3782 *Macromolecules* **2008**, *41*, 3782−3784

Organo-Catalyzed ROP of ϵ-Caprolactone: Methanesulfonic Acid Competes with Trifluoromethanesulfonic Acid

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Received March 20, 2008
Revised Manuscript Received April 18, 2008

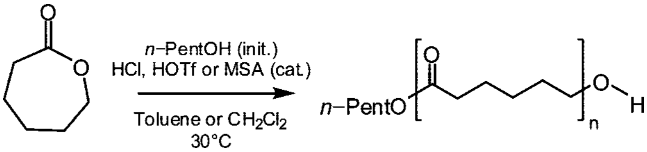
Introduction. In the past two decades, a broad variety of metal complexes have been evaluated as catalysts for the ring-opening polymerization (ROP) of lactones and dilactones. In particular, well-defined complexes combining an ancillary ligand and an initiating group have allowed for tremendous improvements in terms of activity and control.[1] Spectacular progress has also been achieved over the past few years in organo-catalyzed ROP.[2] This metal-free approach is particularly desirable when the resulting polyesters are to be used within medicinal or microelectronic devices. In this respect, Hedrick and Waymouth have developed a variety of systems (4-aminopyridines,[3] *N*-heterocyclic carbenes,[4] thiourea/amine combinations,[5] guanidines,[6] phosphazenes[7]) that efficiently promote the ROP of lactide and lactones via nucleophilic, basic, or bifunctional activation.[8,9]

Comparatively, the ROP of (di)lactones promoted by Brönsted acids has been less studied. In the late 1980s, Kricheldorf et al. demonstrated the feasibility of the trifluoromethanesulfonic acid (HOTf)-catalyzed ROP of lactide, but the polymerization was far from living even in the optimum conditions.[10] In the early 2000s, the groups of Endo and Jérôme reported the polymerization of δ-valero- and ϵ-caprolactones using hydrochloric acid ($HCl\cdot OEt_2$) as a catalyst and an alcohol as initiator. With such combinations, the polymerization is well-controlled, but it proceeds slowly (>24 h at room temperature for monomer to initiator ratios ranging from 70 to 100) despite the large amounts of acid used (≥4 equiv relative to the initiator).[11−13] Recently, we found that, in the presence of a protic initiator, HOTf promotes and controls the ROP of lactide at room temperature.[14] This combination also proved efficient for the homopolymerization of ϵ-caprolactone and for its copolymerization with lactide.[15]

The increasing interest for acid-catalyzed ROP of (di)lactones prompted us to investigate the influence of the acidity of the catalyst on its activity. The widely available and environmentally benign methanesulfonic acid (MSA) was chosen as a much weaker acid than HOTf,[16] and we report here a detailed comparison of HOTf and MSA in the ROP of ϵ-caprolactone.[17] Both acids induce controlled and living polymerizations at 30 °C in the presence of primary as well as secondary alcohols. The reaction proceeds faster in toluene than in chlorinated solvents, and despite a difference in pK_a of more than 10 units,[18] MSA proved as active as HOTf. In addition, the two acids exhibit completely different behavior upon varying the catalyst to initiator ratio: the activity of HOTf is optimal for a ratio of about 1:1, whereas that of MSA keeps increasing above the stoichiometric ratio, allowing to significantly decrease the polymerization time while retaining very good control.

Results and Discussion. In the context of acid-catalyzed ROP, methanesulfonic acid (MSA) appeared an interesting alternative for the extremely acidic HOTf (Hammett acidity $H_0 \sim -14$) and the highly corrosive HCl. MSA ($H_0 \sim -1$) is produced industrially in large scale by oxidation of methanethiol, and as a part of the natural sulfur cycle,[19] it is considered as environmentally benign. The activity of the three acids HCl, HOTf, and MSA toward the ROP of ϵ-CL was assessed in identical conditions: initiator = *n*-PentOH, monomer/catalyst/initiator ratio = 40/1/1, temperature = 30 °C, $[\epsilon\text{-CL}]_0 = 0.9$ M, solvent = dichloromethane (DCM) or toluene (Table 1). Accordingly, MSA proved slightly more active than HOTf, complete monomer conversion being respectively achieved within 2 vs 7 h in DCM (runs 3 and 2). For comparison, only 22% of the monomer is polymerized with HCl even after 24 h (run 1). Replacement of DCM for toluene allows to slightly decrease the polymerization times for MSA and to a greater extent for HOTf and HCl: complete monomer conversion is achieved after 19 h with HCl (run 4) and only requires 90 min with HOTf and MSA (runs 5 and 6). Although it is difficult to precisely rationalize the solvent effect, it is likely that the higher polymerization kinetics observed in toluene compared with DCM result from a slightly tighter interaction between the acid catalyst and the monomer in the less polar solvent. In all cases, the number-average molecular weights M_n of the resulting poly(ϵ-caprolactone) (PCL) (as determined by SEC analyses with polystyrene standards and a correction factor[20] of 0.56) match well that anticipated theoretically (4648 g/mol), the polydispersity index M_w/M_n being slightly lower for MSA (1.07) than for HOTf (1.15) and HCl (1.22). Overall, these results substantiate the superiority of sulfonic acids over HCl in promoting the ROP of ϵ-CL and suggest that the activity of these acid catalysts does not simply correlate their acidity.

Table 1. Polymerization of ϵ-Caprolactone (ϵ-CL) Promoted by HCl, HOTf, or MSA[a]



run	catalyst	H_0[b]	solvent	time (h)[c]	M_n[d,e]	M_w/M_n[d]
1	HCl	−8	DCM	24 (22%[f])	1610	1.19
2	HOTf	−14	DCM	7	3500	1.22
3	MSA	−1	DCM	2	4280	1.07
4	HCl	−8	toluene	19	3500	1.22
5	HOTf	−14	toluene	1.5	4500	1.15
6	MSA	−1	toluene	1.5	4300	1.07

[a] Polymerizations of 0.9 M solutions of ϵ-caprolactone carried out at 30 °C with *n*-PentOH as initiator for a monomer/initiator/catalyst ratio of 40/1/1. [b] Hammett acidity.[18] [c] Polymerization time necessary to achieve monomer conversion >98% according to ^{1}H NMR spectroscopy. [d] Number-average molecular weight (M_n) and polydispersity index (M_w/M_n) obtained from size exclusion chromatography analysis (in tetrahydrofuran, THF) using polystyrene standards and a correction factor[20] of 0.56. [e] $M_{n(th)} = 4648$ g/mol, as calculated from the molecular weight of ϵ-caprolactone (114 g/mol) × the monomer/initiator ratio plus the molecular weight of the initiator (88 g/mol). [f] Monomer conversion.

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10.1021/ma800626q CCC: $40.75

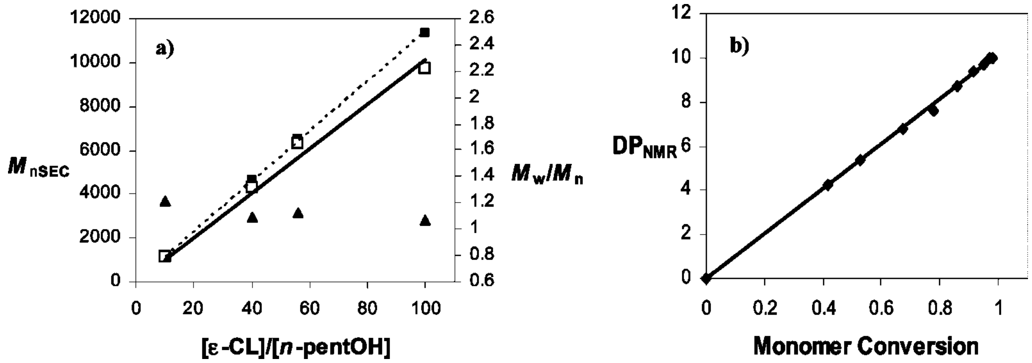


Figure 1. (a) Plot of number-average molecular weight M_n (estimated by size exclusion chromatography SEC and a correction factor of 0.56) vs ϵ-caprolactone (monomer) to initiator ratio (solid line) (toluene, 30 °C, [MSA]/[*n*-PentOH]$_0$ = 1, [ϵ-CL]$_0$ = 0.9 M). Broken line shows the $M_{n(th)}$ values calculated from the molecular weight of ϵ-caprolactone (114 g/mol) × [ϵ-CL]$_0$/[*n*-PentOH] plus the molecular weight of *n*-PentOH (88 g/mol). ▲ represents M_w/M_n. (b) Plot of DP (estimated by ^{1}H NMR spectroscopy) vs ϵ-caprolactone conversion (estimated by ^{1}H NMR spectroscopy) (Tol-d8, 30 °C, [ϵ-CL]$_0$/[MSA]/[*n*-PentOH]$_0$ 10/1/1, [ϵ-CL]$_0$ = 0.9 M).

In order to compare further the behavior of HOTf and MSA, polymerizations of ϵ-caprolactone were carried out with both systems, varying the nature of the initiator as well as the monomer to initiator ratio (Table S1).[21] Both primary and secondary alcohols (*n*-PentOH, *i*-PrOH, and CyOH) are convenient initiators with the two acids, and PCL of controlled molecular weights, narrow distribution, and complete end-group fidelity[22] were obtained. Variation of the monomer to initiator ratio from 10 to 100 gives access to PCL with molecular weights up to 11 000 g/mol and narrow molecular weight distributions ($1.07 < M_w/M_n < 1.21$). After complete monomer conversion, the acid catalyst can be easily and quantitatively removed from the polymer sample without affecting its properties, either by addition of diisopropylethylamine followed by aqueous washing or by treatment with a basic resin (such as Amberlyst A21). With both acids, the experimental M_n values vary linearly with the monomer to initiator ratio and agree well with those calculated from the monomer feed (Figure 1a, for MSA-catalyzed ROP). The degree of polymerization (DP_{NMR} determined by ^{1}H NMR) also increases linearly with the monomer conversion (Figure 1b).[21] These linear relationships support the controlled character of the polymerizations. In addition, the living character of the HOTf- and MSA-catalyzed polymerizations was supported by second-feed experiments. As a representative example, a PCL with M_n = 4280 g/mol and M_w/M_n = 1.07 was first prepared by complete polymerization of 40 equiv of ϵ-caprolactone with MSA/*n*-PentOH (1/1) in toluene. Polymerization was then restarted by subsequent addition of 40 equiv of ϵ-caprolactone to afford a PCL with M_n = 8489 g/mol and M_w/M_n = 1.09 after complete conversion of the monomer (Figure S4).[21]

Aiming at improving further the ROP of ϵ-caprolactone catalyzed by sulfonic acids, the influence of the catalyst to initiator ratio was then investigated.[21] In marked contrast with that observed so far, HOTf and MSA exhibited here completely different behaviors. As a representative example, the polymerization of 40 equiv of ϵ-caprolactone that required 90 min at 30 °C in toluene with both HOTf and MSA for catalyst to initiator ratio = 1 is complete within only 30 min when the MSA to initiator ratio is increased to 3, whereas monomer conversion only reaches 33% with HOTf under the same conditions. As illustrated in Figure 2, the activity of HOTf progressively increases with the amount of catalyst up to [HOTf]/[*n*-PentOH]$_0$ = 1 but significantly decreases when the catalyst is added in excess relative to the initiator. This behavior makes MSA particularly attractive, since the polymerization times can be noticeably shortened, while retaining very good control, as illustrated by the preparation of a PCL with M_n = 9300 g/mol and M_w/M_n = 1.10 within only 2 h at 30 °C ([ϵ-CL]$_0$/[MSA]/[*n*-PentOH]$_0$ = 100/3/1).

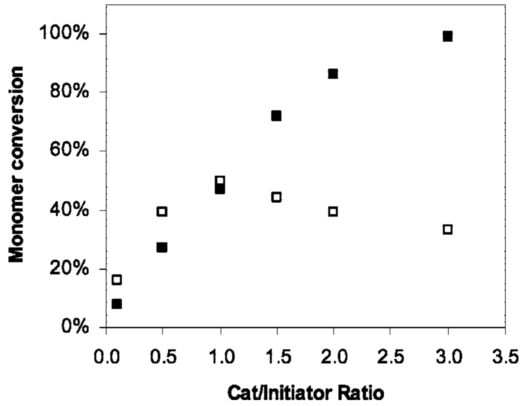
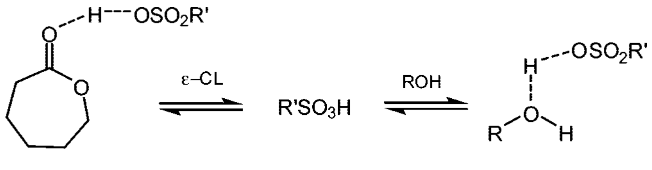


Figure 2. Influence of the catalyst to initiator ratio on the monomer conversion after 30 min for the ROP of ϵ-caprolactone catalyzed by MSA (■) and HOTf (□), in toluene at 30 °C, [ϵ-CL]$_0$/[*n*-PentOH]$_0$ = 40/1, [ϵ-CL]$_0$ = 0.9 M.

Scheme 1. Competitive Monomer Activation and Alcohol Deactivation[a]



[a] R refers to the initiating or propagating alcohol, R′ = CF$_3$, CH$_3$.

The pronounced difference observed between HOTf and MSA upon varying the catalyst to initiator ratio may result from the competition between the activation of the monomer and the deactivation of the initiating/propagating alcohol, as illustrated in Scheme 1. Excess amounts of the strong acid HOTf would slow down the polymerization as a result of strong deactivation of the alcohol, whereas increasing the quantity of MSA would accelerate the polymerization as the result of more efficient monomer activation.

In conclusion, both HOTf and MSA induce reproducible, controlled and living polymerizations of ϵ-caprolactone at 30 °C in the presence of primary as well as secondary alcohols. The reaction proceeds faster in toluene than in chlorinated solvents, and despite a difference in pK_a of more than 10 units, MSA proved as active as HOTf. The activity of HOTf is optimal for a catalyst to initiator ratio of 1, suggesting that the deactivation of the initiating/propagating alcohol competes with the activation of the monomer. In marked contrast, the activity of MSA keeps increasing above the stoichiometric ratio, allowing to decrease significantly the polymerization time while retaining very good control. Accordingly, MSA appears an efficient, cheap, and environmentally benign catalyst for the preparation of PCL of controlled molecular weights and narrow polydispersities. Current efforts aim at taking advantage of this new catalytic system to prepare complex architectures and at determining further the precise mode of action of such sulfonic acids.

Acknowledgment. We are grateful to Arkema, the CNRS, and the UPS for financial support of this work. Fruitful discussions with Dr. L. Maron (LPCNO, Toulouse) have been particularly appreciated.

Supporting Information Available: Experimental details, Table S1, and Figures S1−S5. This material is available free of charge via the Internet at http://pubs.acs.org.

References and Notes

(1) (a) Löfgren, A.; Albertsson, A.-C.; Dubois, P.; Jérôme, R. *Rev. Macromol. Chem. Phys.* **1995**, *C35*, 379–418. (b) O'Keefe, B. J.; Hillmyer, M. A.; Tolman, W. B. *J. Chem. Soc., Dalton Trans.* **2001**, 2215–2224. (c) Lou, X.; Detrembleur, C.; Jérôme, R. *Macromol. Rapid Commun.* **2003**, *24*, 161–172. (d) Albertsson, A.-C.; Varma, I. K. *Biomacromolecules* **2003**, *4*, 1466–1486. (e) Dechy-Cabaret, O.; Martin-Vaca, B.; Bourissou, D. *Chem. Rev.* **2004**, *104*, 6147–6176. (f) Wu, J.; Yu, T.-L.; Chen, C.-T.; Lin, C.-C. *Coord. Chem. Rev.* **2006**, *250*, 602–626.

(2) (a) Bourissou, D.; Moebs-Sanchez, S.; Martin-Vaca, B. *C. R. Chim.* **2007**, *10*, 775–794. (b) Kamber, N. E.; Jeong, W.; Waymouth, R. M.; Pratt, R. C.; Lohmeijer, B. G. G.; Hedrick, J. L. *Chem. Rev.* **2007**, *107*, 5813–5840.

(3) Nederberg, F.; Connor, E. F.; Moller, M.; Glauser, T.; Hedrick, J. L. *Angew. Chem., Int. Ed.* **2001**, *40*, 2712–2715.

(4) (a) Dove, A. P.; Pratt, R. C.; Lohmeijer, B. G. G.; Culkin, D. A.; Hagberg, E. C.; Nyce, G. W.; Waymouth, R. M.; Hedrick, J. L. *Polymer* **2006**, *47*, 4018–4025. (b) Dove, A. P.; Pratt, R. C.; Lohmeijer, B. G. G.; Li, H.; Hagberg, E. C.; Waymouth, R. M.; Hedrick, J. L. *N-Heterocyclic Carbenes in Synthesis*; Nolan, S. P., Ed.; Wiley-VCH: Weinheim, 2006; pp 275−296.

(5) (a) Dove, A. P.; Pratt, R. C.; Lohmeijer, B. G. G.; Waymouth, R. M.; Hedrick, J. L. *J. Am. Chem. Soc.* **2005**, *127*, 13798–13799. (b) Pratt, R. C.; Lohmeijer, B. G. G.; Long, D. A.; Lundberg, P. N. P.; Dove, A. P.; Li, H. B.; Wade, C. G.; Waymouth, R.; Hedrick, J. L. *Macromolecules* **2006**, *39*, 7863–7871.

(6) (a) Pratt, R. C.; Lohmeijer, B. G. G.; Long, D. A.; Waymouth, R. M.; Hedrick, J. L. *J. Am. Chem. Soc.* **2006**, *128*, 4556–4557. (b) 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) (a) Zhang, L.; Nederberg, F.; Messman, J. M.; Pratt, R. C.; Hedrick, J. L.; Wade, C. G. *J. Am. Chem. Soc.* **2007**, *129*, 12610–12611. (b) Zhang, L.; Nederberg, F.; Pratt, R. C.; Waymouth, R. M.; Hedrick, J. L.; Wade, C. G. *Macromolecules* **2007**, *40*, 4154–4158.

(8) For theoretical and experimental mechanistic studies on organocatalyzed ROP, see: (a) Lai, C.; Lee, H. M.; Hu, C. *Tetrahedron Lett.* **2005**, *46*, 6265–6270. (b) Csihony, S.; Nyce, G. W.; Sentman, A. C.; Waymouth, R. M.; Hedrick, J. L. *Polym. Prep. (Am. Chem. Soc., Div. Polym. Chem.)* **2004**, *45*, 319–320. (c) Movassaghi, M.; Schmidt, M. A. *Org. Lett.* **2005**, *7*, 2453–2456. (d) Simon, L.; Goodman, J. M. *J. Org. Chem.* **2007**, *72*, 9656–9662.

(9) *O*-Carboxyanhydrides proved activated equivalents for 2,5-dioxane-1,4-diones toward DMAP-catalyzed ROP: (a) Thillaye du Boullay, O.; Marchal, E.; Martin-Vaca, B.; Cossio, F. P.; Bourissou, D. *J. Am. Chem. Soc.* **2006**, *128*, 16442–16443. (b) Thillaye du Boullay, O.; Bonduelle, C.; Martin-Vaca, B.; Bourissou, D. *Chem. Commun.* **2008**, 1786–1788.

(10) (a) Kricheldorf, H. R.; Dunsing, R. *Makromol. Chem.* **1986**, *187*, 1611–1625. (b) Kricheldorf, H. R.; Kreiser, I. *Makromol. Chem.* **1987**, *188*, 1861–1873.

(11) (a) Shibasaki, Y.; Sanada, H.; Yokoi, M.; Sanda, F.; Endo, T. *Macromolecules* **2000**, *33*, 4316–4320. (b) Sanda, F.; Sanada, H.; Shibasaki, Y.; Endo, T. *Macromolecules* **2002**, *35*, 680–683. (c) Lou, X.; Detrembleur, C.; Jérôme, R. *Macromolecules* **2002**, *35*, 1190–1195.

(12) For the preparation of di- and triblock copolymers from poly(ethylene glycol) macroinitiators, see: Kim, M. S.; Seo, K. S.; Khang, G.; Lee, H. B. *Macromol. Rapid Commun.* **2005**, *26*, 643–648.

(13) Carboxylic acids have also been evaluated as catalysts for the ROP of ϵ-caprolactone. See ref 11b and Persson, P. V.; Schröder, J.; Wickholm, K.; Hedenström, E.; Iversen, T. *Macromolecules* **2004**, *37*, 5889–5893.

(14) Bourissou, D.; Martin-Vaca, B.; Dumitrescu, A.; Graullier, M.; Lacombe, F. *Macromolecules* **2005**, *38*, 9993–9998.

(15) (a) Basko, M.; Kubisa, P. *J. Polym. Sci., Part A: Polym. Chem.* **2006**, *44*, 7071–7081. (b) Basko, M.; Kubisa, P. *J. Polym. Sci., Part A: Polym. Chem.* **2007**, *45*, 3090–3097.

(16) For a recent discussion on the environmental benefits of MSA in the context of electrochemical processes, see: Gernon, M. D.; Wu, M.; Buszta, T.; Janney, P. *Green Chem.* **1999**, 127–140.

(17) Propylsulfonic acid immobilized on silica also proved effective for the controlled ROP of ϵ-caprolactone: Wilson, B. C.; Jones, C. W. *Macromolecules* **2004**, *37*, 9709–9714.

(18) (a) Bordwell, F. G. *Acc. Chem. Res.* **1988**, *21*, 456–463. (b) Pataï, S.; Rappoport, Z. In *The Chemistry of Sulphonic Acids, Esters and their Derivatives*; John Wiley and Sons: New York, 1991; p 251.

(19) Baker, S. C.; Kelly, D. P.; Murrell, J. C. *Nature (London)* **1991**, *350*, 627–628.

(20) Save, M.; Schappacher, M.; Soum, A. *Macromol. Chem. Phys.* **2002**, *203*, 889–899.

(21) See Supporting Information for details.

(22) The quantitative incorporation of the protic initiator in the resulting PCL was confirmed by ^{1}H NMR spectroscopy and electrospray-ionization mass spectrometry (Figures S1 and S2).[21]

MA800626Q