

Supplementary Information

New amphiphilic block copolymers from lactic acid and cholinium building units

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Materials

2-dimethylaminoethyl methacrylate (98%, Aldrich), 2-bromoethanol (95%, Aldrich), silver lactate (97%, Aldrich), 4-Cyano-4-[(dodecylsulfanylthiocarbonyl)sulfanyl]pentanol (Aldrich), 2,2'-Azobis(2-methylpropionitrile) (AIBN, 98%, Aldrich), 1,8-Diazabicyclo[5.4.0]undec-7-ene (DBU) (98%, Aldrich), benzoic acid (BA) (99.5%, Aldrich), ethyl acetate (99.5%, Aldrich), dichloromethane (99.5%, Aldrich), methanol (99.8%, Aldrich), diethyl ether (99.5%, Aldrich) were used as received without further purification. Dialysis membranes (Pur-A-Lyzer, MWCO 3.5 kDa, Aldrich) with cut-off molecular weight of 3500 kDa were used.

Monomer synthesis

Detailed monomer synthesis is explained elsewhere¹. Commercially available 2-dimethylaminoethylmethacrylate monomer was quaternized with 2-bromoethanol at room temperature to give the corresponding 2-cholinium bromide methacrylate monomer. Salt

metathesis reaction was employed with silver lactate to form the desired final monomer, 2-cholinium lactate methacrylate. The monomer was later characterized by ^1H NMR.

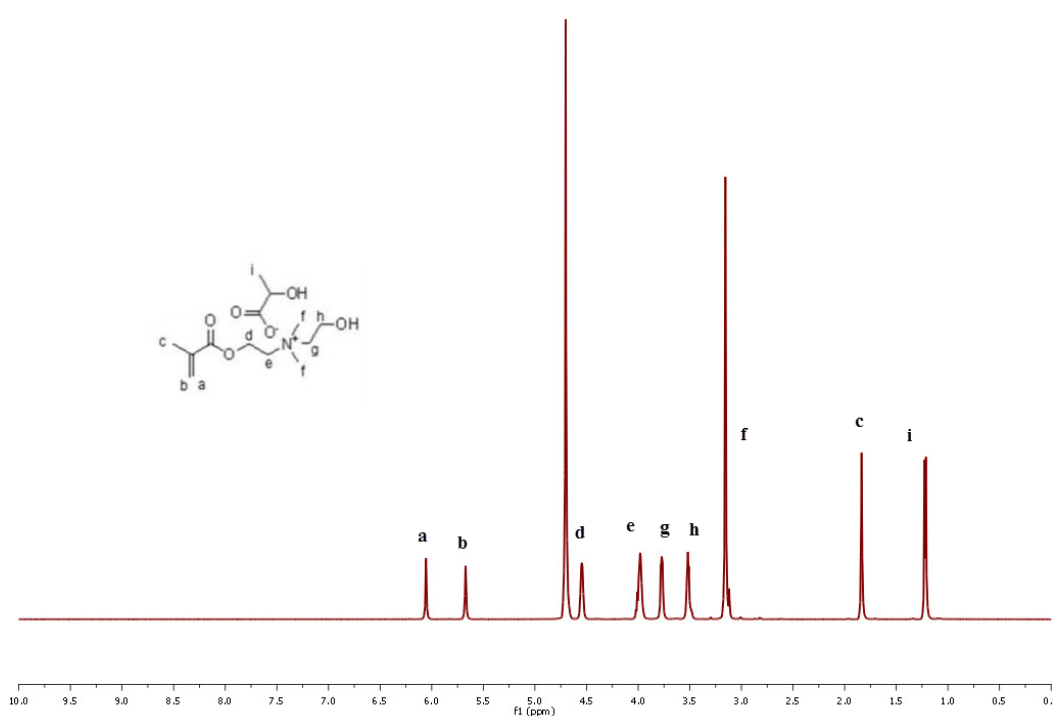


Figure S1. ^1H NMR spectrum of 2-cholinium lactate methacrylate monomer

Catalyst preparation

Benzoic acid (BA) was dissolved in diethyl ether (15% solid) and put into round bottom flask equipped with a dropping funnel containing equimolar amount of diazabicyclo[5.4.0]undec-7-ene (DBU) dissolved in diethyl ether (20% solid). DBU solution was slowly dropped onto benzoic acid solution to form a white precipitate. The salt formed (DBU:BA) was washed with excess diethyl ether and dried under vacuum prior to use.

Synthesis of Poly(L-lactide) Macro-RAFT agent

Ring opening polymerization of L-lactide was conducted by using hydroxyl terminated 4-cyano-4-[(dodecylsulfanylthiocarbonyl)sulfanyl]pentanol chain transfer agent (CTA) as the initiator and DBU:BA salt as the catalyst in the presence of dichloromethane as the solvent at 40°C. In a typical reaction, 0.3 g of initiator, 5.32 g of L-lactide, 1.05 g of catalyst and 22.5 g of dichloromethane were mixed in one-neck round bottom flask and the reaction was conducted for 42 hours. Conversion of the monomer to polymer was followed by ^1H NMR. Final polymer was precipitated in cold methanol to get rid of unreacted monomer. Two polymers with different molecular weights were prepared, molecular weights being 3500 and 7100 g/mol as calculated from ^1H NMR.

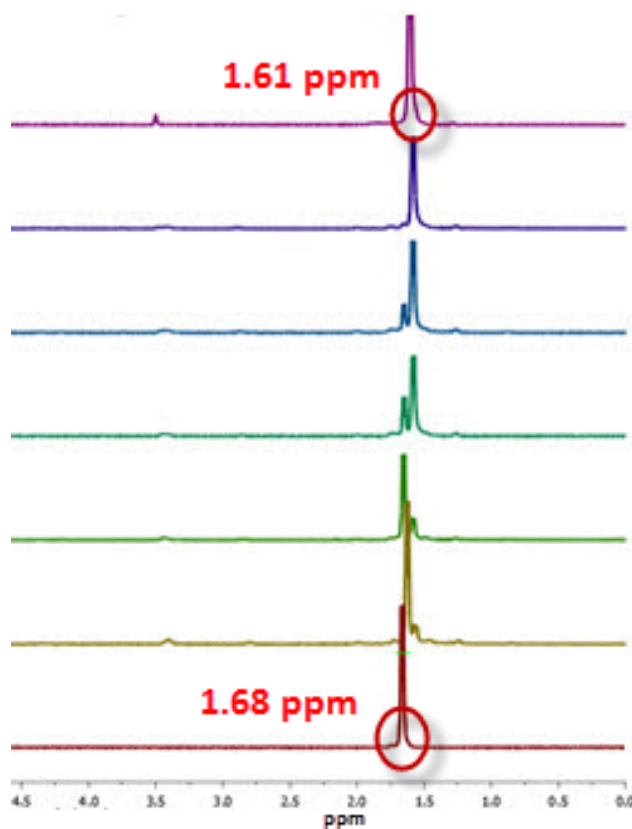


Figure S2. ^1H NMR spectra taken during the polymerization showing the monomer to polymer conversion from bottom to top

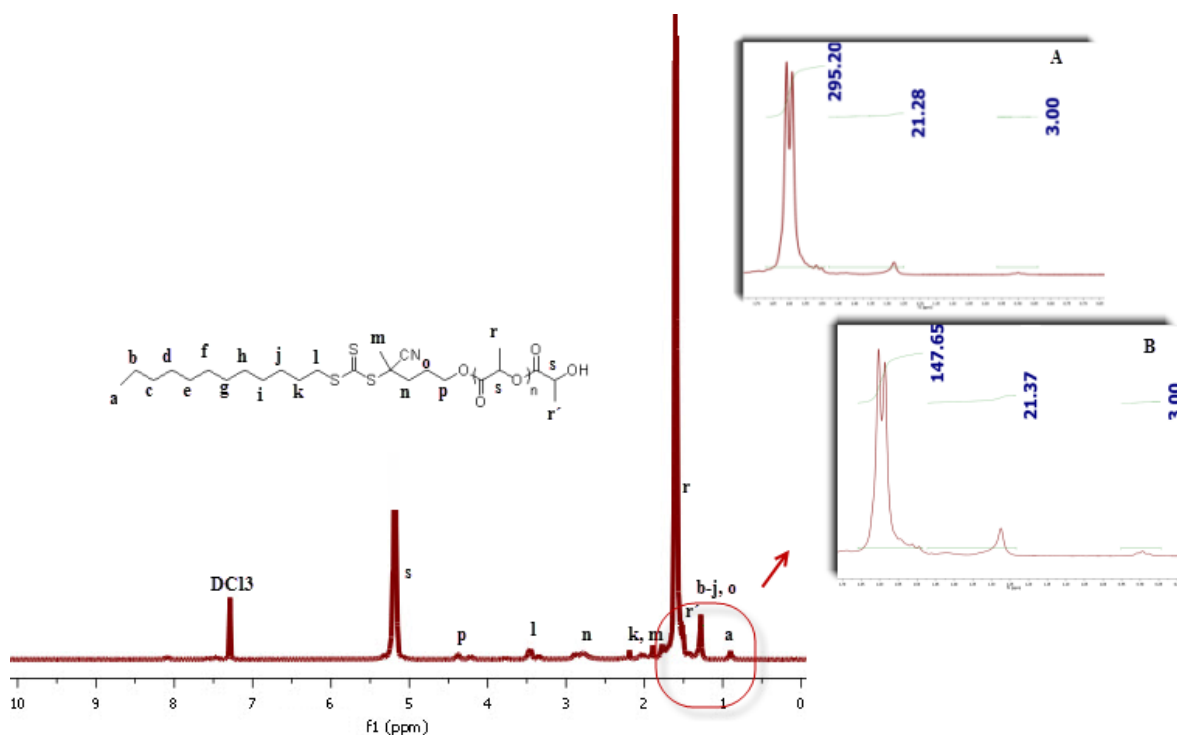


Figure S3. ^1H NMR spectrum of PLA macro RAFT agent, inner images shows the integral values used to determine the calculated molecular weights of the polymers. A) PLA7.0K B) PLA3.5K

Synthesis of Poly(L-lactide)-poly(2-cholinium lactate methacrylate) Block Copolymers (PLA-PIL)

Poly(L-lactide) macro-CTA (MCTA) is used to conduct the polymerization of 2-cholinium lactate methacrylate monomer through RAFT polymerization. In a typical reaction, 0.2 g of MCTA and 0.89 g of monomer is dissolved in methanol/DCM (5.9 ml + 2.0 ml) in a one-neck round-bottom flask. N_2 was purged through the flask and 0.0025 g of AIBN added at 70°C in 1.0 ml of methanol. The reactions were conducted for 24 hours. Conversion of the monomer to polymer was followed by ^1H NMR. Resulting crude product was washed with acetone and dichloromethane.

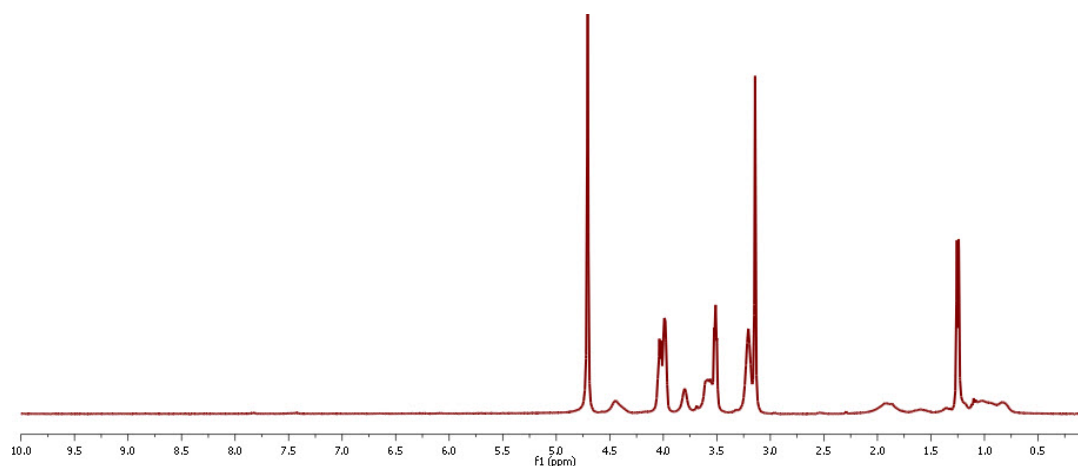


Figure S4. ^1H NMR spectrum of the PLA-PIL block copolymer after polymerization. Signals arising from ionic liquid monomer (6.09 and 5.70 ppm) disappear at the end of the reaction

Preparation and characterization of self-assembled PLA-PIL micelles

Amphiphilic block copolymers were dissolved in deionized water to have a concentration of 5mg/ml. Simply, 50 mg of block copolymer was dissolved in 10 ml **deionized water** and remained under mechanical stirring for 24 hours at room temperature until all material was completely dissolved. The solutions were then poured into dialysis membranes having 3500 kDa cut-off molecular weight and dialyzed against excess deionized water for 48 hours at room temperature under strong agitation. Dialyzed solutions were poured into vials and diluted dropwise to 1 mg/ml to prevent multiple scattering and analyzed by dynamic light scattering and TEM. Before the analysis, the solutions were filtered through 0.45 μm regenerated cellulose syringe filters.

Characterization

The ^1H NMR measurements were carried out on a Bruker AC-400 instrument with the following experimental conditions: spectral width 20 ppm with 32 K data points, flip angle 90, relaxation delay of 18 s, digital resolution of 0.24 Hz/pt. Gel permeation chromatography was conducted on Agilent PL-GPC 50 integrated GPC system with refractive index detector to detect the molecular weights of the polymers. The eluent was THF containing 10 mM of lithium bis(trifluoromethanesulfonyl) imide. Narrow molecular weight polystyrene standards were used for calibration. The mean size of the nanoparticles was determined by dynamic light scattering (DLS) method. The intensity average particle diameter was measured at 25°C and 173° backscatter angle by using dynamic light scattering Malvern ZetaSizer Nano-S instrument equipped with a 633 nm red laser. Transmission electron microscopy (TEM) was performed on a TECNAI G² 20 TWIN (200 kV).

Reference

¹ M. Isik, R. Gracia, L. C. Kollnus, L. C. Tome., I. M. Marrucho, D. Mecerreyes, *ACS Macro Lett*, 2013, **2**, 975.