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Novel Direct Synthetic Approach to Thiol-Functionalized Poly(ε-caprolactone) by Highly Chemselective and Low Costly Rare Earth Phenolate Catalysts

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INTRODUCTION Thiol-functionalized biodegradable polyesters have been paid much attention for their applications in various fields including stabilizing gold or silver nanoparticles.[1,2] To the best of our knowledge, there have been several chemical strategies to prepare the polyesters with thiol functionalities,[3–5] all of which involves protecting/deprotecting procedures of thiol groups. In 2005, Martinelle et al. reported a direct route to synthesize thiol-functionalized poly(ε-caprolactone) (PCLSH) via ring-opening polymerization (ROP) by using costly enzymic catalyst of *Candida antarctica* lipase B (CALB).[6] After 24-h polymerization at 60 °C, the product ($M_{n,SEC}$ = 2.9 kDa and PDI = 1.42) contained 70% PCLSH. Recently, Li and coworkers presented ROP of CL catalyzed by $Sn(OTf)_2$ in the presence of 2-mercaptoethanol.[7] However, the fraction of thiol-terminated PCL was not addressed.

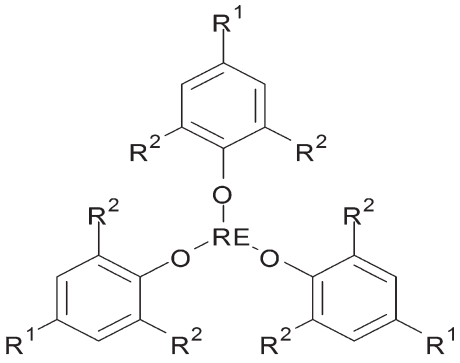
Earlier works of Feijen, Jerôme, and our group have demonstrated that low costly rare earth phenolates (REPs) and amides could catalyze living ROPs of lactones and cyclic carbonates.[8–11] In this study, we firstly report that REPs are efficient and chemselective catalysts for direct synthesis of PCLSH initiated by ω-mercapto-alcohol under mild conditions. Through this convenient synthetic approach, well-defined PCLSH polymers were obtained without tedious protecting/deprotecting steps providing a potential industrial scale application for mass manufacture of PCLSH in the benefit of relatively low cost of REP catalyst. Moreover, by using the obtained PCLSH, well-separated silver nanoparticles (SNPs) with an average size of 3 nm are prepared.

RESULTS AND DISCUSSION

A series of REPs (Scheme 1) including dysprosium, lanthanum, and yttrium tris(2,6-di-*tert*-butyl-4-methyl phenolate)s (**1a**, **1b** and **1c**), and yttrium triphenolate (**2**) can efficiently catalyze controlled ROP of CL initiated by hydroxyl end of 6-mercaptohexanol (MH) (Scheme 2). The polymerization results are listed in Table 1. The ROPs of CL are carried out at 60 °C giving yields over 90% for 3 h except the case of catalyst **2**. The molecular weights of synthesized PCLSHs vary from 4.6 to 29.9 kDa (PDI < 1.6) according to SEC analyses (Fig. S1 in the supporting information), which can be controlled by the change of feeding ratio [CL]/[I]. The fractions of PCLSHs are more than 73% for different REPs according to the ^{1}H-NMR analyses and up to 87% in the case of **1a** (Table 1, run 1). 2-Mercaptoethanol (ME) can be also used as the initiator. 77% PCLSH (Table 1, run 6) was prepared at 50 °C for 1 h ROP (its ^{1}H-NMR spectrum is shown in Fig. S2). Through control experiments using REP catalyst **1b**, it was found that little thiol groups of hexathiol (HT) initiated ROP of CL to form thiolester. When the ROP was initiated by a mixture of HT and isopropanol (*i*PrOH), all produced PCLs had *i*PrO-end group and no thiolester was detected consistent with the report of living ROP initiated by *i*PrOH with quantitative efficiency.[8] It can be concluded that REP catalyzed ROP of CL showed chemselectivity toward OH and SH.

The characteristic signals of PCL backbone (H^h, H^k, H^r, and H^t) are clearly shown in ^{1}H-NMR spectrum (Fig. 1). The methylene protons (H^b) adjacent to the free thiol group derived from MH initiator are split into a quartet. The ^{1}H-^{1}H COSY analysis (Fig. S3) provides more information about the structure. The signals of H^a, H^c, H^d, H^e, H^f, and H^g attributed to MH are overlapped by those of CL units. The coupling signal of H^a and H^b reveals that the H^a signal is overlapped by H^r of CL units (Fig. S3, area A) indicating that the produced

Additional Supporting Information may be found in the online version of this article. Correspondence to: J. Ling (E-mail: lingjun@zju.edu.cn)



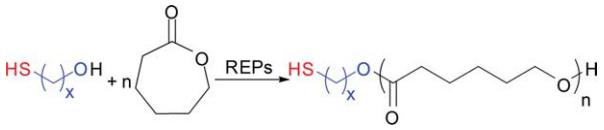
1a: RE=Dy, R^1=Me, R^2=^{t}Bu
1b: RE=La, R^1=Me, R^2=^{t}Bu
1c: RE=Y, R^1=Me, R^2=^{t}Bu
2: RE=Y, R^1=H, R^2=H

SCHEME 1 Structures of rare earth phenolates.

PCLSH contains free thiol end group. The signal of H^c is overlapped by H^k according to the coupling signal of H^c and H^b (Fig. S3, area B). Area C between H^z and H^y demonstrates that a hydroxyl group is attached to the other end of PCL. The presence of the initiator residue in PCL is further confirmed by the fully-assigned signals in ^{13}C-NMR (Fig. 2) and ^{1}H-^{13}C HMQC spectra (Fig. S4). The fractions of PCLSHs are calculated by the comparison of the integral of the peak H^b with that of H^z (see footnote of Table 1).[6] The remaining of polymers are pure PCL and no thiol ester is detected by either ^{1}H-NMR or ^{13}C-NMR.

REP shows highly chemselectivity that its phenolate ligands prefer to being exchanged with hydroxyl group rather than thiol group of MH and form rare earth alkoxides allowing CL propagation, as a coordination-insertion polymerization mechanism[8,10,12,13] and fast ligand exchange reactions are speculated.[8–10]

The stabilization of silver nanoparticles (SNPs) by PCLSH has been investigated. The produced PCLSH has been directly used as prepared without any further purification.



SCHEME 2 ω-Mercapto-alcohol (x = 2, 6) initiated ROP of ε-caprolactone catalyzed by rare earth phenolate (REP). [Color figure can be viewed in the online issue, which is available at wileyonlinelibrary.com.]

The similarity of the FTIR spectra of free PCLSH and PCLSH-modified SNPs (Fig. S5) demonstrates the presence of PCLSH as an essential component of the composite SNPs in accordance with previous reports.[14,15] The PCLSH-capped SNPs are confirmed by UV-vis analysis (Fig. S6). The characteristic plasmon absorption band of SNPs at 455 nm is observed differing from a maximum at 390 nm of the absorption of uncapped silver colloids,[16] which suggests the *S*-Ag bond formation of the nanoparticles.[15] Well-separated SNPs with an average size of 3 nm are characterized by TEM (Fig. 3) which are smaller than those encapped by $C_{12}H_{26}S$ and $C_9H_{20}S$.[14,15]

EXPERIMENTAL

ε-Caprolactone (CL) (Acros, 99%) was distilled under reduced pressure prior to use. The catalysts **1a**, **1b**, **1c**, and 2 were synthesized according to the literature.[11] MH (Aldrich, 97%), ME (Shanghai Jingchun, AR), sodium borohydride ($NaBH_4$) (Sinopharm, 96%), silver nitrate ($AgNO_3$) (Shanghai Jingxihuagong, 99.8%), tetra-*n*-octylammonium bromide [$(n$-$C_8H_{17})_4NBr$] (Alfa Aesar, 98%), and other chemicals were purchased and used without purification.

Polymerizations were carried out in previously flamed and argon-purged 20-mL ampules. As an example (Table 1, run 1), MH (24 mg, 0.18 mmol) was mixed with **1a** (0.6 mL, 0.066 mol/L) in 3 mL toluene. The reaction proceeded for 3 h after addition of CL (0.834 g, 7.32 mmol). The polymer was precipitated in cold methanol, filtrated, and dried *in vacuo* at room temperature.

TABLE 1 Ring Opening Polymerization of ε-Caprolactone by Rare Earth Phenolates in Toluene

Run	I[a]	REP	$\frac{[CL]}{[I]}$	$\frac{[I]}{[REPs]}$	T (°C)	T (h)	Yield[b] (%)	SH[c] (%)	$M_{n,\ theo}$[d] (kDa)	$M_{n,\ NMR}$[e] (kDa)	$M_{n,\ SEC}$[f] (kDa)	PDI[f]
1	MH	**1a**	42	4	60	3	90.1	87	4.4	5.9	11.0	1.52
2	MH	**1b**	41	5	60	3	91.1	84	4.4	6.6	13.4	1.57
3	MH	**1b**	96	4	60	3	94.9	73	10.5	12.4	29.9	1.50
4	MH	**1c**	47	5	60	3	90.2	80	5.0	5.0	12.6	1.53
5	MH	**2**	16	4	100	4	90.6	80	1.8	2.8	4.6	1.35
6	ME	**1c**	6	5	50	1	90.0	78	0.7[g]	0.8[h]	1.7	1.35

[a] I refers to initiator.
[b] Yield refers to isolated yield.
[c] Determined by $I(H^b)/I(H^z) \times 100\%$ according to ^{1}H NMR analysis.
[d] Calculated by $[CL]/[I] \times$ Yield $\times$ 114 + 134.
[e] Determined by $\{[I(H^{t+g}) - I(H^b)]/I(H^z) + 1\} \times 114 + 134$ according to ^{1}H NMR analysis.
[f] Determined by SEC.
[g] Calculated by $[CL]/[I] \times$ Yield $\times$ 114 + 78.
[h] $[I(H^g)/I(H^z) + 1] \times 114 + 78$ according to ^{1}H NMR analysis.

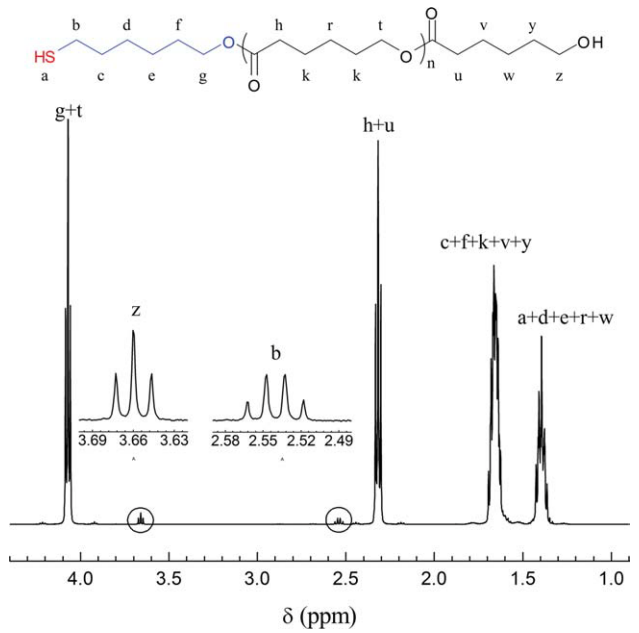


FIGURE 1 ^{1}H-NMR spectrum of PCLSH (Table 1, run 1).

The silver nanoparticle was prepared by *in situ* method. About 2 mL (0.06 mol/L) $(n\text{-}C_8H_{17})_4NBr$ in toluene was mixed with 1 mL (0.065 mol/L) aqueous solution of $AgNO_3$ under rapid stirring. Subsequently, 0.197 g PCLSH (Table 1, run 3) in 1 mL toluene was added followed by slow addition of 2.0 mL (0.29 mol/L) freshly prepared aqueous solution of $NaBH_4$. The reaction mixture was stirred for 12 h in dark. The organic phase was separated and concentrated by evaporation at room temperature and finally dissolved in 20 mL chloroform.

^{1}H-NMR, ^{13}C-NMR, ^{1}H-^{1}H COSY, and ^{1}H-^{13}C HMQC spectra were recorded on a Bruker Avance III 500 (^{1}H: 500 MHz and ^{13}C: 125 MHz) spectrometer in $CDCl_3$ with tetramethylsilane as the internal reference. SEC measurements were performed on a Waters 1515 apparatus with two PL mixed-C columns. THF was used as the eluent at 40 °C with a flow rate of 1.0 mL/min using commercial polystyrene standards for calibration. FTIR spectra were recorded on a Vector 22 FTIR spectrometer using KBr pellet. A Varian CARY 100 Bio UV-vis spectrophotometer was used for the recording of UV-vis absorption of free PCLSH and silver nanoparticles stabilized by PCLSH in chloroform. TEM were obtained from a JEM-1200 operating at 80 kV. The sample was prepared by dipping the TEM copper grid to a dilute dispersion of silver nanoparticles in $CHCl_3$ and solvent was evaporated at room temperature.

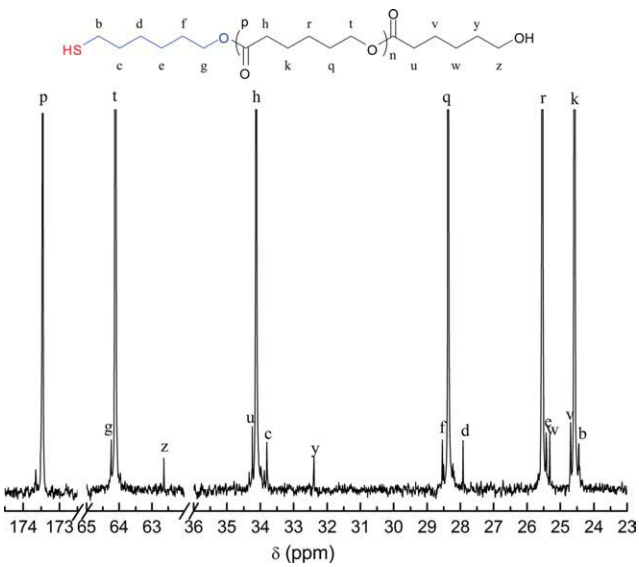


FIGURE 2 ^{13}C-NMR spectrum of PCLSH (Table 1, run 1).

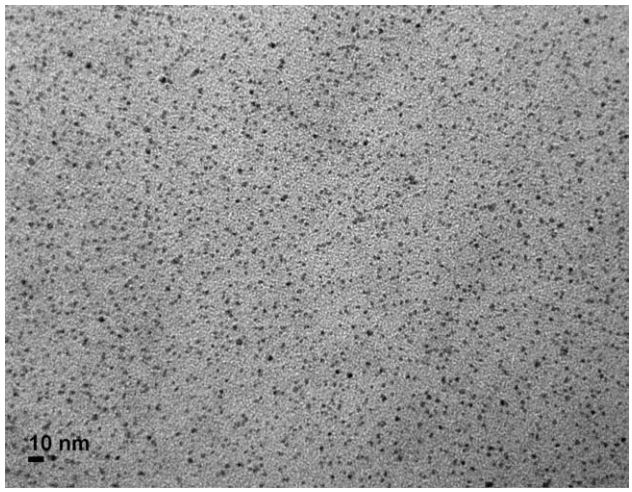


FIGURE 3 TEM images of silver nanoparticles stabilized by PCLSH (Table 1, run 3).

CONCLUSIONS

In conclusion, the feasibility of direct synthesis of thiol-functionalized PCL catalyzed by highly chemselective and low costly REP catalysts has been demonstrated in this study for the first time. The advantages of using this synthetic approach are: (1) Tedious protecting/deprotecting steps of thiol groups are no longer necessary. (2) High fractions of the well-defined PCLSH can be obtained with controlled molecular weight and moderate polydispersity indexes under mild condition. (3) The inexpensive REP catalysts provide a potential industrial scale application for mass manufacture of PCLSH. Well-separated silver nanoparticles stabilized by the obtained PCLSH are prepared with potential applications in biotechnology and material science.

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