Triazabicyclodecene: A Simple Biphenyl Organocatalyst for Acyl Transfer and Ring-Opening Polymerization of Cyclic Esters

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To harness the ability of macromolecules to generate interesting and functional microstructures, it is of utmost importance to have control over the size and distribution of the different polymer segments. For applications in microelectronics and in living systems, the resulting polymers should be free of any metal residues. These requirements have motivated the development of novel chemistry, such as the controlled radical polymerizations mediated by nitroxide and dithioester intermediates. Our own work has focused on the development of metal-free organocatalytic ring-opening polymerizations (ROPs) of cyclic esters and has led us to investigate the reactivity of known transesterification agents such as 4-(dimethylamino)pyridine and phosphines as well as the more recently developed N-heterocyclic carbenes (NHCs) and bifunctional amino-thioureas.

We have proposed a monomer-activated mechanism for NHCs wherein the highly nucleophilic NH attacks the carbonyl group to accelerate transesterification. Alternatively, the strongly basic NHC could activate the alcohol for transesterification through formation of a hydrogen bond. The bifunctional amino-thiourea catalysts were proposed to simultaneously activate the alcohol of the initiating/propagating species and the carbonyl of the monomer through hydrogen bonding. Interesting parallels exist between the chemistry of these catalysts and another strongly basic organic molecule, the commercially available guanidine 1,5,7-triazabicyclo[4.4.0]dec-5-ene (TBD). First, the $p_K_a$ values of the conjugate acid of TBD in organic solvents such as THF and MeCN are close to those determined experimentally and computationally for those of the NHCs ($p_K_a = 26$ vs $17-26$). TBD has been applied as a strongly basic catalyst for a variety of reactions, including Michael additions, Wittig reactions, and transesterification reactions. More importantly, Corey has shown that bicyclic guanidine catalysts exhibit bifunctional hydrogen-bonding capabilities in the enantioselective Strecker synthesis of $\alpha$-aminoaldehydes and $\alpha$-amino acids, and TBD was shown to react with malonate attack of both disubstituted nitrogens at the carbonyl groups to form betaine-like structures. This prompted us to study the chemistry of TBD with respect to transesterification and ROP.

In initial studies, we found the reaction of TBD with vinyl acetate to be especially revealing. Combination of the reagents in 1:1 stoichiometry as monitored by $^1$H NMR spectroscopy results in rapid, quantitative formation of acetaldehyde and N-acetylTBD as a stable, neutral compound (Scheme 1). Addition of benzyl alcohol to N-acetylTBD results in the rapid quantitative formation of benzyl acetate and regenerates TBD, completing a single TBD-catalyzed transesterification turnover. The acylation of TBD and subsequent esterification indicate that guanidines such as TBD might function not merely as general base catalysts. These results may suggest a novel catalytic role for guanidines, a substructure common to many bioactive natural products.

Having found TBD to be an efficient acyl-transfer and transesterification catalyst, we explored its activity for the ROP of cyclic esters. Polymerization of L-lactide (LLA) in CH$_2$Cl$_2$ with TBD at only 0.1% relative to monomer with 1% of 4-pyrenebutanol added as an initiator (targeted degree of polymerization (DP) = 100) generated poly(LLA) in seconds at room temperature, activity rivaling that of the most active metal catalysts. The resulting polymer had a molecular weight of $M_n$ = 24 200 g mol$^{-1}$ and a narrow polydispersity ($PDI = M_w/M_n = 1.19$). Different molecular weights could be achieved by varying the concentration of initiator (Table 1). Simultaneous refractive index and UV absorbance monitoring by gel permeation chromatography (GPC), together with $^1$H NMR spectroscopy, shows that the UV-active 4-pyrenebutanol initiator is fully incorporated into the polymer in all cases, demonstrating end-group fidelity (Figure 1, inset). Quenched aliquots taken during TBD-catalyzed polymerizations show a linear increase of $M_n$ with conversion (Figure 1). A slight decrease in PDI from $\sim$1.25 to $\sim$1.20 as conversion approaches 90% suggests that broadening of the molecular weight distribution occurs during the initial stages of polymerization, due to the high activity of the catalyst. If reaction mixtures are left to stand, TBD-catalyzed transesterification of the poly(LLA) leads to increased PDIs, but TBD can be quenched at short reaction times simply by addition of benzoic acid.

Encouraged by TBD’s high activity for lactide polymerization, we examined its ability to catalyze the ROP of $\delta$-valerolactone (VL) and $\epsilon$-caprolactone (CL). Polymerization of VL proceeded more slowly than that of LLA; nevertheless, a 1.75 M benzene solution of VL was polymerized with only 5% TBD to $\sim$90% conversion within 30 min (Figures 1 and S1). The longer reaction time allows greater control of the PDI: the poly(VL) had an $M_n$ of 14 500 g mol$^{-1}$ and PDI = 1.09. ROP of CL is complicated by the onset of transesterification and broadening of the PDI, reflecting the high tendency of poly(CL) chain ends to transesterify. Still, at $[M_0]/[I_0]$ ratios of 50 and 100, the polymerizations reached $\sim$75% conversions in...
In copolymerizations of the cyclic esters. At room temperature, the catalyst for a variety of transformations would suggest that TBD functions by deprotonating or activating the alcohol for nucleophilic catalysis. However, the less active than TBD for the polymerization of lactide (30 min to reach 92% conversion at 0.1% TBD loading while retaining low 5 and 8 h, respectively, at 0.5% TBD loading while retaining lowactivities, the incipient alkoxy to generate the TBD amide. Hydrogen-bond activation of the incoming alcohol should facilitate esterification, liberating the ester and regenerating TBD. By this mechanism, TBD functions as a deceptively simple bifunctional transesterification catalyst, analogous to the amino-thioureas we have used previously.6

In summary, we have found TBD to be a very active catalyst for ROP of LLA, VL, and CL, providing polymers of controlled molecular weight and polydispersity. While pseudo-anionic mechanisms are plausible, TBD appears to be uniquely capable of activating both monomer and initiator, which may explain its heightened reactivity. The ready commercial availability, ease of use, and controlled high activity of TBD make it a highly accessible catalyst for solution-phase ROP of cyclic esters.

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Supporting Information Available: Full experimental details, tables, and figures of polymerization. This material is available free of charge via the Internet at http://pubs.acs.org.

References

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Table 1. Results for Base-Catalyzed ROP of Cyclic Esters

<table>
<thead>
<tr>
<th>monomer</th>
<th>catalyst (%)</th>
<th>$\left[\text{M}^0\right]$</th>
<th>time (s)</th>
<th>conversion (%)</th>
<th>$M_\text{n}$ ($g\text{ mol}^{-1}$)</th>
<th>PDI (a)</th>
</tr>
</thead>
<tbody>
<tr>
<td>LLA</td>
<td>0.1</td>
<td>100</td>
<td>20</td>
<td>99</td>
<td>24 200</td>
<td>1.19</td>
</tr>
<tr>
<td>LLA</td>
<td>0.1</td>
<td>500</td>
<td>1 min</td>
<td>95</td>
<td>62 600</td>
<td>1.11</td>
</tr>
<tr>
<td>(\delta)-VL</td>
<td>0.5</td>
<td>25</td>
<td>0.2 h</td>
<td>90</td>
<td>3 800</td>
<td>1.06</td>
</tr>
<tr>
<td>(\delta)-VL</td>
<td>0.5</td>
<td>50</td>
<td>0.25 h</td>
<td>88</td>
<td>7 000</td>
<td>1.05</td>
</tr>
<tr>
<td>(\delta)-VL</td>
<td>0.5</td>
<td>100</td>
<td>0.5 h</td>
<td>91</td>
<td>14 500</td>
<td>1.09</td>
</tr>
<tr>
<td>(\epsilon)-CL</td>
<td>0.3</td>
<td>200</td>
<td>0.5 h</td>
<td>77</td>
<td>16 500</td>
<td>1.12</td>
</tr>
<tr>
<td>(\epsilon)-CL</td>
<td>0.5</td>
<td>50</td>
<td>5 h</td>
<td>86</td>
<td>2 800</td>
<td>1.10</td>
</tr>
<tr>
<td>(\epsilon)-CL</td>
<td>0.5</td>
<td>100</td>
<td>8 h</td>
<td>72</td>
<td>16 900</td>
<td>1.16</td>
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<tr>
<td>(\epsilon)-CL</td>
<td>0.5</td>
<td>200</td>
<td>8 h</td>
<td>52</td>
<td>20 900</td>
<td>1.16</td>
</tr>
</tbody>
</table>

(a) Solvent for LLA was CH$_2$Cl$_2$; for \(\delta\)-VL and \(\epsilon\)-CL, C$_6$D$_6$ was used. * Percentage relative to monomer. † Measured by $^1$H NMR. ‡ Measured by GPC in THF.