Note: variations of peak positions are attributed to different compositions of DMSO/$CDCl_3$ solvent mixtures.

Polymerization (exemplary procedure)

Poc-Sar (225 mg, 1.076 mmol, 50 equiv) were dried in high vacuum and flushed with nitrogen 5 times, and then, 1.3 mL of DMSO, 0.1 mL of benzylamine solution in DMSO (23 mg in 1 mL of DMSO, 0.1 mL = 1 equiv) and 30 µl of DIPEA (0.172 mmol, 8 equiv) were added. The reaction vial was heated to 60 °C and allowed to react for 24 h. The polymer was isolated by precipitation in acetone, filtration, and drying in vacuum (or by dialysis against water for 2 days and freeze-drying). Yield: ~75%.

Table S1. Molecular characteristics of polysarcosines prepared by reaction of $BnNH_2$ with Poc-Sar ($[Poc\text{-}Sar]_0$ = 0.77 M) in 2 vol% tertiary amine base (TEA or DIPEA) in DMSO at 60 °C for 24 h.

entry	$[Poc\text{-}Sar]_0/[BnNH_2]_0$	M_n^{cal}	M_n^{NMR} (g mol^{-1})	M_p^{MALDI} (g mol^{-1})	M_p^{SEC} (g mol^{-1})*	M_n^{SEC} (g mol^{-1})*	M_w^{SEC} (g mol^{-1})*
			Figure S5	Figure S6	Figure S7		
1	50	3660	3650	3200	5090	4580	5080
2	68	4940	4440	3900	5960	5150	5750
3	96	6930	7780	7600	9260	8140	8970
4	194	13900	16500	–	14840	12970	14060
5	307	21940	20000	–	15220	(10920)	(13110)

* Eluent: 0.058 M LiBr in NMP, polystyrene calibration

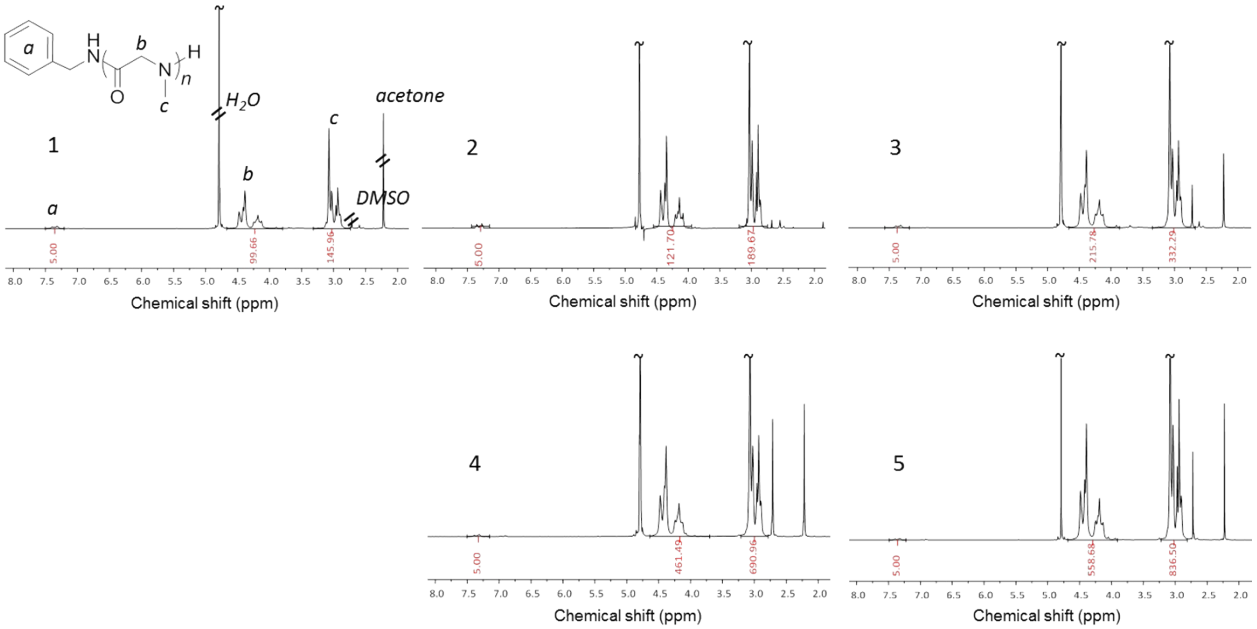

Figure S5. ^{1}H-NMR spectra (600 MHz, D_2O) of polysarcosine, Table S1 entries 1-5. Signal of aromatic protons (δ 7.2-7.5 ppm, *a*, phenyl end group) was normalized to 5H and the molar mass calculated by M_n^{NMR} = (integral(CH_2, *b*)/2·71.1 + 107.2) g mol^{-1}.

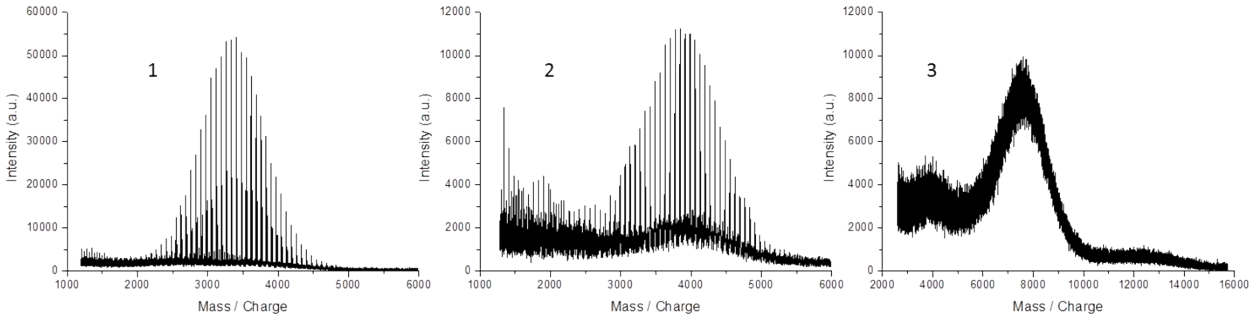

Figure S6. MALDI-TOF mass spectra of polysarcosine (Na^+/K^+ adducts), Table S1 entries 1-3. Note: Higher molar mass polysarcosines (entries 4-5) could not be analyzed.

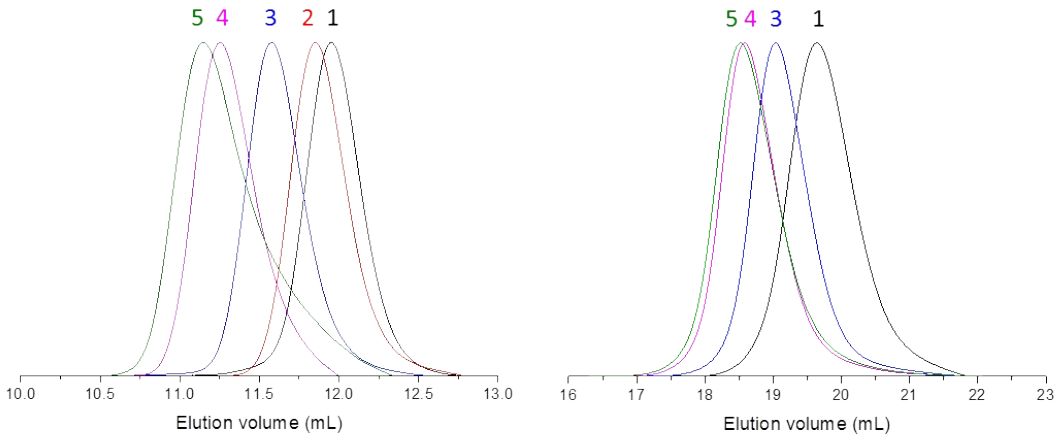

Figure S7. SEC RI traces of polysarcosines, Table S1 entries 1-5 (eluent: 0.058 M LiBr in NMP) (left) and entries 1, 3-6 (eluent: 0.1 N aqueous $NaNO_3$) right). Note: SEC analysis of high molar mass polysarcosine 5 in NMP appeared to be disturbed by polymer–stationary phase interactions, as indicated by a pronounced tailing of the peak toward higher elution volume. On the other hand, SEC analysis in water revealed symmetric peaks (no tailing) for all polysarcosine samples but, however, overall too low molar mass averages (M_n^{SEC} < 4500 g mol^{-1}, PEO calibration) and just marginal differences between the high molar mass samples 4-5.