Green Chemistry

Accepted Manuscript

ROYAL SOCIETY OF CHEMISTRY

www.rsc.org/greenchem

Journal Name

RSCPublishing

ARTICLE

Rational investigations in the ring opening of cyclic carbonates by amines

Cite this: DOI: 10.1039/xoxxoooooox

M. Blain,[a,b] L. Jean-Gérard,[a] R. Auvergne,[b] D. Benazet,[c] S. Caillol,[b,*] and B. Andrioletti[a,*]

Received ooth January 2012,
Accepted ooth January 2012

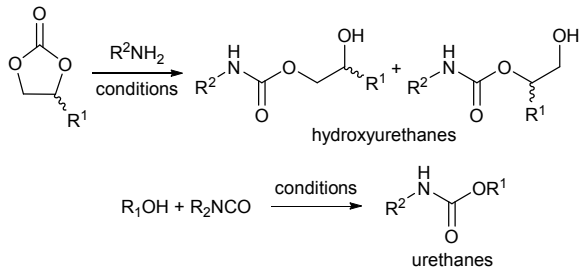
DOI: 10.1039/xoxxoooooox

www.rsc.org/

Non-isocyanate polyurethanes (NIPU's) constitute a promising alternative for more classical polyurethanes (PU's) as they may display mechanical properties that can match those of PU's and their synthesis does not involve the use of toxic isocyanates. Yet, because of the lower reactivity of carbonates *versus* isocyanates, the synthesis of NIPU's is not straightforward and generally requires the use of a catalyst. Recently, several groups have reported on the use of different ranges of catalysts for promoting the nucleophilic attack of the amine on the carbonate. However, many of these studies involve the use of highly reactive amine and/or carbonate proscribing a complete panorama of the potentialities of the reaction. Herein, we propose a rational study of the catalyzed aminolysis of four representative cyclic carbonates that reveals that the thiourea organocatalyst **1** outperforms in many aspects, classical inorganic or other organic catalysts.

Introduction

With a global production of 14Mt in 2006 and 17.5 Mt in 2011, PUs are the 6th most widely used polymer.[1] Despite this undeniable success, increasing concerns related to the use of (poly)isocyanate monomers as key reagents for the synthesis of PU's have stimulated the search for alternative synthetic strategies that could afford macromolecules with similar (mechanical) properties without requiring the use of toxic building blocks. In this context, a recent infatuation in the long-known aminolysis of carbonates has emerged.[2–7] Indeed, the aminolysis of carbonates affords carbamate functions structurally related to the structure obtained when an alcohol reacts with an isocyanate (Scheme 1). When a cyclic carbonate is reacted with a polyamine a poly-hydroxyurethane (PHU) is obtained.[8–12]



Scheme 1 carbonate vs isocyanate strategy

Considering the structural similarities between PU's and PHU's a considerable effort is currently devoted to understanding[13,14] and optimizing the ring opening of cyclic carbonates by amines.[15,16]

Due to the well-known lower reactivity of cyclic carbonates compared with isocyanates,[4,5] the use of a catalyst is generally required for promoting the nucleophilic attack of the amine on the carbonyl group of the carbonate.[17,18] A noticeable exception involves the use of linear primary amines which nucleophilicity is generally sufficient for reacting with the carbonate without requiring the use of a catalyst, even at room temperature (*vide infra*).[16] As most PU's are industrially formulated and processed at room temperature, it is highly desirable to propose a reliable access to PHU's that could proceed in similar conditions. In addition, synthesizing PHU's at room temperature would undoubtedly limit the possibility to favor side reactions, such as the degradation of carbamates to amide or ureas that could 1) limit the chain growth, or 2) result in polymers with unwanted functionalities or structure.

In this context, some of us[19–22] and others[4,7,12,15,23–25] have decided to re-investigate the long-known catalysed aminolysis of carbonates. However, to date, a survey of the corresponding literature data reveals the absence of a clear trend regarding the influence of the amine, the catalyst, and the temperature. Accordingly, we decided to embark a rational study on the aminolysis of carbonates with the aim of providing polymer chemists an extensive study on the catalyzed aminolysis of carbonates within a context of sustainable chemistry. Different

factors have been investigated. In a first instance, we have investigated the solvent free reaction of different amines with the propylene carbonate (which was selected as a typical cyclic carbonate), in the absence of catalyst. The objective was to determine a system amine/carbonate that would exhibit a moderate reactivity in order to evaluate precisely the catalytic effect. After this preliminary screening, a large range of inorganic and organic catalysts were tested. The conversion, the selectivity and the color of the reaction mixture were considered for this study. Once the optimal reaction time had been determined, the reactivity of several amines with different carbonates was investigated providing a rather complete overview of the scope of the reaction.

Results and discussion

Choice of the amine

Propylene carbonate (PC) being relatively unreactive, and readily available, it was chosen as the prototypal 5-membered cyclic carbonate partner for selecting the most appropriate, non-functionalized amine for the study. In order to provide data directly usable by polymer chemists, it was decided to perform the screening neat, as polyurethanes are generally synthesized in the absence of solvent. PC being an excellent "green" solvent, the screening was performed at 25°C. A clear reaction mixture was obtained with the variously substituted amines investigated (Figure 1).

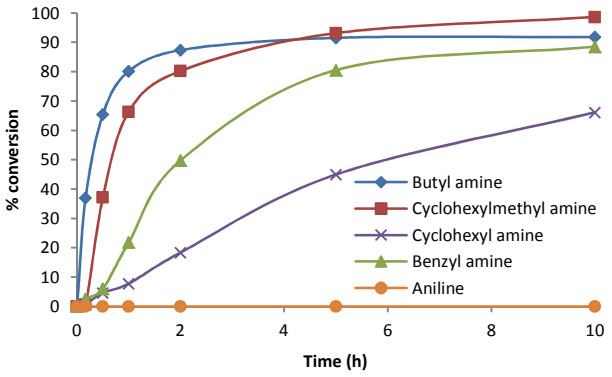


Fig. 1 Conversion of PC with different amines

As expected, a quantitative GC-MS analysis revealed that the less hindered, more nucleophilic butyl-, cyclohexylmethyl- and benzyl-amines displayed the highest reactivities with an almost complete conversion in about 10 hours, even in the absence of catalyst. Conversely, the more sterically demanding cyclohexylamine displayed a limited reactivity with a conversion limited to 66% after 10 hours of stirring at room temperature. At last, the poorly reactive aniline did not react in these conditions. In light of these results, we decided to retain the cyclohexylamine as nucleophile for the catalyst screening.

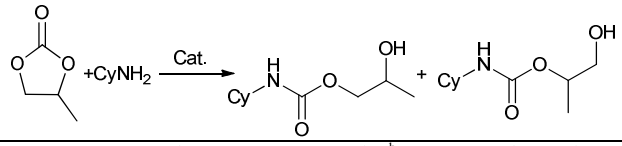
Determination of the optimal catalyst

Both inorganic salts and organocatalysts were investigated.

Inorganic Lewis acids

A large range of little toxic metal salts were first investigated. It was expected that the Lewis character would enhance the reactivity of the carbonate function[26,22] (Table 1).

Table 1 Lewis acid-catalyzed aminolysis of CP with cyclohexylaminea.



Entry	Catalyst	% Conversion[b] CP	Observations
1	none	9(45)	colorless
2	$MgBr_2$	51(71)	Suspension
3	$Yb(OTf)_3$	53(77)	turbid
4	$Fe(OTf)_3$	40(64)	brown
5	$FeCl_3$	41(67)	brown
6	$Bi(OTf)_3$	48(70)	white
7	$Ti(OiPr)_4$	12(57)	turbid

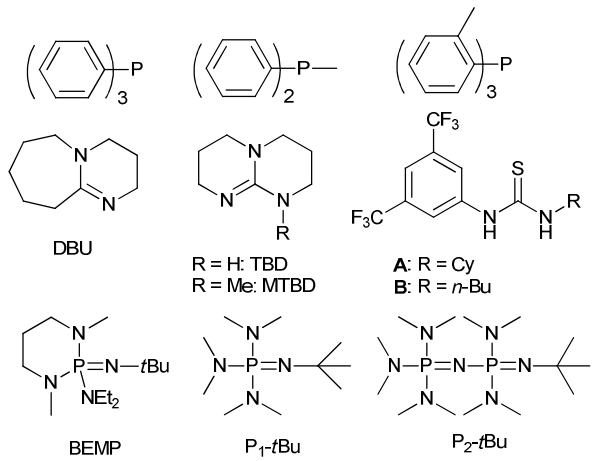
[a] CP/cyclohexylamine: 1/1, 25°C, catalyst loading : 5 mol%, 1 hr. [b] in parenthesis, conversion after 5 hr.

As mentioned before, the non-catalyzed aminolysis of CP with the cyclohexylamine proceeds to a very limited extent, with a conversion of 9% after 1 hr, and 45% after 5 hr of stirring at 25°C. At the exception of $Ti(OiPr)_4$ (entry 7), all the Lewis acids catalyze the aminolysis reaction with a conversion reaching about 50% after 1 hr when Mg, Yb or Bi salts were used. When the reaction was allowed to proceed for 5 hr, in every case, the conversions increased, reaching a plateau of about 60-75%. Hence, an interesting catalytic effect is observed. However, for macromolecular applications, chemicals (the catalyst in our case) that afford color have to be proscribed because colorless polymers are generally highly desirable. Similarly, insoluble catalysts should also be banned. Considering our observations (Table 1) and these aforementioned limitations, organocatalysts were evaluated as well.

Organocatalysts

A series of organocatalysts encompassing phosphines, bases, phosphazenes and thioureas was evaluated in the conditions considered for the screening of the inorganic catalysts (Scheme 2)

We first evaluated 3 different phosphines stable enough for allowing an easy handling. Accordingly, 2 triarylphosphines and a monoalkylbiarylphosphine were investigated (Table 2, entries 2-4)[27].

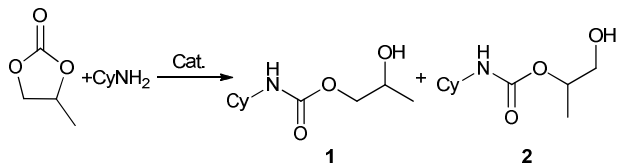


Scheme 2 Oganocatalysts used in the study

Disappointing results were obtained as the conversions did not exceed those obtained for the non-catalyzed reactions. 5 nitrogen-containing bases were also evaluated[28,29,30] (Table 2, entries 5-9). All of them catalyzed the aminolysis of CP, the best catalyst being TBD. This result is in agreement with former results from the literature that proposed that TBD could activate both the carbonate and the nucleophile.[15,31] In contrary, phosphazenes that have been proposed as potent organocatalysts for similar reactions[32,33] appeared poorly efficient in our conditions (entries 10-11). Interestingly, the thioureas **A** and **B**[34,35] revealed also a powerful catalytic effect with a conversion of 66% in the case of the phenylcyclohexyl thiourea **A**, matching the conversion obtained with TBD. Noticeably, in our study, the organocatalysts generally outperformed the inorganic catalysts in terms of efficiency but also because they did not color the reaction mixture. Of note, no significant selectivity for carbamate **1** or **2** was observed during our screening.

From a mechanistic point of view, even if TBD and a thiourea display different structures, it is expected that the catalytic effect could be attributed to similar activation modes of the carbonate. Indeed, it is commonly admitted that a thiouruea is able to activate a carbonyl function by establishing two hydrogen bonds with the CO of the carbonyl function in a 6-membered ring fashion. Conversely, as TBD is a strong base, it is very easily protonated (we observed a reversible protonation of TBD just on standing in air). Based on this assumption, the resulting guanidinium is able to activate the carbonyl similarly to the thiourea. These analogies may explain why TBD and the thiourea display similar performances.

Table 2 Organocatalyzed aminolysis of CP with cyclohexylaminea.



Entry	Catalyst	% Conversion CP	Product ratio 1: 2
1	none	9	35:65
2	PPh_3	12	50:50
3	$MePPh_2$	9	55:45
4	Tri(*o*-toly)phosphine	7	63:37
5	DABCO	17	54:46
6	DMAP	24	55:45
7	DBU	38	42:58
8	TBD	66	56:44
9	MTBD	20	50:50
10	BEMP	24	55:45
11	P1-*t*Bu	18	44:56
12	**A**	66	45:55
13	**B**	61	48:52

[a] CP/cyclohexylamine:: 1/1, 25°C, catalyst loading: 5 mol%, 1 hr.

In light of the results presented in Tables 1 and 2, it was decided to complete our study using the TBD and the thiourea **A** as catalysts.

Effect of the temperature

After selecting the two most promising catalysts, the influence of the temperature was investigated. To this end, PC and the cyclohexylamine were reacted at different temperatures in the presence of TBD and **A**, respectively (Figure 2). As expected, an increase of the temperature up to 100°C results in a sharp increase of the kinetics of the reaction. Hence, the conversions reached 66% and 90% in 12 min when **A** and TBD were used as catalysts, respectively. After 1 hr, the conversion is complete in the presence of TBD and attains 90% when **A** is employed. Thus, it appears that an increase of the temperature results in a higher conversion of CP and reveals a higher catalytic activity of TBD compared with the thiourea. However, it should be noted that this enhanced reactivity proceeds at the expense of the selectivity toward the carbamates. Indeed, the presence of impurities was detected in the ^{1}H NMR spectra of the carbamates when TBD is used (see the supporting information material).

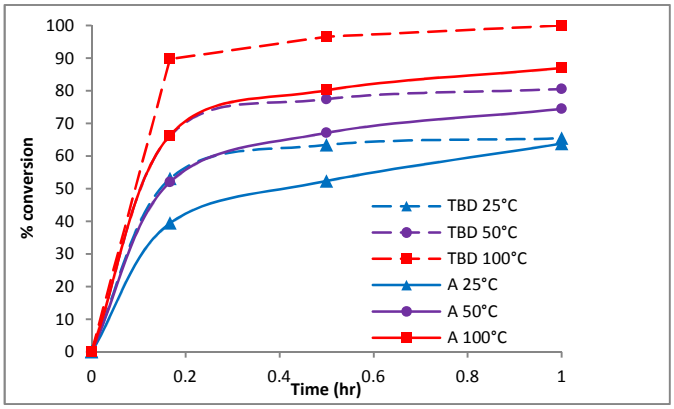


Fig. 2 Reaction of CP with the cyclohexylamine at different temperatures using TBD and **A** as catalysts.

Catalyst loading

Next we investigated the catalyst loading. Different catalytic charges and reaction were screened (Figure 3).

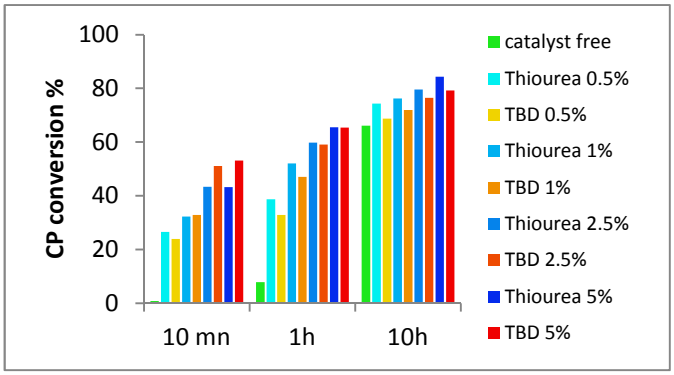
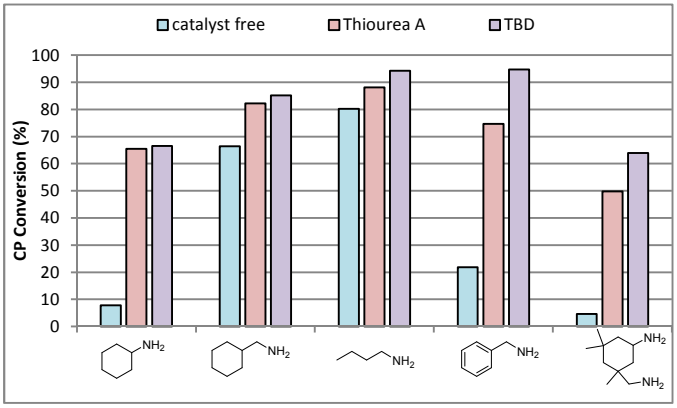


Fig. 3 Effect of the catalyst loading on the aminolysis of CP with cyclohexylamine.

Interestingly, after 10 minutes of reaction, the thiourea **A** is a more efficient catalyst than TBD when the catalyst loading is maintained below 1 mol%. However, when increasing the catalytic charge up to 5 mol%, TBD becomes more efficient than **A**. There observations are confirmed after 1hr of reaction, but thiourea **A** becomes more efficient than TBD with a prolonged reaction time (10 hr). Thus, for large scale application it is worth noting that the thiourea A is more promising than TBD because low catalyst loadings are tolerated. This observation contrasts with what is generally reported in the literature.[15]

Scope of the reaction: amine

Having in hands a promising protocol, we decided to investigate the scope of the reaction and tested 4 additional amines displaying different nucleophilicities: the cyclohexylmethylamine, butylamine, benzylamine and the industrially relevant IPDA diamine were reacted with 1 (or 2) equivalent of CP, in the presence of the two selected organocatalysts, at 25°C for 1 hr (Figure 4).



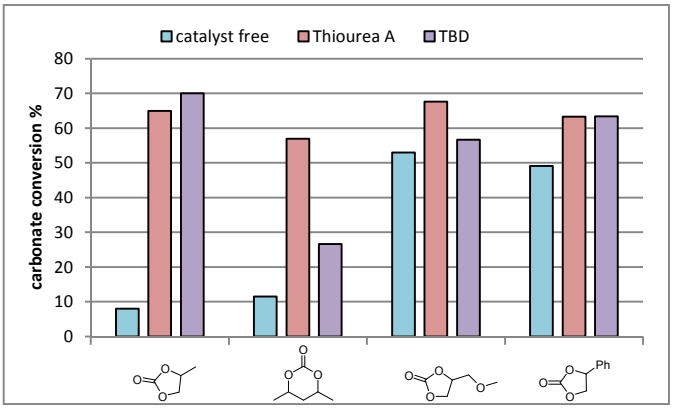
[a] CP/ amine: 1/1, (CP/IPDA: 2/1), 25°C, catalyst: 5 mol%, 1h.

Fig. 4 Reaction of CP with different amines in the presence of TBD or **A**[a].

A careful analysis of the chart (Figure 4) reveals that the catalytic effect of both TBD and **A** is very limited when highly nucleophilic amines are used. In contrast, a dramatic effect is observed in the case of sterically hindered or deactivated amines. Thus, when benzylamine reacts to a limited extent with PC in the absence of catalyst (conv. 28%), in the presence of **A** or TBD, the conversion increased to 74% and 94%, respectively. An even more impressive effect is observed in the case of IPDA. Whereas IPDA is almost unreactive towards PC in the absence of catalyst, important conversions of 50% and 63% were measured in the presence of **A** and TBD, respectively. In these conditions, the two catalysts displayed a very similar catalytic activity.

Scope of the reaction: carbonate

To complete the study, we also screened a series of carbonates, namely the 4-(methoxymethyl)-1,3-dioxolan-2-one, 4-phenyl-1,3-dioxolan-2-one and 4,6-dimethyl-1,3-dioxan-2-one, a representative 6 membered ring carbonate. The cyclohexylamine was chosen as a nucleophile, and both organocatalysts **A** and TBD were investigated.



Carbonate/ amine: 1/1, 25°C, catalyst: 5 mol%, 1h.

Fig. 5 Reaction of different carbonates with the cyclohexylamine in the presence of TBD or **A**.

Interestingly, when screening the different carbonates in these conditions, at the exception of PC, the thiourea **A** revealed a superior or equal activity to TBD (Figure 5). This observation is in sharp contrast with what it is generally admitted in the literature.[15] Whereas both 4-(methoxymethyl)-1,3-dioxolan-2-one and 4-phenyl-1,3-dioxolan-2-one displayed a high reactivity in our conditions with conversions reaching 68 and 63%, respectively in the presence of catalyst **A**, the 6-membered ring 4,6-dimethyl-1,3-dioxan-2-one was only proved reactive in the presence of the thiourea **A** (57% conversion). This observation also contrasts with common beliefs that consider that 6-membered rings are generally more reactive than their 5-membered ring analogues.[13]

Conclusions

To the best of our knowledge, for the first time, a rational study about the aminolysis of cyclic carbonates is reported. Our work demonstrates that in general, organocatalysts display a higher catalytic activity than inorganic Lewis acids. In addition, they generally do not bring color or turbidity to the reaction mixture. This observation is absolutely crucial for future macromolecular applications. Advantageously, this study has been carried out in the absence of solvent which is also relevant for subsequent extension in polycondensation reactions. Our screening also reveals that TBD and the cyclohexylphenyl thiourea **A** outperform the other catalysts investigated. This observation confirms precedent from the literature. However, in our conditions, the thiourea **A** seems more promising as it cleanly catalyzes the aminolysis of carbonates even at very low catalyst loading. In addition, it was proven more efficient when functionalized 5-membered ring or 6-membered ring carbonates were used.

Work is currently underway in our Laboratories to extend this methodology to polycarbonates and polyamines.

Experimental

Chemicals

All the catalysts and IPDI were used as received except the thioureas synthesized according to the reported literature procedure.[34] Propylene carbonate (PC) was purified by distillation. Glycerol carbonate (GC) was purified by column chromatography using ethyl acetate and hexane (60:40) as eluent. 4-(methoxymethyl)-1,3-dioxolan-2-one and 4,6-dimethyl-1,3-dioxan-2-one were synthesized according to the reported literature procedure.[36]

General procedure for the aminolysis of carbonates with GC/MS quantitative analysis

In a typical procedure, carbonate (1 equiv), amine (1 equiv) and diphenyl ether (0.15 equiv internal standard) were stirred together during the time and at the temperature shown in the table in an open air reaction tube with the quantity of catalyst used in the table.

General procedure for the aminolysis of carbonates

In a typical procedure, the carbonate (2.6 mmol), amine (2.6 mmol) and the catalyst (5 mol%) were stirred together for the appropriate time in an open vessel thermostated at 25°C.

Acknowledgements

The Association Nationale de la Recherche et de la Technologie (ANRT) and Juxta are deeply acknowledged for their financial support so as Mrs. Audrey Ledoux for her initial contribution to this work.

Notes and references

a ICBMS-UMR 5246 Université Claude Bernard-Lyon 1
Equipe de CAtalyse, SYnthèse et ENvironnement (CASYEN)
Domaine Scientifique de la Doua-Bât. Curien/CPE, 2° étage aile C
43 Boulevard du 11 Novembre 1918, 69622 Villeurbanne Cedex-France.
b Ecole Nationale Supérieure de Chimie de Montpellier
8, Rue Ecole Normale, 34296 Montpellier-France.
c JUXTA, 5 rue de la Jalesie, BP 71039, 25401 Audincourt cedex-France.

† Electronic Supplementary Information (ESI) available: Synthetic protocols for the preparation of the carbonates (when not commercially available), the catalysts, and complete characterization of the different reaction products. See DOI: 10.1039/b000000x/

(1) a) Shen, L.; Haufe, J.; Patel, M. K. *Report of Utrecht University commissioned by European Polysaccharide Network of Excellence and European Bioplastics* **2009**; b) Panorama du marché du polyuréthane et état de l'art de ses techniques de recyclage, rapport Ademe **2014** (http://www2.ademe.fr/servlet/getDoc?cid=96&m=3&id=91921&p1=30&ref=12441).

(2) Nohra, B.; Candy, L.; Blanco, J.-F.; Guerin, C.; Raoul, Y.; Mouloungui, Z. *Macromolecules* **2013**, *46*, 3771–3792.

(3) Kathalewar, M. S.; Joshi, P. B.; Sabnis, A. S.; Malshe, V. C. *RSC Adv.* **2013**, *3*, 4110–4129.
(4) Kreye, O.; Mutlu, H.; Meier, M. a. R. *Green Chem.* **2013**, *15*, 1431–1455.
(5) Delebecq, E.; Pascault, J.; Boutevin, B.; Ganachaud, F. *Chem. Rev.* **2013**, *113*, 80–118.
(6) Rokicki, G.; Piotrowska, A. *Polymer (Guildf).* **2002**, *43*, 2927–2935.
(7) Bürgel, T.; Fedtke, M.; Franzke, M. *Polym. Bull.* **1993**, *30*, 155–162.
(8) Steblyanko, A.; Choi, W.; Sanda, F.; Endo, T. *J. Polym. Sci. Part A Polym. Chem.* **2000**, *38*, 2375–2380.
(9) Tomita, H.; Sanda, F.; Endo, T. *J. Polym. Sci. Part A Polym. Chem.* **2001**, *39*, 3678–3685.
(10) Tomita, H.; Sanda, F.; Endo, T. *J. Polym. Sci. Part A Polym. Chem.* **2001**, *39*, 851–859.
(11) Kihara, N.; Endo, T. *J. Polym. Sci. Part A Polym. Chem.* **1993**, *31*, 2765–2773.
(12) Annunziata, L.; Diallo, A. K.; Fouquay, S.; Michaud, G.; Simon, F.; Brusson, J.-M.; Carpentier, J.-F.; Guillaume, S. M. *Green Chem.* **2014**, *16*, 1947–1956.
(13) Tomita, H.; Sanda, F.; Endo, T. *J. Polym. Sci. Part A Polym. Chem.* **2001**, *39*, 162–168.
(14) Nohra, B.; Candy, L.; Blanco, J.-F.; Raoul, Y.; Mouloungui, Z. *Eur. J. Lipid Sci. Technol.* **2013**, *115*, 111–122.
(15) Lambeth, R. H.; Henderson, T. J. *Polymer (Guildf).* **2013**, *54*, 5568–5573.
(16) Diakoumakos, C. D.; Kotzev, D. L. *Macromol. Symp.* **2004**, *216*, 37–46.
(17) Helou, M.; Guillaume, S.; Carpentier, J.-F.; Miserque, O. WO2010012562A1 **2010**.
(18) Ochiai, B.; Inoue, S.; Endo, T. *J. Polym. Sci. Part A Polym. Chem.* **2005**, *43*, 6282–6286.
(19) Benyahya, S.; Desroches, M.; Auvergne, R.; Carlotti, S.; Caillol, S.; Boutevin, B. *Polym. Chem.* **2011**, *2*, 2661–2667.
(20) Benyahya, S.; Habas, J.-P.; Auvergne, R.; Lapinte, V.; Caillol, S. *Polym. Int.* **2012**, *61*, 1666–1674.
(21) Besse, V.; Auvergne, R.; Carlotti, S.; Boutevin, G.; Otazaghine, B.; Caillol, S.; Pascault, J.-P.; Boutevin, B. *React. Funct. Polym.* **2013**, *73*, 588–594.
(22) Soules, A.; Caillol, S.; Joubert, J.-P.; Martins, J.; Boutevin, B. WO 2013/060950 **2013**.
(23) Tomita, H.; Sanda, F.; Endo, T. *J. Polym. Sci. Part A Polym. Chem.* **2000**, *39*, 860–867.
(24) Webster, D. C.; Crain, A. L. *Prog. Org. Coatings* **2000**, *40*, 275–282.
(25) Webster, D. C. *Prog. Org. Coatings* **2003**, *47*, 77–86.
(26) Darensbourg, D. J.; Holtcamp, M. W. *Coord. Chem. Rev.* **1996**, *153*, 155–174.
(27) Myers, M.; Connor, E. F.; Glauser, T.; Möck, A.; Nyce, G.; Hedrick, J. L. *J. Polym. Sci. Part A Polym. Chem.* **2002**, *40*, 844–851.
(28) Nederberg, F.; Lohmeijer, B. G. G.; Leibfarth, F.; Pratt, R. C.; Choi, J.; Dove, A. P.; Waymouth, R. M.; Hedrick, J. L. *Biomacromolecules* **2007**, *8*, 153–160.
(29) Helou, M.; Miserque, O.; Brusson, J.-M.; Carpentier, J.-F.; Guillaume, S. M. *Chemistry* **2010**, *16*, 13805–138013.
(30) Alsarraf, J.; Ammar, Y. A.; Robert, F.; Cloutet, E.; Cramail, H.; Landais, Y. *Macromolecules* **2012**, *45*, 2249–2256.
(31) Kiesewetter, M. K.; Scholten, M. D.; Kirn, N.; Weber, R. L.; Hedrick, J. L.; Waymouth, R. M. *J. Org. Chem.* **2009**, *74*, 9490–9496.
(32) Zhang, L.; Nederberg, F.; Messman, J. M.; Pratt, R. C.; Hedrick, J. L.; Wade, C. G. *J. Am. Chem. Soc.* **2007**, *129*, 12610–12611.
(33) Zhang, L.; Nederberg, F.; Pratt, R. C.; Waymouth, R. M.; Hedrick, J. L.; Wade, C. G. *Macromolecules* **2007**, 4154–4158.
(34) Pratt, R. C.; Lohmeijer, B. G. G.; Long, D. A.; Lundberg, P. N. P.; Dove, A. P.; Li, H.; Wade, C. G.; Waymouth, R. M.; Hedrick, J. L. *Macromolecules* **2006**, *39*, 7863–7871.
(35) Dove, A. P.; Pratt, R. C.; Lohmeijer, B. G. G.; Waymouth, R. M.; Hedrick, J. L. *J. Am. Chem. Soc.* **2005**, *127*, 13798–13799.
(36) Nogawa, M.; Sugawara, S.; Iizuka, R.; Shimojo, M.; Ohta, H.; Hatanaka, M.; Matsumoto, K. *Tetrahedron* **2006**, *62*, 12071–12083.