Supporting Information

The effect of temperature on the kinetics of enhanced amide bond formation from lactic acid and valine driven by deep eutectic solvents

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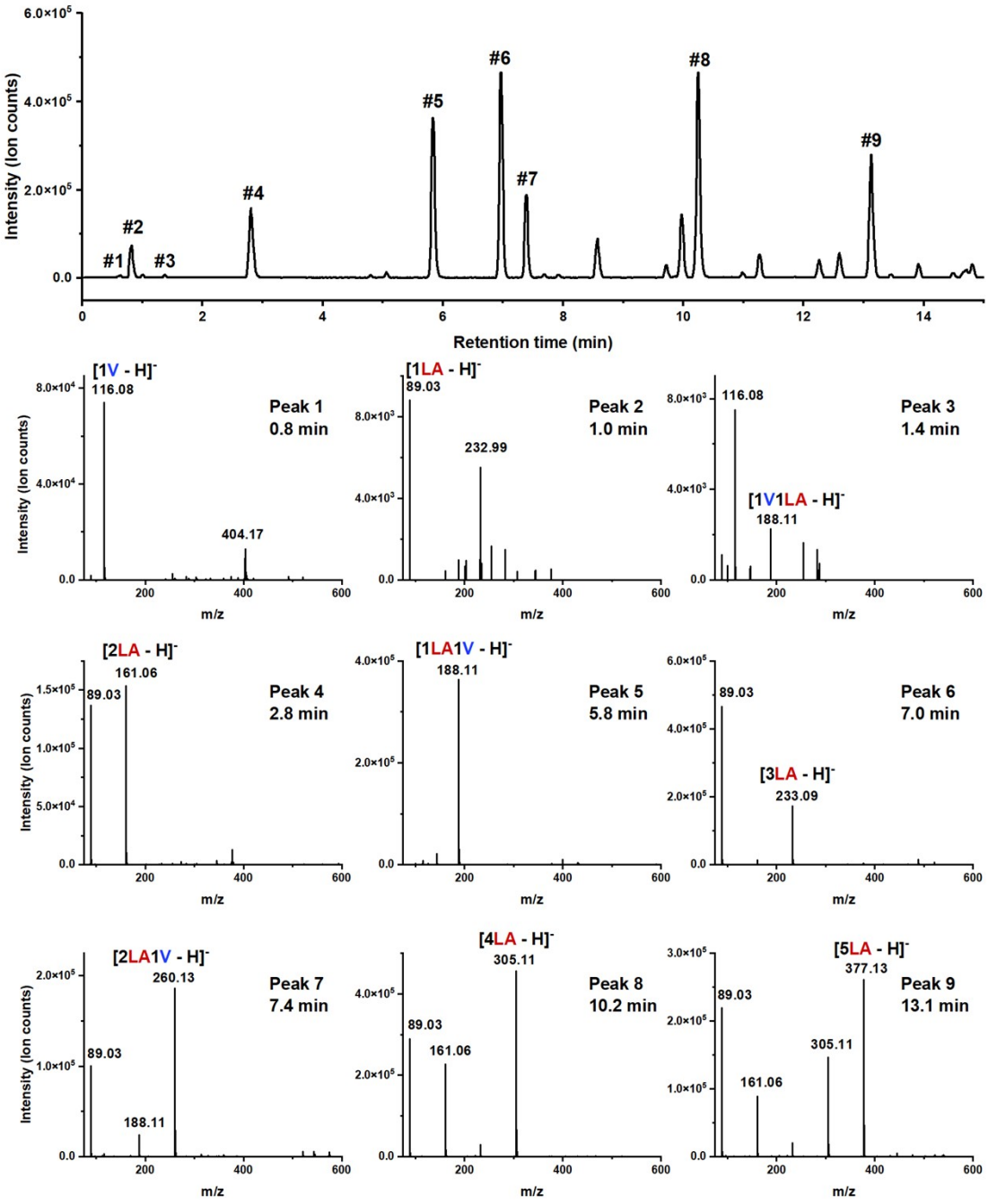

1. LC-MS analysis

Figure S1. LC-MS analysis of the control experiment without TEACl. The molar ratio of LA and V is 10:1. The sample was prepared by heating at 85°C for 24 hours.

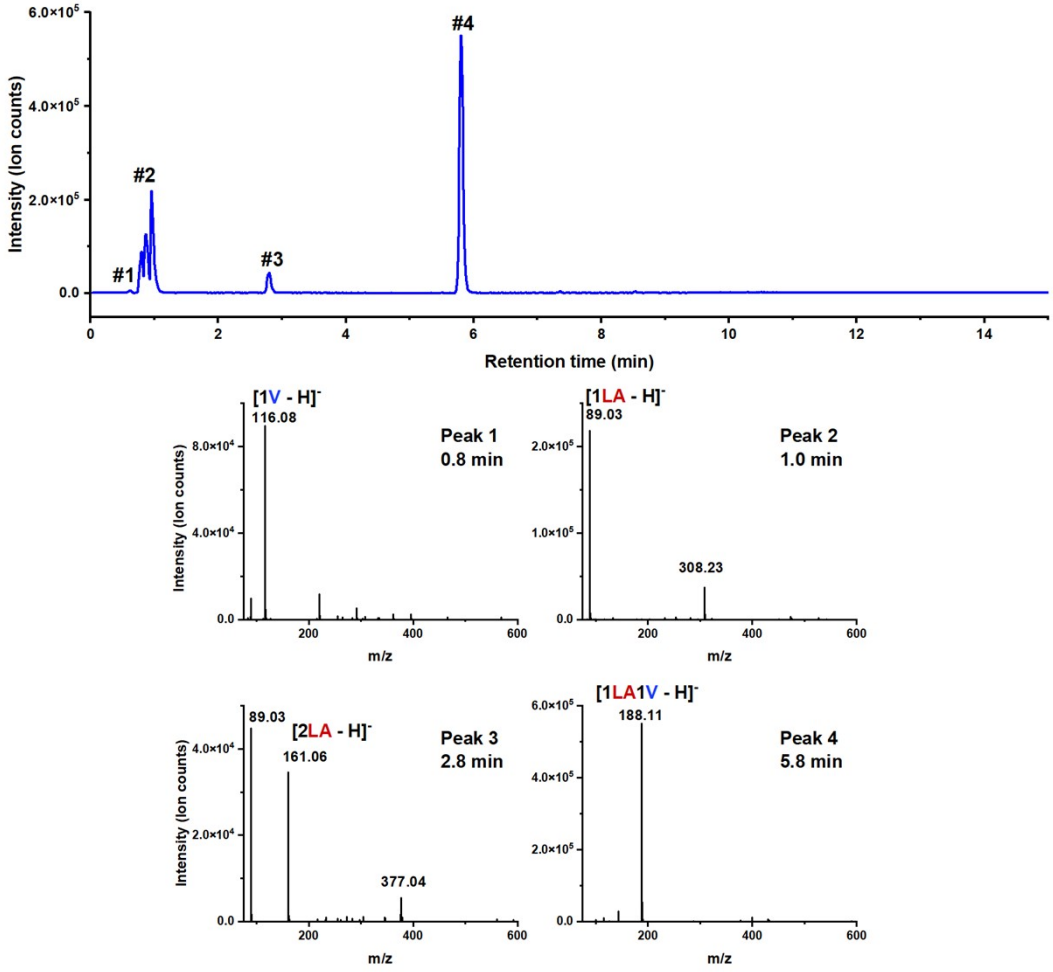

Figure S2. LC-MS analysis of the TEACl/LA/V mixture (molar ratio of 10:10:1). The sample was prepared by heating at 85℃ for 24 hours.

2. The reaction using valine dimer

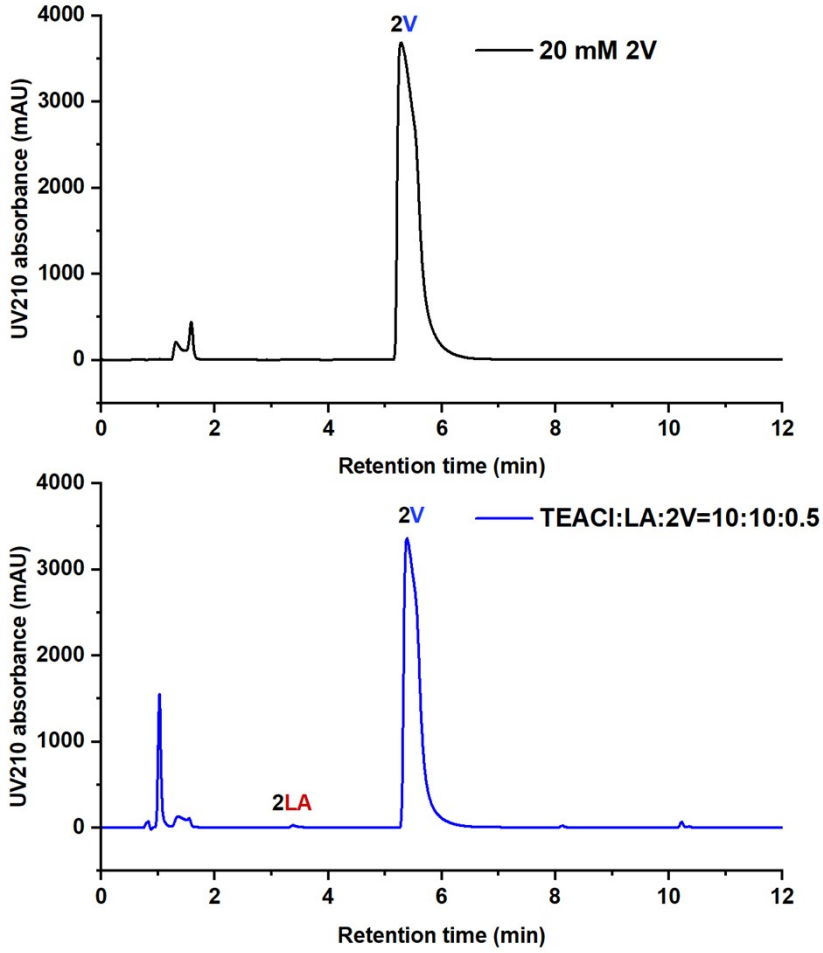

Figure S3. LC-UV analysis of the reaction mixture using valine dipeptide (2V). The top figure is the result of using 20 mM 2V aqueous solution. The bottom chromatogram shows the products of TEACl/LA/2V (molar ratio of 10:10:0.5).

3. Characterization of the 1LA-1V standard compounds

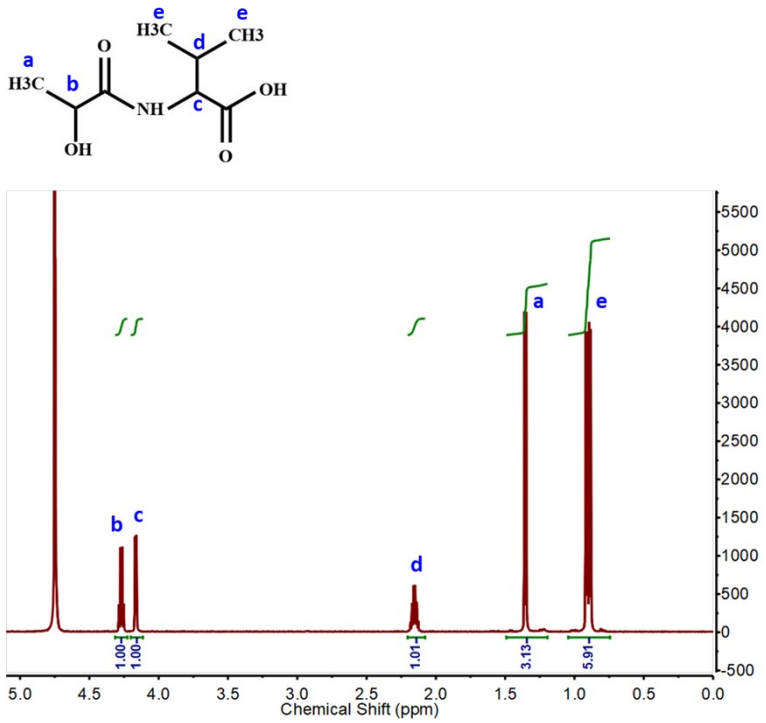

Figure S4. [1]H NMR of 1LA-1V standard compound.

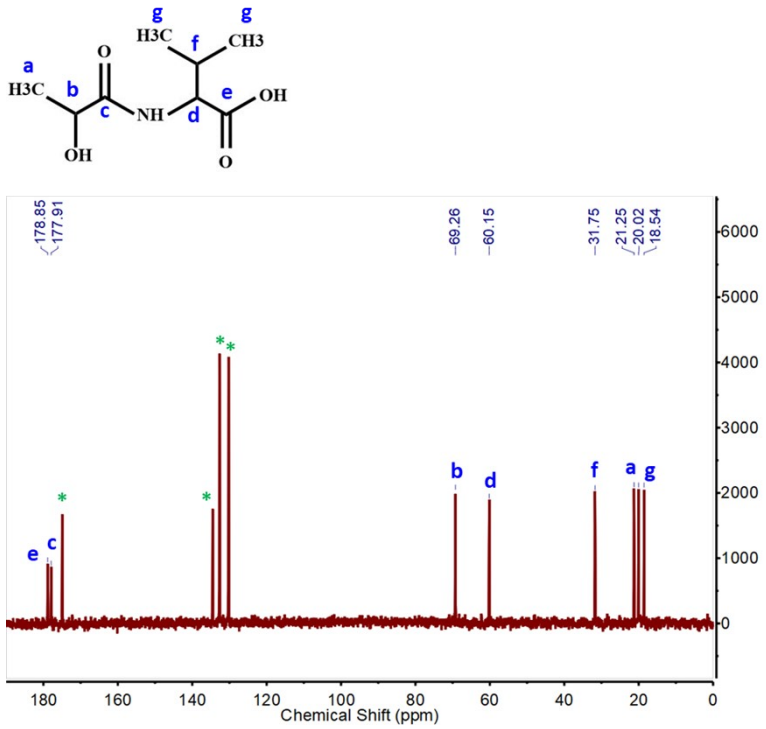

Figure S5. [13]C NMR of 1LA-1V standard compound. The peaks marked by asterisk (*) correspond to the internal standard KHP.

Table S1. UV response factors used in this study.

Compound	UV calibration factor, k [µmole/(mAU*min)]
1LA	1.45×10^{-4}
2LA	4.41×10^{-5}
3LA	3.19×10^{-5}
4LA	2.39×10^{-5}
5LA	1.91×10^{-5}
1LA-1V	6.92×10^{-6}
1V-1LA	4.41×10^{-5}

4. The determination of water evaporation rate constant

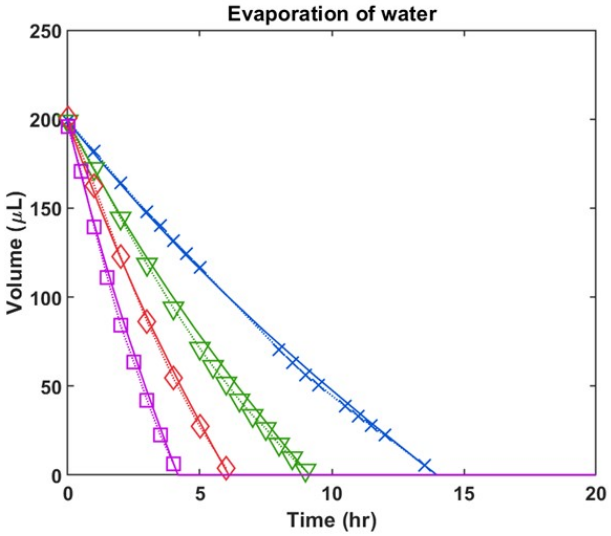

Figure S6. The amount of water left in the reactor at different temperatures from 85°C (purple), 75°C (red), 65°C (green) to 55°C (blue). Solid lines are the model predictions. The experimental data points are represented by □, ◇, ▽ and × symbols, respectively.

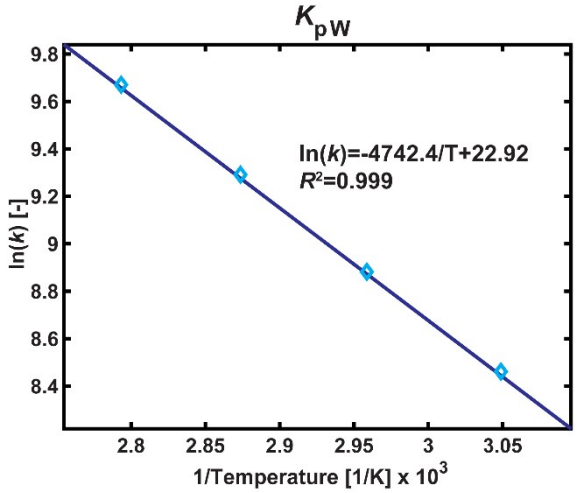

Figure S7. Arrhenius plot of the water evaporation rate constants.

5. The Arrhenius plot of rate constants for the reaction without TEACl

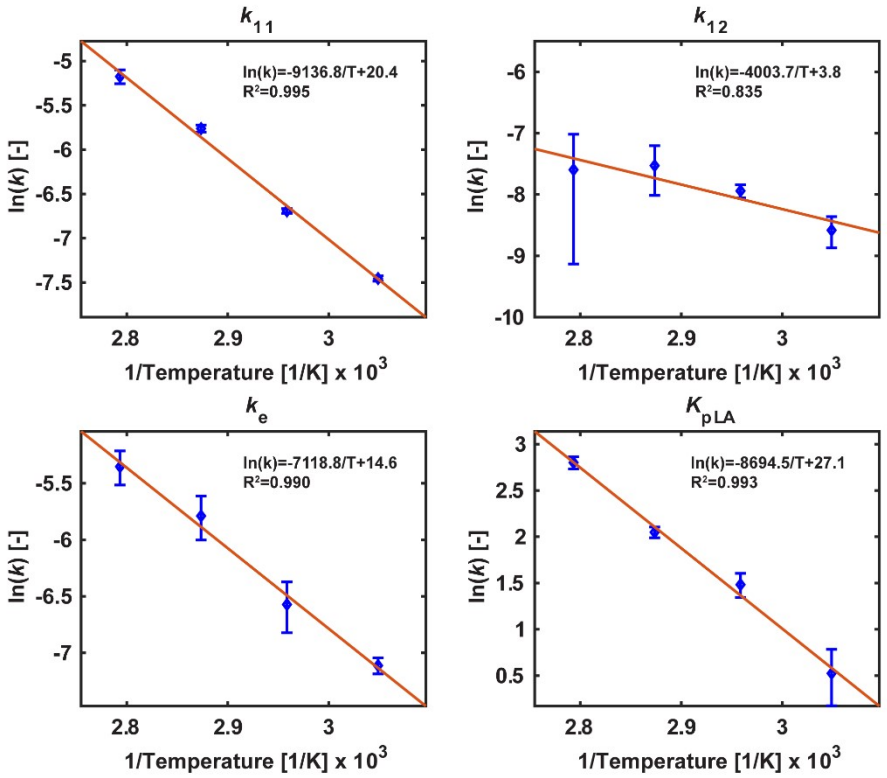

Figure S8. The Arrhenius plots of the four rate constants evaluated from the control experiment without TEACl. The estimated rate constants at each temperature are plotted along with their 95% confidence intervals.

6. The effect of DESs on the polymerization of lactic acid

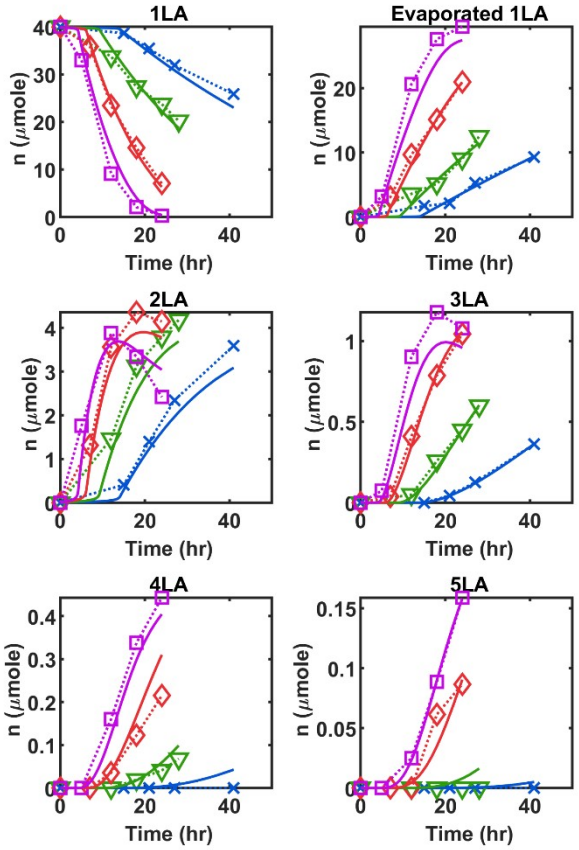

Figure S9. Oligomer distribution versus time profile for the lactic acid polymerization without valine and TEACl. The reaction temperatures are denoted as different colors: purple (85°C), red (75°C), green (65°C) and blue (55°C). Solid lines are the model predictions. The experimental data points are represented by ▫, ◇, ▽ and ╳ symbols, respectively.

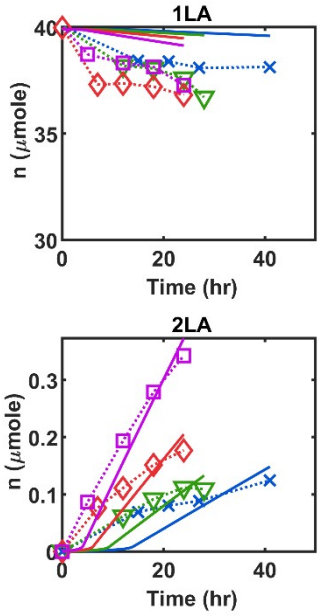

Figure S10. Oligomer distribution versus time profile for the lactic acid polymerization without valine in the presence of TEACl. The molar ratio of TEACl:LA was 1:1. The reaction temperatures are denoted as different colors: purple (85 C), red (75°C), green (65°C) and blue (55°C). Solid lines are the model predictions. The experimental data points are represented by ▫, ◇, ▽ and ╳ symbols, respectively.

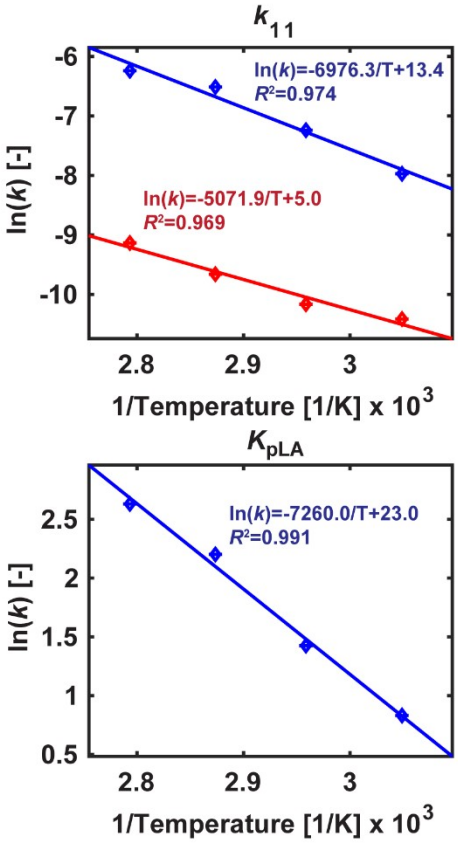

Figure S11. The Arrhenius plots of the rate constants for the lactic acid polymerization without valine. Red and blue lines represent the rate constants of TEACl/LA (molar ratio of 10:10) and the control without TEACl (0:10). The estimated rate constants at each temperature are plotted along with their 95% confidence intervals.

7. The reaction using different DESs

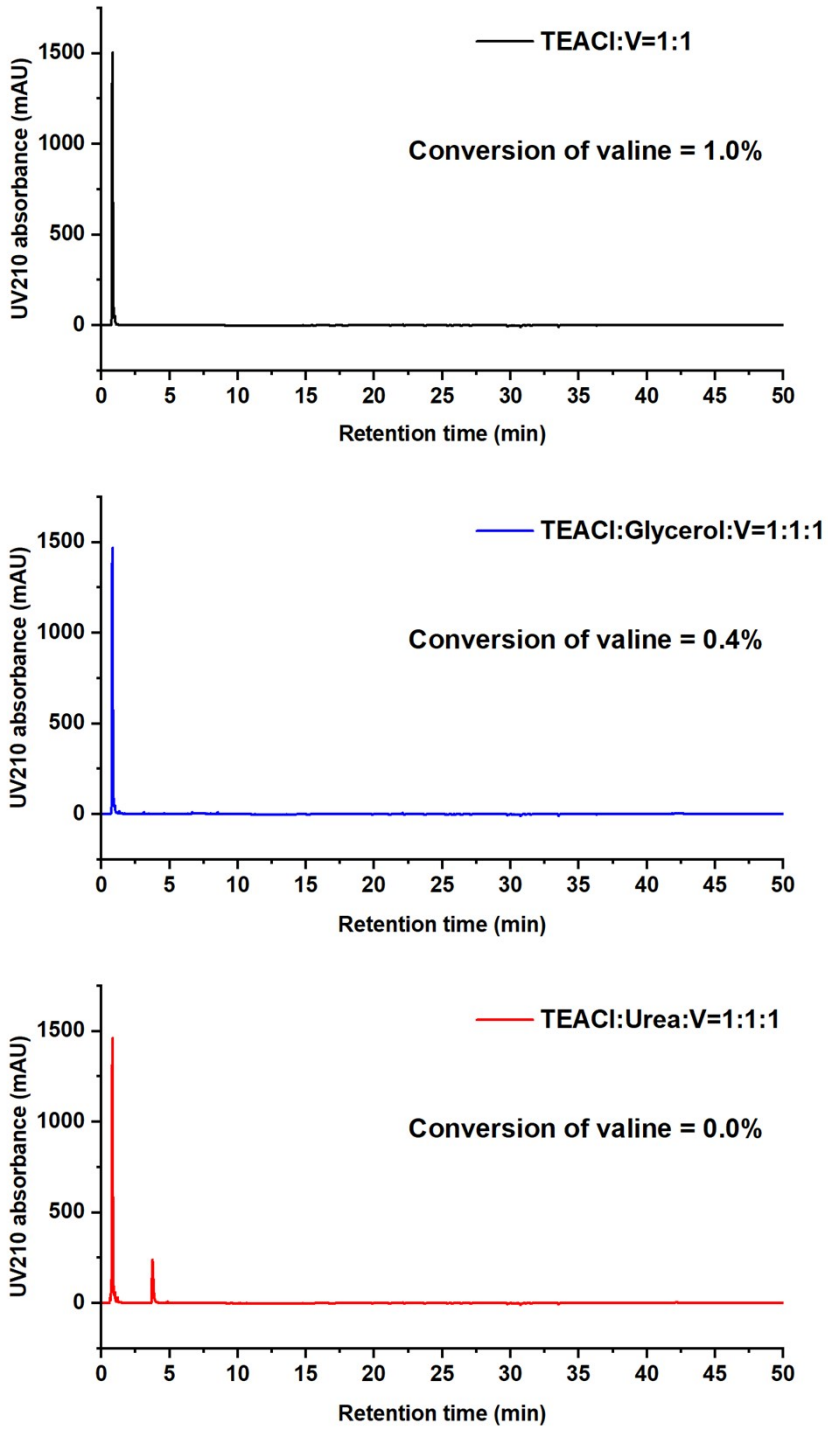

Figure S12. LC-UV chromatograms of the reaction mixtures without lactic acid. The reaction mixtures were prepared by drying at 85℃ for 24 hours. The conversion of valine was measured by ^{1}H NMR analysis.

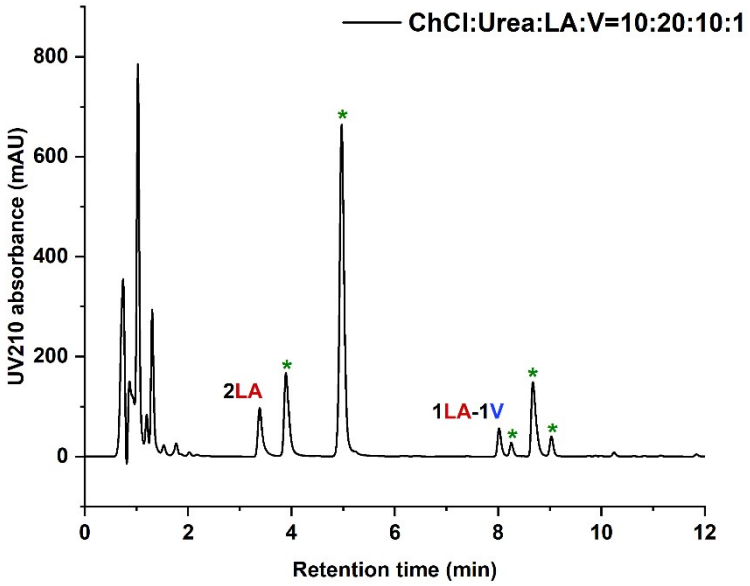

Figure S13. LC-UV chromatograms of the reaction mixtures using choline chloride (ChCl), urea, lactic acid and valine. The reaction mixtures were prepared by drying at 85℃ for 24 hours. The green asterisks indicate the potential side products of lactic acid and valine with urea.

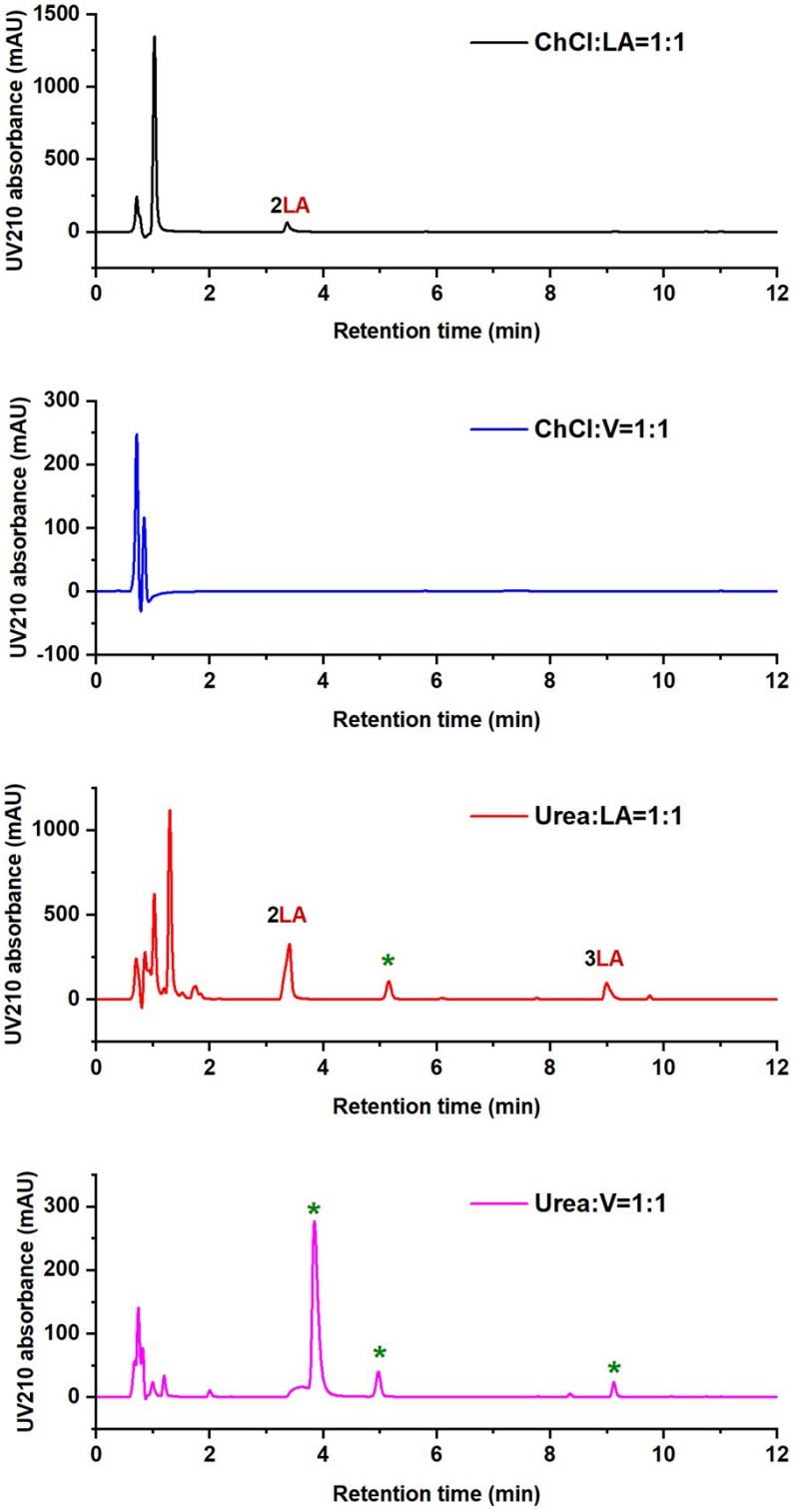

Figure S14. LC-UV chromatograms of the reaction mixtures using ChCl/LA, ChCl/V, Urea/LA, and Urea/V. The reaction mixtures were prepared by drying at 85℃ for 24 hours. The green asterisks indicate the potential side products of lactic acid and valine with urea.

8. The rate constant of each step in different reaction mixtures

Table S2. Rate constants for LA/V copolymerization. The molar ratio of the LA/V mixture was 10:1.

T (℃)	k_{11} (L·mol^{-1}·h^{-1})	k_{12} (L·mol^{-1}·h^{-1})	k_e (L·mol^{-1}·h^{-1})	K_{pLA} (μmol cm^{-1}·h^{-1})
85	0.00566	0.000502	0.00473	16.463
75	0.003147	0.000537	0.00306	7.760
65	0.00124	0.000356	0.00140	4.405
55	0.000578	0.000187	0.000815	1.689

Table S3. Rate constants for TEACl/LA/V reaction The molar ratio of the TEACl/LA/V mixture was 10:10:1.

T (℃)	k_{11} (L·mol^{-1}·h^{-1})	k_e (L·mol^{-1}·h^{-1})
85	0.000693	0.414
75	0.000295	0.225
65	0.000144	0.0947
55	0.0000914	0.0205

Table S4. Rate constants for LA polymerization.

T (℃)	k_{11} (L·mol^{-1}·h^{-1})	K_{pLA} (μmol cm^{-1}·h^{-1})
85	0.00195	13.890
75	0.00148	9.039
65	0.000718	4.161
55	0.000345	2.295

Table S5. Rate constants for TEACl/LA reaction. The molar ratio of TEACl:LA was 1:1.

T (℃)	k_{11} (L·mol^{-1}·h^{-1})
85	0.000108
75	0.0000638
65	0.0000385
55	0.0000300

Table S6. Rate constants for water evaporation.

T (℃)	K_{pw} (μmol cm^{-1}·h^{-1})
85	15845
75	10843
65	7200
55	4726

9. The copolymerization using different concentrations of valine

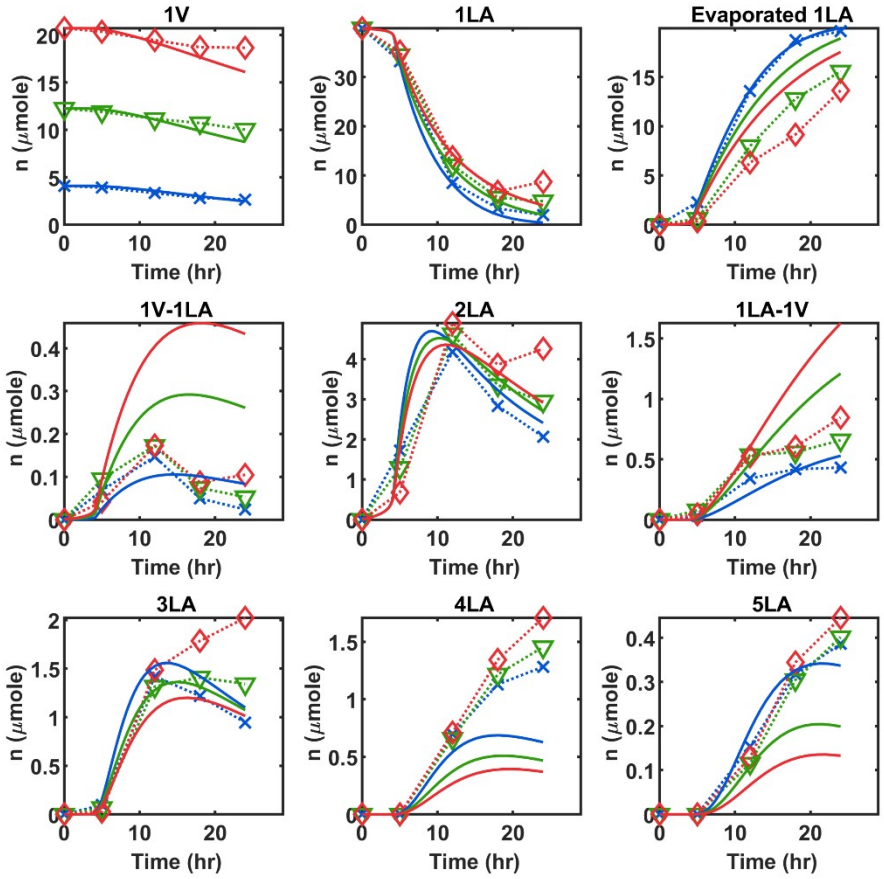

Figure S15. Oligomer distribution versus time profile for the control experiment under different LA/V ratios. The results for different LA/V ratios are denoted as different colors: blue (10:1), green (10:3), and red (10:5). Solid lines are the model predictions. The experimental data points are represented by the same colors and by the ×, ▽ and ◇ symbols, respectively. All simulations were performed by using the rate constants obtained from the 10:1 experiment. The reaction temperature was 85°C.

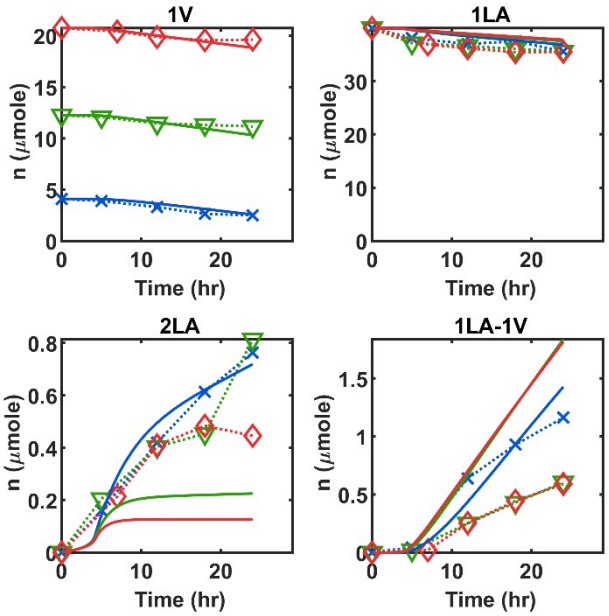

Figure S16. Oligomer distribution versus time profile for the reaction with TEACl under different TEACl/LA/V ratios. The results for different LA/V ratios are denoted as different colors: blue (10:10:1), green (10:10:3), and red (10:10:5). Solid lines are the model predictions. The experimental data points are represented by the same colors and by the ×, ▽ and ◇ symbols, respectively. All simulations were performed by using the rate constants obtained from the 10:10:1 experiment. The reaction temperature was 85°C.

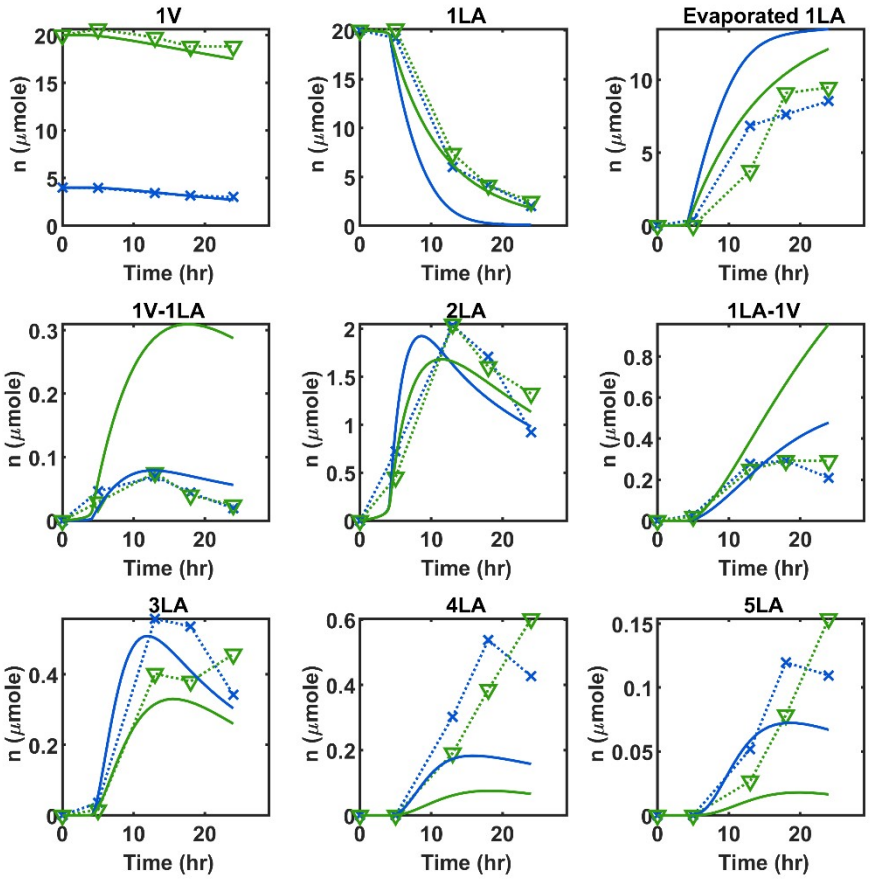

Figure S17. Oligomer distribution versus time profile for the control experiment by reducing the concentration of LA. The results for different LA/V ratios are denoted as different colors: blue (5:1) and green (5:5). Solid lines are the model predictions. The experimental data points are represented by the same colors and by the ×, ▽ and ◇ symbols, respectively. All simulations were performed by using the rate constants obtained from the 10:1 experiment. The reaction temperature was 85°C.

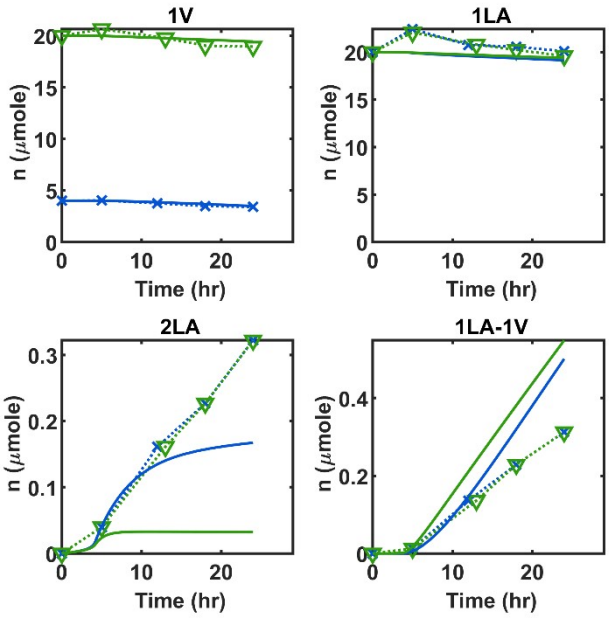

Figure S18. Oligomer distribution versus time profile for the reaction with TEACl by reducing the concentration of TEACl and LA. The results for different TEACl/LA/V ratios are denoted as different colors: blue (5:5:1) and green (5:5:5). Solid lines are the model predictions. The experimental data points are represented by the same colors and by the ×, ▽ and ◇ symbols, respectively. All simulations were performed by using the rate constants obtained from the 10:10:1 experiment. The reaction temperature was 85°C.

10. The copolymerization using different quaternary ammonium salts

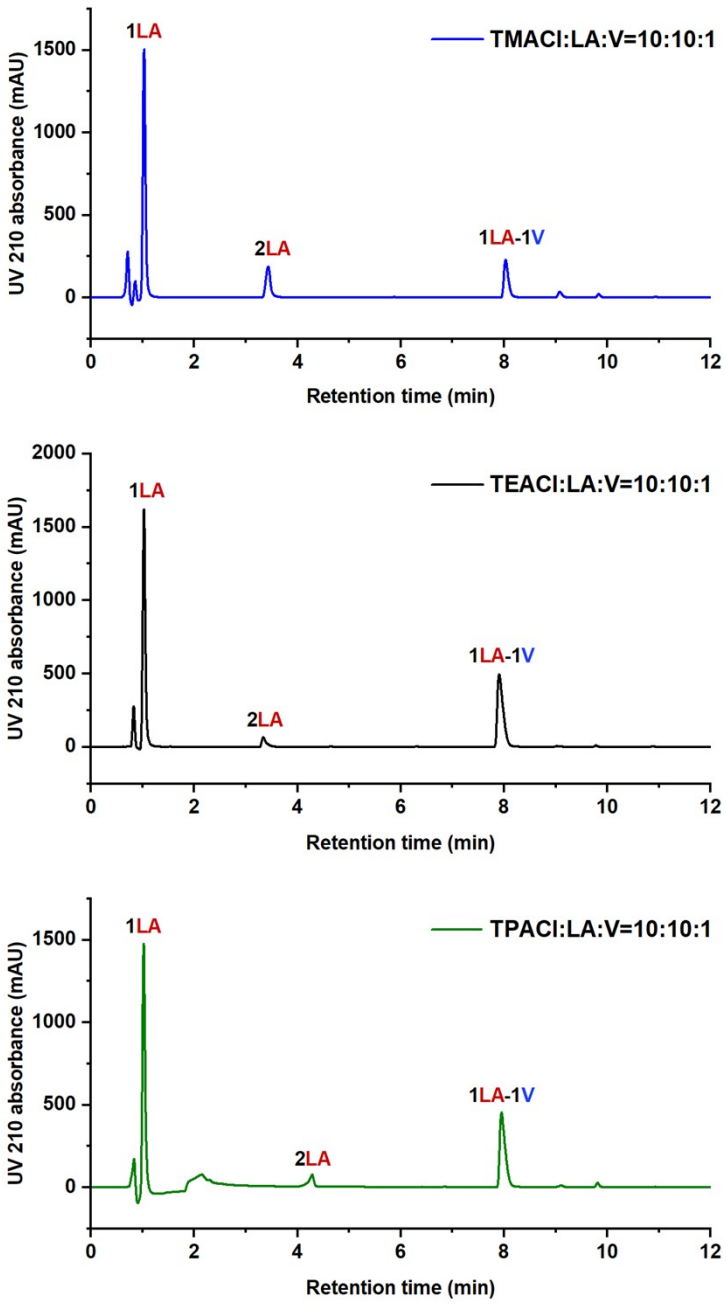

Figure S19. LC-UV chromatograms of the reaction mixtures with different quaternary ammonium salts such as tetramethyl ammonium chloride (TMACl), tetraethyl ammonium chloride (TEACl), and tetrapropyl ammonium chloride (TPACl). The reaction mixtures were prepared by drying at 85℃ for 24 hours.

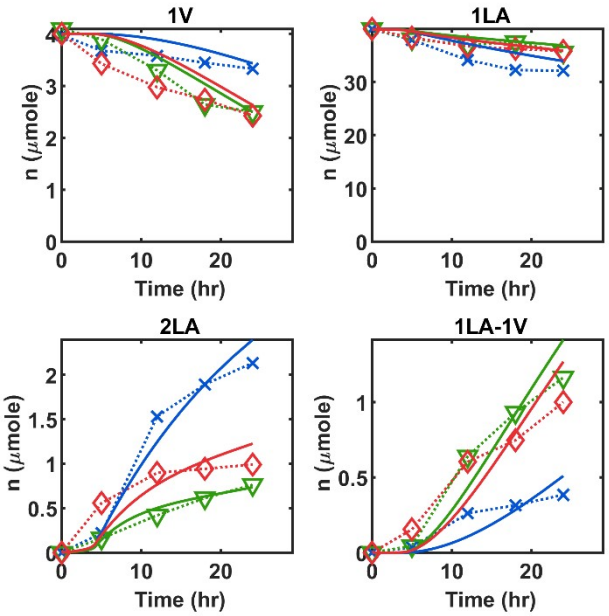

Figure S20. Oligomer distribution versus time profile for the reaction with different quaternary ammonium salts. The results for different salts are denoted as different colors: blue (TMACl), green (TEACl), and red (TPACl). Solid lines are the model predictions. The experimental data points are represented by the same colors and by the ▽, ◇ and × symbols, respectively. The reaction temperature of 85°C. The molar ratio of salts/LA/V was 10:10:1 for each experiment.