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SHORT COMMUNICATION

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Cooperative Catalysis of Cyclic Carbonate Ring Opening: Application Towards Non-Isocyanate Polyurethane Materials

Vince M. Lombardo,[a][‡] Elizabeth A. Dhulst,[b][‡] Emily K. Leitsch,[b] Nathan Wilmot,[c] William H. Heath,[c] Anthony P. Gies,[c] Matthew D. Miller,[c] John M. Torkelson,*[b] and Karl A. Scheidt*[a]

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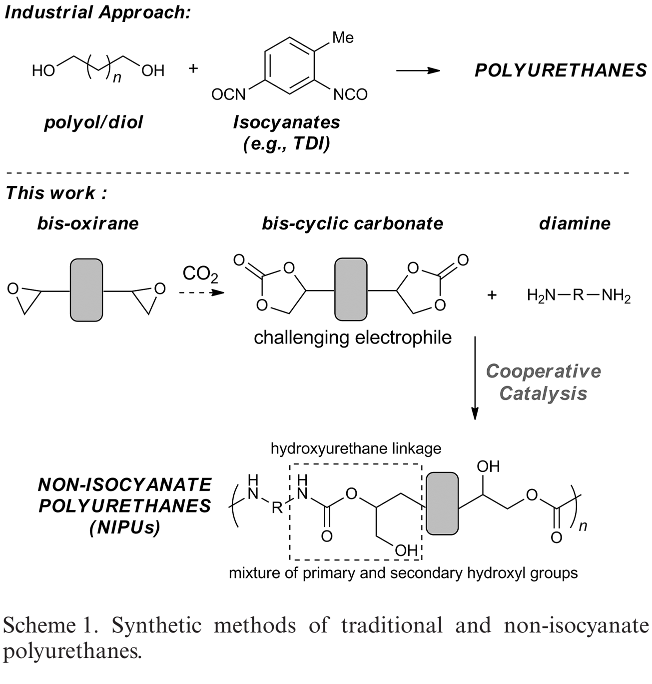
The reaction between cyclic carbonates and amines to produce hydroxyurethanes is an important alternative to current urethane chemistry. In order to address the issue of slow reaction rates, an efficient ring opening of cyclic carbonates with amines has been achieved utilizing cooperative catalysis. A new Lewis acid/Lewis base combination substantially decreases the reaction times for small molecule systems to reach complete conversion. Although triazabicyclodecene (TBD) has a substantial impact on the reaction rate, the addition of lithium triflate (LiOTf) as a co-catalyst allows for the fastest ring opening reported in the current literature. Cooperative catalysis is also applied to the synthesis of polymers containing hydroxyurethane linkages and is able to achieve rapid conversion of the bis-cyclic carbonate and diamine precursors when compared with the uncatalyzed reaction.

Introduction

Polyurethanes (PU) are highly versatile materials with a broad array of applications ranging from flexible and rigid foams to elastomers and adhesives.[1] PUs are commonly formed from the step-growth reactions of multifunctional isocyanates with multifunctional alcohols, with worldwide production exceeding 12 billion kg per year in 2010.[2] The synthesis of PUs differs from that of most other polymers because of the near-room-temperature cure, which is the result of the rapid reaction between alcohol and isocyanate groups at ambient conditions. However, overexposure to isocyanates can be harmful to your health if not handled correctly. Additionally, there are increasing regulatory pressures by state and federal agencies. As a result, there is a clear need to develop new chemical strategies that result in PUs and related materials.[3]

The challenges associated with PU synthesis can be partially addressed by the development of non-isocyanate polyurethanes (NIPUs), in which the urethane linkage is formed in the absence of isocyanate moieties. Groszos described the first synthesis of a NIPU, which involved the reaction of bis-cyclic carbonate with a diamine resulting in hydroxy carbamate formation (Scheme 1), the latter of which contains the urethane unit with an additional hydroxy group.[4] As a consequence, the polymer resulting from such reactions is sometimes referred to as polyhydroxyurethane[5] (PHU) in addition to be being called NIPU.[6] Cyclic carb-



Scheme 1. Synthetic methods of traditional and non-isocyanate polyurethanes.

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[a] Department of Chemistry, Center for Molecular Innovation and Drug Discovery, Northwestern University
2145 Sheridan Road, Evanston, IL 60208, USA
E-mail: scheidt@northwestern.edu
http://sites.northwestern.edu/scheidt/
[b] Department of Chemical and Biological Engineering, Department of Materials Science and Engineering
Northwestern University,
2145 Sheridan Road, Evanston, IL 60208, USA
E-mail: j-torkelson@northwestern.edu
http://torkelson.northwestern.edu
[c] The Dow Chemical Company
2301 N. Brazosport Boulevard, Freeport, TX 77541, USA
[‡] These authors contributed equally to this work.

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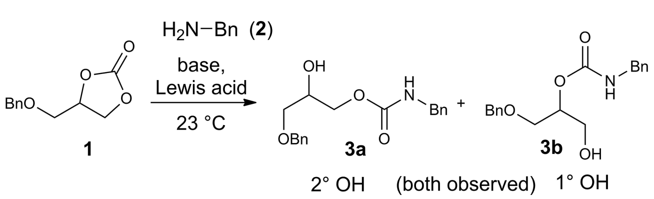
onates are an attractive alternative to isocyanates because of their ease of synthesis from inexpensive glycidyls/bis-oxiranes,[7] low toxicity, and biodegradability.[8] However, the aminolysis of five-membered cyclic carbonates has poor ambient temperature reactivity and has been studied most commonly in solvent at elevated temperatures, with reaction times of many hours or days.[9] Although there have been many research efforts recently devoted to NIPU or PHU,[5b,5d,9,10] there remains a significant need to develop successful approaches to synthesize NIPU with rapid and effective ambient temperature reactions comparable to those used in conventional PU synthesis.

Results and Discussion

Given our interest in the area of cooperative catalysis,[11] we initiated a platform to investigate cyclic carbonate ring openings using an oxophilic Lewis acid in conjunction with an organic Lewis base to simultaneously activate the electrophile (carbonate) and nucleophile (amine, see Table 1). After initial screening of various Lewis acids and bases in the model reaction of small-molecule cyclic carbonate **1** and benzylamine **2**, we determined that the cooperative use of lithium salts with 1,8-diazabicycloundec-7-ene (DBU) achieved fast ring opening in reactions initiated at room temperature with high catalyst loading and in the absence of solvent. The reactions are exothermic, which can result in some temperature rise during a rapid reaction. In particular, with lithium triflate (LiOTf) at 0.20 mol/mol amine (0.61 mol/L) and DBU as base at 0.40 mol/mol amine (1.22 mol/L), a stoichiometrically balanced reaction of benzyl glycerol carbonate and benzylamine in the absence of solvent led to full conversion (> 99 % reaction of functional groups) in 35 min to a mixture of **3a** and **3b** (Table 1, entry 4). This compares to reaction times of 1440 min in the absence of both LiOTf and DBU (Table 1, entry 1), and 120 min in the presence of DBU alone (Table 1, entry 3).

Table 1. Cooperative catalysis screening results.



Entry	Lewis acid (mol-%)[a]	Base (mol-%)[a]	Time [min][b]
1	None	None	1440
2	LiOTf (10)	None	720
3	None	DBU (40)	120
4	LiOTf (20)	DBU (40)	35
5	LiOTf (10)	DBU (10)	75
6	None	TBD (10)	30
7	LiOTf (10)	TBD (10)	10

[a] Relative to mol amine. [b] Indicates time to achieve > 99 % conversion of **1** to **3a** and **3b**.

When the dual catalyst loading was decreased, 0.10 mol/mol amine (0.36 mol/L) of each of LiOTf as acid and DBU as base, the reaction time to full conversion was 75 min, more than a factor of 2 greater than that with the higher dual catalyst concentration described above. This result led us to consider the use of a guanidine base, triazabicyclodecene (TBD), in place of DBU. Commonly used in organic synthesis,[12] TBD, ca. 1 pK_a unit more basic than DBU,[13] has proven effective in the ring-opening polymerization of lactones,[14] and has recently been reported to facilitate the aminolysis of cyclic carbonates at ambient temperature in dimethyl sulfoxide.[10] Interestingly, the use of TBD alone at 0.10 mol/mol amine (0.37 mol/L) in the cyclic carbonate ring-opening reaction afforded full conversion in 30 min, a better result than achieved by the dual catalysis system of LiOTf/DBU at similar concentrations of each component (see Table 1). Ultimately, the unique combination of LiOTf and TBD, each at 0.10 mol/mol amine (0.36 mol/L), as a dual catalysis system resulted in full conversion within 10 min of the reaction initiated at room temperature. To the best of our knowledge, these conditions are the fastest cyclic carbonate ring-openings reported in the literature.[9b,15] While previous research has reported that lithium salts are able to accelerate the ring opening of five-membered cyclic carbonates,[9d,16] our study has not found that LiOTf by itself (Table 1, entry 2) rapidly accelerates the ring-opening reaction of cyclic carbonates with an amine when compared with TBD. However, the comparison of reactions in the presence of TBD but without LiOTf (Table 1, entry 6) and in the presence of TBD and LiOTf (Table 1, entry 7) indicates that cooperative catalysis occurs when both Lewis acid and Lewis base are present.

The profound impact on the ring opening of cyclic carbonates by the combination of TBD and LiOTf indicates that the catalysts work cooperatively. TBD can act as a bifunctional base or as a nucleophile to catalyze numerous reactions as well as the aminolysis of esters and carbonates.[17] TBD has recently been found to open cyclic carbonates to form an activated TBD amide intermediate, which is then displaced by an amine.[10] Lithium salts have been shown to increase the IR stretch of cyclic carbonates (1785 to 1791 cm^{-1}), which indicates an increase in the electrophilicity of the carbonyl carbon.[9d] It is proposed in Figure 1 that lithium triflate increases the electrophilicity of the cyclic carbonate **4** forming a Lewis acid activated cyclic carbonate **5** which can then be attacked by TBD forming tetrahedral intermediate **6**, followed by collapse to the activated carbamate **7**. Nucleophilic attack of the activated carbamate **7** by an amine and subsequent deprotonation of the amine by TBD generates a mixture of carbamate **a** and **b** products, as well as releasing TBD for further cyclic carbonate ring opening.

We have considered the effects of different substrates and amines on reaction time to > 99 % conversion of starting material and the ratio of carbamate products **a** and **b** (Table 2). The fastest reaction times were achieved with the electron-withdrawing *para*-CF_3 benzyl substituent, which is expected due to electronic effects.[8] In addition, the phenyl-substituted carbonate offered similar reaction times with the advantage of being easily obtained from abundantly

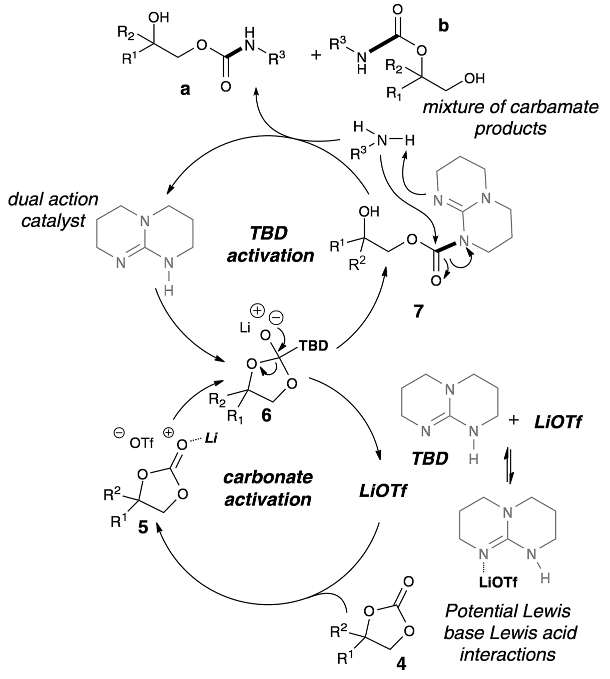
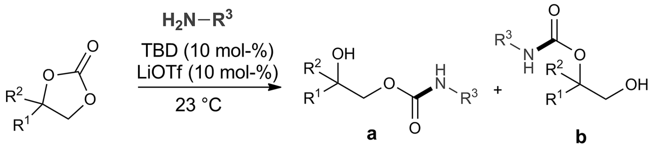


Figure 1. Proposed cooperative catalytic cycles of TBD and LiOTf (catalytic cycle shown produces isomer a).

available styrene oxide. Ratios of carbamate products **a** and **b** remained relatively unchanged when modifying the carbonate backbone or when altering the amines. Interestingly, a significant ratio difference was observed when utilizing disubstituted carbonate, which not only offered rapid reaction times but also a single carbamate product **a**.

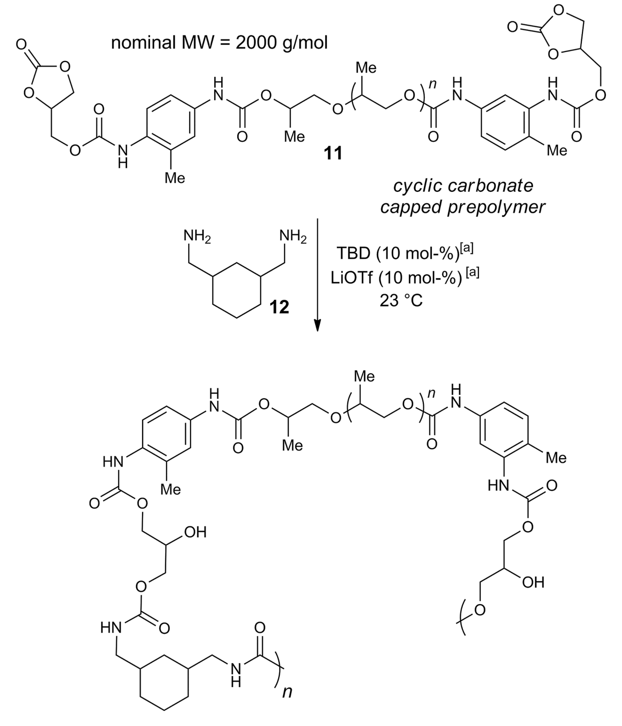
Table 2. Products of the model cyclic carbonate reactions.



Carbonate	R^3	Time[a] [min]	a/b	Yield [%]
$R^1 = CH_2OBn$	Bn	10	4:1	80
$R^2 = H$	Cy	15	4:1	83
	Hex	10	4:1	85
$R^1 = Ph$	Bn	< 3	3:1	92
$R^2 = H$	Cy	< 3	3:1	93
	Hex	< 3	3:1	90
$R^1 = Me$	Bn	3	1:0	85
$R^2 = Ph$	Cy	3	1:0	85
	Hex	3	1:0	84
$R^1 = 4\text{-}F_3CC_6H_4$	Bn	1	3.5:1	95
$R^2 = H$	Cy	1	3.5:1	91
	Hex	1	3.5:1	90

[a] Indicates time to achieve > 99% conversion of the cyclic carbonate to **a** and **b**.

Having shown the utility of TBD/LiOTf cooperative catalysis in substantially increasing the speed and effectiveness of model reactions between small-molecule cyclic carbonates and amines, we also sought to demonstrate cooperative catalysis in the production of polymers by the reaction of difunctional cyclic carbonate molecules and difunctional amines. Conventional PU synthesis often involves a reaction between a prepolymer consisting of a polyether diol of molecular weight (MW) between 600 and 2000 g/mol and a low MW diisocyanate.[18] As shown in Scheme 2, we have chemically functionalized a traditional polyurethane prepolymer [Voranol 220-056N from The Dow Chemical Company, with nominal MW = 2000 g/mol, reacted in excess 2,4-toluene diisocyanate (TDI)] to be end-capped with glycerol carbonate, resulting in a mixture of dicyclic carbonate **11** and low MW dicyclic carbonate. This solution was mixed at stoichiometric balance with a low MW diamine, 1,3-cyclohexane bis(methylamine) **12**, with the reaction initiated at 23 °C (Scheme 2). Comparisons were made between reactions in the presence of 0.10 mol/mol amine (0.133 mol/L) of each of TBD and LiOTf (premixed into the dicyclic carbonate mixture before addition of diamine) and in the absence of catalyst. The concentrations of TBD and LiOTf used in the synthesis of this polymer are roughly a factor of three lower than those present in the reactions of the small-molecule monofunctional cyclic carbonate and amine reactions described above. This reflects the facts that the catalyst system has limited solubility in the polymer and that large quantities of residual catalyst in the polymer can have deleterious effects on its properties and substantially increase cost.



Scheme 2. Polymerization reaction, utilizing cooperative catalysis, between dicyclic carbonate capped prepolymer mixture (low MW structure not shown) and low MW diamine to produce polymer (secondary alcohol product not shown). [a] relative to mol amine.

Major differences in fractional conversion of functional groups, p (with $0 \leq p \leq 1$), were observed in the presence and absence of the TBD/LiOTf catalyst. For example, after 2 min, $p = 0.39$ (39% conversion) with catalyst and 0.06 without catalyst and after 60 min, $p = 0.56$ with catalyst and 0.30 without catalyst. A possible contributor to the extraordinary difference in fractional conversion after 2 min is a temperature rise resulting from the exothermic nature of the reaction, which would be greater in the faster reacting system. Figure 2 demonstrates that both the catalyzed and uncatalyzed reactions provide acceptable fits to results expected for second-order reactions, i.e., first order in cyclic carbonate concentration and first order in amine concentration. Second-order reactions at stoichiometric balance should obey the following Equation (1):

$$c_o/c = 1/(1 - p) = 1 + kc_o t \qquad (1)$$

in which c_o is the initial functional group concentration, c is the functional group concentration at reaction time t, and k is the second-order reaction rate parameter. With approximate linearity in c_o/c for both uncatalyzed and catalyzed reactions, the catalyzed reaction exhibits a k value that is about twice that of the uncatalyzed reaction. The slower nature of the reaction observed with the synthesis of polymer as compared with the reaction of small-molecule model compounds results from the fact that both the functional groups and catalyst loading are at much lower concentrations at the outset of the polymer synthesis as compared with the reaction of the model small-molecule system. Nonetheless, the achievement of substantial conversion within minutes demonstrates the effectiveness of the TBD/LiOTf system in catalyzing the synthesis of PHU at ambient temperature by the reaction of bis-cyclic carbonate with diamine.

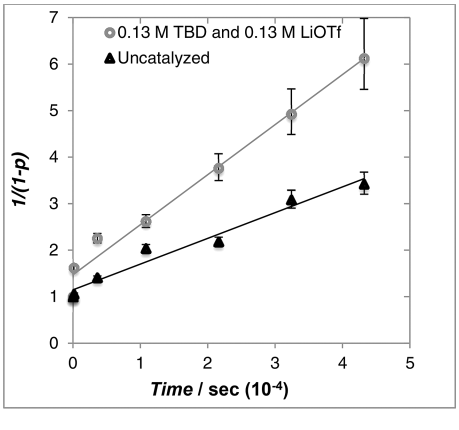


Figure 2. Carbonate conversion fit to integrated second-order rate equations for reactions in the presence and absence of catalyst. Slopes provide kc_o values for the reactions. Calculated k values: $k_{uncat} = 4.0 \times 10^{-5}$ L mol^{-1} s^{-1} and $k_{cat} = 8.1 \times 10^{-5}$ L mol^{-1} s^{-1} (with $c_{o,uncat} = 1.4$ M and $c_{o,cat} = 1.3$ M).

Evidence of the robust nature of the material synthesized in the presence of the catalyst system is provided by its molecular weight gain and tensile properties. Using gel permeation chromatography, the prepolymer **11** can be seen to increase in M_n from 2600 g/mol in the macromer to oligomers with M_n of about 5000, 9000, and 13000 g/mol corresponding to 2, 3–4, and 5 prepolymer units incorporated into oligomers (see the Supporting Information). The material exhibited a Young's modulus of 3.2 MPa and an elongation at break of 360% at room temperature, the latter being consistent with traditional PU elastomer properties and the former with traditional rubber properties reported in the literature.[19]

Conclusions

A rapid opening of cyclic carbonates has been demonstrated using a cooperative catalysis system involving TBD and LiOTf. These new conditions are applicable to a variety of carbonates and amines offering rapid reaction times in all cases. This catalyst system has also been applied to polymer synthesis and has demonstrated the ability to achieve high conversion in the reactions between cyclic-carbonate-capped prepolymers and diamines at ambient temperature. These results have laid a foundation for further studies with the goal of a step-growth polymerization of bis-cyclic carbonates and diamines utilizing our cooperative catalysis conditions.

Experimental Section

Typical Procedure: Epoxide (1.00 mmol) was added to tetra-butyl ammonium iodide (TBAI, 0.100 mmol), and the reaction was heated to 80 °C and stirred until completion as determined by ^{1}H NMR spectroscopy. Upon completion, the reaction mixture was dissolved in dichloromethane, washed with water, dried with magnesium sulfate, filtered, and concentrated in vacuo to afford the carbonate. Lithium triflate (0.100 equiv.) and 1,5,7-triazabicyclo[4.4.0]dec-5-ene (TBD, 0.100 equiv.) were added to a 2 dram vial inside a glove box. The appropriate five-membered cyclic carbonate (1.00 equiv.) was then added and the mixture was stirred for 10 min. The appropriate amine (1.00 equiv.) was then added and the mixture was stirred until completion. The reaction was monitored by LC/MS until > 99% consumption of the starting carbonate was achieved. Upon completion, the reaction mixture was dissolved in a hexanes/dichloromethane mixture and purified by column chromatography.

Supporting Information (see footnote on the first page of this article): Representative experimental procedures for small molecule and polymeric reactions and NMR spectra of the products.

Acknowledgments

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