JACS
JOURNAL OF THE AMERICAN CHEMICAL SOCIETY

Article

pubs.acs.org/JACS

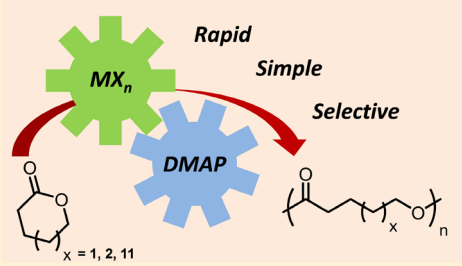
Dual Catalysis for Selective Ring-Opening Polymerization of Lactones: Evolution toward Simplicity

Stefan Naumann,[†] Philip B. V. Scholten, James A. Wilson, and Andrew P. Dove*

Department of Chemistry, University of Warwick, CV4 7AL Coventry, U.K.

Supporting Information

ABSTRACT: Much work has been directed to the design of complex single-site catalysts for ring-opening polymerization (ROP) to enhance both activity and selectivity. More simply, however, cooperative effects between Lewis acids and organocatalytic nucleophiles/Lewis bases provide a powerful alternative. In this study we demonstrate that the combination of *N*-heterocyclic carbenes, 1,8-diazabicycloundec-7-ene (DBU) and 4-dimethylaminopyridine (DMAP) with simple Lewis acids enables the ROP of the macrolactone pentadecalactone in a rapid and efficient manner. Remarkably, regardless of the nature of the nucleophile, the order of activity was observed to be $MgX_2 \gg YCl_3 \gg AlCl_3$ and $MgI_2 > MgBr_2 > MgCl_2$ in every case. The minimal influence of the organobase on polymerization activity allows for the use of simple and inexpensive precursors. Furthermore, extension of the study to other cyclic (di)ester monomers reveals the choice of Lewis acid to lead to monomer selective ROP activity and hence control over copolymer composition by choice of Lewis acid. This approach could lead to the realization of complex polymer structures with tunable physical properties from simple catalyst combinations.



INTRODUCTION

Organic catalysts for the ring-opening polymerization (ROP) of cyclic ester monomers (among others) have become an important tool in polymer synthesis.[1−5] The simplicity, versatility and high activity of several species has led to them being widely applied in preference of more traditional metallo-organic catalysts such as $Sn(Oct)_2$. Of the most widely applied organic catalysts is the commercially available 1,8-diazabicycloundec-7-ene (DBU).[6] Despite its ease of use and high activity for the ROP of lactide, the ROP of small ring lactone monomers, such as ε-caprolactone (CL) and δ-valerolactone (VL), does not proceed efficiently without an added (and toxic)[7] thiourea cocatalyst. Furthermore, DBU has been shown to be inactive for the ROP of large ring lactones such as ω-pentadecalactone (PDL).[8] While 1,5,7-triazabicyclo[4.4.0]dec-5-ene (TBD) is significantly more active as a catalyst such that PDL polymerization is possible,[8] the same lack of control is demonstrated when the ROP of small ring lactones is investigated.[6] While the judicious choice of catalyst can yield better results,[2] we sought a universal, and simple solution to provide well controlled polymerization of a wide range of cyclic ester monomers.

The concept of dual catalysis, where a Lewis acid supports a nucleophile to gain an increased catalytic effect, broadly falls in the categories of cooperative (synergistic)[9] or cascade catalysis,[10] depending on the proposed polymerization mechanism and is related to the chemistry of frustrated Lewis pairs.[11] While these methodologies have been applied to great success in organic chemistry,[12−15] they remain largely under-explored where polymerization catalysis is concerned, although offering the prospect of much increased reaction rates for a wide scope of monomers.[16,17]

Since Dubois and Jérôme found in the early 1990s that the addition of bases such as picoline or phosphines enhanced the activity of $Al(O^iPr)_3$-catalyzed ROP of lactide,[18,19] several other groups have investigated the combination of organic bases with metal salts to result in enhanced ROP activity and/or stereoselectivity in the ROP of lactide,[20−29] complemented by metal-free, fully organocatalytic studies for dual polymerization catalysis.[4,30−32] Importantly, in all cases, the presence of both Lewis acid and organic base has been essential in order to observe the enhanced polymerization activity and selectivity. Despite this promise, studies have remained very limited.[16] We postulated that the introduction of readily available metal-based Lewis acids in the ROP of a range of cyclic ester monomers would facilitate the ring-opening by activation of even the most challenging monomers while retaining good control over monomers that are more susceptible to ROP.

In order to identify highly active dual catalysis systems for ROP, PDL was selected as an exemplar monomer on account of the inactivity of all but one organic catalyst in this process.[8] Furthermore, there is increased current interest in poly(ω-pentadecalactone) (PPDL), as a consequence of its potentially renewable nature as well as the similarity of its properties to that of linear low density polyethylene.[33−35] Inspired by the work of Buchmeiser and co-workers, we sought to study the *N*-heterocyclic carbene (NHC)-adducts with Lewis acids ($SnCl_2$, $Sn(OAc)_2$, $AlCl_3$, $MgCl_2$) that were prepared and isolated to

Received: September 9, 2015
Published: October 27, 2015

DOI: 10.1021/jacs.5b09502
J. Am. Chem. Soc. 2015, 137, 14439−14445

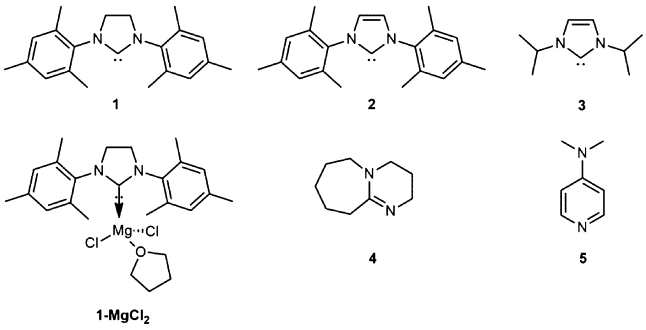


Figure 1. Structures of precatalyst **1-MgCl$_2$** and all nucleophiles used in this study.

serve as latent catalysts for the synthesis of polyurethanes and ROP of CL after thermal activation.[20−22] In these studies, it was shown that cooperation between NHC **1** (Figure 1) and metal halide not only modulated the polymerization rates, but was crucial for any polymerization to occur.

Herein we explore the cooperative effects between Lewis acids and organobases for the ROP of cyclic (di)esters. The first part of this work examines the application of isolated NHC-adduct **1-MgCl$_2$** (Figure 1) for the polymerization of PDL. The insights won from these investigations then serve in a stepwise process to evolve toward a more simple, yet highly effective catalytic system that is active beyond PDL. Furthermore, a broadening of the scope of both Lewis acids and nucleophiles is used to map out key parameters for the cocatalysts studied, critically demonstrating that the choice of Lewis acid is decisive for the monomer selectivity.

RESULTS AND DISCUSSION

Polymerization of PDL Using a Thermally Labile NHC-MgCl$_2$ Complex. Precatalyst **1-MgCl$_2$** was prepared following the previously reported convenient one-step procedure, directly reacting NHC **1** with $MgCl_2$ in THF at room temperature.[22] To investigate the general reactivity of **1-MgCl$_2$** toward PDL, polymerizations were conducted in toluene at elevated temperatures ($[PDL]_0$ = 1.0 M), using benzyl alcohol (BnOH) as initiator (**1-MgCl$_2$**:BnOH = 1:1). Under these conditions PPDL was formed (Table 1) such that after 6 h at

Table 1. Polymerization of PDL Using 1-MgCl$_2$[a]

#	T [°C]	1-MgCl$_2$:BnOH:PDL	conv.[b] [%]	M_n[c] [g mol^{-1}]	M_p[c] [g mol^{-1}]	$Đ_M$[c]
1	80	1:1:50	72	9600	25 500	2.50
2	110	1:1:20	98	6700	12 800	1.97
3	110	1:1:50	96	13 800	41 500	2.67
4	110	1:1:100	98	34 900	70 100	2.09
5	110	1:1:200	82	66 200	110 100	1.80

[a]Conditions: 6 h, $[M]_0$ = 1.0 M in toluene. [b]Monomer conversion determined by ^{1}H NMR spectroscopy. [c]Determined by SEC analysis ($CHCl_3$, PS standards).

80 °C, 72% monomer conversion was found, immediately putting the activity of this precatalyst on par with the performance of a recently described magnesium-based complex for PDL polymerization.[36] A further increase of the reaction temperature to 110 °C yielded near quantitative monomer conversion without negatively influencing the molecular weight distribution (Table 1, entry 3). To further establish the activity of **1-MgCl$_2$**, the target DP of the polymerization setup was

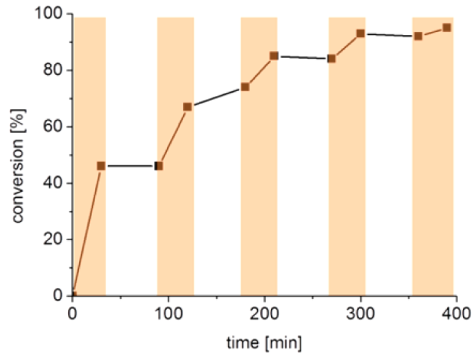


Figure 2. Stepwise conversion versus time for several heating (110 °C, shaded) and room temperature cycles (**1-MgCl$_2$**/BnOH/PDL = 1:1:200).

varied (DP = 20, 50, 100, 200). Notably, all these polymerizations achieved high conversion after 6 h, with a linear dependence of the number-average molecular weight (M_n) and target DP observed (Figure S3). Further analysis of the polymerization kinetics ([M]/[I] = 200) revealed a pseudo-first-order process (Figure S4) and evolution of molecular weight against monomer conversion revealed a linear relationship (Figure S5) that is indicative of a controlled polymerization. Notably the scatter at high monomer conversions can be accounted for by the increasing quantity of cyclic oligomers that inherently result from the ROP of macrolactones.[37,38]

As a result of the latent properties of the precatalyst[22] and the entropy-driven nature of the PDL polymerization, no monomer conversion was observed at room temperature. However, this enabled the polymerization to be stopped and restarted several times over the course of more than 6 h, using 110 °C/room temperature cycles (Figure 2) providing an "on-demand" thermal activation. The slight deviation from ideal step-like conversion is most probably related to the highly viscous polymerization solution, which necessitated a warming prior to sample removal at the end of the room temperature intervals. A linear increase of the molecular weight with conversion (Figure 3) was still observed, which indicates that the resting phases did not quench the catalytically active species or induce side reactions, which overall underlines the robustness of the catalytic setup based on **1-MgCl$_2$**.

Importantly, control experiments demonstrated that $MgCl_2$ or free NHC **1** alone could not induce any polymerization under the same conditions (110 °C, 6 h).[8,39,40] The observed

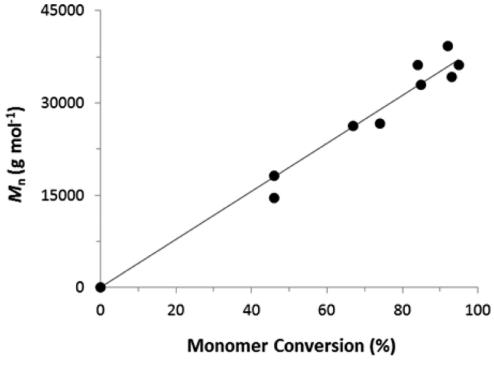
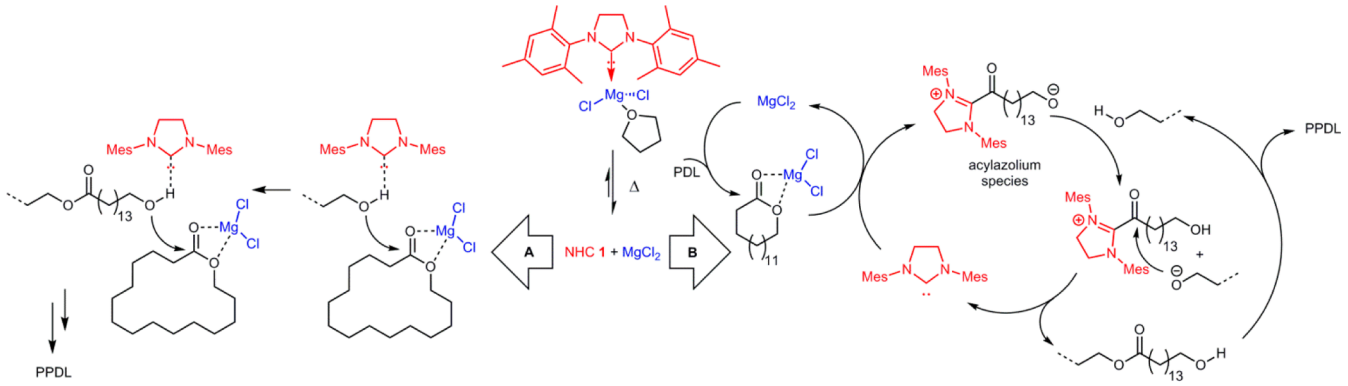


Figure 3. Number-average molecular weight versus conversion relating to the different heating cycles. (**1-MgCl$_2$**/BnOH/PDL = 1:1:200, 110 °C/room temperature, $[M]_0$ = 1.0 M in toluene).

DOI: 10.1021/jacs.5b09502
J. Am. Chem. Soc. 2015, 137, 14439−14445

Scheme 1. Proposed Mechanisms for the Catalytic Joint Action of NHC 1 and $MgCl_2$ after Thermally Induced Dissociation of the Precatalyst Complex[a]



[a]Pathway **A** represents cooperative catalysis between Lewis acid and activating Brønsted base, while **B** shows a cascade of ring-opening and nucleophilic substitution.

high activity when both components are combined can only result from cooperative action, most probably involving complex dissociation and monomer activation by the Lewis acid, which facilitates nucleophilic ring-opening of PDL by either activated alcohol (initiator or OH-terminated growing polymer chain, Scheme 1, **A**) or by the NHC itself (**B**). Both operating pathways of the NHC, its behavior rather as a base (**A**) or as a nucleophile (**B**), have been widely proposed in NHC organopolymerization reactions.[3,5] While the details of the corresponding mechanisms will depend on some key properties of the NHC (steric congestion, pK_a value), it is obvious that the rate determining ring-opening step[41] will be favored by coordination of the ester functionality to a suitable Lewis acid by increasing the positive polarization on the carbonyl carbon, the attacking site for all nucleophiles. Pathway **A** therefore is a typical example for cooperative catalysis, while **B** embodies cascade catalysis, where Lewis acid activation first enables the formation of the acylazolium species, which is then itself an activated form of the monomer to be incorporated into the polymer. The pseudo-first-order kinetics observed indicate fast initiation and a constant concentration of active species and hence point to a fast and complete dissociation of **1-MgCl$_2$** when triggered by heating. In turn, this suggested that separate addition of NHC **1** and $MgCl_2$, as opposed to the introduction of the preformed adduct **1-MgCl$_2$**, should display an equal catalytic effect for the polymerization of PDL. Indeed, polymerization with **1**:$MgCl_2$ in a 1:1 molar ratio led to virtually identical polymer when compared to the action of **1-MgCl$_2$** (Figure 4) and opened up the possibility to conveniently broaden the investigation into further nucleophile and Lewis acid dual catalysis pairs.

Dual Catalysis Using NHC/Lewis Acid Pairs for Preparation of PPDL. The decoupling of nucleophile and Lewis acid enables a more thorough investigation of the effects of each component. To this end, a stepwise increase of the $MgCl_2$:**1** molar ratio from 0.25 to 5.0 equiv was shown to result in a considerable increase of monomer conversion (see Table S1). In the next series of experiments, NHC **1** was applied in the presence of a range of Lewis acids for the polymerization of PDL under otherwise unchanged conditions (Table 2).

The results immediately emphasized the dominant role that is played by the metal component and were surprising in their clarity. The addition of $FeCl_3$, $ZnCl_2$, $B(Ph)_3$ and $Bi(OTf)_3$ did not induce any polymerization (Table 2, entries 8–11), while

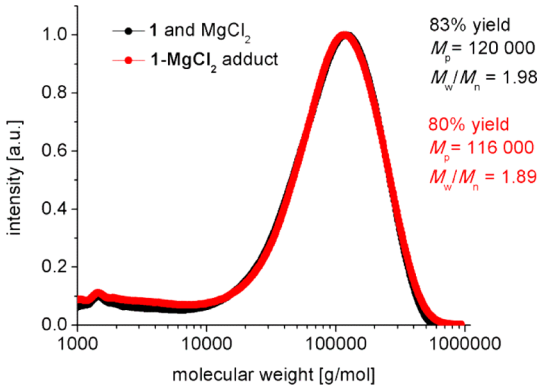


Figure 4. Direct comparison of PPDL derived from **1-MgCl$_2$** (red) and by separate addition of **1** and $MgCl_2$ (black) under identical conditions (110 °C, 4 h, cat/BnOH/PDL = 1:1:200, $[M]_0$ = 1.0 M in toluene).

Table 2. Polymerization of PDL Using NHC 1 with Different Lewis Acid Cocatalysts[a]

#	Lewis acid	conv.[b] [%]	M_n[c] [g mol^{-1}]	M_p[c] [g mol^{-1}]	$Đ_M$[c]
1	$MgCl_2$	83	61 200	120 000	1.97
2	$MgBr_2$	98	82 800	162 000	1.96
3	$MgBr_2$[d]	81	64 700	126 000	1.94
4	MgI_2	99	63 400	118 000	1.92
5	MgI_2[d]	98	42 300	84 100	2.31
6	YCl_3	37	26 400	55 400	2.06
7	$AlCl_3$	1	–	–	–
8	$ZnCl_2$	–	–	–	–
9	$FeCl_3$	–	–	–	–
10	$Bi(OTf)_3$	–	–	–	–
11	$B(Ph)_3$	–	–	–	–

[a]Conditions: NHC/Lewis acid/BnOH/PDL = 1:1:1:200, $[M]_0$ = 1.0 M in toluene, 4 h, 110 °C. [b]Monomer conversion determined by ^{1}H NMR spectroscopy. [c]Determined by SEC analysis ($CHCl_3$, PS standards). [d]Polymerization time = 2 h.

the strong Lewis acid $AlCl_3$ effected an extremely low monomer conversion. In fact, while not an exhaustive study, the only non-magnesium cocatalyst found to display significant activity was YCl_3 (Table 2, entry 6), application of which led to conversion about half as high as observed with $MgCl_2$ under comparable conditions. Strikingly, the heavier halide analogues $MgBr_2$ and

DOI: 10.1021/jacs.5b09502
J. Am. Chem. Soc. 2015, 137, 14439–14445

MgI_2 outperformed $MgCl_2$ and enabled virtually complete monomer conversion, under formation of high molecular weight PPDL with $Đ_M < 2$. Use of $MgBr_2$ delivered repeatedly higher molecular weight compared to the other magnesium halides, suggesting the possibility to influence the polymer properties by choice of the Lewis acid. Notably, MgI_2 effected almost complete conversion after only 2 h of reaction time (Table 2, entry 5).

A number of factors can be expected to regulate the performance of the different Lewis acids. Solubility certainly exerts some influence, though not a decisive one. While use of $MgCl_2$ entailed suspensions, which remained turbid even at reaction temperature (toluene, 110 °C), $MgBr_2$ and MgI_2 were observed to be clear solutions after heating which indicates dissolution of the Lewis acid in the polymerization media and may potentially explain their higher ROP activity. However, solutions of $AlCl_3$ and $B(Ph)_3$ were homogeneous at room temperature and YCl_3 readily dissolved when heated so this cannot be the limiting factor. The behavior in solution is harder to evaluate, but it is clear that the solution conformation of the Lewis acid and coordination to the monomer must compete with other ways to saturate the electron deficiency of the Lewis acids. In agreement with previous studies into Lewis acid-activated processes, the greater catalytic activity of MgI_2 over $MgCl_2$ and $MgBr_2$ may be explained by its cationic character that results from dissociation of one iodide ligand.[42−45] However, the stark differences in reactivity between MCl_x salts will be a compromise between complexation with the NHC, thus modulating the concentration of "free" catalyst species in solution, as well as the ability of the Lewis acid to bind and hence activate the (macro)lactone.[20−22,46] Activation will be restricted by fundamental aspects like geometry (ion radii), charge density and ligands on the metal, necessarily rendering some Lewis acids a better fit than others. Notably, the relative importance of the contributions discussed above can be evaluated by varying both organobase and monomer (see below).

Beyond the screening of different Lewis acids, two other NHCs (**2** and **3**, Figure 1) were prepared and studied. Strikingly, despite the different electronic and steric demands of these NHCs, the ROP of PDL in combination with a range of Lewis acids yielded very similar results to those obtained from the action of NHC **1** (Table 3, compare Table 2). In all three cases, monomer conversions of the polymerizations were comparable and the same trend of Lewis acid activation was observed such that the activity in the order of $MgX_2 > YCl_3 > AlCl_3$ was again found. The absence of different behavior between these dual catalysis systems is surprising. NHCs **2** and **3** commonly show very different abilities in the organo-polymerization of lactones and other monomers,[3,5] with the stronger nucleophile **3** able to induce very fast and sometimes uncontrolled polymerization, while **2** (and **1**) are much more limited as a consequence of steric hindrance and electronic effects.[47−50] Application of **3**, however, is not without impact on the PPDL properties, entailing a significant broadening of the molecular weight distribution, in line with its high propensity for catalyzing transesterification, which also explains the overall lower molecular weights.

It can be deduced that the high activity of MgX_2 for PDL polymerization is not specific for NHC **1**, but clearly also enables the use of other NHCs. The remarkable similarities of the results obtained from the different NHCs **1**−**3** further suggest that competitive complexation by the NHC is not a relevant contribution to the overall activity. In general the differences between the nucleophiles are marginalized by the decisive choice of Lewis acid. Indeed, use of a strongly active NHC such as **3** introduces adverse effects like increased transesterification. Importantly, this might indicate that the activation provided by the Lewis acid is strong enough to enable much weaker, yet potentially more selective nucleophiles or Lewis bases for PDL polymerization, providing alternatives for the use of the more sensitive and reactive NHCs.

Table 3. Polymerization of PDL Using NHCs with Different Lewis Acid Cocatalysts[a]

#	NHC	Lewis acid	conv.[b] [%]	M_n[c] [g mol^{-1}]	M_p[c] [g mol^{-1}]	$Đ_M$[c]
1	**2**	$MgCl_2$	82	17 500	43 100	2.50
2	**2**	$MgBr_2$	97	37 300	68 700	1.96
3	**2**	MgI_2	98	32 000	55 300	1.89
4	**2**	MgI_2[d]	85	67 500	113 500	1.70
5	**2**	YCl_3	46	30 500	52 600	1.87
6	**2**	$AlCl_3$	0	–	–	–
7	**3**	$MgCl_2$	88	21 600	61 100	2.87
8	**3**	$MgBr_2$	96	21 100	68 700	3.25
9	**3**	MgI_2	98	18 500	42 300	2.68
10	**3**	MgI_2[d]	80	15 700	35 300	2.53
11	**3**	YCl_3	52	8400	33 000	3.54
12	**3**	$AlCl_3$	1	–	–	–

[a]Conditions: NHC/Lewis acid/BnOH/PDL = 1:5:1:200, $[M]_0$ = 1.0 M in toluene, 2 h, 110 °C. [b]Monomer conversion determined by ^{1}H NMR spectroscopy. [c]Determined by SEC analysis ($CHCl_3$, PS standards). [d]Polymerization time = 30 min.

Dual Catalysis Using DBU or DMAP in the Presence of Lewis Acids for Preparation of PPDL. The absence of a nucleophile-dependent effect when NHCs were employed with Lewis acids in the ROP of PDL motivated the study of weaker, less air-sensitive and more readily available Lewis base catalysts. To this end, 1,8-diazabicycloundec-7-ene (DBU, **4**, Figure 1) and 4-dimethylaminopyridine (DMAP, **5**) were studied in combination with a range of Lewis acids. Both compounds are routinely used, robust and readily available organocatalysts, but both have also been shown to be inactive for PDL polymerization.[8] DMAP in particular is a comparatively weak nucleophile that shows no or extremely low propensity to polymerize CL[8,51,52] and a relatively slow polymerization of lactide.[53] The presence of Lewis acid activators changes this behavior profoundly (Table 4). In combination with MgI_2, DBU was revealed to be the most active cocatalyst for PDL polymerization found so far. After 30 min (Table 4, entry 1),

Table 4. Polymerization of PDL Using DBU or DMAP with Different Lewis Acid Cocatalysts[a]

#	Nu	Lewis acid	conv.[b] [%]	M_n[c] [g mol^{-1}]	M_p[c] [g mol^{-1}]	$Đ_M$[c]
1	**4**	MgI_2[d]	96	70 700	119 400	1.80
2	**4**	YCl_3	54	39 800	63 200	1.75
3	**4**	$AlCl_3$	2	–	–	–
4	**5**	MgI_2	95	59 900	97 600	1.65
5	**5**	YCl_3	56	45 600	75 900	1.76
6	**5**	$AlCl_3$	3	–	–	–

[a]Conditions: Nu/Lewis acid/BnOH/PDL = 1:5:1:200, $[M]_0$ = 1.0 M in toluene, 2 h, 110 °C. [b]Monomer conversion determined by ^{1}H NMR spectroscopy. [c]Determined by SEC analysis ($CHCl_3$, PS standards). [d]Polymerization time = 30 min.

DOI: 10.1021/jacs.5b09502
J. Am. Chem. Soc. 2015, 137, 14439−14445

almost quantitative monomer consumption had occurred, while at the same time the molecular weight remained high and the molecular weight distribution was lower than in the case of NHC cocatalysis. Furthermore, the same order of activity of MgX_2 > YCl_3 > $AlCl_3$ was again observed (Table 4, entries 2 and 3). An even stronger testament to the activation power of MgI_2 is its ability to also enable DMAP to achieve a very high monomer conversion of 95%, albeit requiring a longer polymerization time (2 h). Notably, the combination of DMAP/MgI_2 also delivered a lower dispersity ($Đ_M$ = 1.65), underlining the benefits of using a Lewis base with low propensity for transesterification side reactions (Table 4, entry 4). Cocatalysis with YCl_3 and $AlCl_3$ delivered intermediate and no activity respectively, in line with observations with NHC nucleophiles (Table 4, entries 5 and 6).

The observed strong similarities resulting from the use of the organobase cocatalysts **1**−**5** further underline that the Lewis acid-monomer interaction is the decisive factor in this type of dual catalysis, indicating that the superiority of magnesium halides is general to PDL polymerization rather than specific to a special type of nucleophile. Remarkably, the activation is sufficiently strong to render DMAP close to NHCs in terms of conversion and polymerization rate. Overall this offers the possibility to complement this strong activation with a mild Lewis base, bestowing both more control and an easier handling on the polymerization setup.

DMAP/Lewis Acid Cocatalysis for the Homo- and Copolymerization of ε-Caprolactone and δ-Valerolactone. To gain further insight into the applicability of the operationally very convenient and robust combination of DMAP and Lewis acid, the catalytic system was extended to other lactone monomers. DMAP and MgI_2 were employed in the ROP of CL, VL, *rac*-lactide (*rac*-LA) and β-butyrolactone (β-BL). Reactions were conducted in THF at 70 °C, retaining the optimized ratio of Nu/Lewis acid/BnOH/Monomer = 1:5:1:200 (Table 5). The results clearly showed that CL was swiftly converted to polymer, reaching quasi-quantitative conversion. Control over the molecular weight was conveniently realized by adjusting the initiator/monomer ratio (Table 5, entry 2). Matrix-assisted laser desorption/ionization time-of-flight mass spectrometry (MALDI ToF MS) analysis of this sample (Figure 5) revealed a single distribution, with the molecular weights in accordance with the calculated mass for BnOH-initiated poly(ε-caprolactone), supporting the proposed polymerization mechanism. VL was also polymerized to yield well-defined material (Table 5, entry 3); however, the polymerization was much slower than expected (38% after 2 h) and the ROP of *rac*-LA displayed only very low monomer conversion. β-BL was not observed to polymerize at all under these conditions. This gradual loss of polymerization activation using MgI_2 as the Lewis acid activator, as the nature of the monomer grows more distant from the original PDL, clearly indicates that the ability to activate is *monomer specific* for a given Lewis base and Lewis acid. We postulated that other Lewis acids might be more suitable in cocatalyzing the polymerization of the smaller-ring lactones as a result of their solution conformation and indeed it was found that YCl_3, inferior to MgI_2 for PDL polymerization, reaches the same VL conversion (38%) after only 10 min (Table 5, entry 6), compared to 2 h for MgI_2 (Table 5, entry 3). Likewise, the ROP of *rac*-LA yielded an increased monomer conversion in the presence of YCl_3 as compared to MgI_2, however, monomers PDL, CL and VL are more effectively polymerized compared to *rac*-LA.

These results clearly demonstrate the broader utility of this type of dual catalysis and highlight that DMAP is enabled to polymerize a range of monomers, provided that a suitable Lewis acid is found to generate the necessary activation. More importantly, since the Lewis acid interacts with the monomers with a certain selectivity, it might also be possible to manipulate the composition of lactone copolymers, depending on the Lewis acid present. As such, copolymerizations of CL and VL (1:1) were undertaken using MgI_2, $MgCl_2$, YCl_3 and $ZnCl_2$ as cocatalysts with DMAP. While only MgI_2 and YCl_3 cocatalysts resulted in isolated polymer, the MgI_2 system showed an overall conversion of 52% after 2 h and displayed a slightly preferred incorporation of VL. Contrasting this, application of YCl_3 entailed a conversion of 58% after only 10 min but displayed an inverted and somewhat stronger preference for CL incorporation (Table S2 and Figures S6 and S7). Both copolymers were well-defined as found by SEC analysis and lay in the expected range of molecular weight.

Table 5. Polymerization of Several Lactones Using DMAP with Different Lewis Acid Cocatalysts[a]

#	Lewis acid	monomer	time [min]	conv.[b] [%]	M_n[c] [g mol^{-1}]	$Đ_M$[c]
1	MgI_2	CL	120	95	28 700	1.33
2	MgI_2	CL[d]	60	>99	4000	1.19
3	MgI_2	VL	120	38	7900	1.13
4	MgI_2	*rac*-LA[e]	120	5	–	–
5	MgI_2	β-BL	120	0	–	–
6	YCl_3	VL	10	38	7700	1.19
7	YCl_3	VL	30	68	13 200	1.47
8	YCl_3	*rac*-LA[e]	240	22	4300	1.11

[a]Conditions: Nu/Lewis acid/BnOH/PDL = 1:5:1:200, $[M]_0$ = 1.0 M in THF, 70 °C. [b]Monomer conversion determined by ^{1}H NMR spectroscopy. [c]Determined by SEC analysis ($CHCl_3$ (THF for poly(*rac*-LA), PS standards). [d]Nu/Lewis acid/BnOH/PDL = 1:5:10:200. [e]$[M]_0$ = 0.75 M.

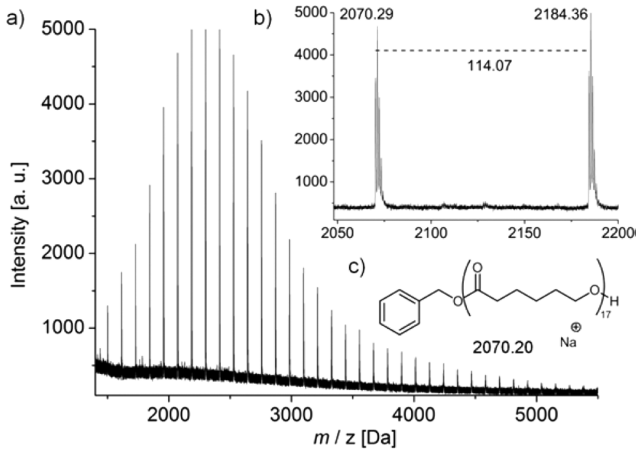


Figure 5. (a) MALDI ToF MS of poly(ε-caprolactone) derived by the action of DMAP/MgI_2, and detail with experimental (b) and calculated (c) polymer masses.

CONCLUSIONS

Dual catalysis as presented in this study is versatile, of broad applicability and very convenient to employ, relying on simple and cheap cocatalysts like the benign magnesium halides and

DOI: 10.1021/jacs.5b09502
J. Am. Chem. Soc. 2015, 137, 14439−14445

DMAP, suggesting a much greater potential to still explore. The concept of monomer selective catalysis simply by polymerization in the presence of different Lewis acids is very attractive by virtue of its simplicity and potential flexibility in view of the as yet unexplored plethora of possible combinations of nucleophiles and Lewis acids. Deeper investigations into this methodology, which to the best of our knowledge has not been described before, are ongoing and certainly add a further illustration to the powerful cooperative effects that can be gained from the complementing action of readily available, simple metal halides and equally well accessible organocatalysts.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/jacs.5b09502.

Experimental details, NMR spectra and further tabular data. (PDF)

■ AUTHOR INFORMATION

Corresponding Author

*a.p.dove@warwick.ac.uk

Present Address

†University of Stuttgart, Department of Chemistry, Institute for Polymer Chemistry, Pfaffenwaldring 55, D-70569 Stuttgart, Germany.

Notes

The authors declare no competing financial interest.

■ ACKNOWLEDGMENTS

Mr. Anthony W. Thomas and Dr. Tara Schiller are gratefully acknowledged for support with polymer characterization. SN gratefully acknowledges his DFG research stipend (NA 1206). The Royal Society are also thanked for the award of an Industry Fellowship to APD.

■ REFERENCES

(1) Kiesewetter, M. K.; Shin, E. J.; Hedrick, J. L.; Waymouth, R. M. *Macromolecules* **2010**, *43*, 2093−2107.
(2) Dove, A. P. *ACS Macro Lett.* **2012**, *1*, 1409−1412.
(3) Fèvre, M.; Pinaud, J.; Gnanou, Y.; Vignolle, J.; Taton, D. *Chem. Soc. Rev.* **2013**, *42*, 2142−2172.
(4) Thomas, C.; Bibal, B. *Green Chem.* **2014**, *16*, 1687−1699.
(5) Naumann, S.; Dove, A. P. *Polym. Chem.* **2015**, *6*, 3185−3200.
(6) Lohmeijer, B. G. G.; Pratt, R. C.; Leibfarth, F.; Logan, J. W.; Long, D. A.; Dove, A. P.; Nederberg, F.; Choi, J.; Wade, C.; Waymouth, R. M.; Hedrick, J. L. *Macromolecules* **2006**, *39*, 8574−8583.
(7) Nachtergael, A.; Coulembier, O.; Dubois, P.; Helvenstein, M.; Duez, P.; Blankert, B.; Mespouille, L. *Biomacromolecules* **2015**, *16*, 507−514.
(8) Bouyahyi, M.; Pepels; Mark, P. F.; Heise, A.; Duchateau, R. *Macromolecules* **2012**, *45*, 3356−3366.
(9) Allen, A. E.; MacMillan, D. W. C. *Chem. Sci.* **2012**, *3*, 633−658.
(10) Muschiol, J.; Peters, C.; Oberleitner, N.; Mihovilovic, M. D.; Bornscheuer, U. T.; Rudroff, F. *Chem. Commun.* **2015**, *51*, 5798−5811.
(11) Stephan, D. W.; Erker, G. *Angew. Chem., Int. Ed.* **2015**, *54*, 6400−6441.
(12) Peters, R. *Cooperative Catalysis*; Wiley: New York, 2015.
(13) Raup, D. E. A.; Cardinal-David, B.; Holte, D.; Scheidt, K. A. *Nat. Chem.* **2010**, *2*, 766−771.
(14) Cohen, D. T.; Scheidt, K. A. *Chem. Sci.* **2011**, *3*, 53−57.
(15) Grossmann, A.; Enders, D. *Angew. Chem., Int. Ed.* **2012**, *51*, 314−325.
(16) Piedra-Arroni, E.; Amgoune, A.; Bourissou, D. *Dalton Trans.* **2013**, *42*, 9024−9029.
(17) Zhang, Y.; Miyake, G. M.; John, M. G.; Falivene, L.; Caporaso, L.; Cavallo, L.; Chen, E. Y.-X. *Dalton Trans.* **2012**, *41*, 9119−9134.
(18) Degée, P.; Dubois, P.; Jérôme, R. *Macromol. Chem. Phys.* **1997**, *198*, 1973−1984.
(19) Degée, P.; Dubois, P.; Jérôme, R.; Jacobsen, S.; Fritz, H.-G. *Macromol. Symp.* **1999**, *144*, 289−302.
(20) Bantu, B.; Pawar, G. M.; Decker, U.; Wurst, K.; Schmidt, A. M.; Buchmeiser, M. R. *Chem. - Eur. J.* **2009**, *15*, 3103−3109.
(21) Bantu, B.; Manohar Pawar, G.; Wurst, K.; Decker, U.; Schmidt, A. M.; Buchmeiser, M. R. *Eur. J. Inorg. Chem.* **2009**, *2009*, 1970−1976.
(22) Naumann, S.; Schmidt, F. G.; Frey, W.; Buchmeiser, M. R. *Polym. Chem.* **2013**, *4*, 4172−4181.
(23) Patel, D.; Liddle, S. T.; Mungur, S. A.; Rodden, M.; Blake, A. J.; Arnold, P. L. *Chem. Commun.* **2006**, 1124−1126.
(24) Pietrangelo, A.; Hillmyer, M. A.; Tolman, W. B. *Chem. Commun.* **2009**, 2736−2737.
(25) Pietrangelo, A.; Knight, S. C.; Gupta, A. K.; Yao, L. J.; Hillmyer, M. A.; Tolman, W. B. *J. Am. Chem. Soc.* **2010**, *132*, 11649−11657.
(26) Arnold, P. L.; Casely, I. J.; Turner, Z. R.; Bellabarba, R.; Tooze, R. B. *Dalton Trans.* **2009**, 7236−7247.
(27) Piedra-Arroni, E.; Brignou, P.; Amgoune, A.; Guillaume, S. M.; Carpentier, J.-F.; Bourissou, D. *Chem. Commun.* **2011**, *47*, 9828−9830.
(28) Brignou, P.; Guillaume, S. M.; Roisnel, T.; Bourissou, D.; Carpentier, J.-F. *Chem. - Eur. J.* **2012**, *18*, 9360−9370.
(29) Piedra-Arroni, E.; Ladavière, C.; Amgoune, A.; Bourissou, D. *J. Am. Chem. Soc.* **2013**, *135*, 13306−13309.
(30) Koeller, S.; Kadota, J.; Peruch, F.; Deffieux, A.; Pinaud, N.; Pianet, I.; Massip, S.; Léger, J.-M.; Desvergne, J.-P.; Bibal, B. *Chem. - Eur. J.* **2010**, *16*, 4196−4205.
(31) Kazakov, O. I.; Datta, P. P.; Isajani, M.; Kiesewetter, E. T.; Kiesewetter, M. K. *Macromolecules* **2014**, *47*, 7463−7468.
(32) Kazakov, O. I.; Kiesewetter, M. K. *Macromolecules* **2015**, *48*, 6121−6126.
(33) Ceccorulli, G.; Scandola, M.; Kumar, A.; Kalra, B.; Gross, R. A. *Biomacromolecules* **2005**, *6*, 902−907.
(34) Cai, J.; Liu, C.; Cai, M.; Zhu, J.; Zuo, F.; Hsiao, B. S.; Gross, R. A. *Polymer* **2010**, *51*, 1088−1099.
(35) Pepels, M. P. F.; Hansen, M. R.; Goossens, H.; Duchateau, R. *Macromolecules* **2013**, *46*, 7668−7677.
(36) Wilson, J. A.; Hopkins, S. A.; Wright, P. M.; Dove, A. P. *Polym. Chem.* **2014**, *5*, 2691−2694.
(37) Pepels, M. P. F.; Souljé, P.; Peters, R.; Duchateau, R. *Macromolecules* **2014**, *47*, 5542−5550.
(38) Di Stefano, S. *J. Phys. Org. Chem.* **2010**, *23*, 797−805.
(39) Kricheldorf, H. R.; Sumbel, M.-V. *Makromol. Chem.* **1988**, *189*, 317−331.
(40) Kricheldorf, H. R.; Sumbel, M. *Eur. Polym. J.* **1989**, *25*, 585−591.
(41) Acharya, A. K.; Chang, Y. A.; Jones, G. O.; Rice, J. E.; Hedrick, J. L.; Horn, H. W.; Waymouth, R. M. *J. Phys. Chem. B* **2014**, *118*, 6553−6560.
(42) Wellmar, A.; Persson, I. *J. Organomet. Chem.* **1991**, *415*, 143−153.
(43) Li, W.-D. Z.; Zhang, X.-X. *Org. Lett.* **2002**, *4*, 3485−3488.
(44) Zhang, X.; Shi, J. *Tetrahedron* **2011**, *67*, 898−903.
(45) Berthet, M.; Davanier, F.; Dujardin, G.; Martinez, J.; Parrot, I. *Chem. - Eur. J.* **2015**, *21*, 11014−11016.
(46) Naumann, S.; Buchmeiser, M. R. *Catal. Sci. Technol.* **2014**, *4*, 2466−2479.
(47) Nyce, G. W.; Glauser, T.; Connor, E. F.; Möck, A.; Waymouth, R. M.; Hedrick, J. L. *J. Am. Chem. Soc.* **2003**, *125*, 3046−3056.
(48) Kamber, N. E.; Jeong, W.; Gonzalez, S.; Hedrick, J. L.; Waymouth, R. M. *Macromolecules* **2009**, *42*, 1634−1639.
(49) Raynaud, J.; Absalon, C.; Gnanou, Y.; Taton, D. *Macromolecules* **2010**, *43*, 2814−2823.
(50) Stukenbroeker, T. S.; Solis-Ibarra, D.; Waymouth, R. M. *Macromolecules* **2014**, *47*, 8224−8230.

DOI: 10.1021/jacs.5b09502
J. Am. Chem. Soc. 2015, 137, 14439−14445

(51) Feng, H.; Dong, C.-M. *J. Polym. Sci., Part A: Polym. Chem.* **2006**, *44*, 5353−5361.
(52) Oshimura, M.; Tang, T.; Takasu, A. *J. Polym. Sci., Part A: Polym. Chem.* **2011**, *49*, 1210−1218.
(53) Nederberg, F.; Connor, E. F.; Moeller, M.; Glauser, T.; Hedrick, J. L. *Angew. Chem., Int. Ed.* **2001**, *40*, 2712−2715.

DOI: 10.1021/jacs.5b09502
J. Am. Chem. Soc. 2015, 137, 14439−14445