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Readily Prepared and Tunable Ionic Organocatalysts for Ring-opening Polymerization of Lactones

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Electronic Supplementary Information

Abstract Highly potent ionic organocatalyst is developed for room-temperature controlled ring-opening polymerization (ROP) of lactones, including δ -valerolactone, ϵ -caprolactone, and δ -hexalactone. The catalysts are prepared by simply mixing tetra-*n*-butyl ammonium hydroxide and a (thio)urea at elevated temperature under vacuum, and used in cooperation with an alcoholic initiator. The performance of the catalyst is readily adjusted and optimized through variation of the (thio)urea precursor, catalyst composition, and reaction condition. Urea-derived catalysts are generally superior to thiourea-derived ones. Provided with proper *N*-substituents, the catalyst affords both high polymerization efficiency and high selectivity for monomer enchainment over macromolecular transesterification, even at high monomer conversion and/or substantially extended reaction time. In addition to acidity, structural symmetry of the urea also proves decisive for the catalytic activity, which enables a catalyst-assisted proton transfer process for the ring-opening of lactone and thus provides a novel mechanistic insight for ROP catalyzed by hydrogen-bonding type bifunctional ionic organocatalysts.

Keywords Organocatalytic polymerization; Ring-opening polymerization; Polyester

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INTRODUCTION

Aliphatic polyesters synthesized by ring-opening polymerization (ROP) of lactones, especially ϵ -caprolactone (CL) and δ -valerolactone (VL), represent classic (bio)degradable polymers that have been extensively studied and widely used.^[1,2] Enormous efforts have been made to forge catalytic ROP into a powerful toolbox for synthesizing aliphatic polyesters with controlled molar mass, narrow molar mass distribution (D_M), and diverse macromolecular structures.^[3–5] In the recent two decades, organocatalysis has shown to be an excellent match for ROP of lactones.^[6–9] In addition to producing metal-free polyesters, organocatalysis can equal or outperform metal-based initiating/catalytic systems in terms of polymerization efficiency and control/selectivity, for which ROP of lactones stands as a typical example.

So far, a large variety of small-molecule organic compounds, including strong organobases, strong Brønsted acids, and hydrogen bond donor-acceptor type bifunctional catalysts, have shown the effectiveness for ROP of lactones.^[7,8] For the monofunctional organobases, such as phosphazene bases (PB)^[10,11] and *N*-heterocyclic carbenes (NHC),^[12,13] catalytic activity will generally be enhanced as the basicity increases. Particularly, a relatively strong base is usually

needed for CL in order to perform the ROP at room temperature (RT) and reach high monomer conversion in a reasonable time scale. However, high basicity almost inevitably leads to low selectivity for monomer enchainment over macromolecular transesterification and thus causes uncontrolled molar mass and macromolecular structure as well as high D_M , especially at high monomer conversion. Better polymerization control has been realized by the use of strong organic Brønsted acids, *i.e.* well-controlled molar mass with relatively low D_M can be achieved at high or complete monomer conversion.^[14–16] However, the catalytic activity is significantly lower than strong organobases. A proper balance between activity and selectivity can be arrived at by bifunctional organocatalysts comprising both a hydrogen bond donating site/molecule and a hydrogen bond accepting site/molecule. The monomer-hydroxyl synergetic activating mechanism favors the reaction between monomer and chain end over transesterification on the open-chain ester groups (*i.e.* polyester).^[6,7,17] The bifunctional organocatalyst can be a single molecule (*e.g.* 1,5,7-triazabicyclo[4.4.0]dec-5-ene, TBD)^[18,19] or bi-component such as 1,8-diazabicyclo[5.4.0]-7-undecene (DBU) plus thiourea (a mild base plus a weak acid)^[20] and DBU/7-methyl-TBD (MTBD) plus sulfonic/phosphoric acid (a mild base plus strong acid).^[21–24] However, such catalysts are usually much less active, especially for CL.

Recently, a new class of bi-component bifunctional catalyst constituted by a strong base and a $-\text{NHCO}(\text{S})-$ type

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hydrogen bond donor (weak acid) has shown both high activity and high selectivity for ROP of cyclic esters.^[19,25–29] In the cases where an alkali metal alkoxide is used as the strong base, the actual bifunctional ionic catalyst and an hydroxy initiator are both generated upon mixing the base and the weak acid.^[19,25–27] This method uses inexpensive and easily accessible chemicals to produce the catalyst, but the structure of the polyester is limited since the initiator only originates from the base. In other cases, the catalyst is generated by combination of a strong and neutral organobases (PB, NHC, and MTBD) with a (thio)urea, then used in cooperation with added hydroxy initiator.^[19,28–30] Because of the independence of catalyst and initiator, this method rivals the previous one for the versatile synthesis of various polyester structures by employing different initiators. However, only complex and expensive organobases have been used so far. In this study, we have developed a new version of the second method by employing a simple and inexpensive organobase, tetra-*n*-butylammonium hydroxide (TBOH), to deprotonate (thio)ureas through a facile dehydration reaction. A series of organocatalysts featured by a tetra-*n*-butylammonium cation and a thiourea or urea anion (thioimide or imide), termed as TUA or UA, are afforded with the catalytic activity and selectivity readily adjusted and optimized to achieve efficient, controlled/selective, and versatile ROP of lactones.

EXPERIMENTAL

Materials

All chemicals were purchased from Aladdin unless otherwise specified. ϵ -Caprolactone (CL; 99%), δ -valerolactone (VL; 98%), δ -hexalactone (HL; 98%), benzyl alcohol (BA; 99%), dichloromethane (DCM; 99.5%), and toluene (Guangzhou Chemical Reagent, AR) were dried by stirring with calcium hydride overnight and distilled. Tetrahydrofuran (THF; 99%) was dried successively by molecular sieve (4 Å), calcium hydride, and *n*-butyllithium (*n*-BuLi) capped with 1,1-diphenyl-ethylene before distilled. 1,3-Dicyclohexylthiourea (TU1; TCI, 98%), 1,3-diphenylthiourea (TU2; TCI, 98%), and 1,3-diphenylurea (U4; TCI, 98%) were vacuum-dried prior to use. 1-[3,5-Bis(trifluoromethyl)phenyl]-3-cyclohexylthiourea (TU3), 1-cyclohexyl-3-phenylthiourea (TU4), 1,3-bis[3,5-bis(trifluoromethyl)phenyl]urea (U1), 1-[3,5-bis(trifluoromethyl)phenyl]-3-(3-trifluoromethyl)phenylurea (U2), 1-[3,5-bis(trifluoromethyl)phenyl]-3-phenylurea (U3), and 1,3-bis[(3-trifluoromethyl)phenyl]urea (U5) were synthesized by the reaction between the corresponding primary/secondary amine and isothiocyanate (for thiourea) or isocyanate (for urea).^[31] Chloroform (Guangzhou Chemical Reagent, AR), methanol (AR), dimethyl sulfoxide (DMSO; Energy Chemical, 99.7%, extra dry, stored with molecular sieve), tetra-*n*-butylammonium hydroxide (TBOH; 0.8 mol·L⁻¹ in methanol), and acetic acid (AcOH; AR) were used as received.

Instrumentation

Size exclusion chromatography (SEC) coupled with RI and UV detectors was conducted in THF at 35 °C using two identical PL gel columns (5 μ m, MIXED-C) at a flow rate of 1.0 mL·min⁻¹. Calibration was done with a series of nar-

rowly dispersed polystyrene (PS) standards to obtain apparent number-average molar mass ($M_{n,SEC}$) and $\bar{M}_w$ of the polymers. NMR spectra were recorded at RT on a Bruker AV600 NMR spectrometer using CDCl₃ or DMSO-*d*₆ as the solvent with tetramethylsilane as the internal standard. ¹H-NMR spectrum was used to calculate the monomer conversion by comparing the integrals of characteristic signals from the remaining monomer with that of the corresponding signals from the polymer. Number-average molar mass of the isolated polymer ($M_{n,NMR}$) was calculated from ¹H-NMR spectrum through comparison of signal integrals from the end group (e.g. methylene or methine protons next to the terminal hydroxyls) with those from the polymer main body (e.g. methylene protons next to the ester groups). Matrix-assisted laser desorption/ionization time-of-flight mass spectrometry (MALDI-TOF MS) measurements were performed on a Bruker Autoflex III Smartbeam MALDI-TOF mass spectrometer. Samples were dissolved in THF (10 mg·mL⁻¹) and mixed with a solution of sodium trifluoroacetate in THF (10 mg·mL⁻¹) in a volume ratio of 5:1. This solution was then mixed with a THF solution of matrix (2,5-dihydroxybenzoic acid, 20 mg·mL⁻¹) in a volume ratio of 1:10. Then, 0.4 μ L of the final solution was spotted on the target plate (dried-droplet method). The reflective positive ion mode was used to acquire the mass spectra of the samples. Calibration was done externally with poly(methyl methacrylate) standards using the nearest neighbor positions.

Preparation of (Thio)ureas

Thioureas/ureas that are not commercially available were synthesized by reactions of the corresponding amine (excess) and isothiocyanate/isocyanate. A typical procedure for TU4 is as follows. 0.405 g of phenyl isothiocyanate (3.0 mmol), 0.45 g of cyclohexylamine (4.5 mmol), and 20 mL of DCM were added in a pre-dried 50 mL Schlenk flask and stirred at RT for 6 h. Then DCM was removed by rotary evaporation and the crude product was washed 3 times with chloroform. The white solid product was collected by filtration and dried under vacuum at 40 °C overnight. Yield = 0.51 g (73%).

The synthesis of ureas followed a similar procedure except that toluene was used as the solvent and the crude product was washed also by toluene.

Preparation of Ionic Organocatalysts

The ionic organocatalysts (TUA/UA) used in this study were prepared by reaction (dehydration) of the corresponding thiourea/urea (excess) and TBOH. A typical procedure for UA2 is as follows. 1.25 mL of TBOH solution (1.0 mmol) and 1.04 g of U2 (2.5 mmol) were mixed with 15 mL of THF in a 50 mL round-bottom Schlenk flask. The mixture was stirred at 40 °C for 1 h followed by slow removal of THF by vacuum distillation. The remaining solid was heated at 80 °C under vacuum with constant pumping of an oil pump for 8 h. Then 5 mL of DMSO and 20 mL of THF were added to afford a homogeneous catalyst solution with the concentration of urea anion being 0.04 mol·L⁻¹.

Polymerization Procedures

Polymerization of CL

A typical procedure for U2CL is given as follows. In a glovebox, a pre-dried 50 mL Schlenk flask was charged with

0.45 mL of UA2 solution (0.018 mmol of UA2 and 0.027 mmol of U2), 9.4 μ L of BA (9.7 mg, 0.09 mmol), and 1.5 mL of THF. Then, 1.0 mL of CL (1.03 g, 9.0 mmol) was injected in the reaction flask and the mixture was stirred for 5 h ($[CL]_0 = 3.0 \text{ mol}\cdot\text{L}^{-1}$), during which aliquots were withdrawn from time to time, quenched with AcOH, and used for $^1\text{H-NMR}$ and SEC analyses. The reaction was finally quenched with *ca.* 0.1 mL of AcOH. The polymer was precipitated in methanol and dried in vacuum. $\text{Conv.}_{(CL)} = 95\%$, $M_{n,th} = 10.8 \text{ kg}\cdot\text{mol}^{-1}$, $M_{n,SEC} = 19.4 \text{ kg}\cdot\text{mol}^{-1}$, $\bar{D}_M = 1.15$. $^1\text{H-NMR}$ (600 MHz, CDCl_3 , δ , ppm): 7.38–7.30 (aromatic protons of BA-derived end group), 5.12–5.10 ($\text{C}_6\text{H}_5\text{CH}_2\text{OCO}-$), 4.09–4.02 ($-\text{OCOCH}_2\text{CH}_2\text{CH}_2\text{CH}_2\text{CH}_2\text{OCO}-$), 3.66–3.62 ($-\text{OCOCH}_2\text{CH}_2\text{CH}_2\text{CH}_2\text{CH}_2\text{OH}$), 2.33–2.27 ($-\text{OCOCH}_2\text{CH}_2\text{CH}_2\text{CH}_2\text{CH}_2\text{O}-$), 1.69–1.34 ($-\text{OCOCH}_2\text{CH}_2\text{CH}_2\text{CH}_2\text{CH}_2\text{O}-$), $M_{n,NMR} = 10.2 \text{ kg}\cdot\text{mol}^{-1}$.

Polymerization of HL

A typical procedure for U2HL2 is given as follows. In a glovebox, a pre-dried 50 mL Schlenk flask was charged with 0.51 mL of UA2 solution (0.021 mmol of UA2 and 0.032 mmol of U2) and 8.5 μ L of BA (8.9 mg, 0.082 mmol), followed by the removal of THF from the reaction flask by vacuum distillation. Then, 0.9 mL of HL (0.93 g, 8.2 mmol) was injected in the reaction flask and the mixture was stirred for 3 h, during which aliquots were withdrawn from time to time, quenched with AcOH, and used for $^1\text{H-NMR}$ and SEC analyses. The reaction was finally quenched with *ca.* 0.1 mL of AcOH. The polymer was precipitated in cold methanol and dried in vacuum. $\text{Conv.}_{(HL)} = 91\%$, $M_{n,th} = 10.4 \text{ kg}\cdot\text{mol}^{-1}$, $M_{n,SEC} = 17.1 \text{ kg}\cdot\text{mol}^{-1}$, $\bar{D}_M = 1.12$. $^1\text{H-NMR}$ (600 MHz, CDCl_3 , δ , ppm): 7.38–7.30 (aromatic protons of BA-derived end group), 5.12–5.09 ($\text{C}_6\text{H}_5\text{CH}_2\text{OCO}-$), 4.95–4.84 ($-\text{OCOCH}_2\text{CH}_2\text{CH}_2\text{CH}_2\text{CH}_2\text{OCO}-$), 3.84–3.76 ($-\text{OCOCH}_2\text{CH}_2\text{CH}_2\text{CH}_2\text{CH}_2\text{OH}$), 2.35–2.22 ($-\text{OCOCH}_2\text{CH}_2\text{CH}_2\text{CH}_2\text{CH}_2\text{O}-$), 1.75–1.45 ($-\text{OCOCH}_2\text{CH}_2\text{CH}_2\text{CH}_2\text{CH}_2\text{O}-$), 1.25–1.16 ($-\text{OCOCH}_2\text{CH}_2\text{CH}_2\text{CH}_2\text{CH}_2\text{O}-$), $M_{n,NMR} = 11.2 \text{ kg}\cdot\text{mol}^{-1}$.

Polymerization of VL

A typical procedure for U3VL is given as follows. In the glovebox, a pre-dried 50 mL Schlenk flask was charged with 0.55 mL of UA3 solution (0.022 mmol of UA3 and 0.033 mmol of U3), 11.4 μ L of BA (11.9 mg, 0.11 mmol), and 2 mL of THF. Then, 1.0 mL of VL (1.11 g, 11.0 mmol) was injected in the reaction flask and the mixture was stirred for 10 min ($[VL]_0 = 3.0 \text{ mol}\cdot\text{L}^{-1}$), during which aliquots were withdrawn from time to time, quenched with AcOH, and used for $^1\text{H-NMR}$ and SEC analyses. The reaction was finally quenched with *ca.* 0.1 mL of AcOH. The polymer was precipitated in methanol and dried in vacuum. $\text{Conv.}_{(VL)} = 95\%$, $M_{n,th} = 9.5 \text{ kg}\cdot\text{mol}^{-1}$, $M_{n,SEC} = 16.1 \text{ kg}\cdot\text{mol}^{-1}$, $\bar{D}_M = 1.08$. $^1\text{H-NMR}$ (600 MHz, CDCl_3 , δ , ppm): 7.77–6.94 (aromatic protons of BA-derived end group), 5.12–5.09 ($\text{C}_6\text{H}_5\text{CH}_2\text{OCO}-$), 4.12–4.03 ($-\text{OCOCH}_2\text{CH}_2\text{CH}_2\text{CH}_2\text{OCO}-$), 3.67–3.63 ($-\text{OCOCH}_2\text{CH}_2\text{CH}_2\text{CH}_2\text{OH}$), 2.37–2.31 ($-\text{OCOCH}_2\text{CH}_2\text{CH}_2\text{CH}_2\text{O}-$), 1.73–1.56 ($-\text{OCOCH}_2\text{CH}_2\text{CH}_2\text{CH}_2\text{O}-$), $M_{n,NMR} = 8.0 \text{ kg}\cdot\text{mol}^{-1}$.

RESULTS AND DISCUSSION

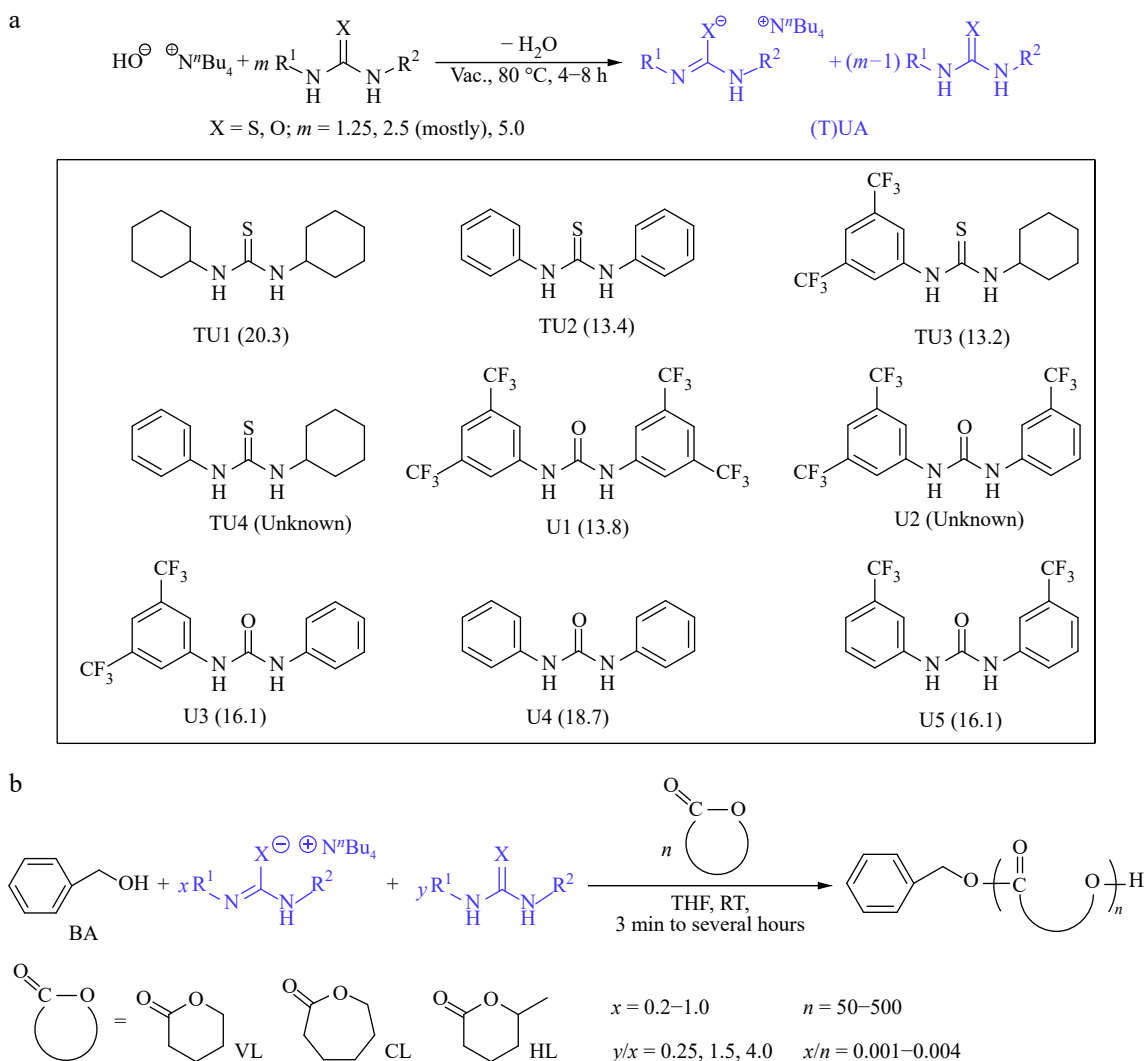
The structures of the synthesized (thio)ureas are confirmed

by $^1\text{H-NMR}$ spectra (Figs. S1–S5, in electronic supplementary information, ESI). The relative acidities of the (thio)ureas are discussed here according to the pK_a values reported in literature.^[31,32] The ionic organocatalyst is prepared by a simple acid-base (dehydration) reaction between TBOH and the (thio)urea at 80 °C under vacuum for at least 4 h. Excess (thio)urea is used to ensure complete consumption of the hydroxide anion. Hence the afforded catalyst (TUA or UA) comprises a (thio)urea anion, a tetra-*n*-butylammonium cation, and a certain amount of neutral (thio)urea (Scheme 1a). The disappearance of $-\text{NH}-$ proton signal and the relocation of aromatic proton signals in $^1\text{H-NMR}$ spectra after the reaction with TBOH confirm the occurrence of deprotonation and a fast proton exchange between the anionic and neutral forms of (thio)urea (Figs. S6 and S7 in ESI). The solubility of the TUA/UA catalysts in the organic media varies with the *N*-substituents. A mixed solvent of DMSO and THF with a volume ratio of 1/4 allows good solubility of all the catalyst, and therefore is used to prepare the catalyst solutions in order to keep a consistency of the amounts of DMSO added to the reactions.

Attempts are first made using TBOH to catalyze the ROP of VL with or without BA added as the initiator (methanol in the original TBOH solution is removed under vacuum). When BA is absent ($[VL]/[\text{TBOH}] = 100/1$), no PVL is formed at RT after 24 h as shown by SEC. In the presence of BA ($[VL]/[\text{BA}]/[\text{TBOH}] = 100/1/1$), ROP of VL occurs but the conversion of VL reaches only < 10% in 24 h. The attempt to polymerize VL by using a non-dehydrated mixture of TBOH and TU1 also fails ($[VL]/[\text{BA}]/[\text{TBOH}]/[\text{TU1}] = 100/1/0.1/0.25$). The same is observed for U2. The explanation can be that the reaction between lactone and hydroxide anion generates a carboxylate species which is a weak and monofunctional base and thus ineffective for catalyzing the ROP of lactone, especially at room temperature. On the other hand, ROP of lactone occurs when (T)UAs are used as the catalysts (Scheme 1b), as will be discussed below. It is therefore further confirmed that hydroxide anion of TBOH is consumed by the dehydration reaction in the catalyst preparation process and as a result, the basicity is transferred from TBOH to the (thio)urea anion.

ROP of the lactone is then performed with (T)UAs as the catalysts and BA as the initiator. The impacts of catalyst structure (*N*-substituents), composition (amount of excess thiourea/urea), catalyst loading, and reaction conditions (monomer concentration, temperature, time, *etc.*), as well as the difference between TUA and UA are investigated. For most of the experiments, aliquots are withdrawn on an irregular basis and analyzed by SEC and $^1\text{H-NMR}$ to monitor polymerization results and to guarantee that ROP is quenched at high monomer conversion.

In the TUA series, TUA1 shows the highest catalytic activity for both CL and VL. High or complete monomer conversion is reached within 10 min using 0.1 mol% of TUA1 loading (TU1CL, TU1VL in Table 1). The turnover frequency (TOF) for CL and VL is calculated to be 6000 and 10800 h^{-1} , respectively. However, molar mass distributions are rather broad indicating poor control of the ROP process (extensive macromolecular transesterification). Changing the



Scheme 1 (a) Illustration for the preparation of ionic organocatalysts. Structural formula of the (thio)ureas used in this study are listed below. In parenthesis are the pK_a values found in Ref. [31]. (b) General reaction scheme for BA-initiated ROP of lactones catalyzed by the (T)UA ionic catalysts. Monomers used in this study are listed below.

Table 1 Conditions and results of ROP of VL/CL catalyzed by TUAs^a

Entry ^b	[M] ₀ /[OH]/[TUA] ^c	Time	Conv. ^d (%)	$M_{\text{n,th}}$ ^e (kg·mol ⁻¹)	$M_{\text{n,SEC}}$ ^f (kg·mol ⁻¹)	D_{M} ^f
TU1CL	100/1/0.1	10 min	>99	10.7	18.8	1.83
TU1VL	100/1/0.1	5 min	90	9.0	14.9	1.39
TU2CL ^a	100/1/1	96 h	35	4.0	6.3	1.15
TU2VL	100/1/1	144 h	51	5.1	7.4	1.16
TU3CL	100/1/1	96 h	9	1.0	1.4	1.13
TU3VL	100/1/1	144 h	33	3.3	5.2	1.11
TU4CL	100/1/0.2	27 h	92	10.5	15.7	1.27
TU4VL1	100/1/0.2	1 h	95	9.5	15.1	1.09
TU4VL2	50/1/0.1	1 h	95	4.8	6.9	1.11

^a Performed at RT (and 60 °C for TU2CL) in THF with [M]₀ being 3 mol·L⁻¹; ^b Thiourea, used for preparation of TUA, and monomer are indicated in the entry name. The molar ratio of TBOH and thiourea for preparation of TUA is 1/2.5, except TU1CL (1/1.25); ^c Molar feed ratio of monomer, BA, and thiourea anion; ^d Monomer conversion determined from ¹H-NMR spectrum of the crude product; ^e Theoretical number-average molar mass calculated from [M]₀/[OH] and monomer conversion; ^f Apparent number-average molar mass and molar mass distribution obtained from SEC analysis of the crude product (THF, 35 °C, PS standards)

N-substituents from cyclohexyl (TU1) to phenyl (TU2) increases the thiourea acidity (Scheme 1) and significantly lowers the catalytic activity of TUA. TUA2-catalyzed ROP of CL and VL appears to be extremely slow even with 1 mol% of catalyst loading and elevated temperature (TU2CL and TU2-

VL in Table 1). The comparison between TUA1 and TUA2 shows that the basicity of anionic part of the catalyst plays a key role in catalytic activity. The poor performance of TUA1/TUA2 is different from what we previously observed for the combination of a PB superbase and TU1/TU2,^[28] indicating

the effect of counterion in this all-organic ionic catalytic system.^[19,25] Poor activity is also shown by the TUA catalyst derived from TU3 which has an acidity close to that of TU2 (Scheme 1; TU3CL and TU3VL in Table 1).

TU4 features an asymmetric structure with a cyclohexyl on one side and a phenyl on the other (Scheme 1). Its acidity is supposedly between that of TU1 and TU2. A better compromise of catalytic activity and polymerization control is therefore exhibited by TUA4 as compared with TUA1 and TUA2. Especially, rapid (TOF = 475 h⁻¹) ROP is achieved for VL with catalyst loading being 0.2 mol% and target degree of polymerization (DP) being 100 or 50 (TU4VL1 and TU4VL2 in Table 1). Well-defined PVL structures and controlled molar mass are confirmed by SEC, ¹H-NMR, and MALDI-TOF MS characterizations (Fig. 1 and Fig. S8 in ESI). Near complete conversion of VL is reached in 1 h, and only a slight increase of D_M (from 1.09 to 1.16) is observed when the reaction time is extended to 22 h (Fig. 1B). This indicates high selectivity of TUA4 for monomer enchainment

over macromolecular transesterification. However, TUA4 still shows a low catalytic activity for CL (TU4CL in Table 1). The generally unsatisfactory performance of TUAs and limited choices of thiourea for optimizing the polymerization efficiency and control encourage us to use ureas in the following studies.

An array of ureas are tested in order to improve the catalytic activity for VL/CL and to gain more insights into the structure-activity relationship of UA catalysts (Scheme 1). U1 carries two trifluoromethyl (–CF₃) groups on each *N*-phenyl, and thus is the most acidic one of the ureas used here. Its p*K*_a value is reported to be close to that of TU2.^[31] However, the polymerization efficiency and control are remarkably improved for CL by use of UA1 according to the catalyst loading (0.2 mol%), reaction time, and monomer conversion achieved (U1CL in Table 2). The distinctly higher catalytic activity of UA1 for CL, as compared with its TUA counterpart (TUA2), may be associated with the stronger binding of urea –NH– to the carbonyl of lac-

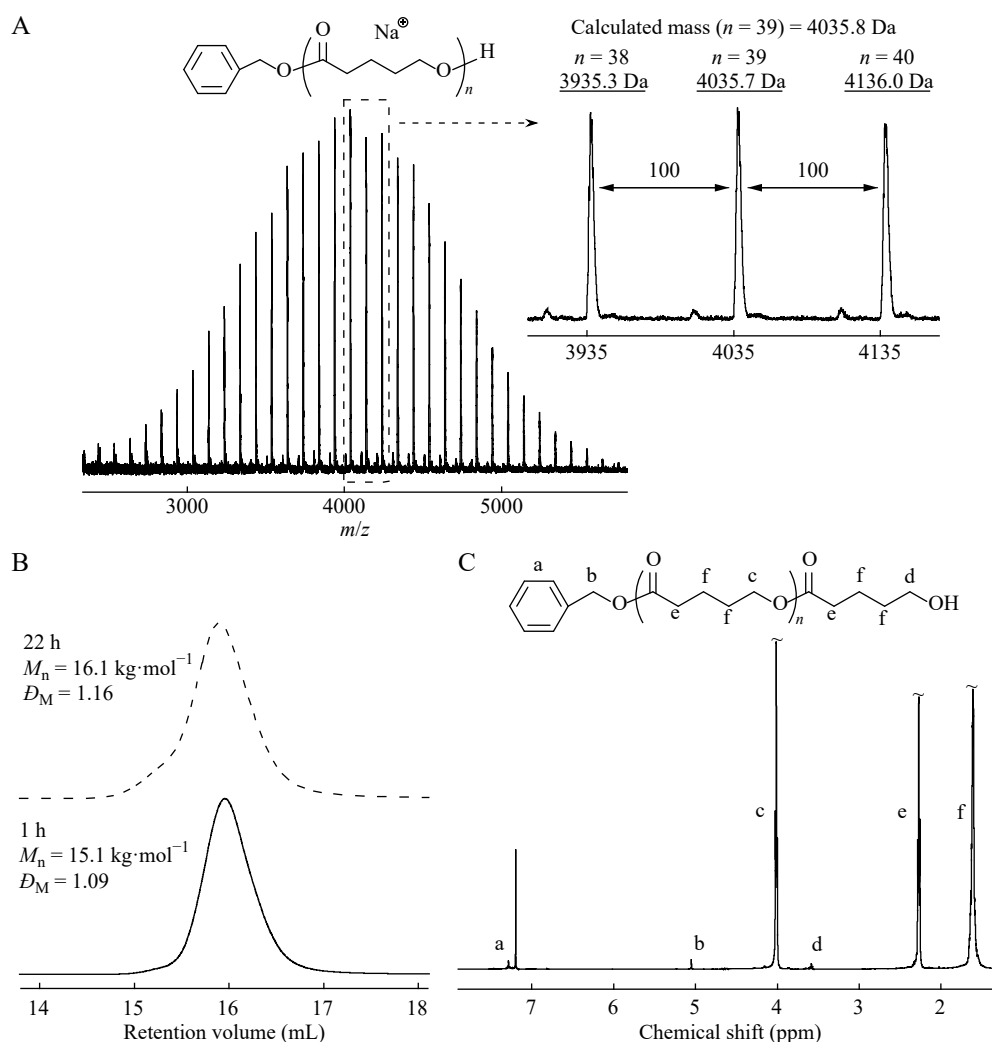


Fig. 1 (A) MALDI-TOF MS spectrum of a low-molar-mass PVL (isolated product) synthesized with TUA4 as the catalyst (TU4VL2 in Table 1). The major and minor mass populations derive from BA-initiated PVL ionized by sodium cation and proton, respectively. (B) SEC traces of PVL (crude product at 1 h and isolated product at 22 h; RI signal) with higher molar mass synthesized using the same catalyst and initiator (TU4VL1 in Table 1). (C) ¹H-NMR spectrum of the isolated product of TU4VL1

Table 2 Conditions and results of ROP of lactones catalyzed by UAs^a

Entry ^b	[M] ₀ /[OH]/[UA] ^c	[M] ₀ (mol·L ⁻¹)	Time	Conv. ^d (%)	$M_{n,th}$ ^e (kg·mol ⁻¹)	$M_{n,SEC}$ ^f (kg·mol ⁻¹)	$\bar{D}_M$ ^f	$M_{n,NMR}$ ^g (kg·mol ⁻¹)
U1CL	100/1/0.2	3	11 h	82	9.4	15.2	1.15	8.1
U2CL	100/1/0.2	3	5 h	95	10.8	19.4	1.15	10.2
U3CL	100/1/0.2	3	2 h	91	10.4	17.1	1.17	9.1
U4CL1	100/1/0.2	3	3 min	99	11.4	20.0	1.81	–
U4CL2	100/1/0.2	1	8 min	89	10.2	17.6	1.11	10.2
U5CL	100/1/0.2	3	20 min	90	10.3	16.9	1.23	12.2
U2VL1	100/1/0.2	3	25 min	91	9.1	15.0	1.09	9.2
U2VL2	500/1/1	3	1 h	97	48.5	64.1	1.12	–
U3VL	100/1/0.2	3	10 min	95	9.5	16.1	1.08	8.0
U4VL1	100/1/0.2	3	4 min	76	7.6	16.5	1.78	–
U4VL2	100/1/0.2	1	3 min	87	8.7	17.5	1.14	8.3
U2HL1	100/1/0.2	3	18 h	73	8.3	15.7	1.16	7.2
U2HL2	100/1/0.2	Bulk	3 h	91	10.4	17.1	1.12	11.2

^a Performed at RT in THF for VL and CL with [M]₀ being 3 mol·L⁻¹; ^b Urea, used for preparation of UA, and monomer are indicated in the entry name. The molar ratio of TBOH and urea for preparation of UA is 1/2.5; ^c Molar feed ratio of monomer, BA, and urea anion; ^d Monomer conversion determined from ¹H-NMR spectrum of the crude product; ^e Theoretical number-average molar mass calculated from [M]₀/[OH] and monomer conversion; ^f Apparent number-average molar mass and molar mass distribution obtained from SEC analysis of the crude product (THF, 35 °C, PS standards); ^g Number-average molar mass calculated from ¹H-NMR spectrum of the isolated product

tone.^[25,33,34] Reducing the number of electron-withdrawing —CF₃ groups in the urea structure increases its pK_a value and thus enhances the basicity of the urea anion, and this leads to a distinct enhancement of catalytic activity. U2 has only one less —CF₃ than U1, yet UA2 allows considerably faster ROP of CL as compared with UA1 (U2CL in Table 2, Fig. S9 in ESI; TOF = 95 h⁻¹). A good control at nearly complete monomer conversion is also achieved. U3 has one less —CF₃ than U2, and UA3 results in higher polymerization rates than UA2 with the same catalyst loading. High conversion and controlled molar mass are achieved in 2 h (U3CL in Table 2; TOF = 227 h⁻¹). However, $\bar{D}_M$ increases markedly with further increased monomer conversion (> 91%). U4 carries no —CF₃ group on the *N*-phenyls. The ROP of CL catalyzed by UA4 (U4CL1 in Table 2) is extremely fast with full conversion achieved in 3 min (TOF > 10000 h⁻¹), but $\bar{D}_M$ is rather high (> 1.8). Reducing the concentration of CL from 3 mol·L⁻¹ to 1 mol·L⁻¹ helps gaining low $\bar{D}_M$ while retaining high polymerization rates (U4CL2 in Table 2; Fig. 2, left). It is therefore clear that the catalytic activity of UA increases with higher basicity (Fig. S10 in ESI), but at the sacrifice of control/selectivity. A balance between basicity and acidity is required to achieve the best compromise between catalytic activity and selectivity.^[34] A lower monomer concentration can help improve the selectivity because of the lowered exothermic effect of ROP and lowered concentration of hydroxyl which render macromolecular transesterification less competitive.

When UA2 is used for the ROP of VL, PVL with low and high molar mass can both be obtained in short reaction time (≤ 1 h; TOF up to 1100 h⁻¹; U2VL1 and U2VL2 in Table 2) with controlled molar mass, low $\bar{D}_M$, and well-defined macromolecular structures (Fig. S11 in ESI). The results are substantially retained at extended reaction time, especially at a higher ratio of hydroxyl to catalyst (Fig. 3). The shoulder on the SEC peak in the case of high DP may be attributed to the

occurrence of intermolecular transesterification.^[35,36] UA3 is also more active for catalyzing ROP of VL as compared with UA2, allowing 95% of monomer conversion in only 10 min and low $\bar{D}_M$ (TOF = 2850 h⁻¹; U3VL in Table 2). UA4 has been demonstrated to be overly active (poorly selective) for CL at a concentration of 3 mol·L⁻¹, and similar result is obtained for VL (U4VL1 in Table 2). Lowering [VL]₀ to 1 mol·L⁻¹ also leads to much better control while retaining a high polymerization rate (TOF = 8700 h⁻¹; U4VL2 in Table 2; Fig. 2, right).

ROP of 5-substituted VLs, *e.g.* HL, can also be afforded by UA2 in both THF and bulk (U2HL1–2 in Table 2). Higher equilibrium conversion (91%) is reached in bulk within 3 h, and the well-defined PHL structures are confirmed by SEC and ¹H-NMR analysis (Figs. S12 and S13 in ESI). The catalytic activity exhibited by UA2 for the ROP of HL is evidently higher than a previously used strong Brønsted acid.^[37]

U5 carries one —CF₃ on each of the *N*-phenyls, and thus is a symmetric structural isomer of U3 (Scheme 1). The pK_a values of U3 and U5 found in the literature are the same,^[31] indicating that their deprotonated forms (the urea anions) have similar basicity, which is also demonstrated by the ¹H-NMR spectra of BA in the presence of UA3 and UA5 (Fig. 4). For instance, when BA is mixed with the catalyst, signal of —OH proton disappears indicating the interaction of hydroxyl with the basic moiety of urea anion, and signal of the methylene proton shows the same upfield shifts indicating that the two catalysts have the similar basicity. Surprisingly, UA5 exhibits a much higher catalytic activity than UA3 for the ROP of CL (U5CL versus U3CL in Table 2; TOF = 1350 and 227 h⁻¹, respectively). One possible reason is that deprotonation of —NH¹— preferably occurs next to the more electron-withdrawing *N*-substituent for an asymmetric urea (Scheme 2a), *i.e.* the 3,5-bis(trifluoromethyl) phenyl side in the case of U3. Therefore, —NH²— remain-

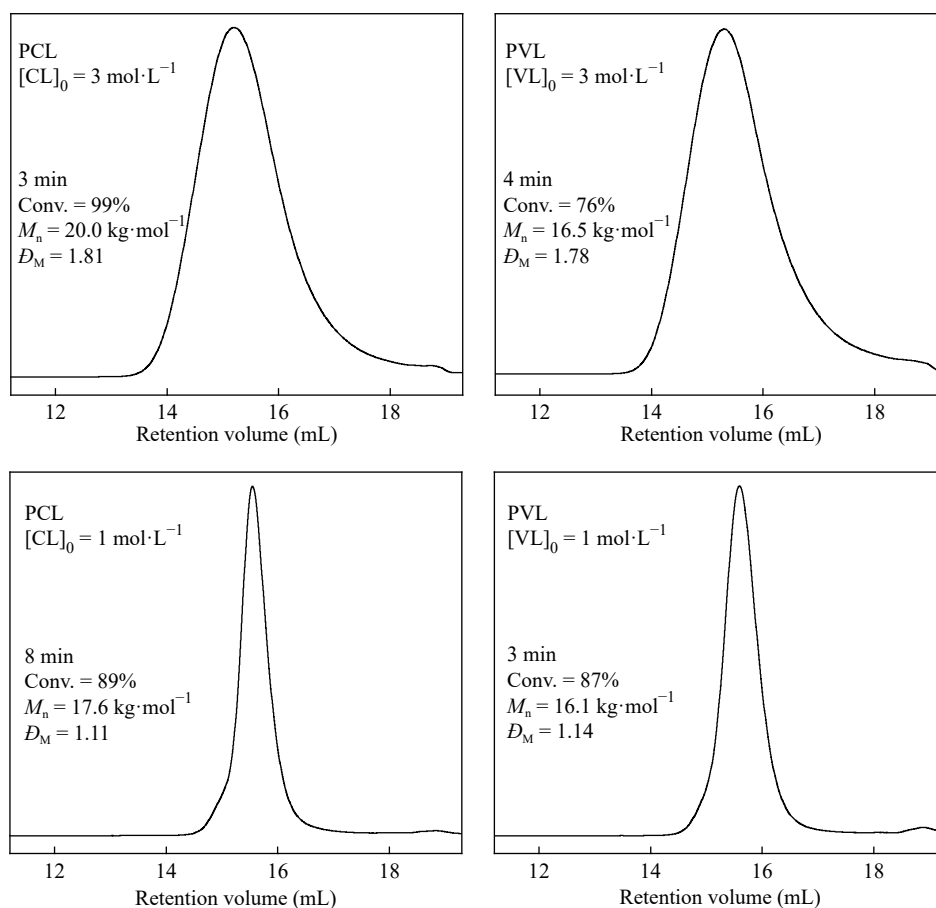


Fig. 2 SEC traces (RI signal in THF at 35 °C) of PVL and PCL synthesized with UA4 as the catalyst at different monomer concentrations (U4CL1, U4CL2, U4VL1 and U4VL2 in Table 2)

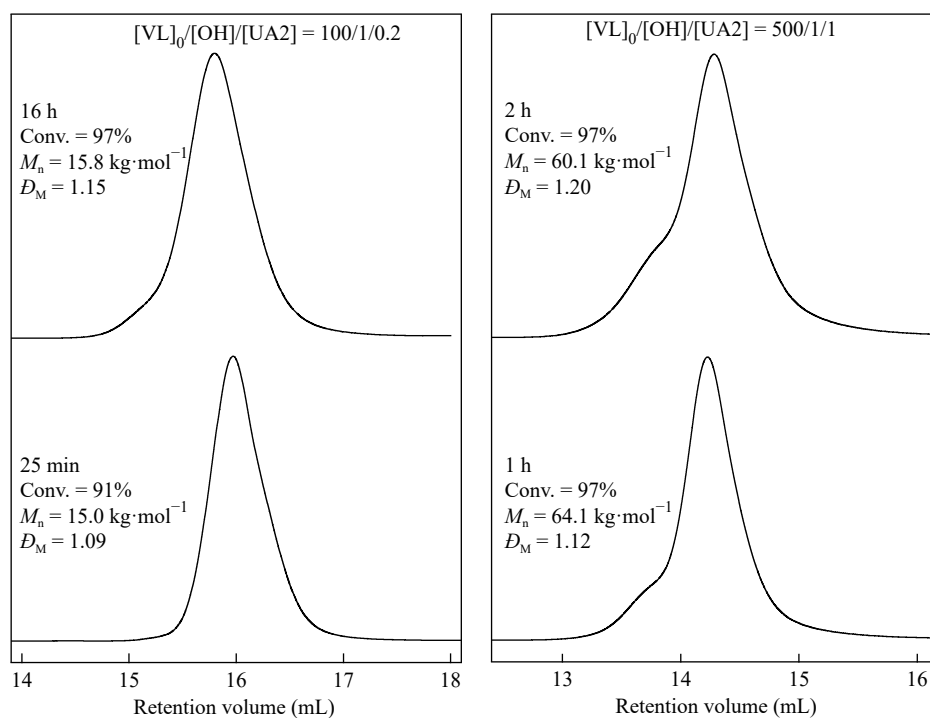


Fig. 3 SEC traces (RI signal in THF at 35 °C) of PVLs synthesized with UA2 as the catalyst at high monomer conversions and extended reaction time. Target DP = 100 (left) and 500 (right) corresponds to U2VL1 and U2VL2 in Table 2, respectively.

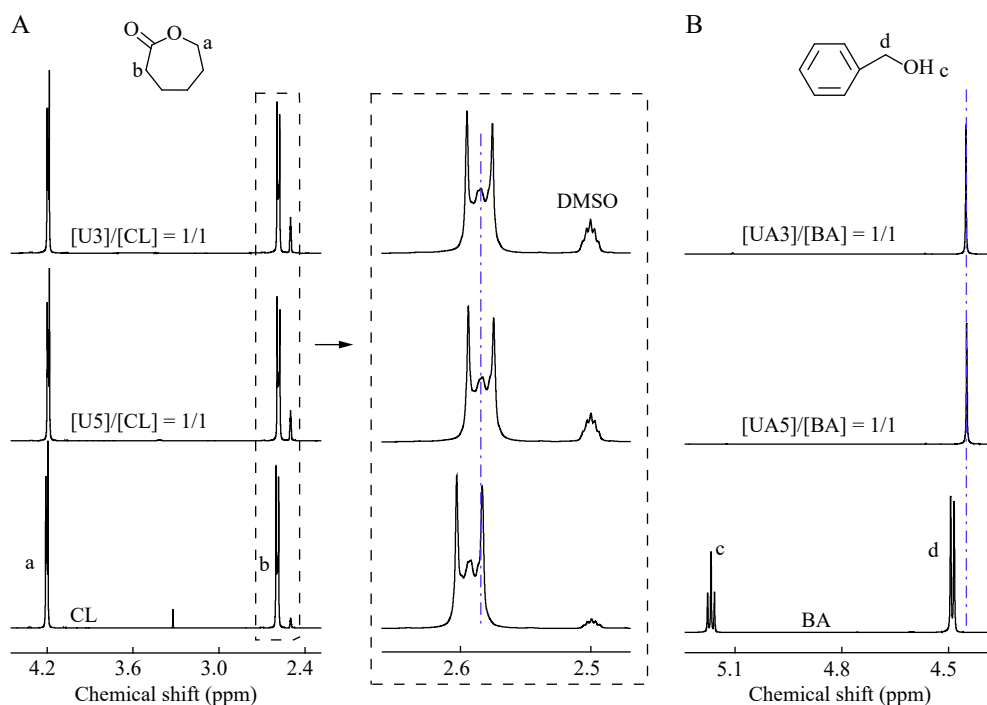
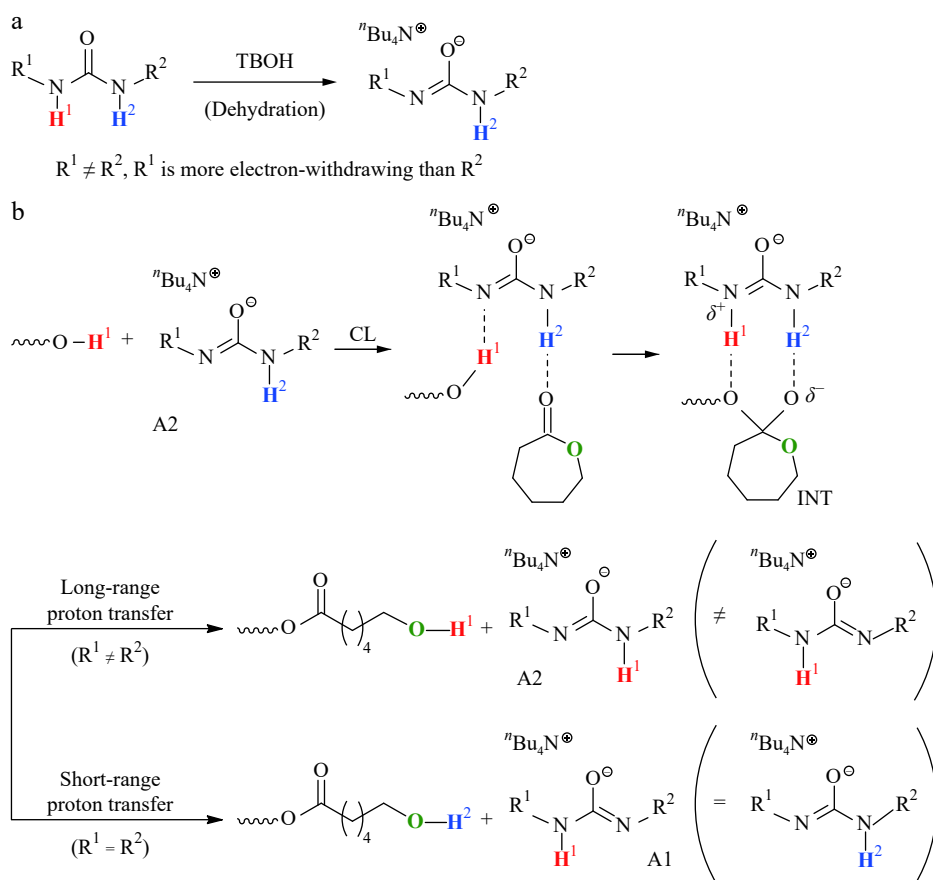


Fig. 4 (A) ^1H -NMR spectra (in DMSO-d_6) of CL and CL mixed with U3 or U5 in a molar ratio of 1/1; (B) Hydroxyl and methylene region of the ^1H -NMR spectra (in DMSO-d_6) of BA and BA mixed with UA3 and UA5. The molar ratio of BA to the urea anion is 1/1. The molar ratio of TBOH to urea for preparation of UA is 1/2.5.



Scheme 2 Plausible explanation for the different catalytic activities of UA3 and UA5: (a) Preferred deprotonation mode of an asymmetric urea; (b) Preferred proton transfer modes for the ring opening of CL catalyzed by urea anions originating from asymmetric and symmetric ureas

ing on the anion of U3 is adjacent to a less electron-withdrawing phenyl so that it becomes a less stronger hydrogen bond donor as compared with that of U5.^[38]

Another possible explanation is also proposed here, which may provide a new mechanistic insight for the ROP of cyclic ester catalyzed by urea anion. The deprotonated $=N-$ and non-deprotonated $-NH_2-$ moieties of the urea anion (A2) are hydrogen-bonded with hydroxyl ($-OH^1$) and CL, respectively, leading to the formation of the tetrahedral intermediate (INT; Scheme 2b).^[25] When the CL ring opens, the oxygen atom of the breaking C—O bond may take a proton that originates from the hydroxyl (H^1 ; long-range proton transfer) resulting in one enchain monomeric unit and A2, or from A2 itself (H^2 ; short-range proton transfer) resulting in A1 (Scheme 2b). When UA derives from an asymmetric urea as U3, A1 has a higher basicity than A2, so the short-range proton transfer is less favored. But for a UA derived from a symmetric urea like U5, A1 and A2 are identical so that the short-range proton transfer prevails and the CL ring opens more smoothly.^[39] It is not yet clear if the catalyst-assisted proton transfer would have an effect on the polymerization control/selectivity, since increased D_M is observed for both U3CL and U5CL at higher CL conversion ($D_M = 1.31$ and 1.36, respectively, at CL conversion of 98%).

The effect of catalyst composition, *i.e.* the ratio of TBOH to thiourea used in the preparation of TUA catalyst, is also investigated (Table S1 in ESI). ROP of VL catalyzed by TUA4 has been performed with the same target DP and the ratio of ionic to neutral parts of (T)UA being 1/0.25, 1/1.5, and 1/4, respectively. The ratio of 1/1.5 is found to give the best compromise between polymerization efficiency and control, and therefore is the catalyst composition used for most of the experiments in this study (Tables 1 and 2). A proper amount of neutral (thio)urea in the catalysts may help activate the cyclic ester through hydrogen bonding to carbonyl and thus enhance the catalytic activity.^[19,25,40] On the other hand, too much neutral (thio)urea may cause overly alleviated activity of the (thio)urea anion through hydrogen bonding between the two parts,^[41,42] as well as a reduction in the achievable monomer conversion by shifting the polymer-monomer equilibrium.^[43]

CONCLUSIONS

In summary, a series of bifunctional ionic organocatalysts are prepared *via* a simple dehydration reaction between TBOH and (thio)ureas. The catalysts can be used in cooperation with an alcoholic initiator to trigger the ROP of lactones at room temperature. Better results are afforded by use of UAs in comparison with TUAs owing to the suitable pK_a range and, presumably, the counterion effect. High polymerization efficiency and excellent control/selectivity can both be achieved at high or nearly complete monomer conversion provided that the urea acidity, catalyst loading, hydroxyl-to-catalyst ratio, monomer concentration, and catalyst composition are appropriately chosen. In addition to the hydrogen-bonding type bifunctional activation mechanism, a catalyst-assisted proton transfer process is suggested for UA derived from a symmetric urea which smoothens the ring opening of

cyclic ester and thus further enhances the polymerization efficiency. Although the rich structural diversity and easy accessibility of (thio)ureas provide good opportunities to finely tune the catalytic activity, the compromise between activity and selectivity is still imperfect for CL. The use of less acidic and/or symmetric urea for the preparation of UA catalyst enhances the polymerization efficiency of CL but also leads to a descent in molar mass control of PCL at high monomer conversion (*e.g.* > 90%) and extended reaction time. Altering the neutral precursor and/or cation of the catalyst may provide new chances for further improvement, which is our ongoing study.

Electronic Supplementary Information

Electronic supplementary information (ESI) is available free of charge in the online version of this article at <http://dx.doi.org/10.1007/s10118-019-2285-1>.

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