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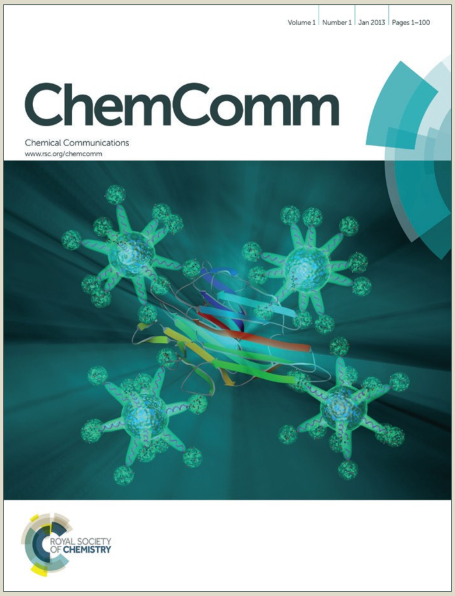

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Photoswitchable ring-opening polymerization of lactide catalyzed by azobenzene-based thiourea†

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The reactivity of catalytic polymerization system with photoresponsive azobenzene-based thiourea/PMDETA as a catalyst could be switched between slow and fast states by alternating exposure to UV and ambient light, because the active site of azobenzene thiourea is blocked via intramolecular hydrogen bonding when the azobenzene thiourea transfers from *E* isomer to *Z* isomer under UV irradiation.

In recent years, the development of switchable catalytic polymerization using external stimuli attracts much attention because this kind of progress can be controlled and give desirable polymers or block copolymers at will.[1] External stimuli, including coordination chemistry,[2] redox processes,[3] lights,[4] and so on,[5] usually induce the change in the state of the catalyst and then control the polymerization progress. In the past several years, some excellent works on redox-controlled switchable polymerization of lactide were reported. For example, Diaconescu and co-workers reported the activity of several group 4 metal alkoxide complexes supported by ferrocene-based ligands can be controlled using redox reagents during the ring-opening polymerization of *L*-lactide and *ε*-caprolactone.[6] Byers and co-workers reported redox-controlled polymerization of lactide catalyzed by bis(imino)pyridine iron bis(alkoxide) complexes, because bis(imino)pyridine iron bis(alkoxide) complex could be "switched" on and off by reversibly reducing and oxidizing the metal center.[7] Furthermore, they applied this redox switchable iron-based catalyst to synthesize block copolymerization of lactide and various epoxides because epoxide polymerization could be "switched off" upon in situ reduction of the iron(III) catalyst and "switched on" upon in situ oxidation, which is orthogonal to what was observed for lactide polymerization.[8] Compared with the redox control, light was more ideal stimulus because it is non-invasive, chromophore-selective, and provides excellent temporal control.[9] Photochemical switches for photo-initiating polymerization processes and mediating small-molecule organic transformations have been commonly used in recent years.[1,9,10] However, photoswitchable catalytic ROP (ring-opening polymerization) of lactones were very rare. For example, a photoswitchable ROP of *ε*-caprolactone and *δ*-valerolactone using dithienylethene-annulated N-heterocyclic carbene catalyst was reported by Bielawski and a visible light regulated ROP using a photoacid as organocatalyst was developed by Xu and Boyer,[11] and no photoswitchable ROP of lactide has been explored until now.

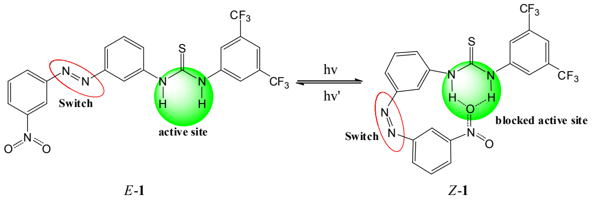

Chart 1 Photoswitchable azobenzene-based thiourea compound **1**.

Poly (lactic acid) (PLA) is a biocompatible and biodegradable polymer and has been widely applied in packaging, agricultural materials, drug delivery, and medical devices.[12] Although the ring-opening polymerization catalyzed by metal complexes was an effective method for the synthesis of polylactide,[13] the organocatalytic ring-opening polymerization of lactide also attracted much attention because of it is more economical, environmentally friendly, and it is not needed to removal metals.[14] Among them, thiourea(TU)/amine base for the ROP of lactide seems to be a good system because of convenient synthesis, high activity, and excellent controllability, and the general mechanism for the H-bonding catalysis in the ROP of lactide have been proposed: the initiating or propagating alcohol and the carbonyl group of lactide were activated by a H-bond acceptor (amine) and a donor (thiourea), respectively.[15] For example, Kiesewetter recently reported a series of excellent works in this area.[16] Herein a

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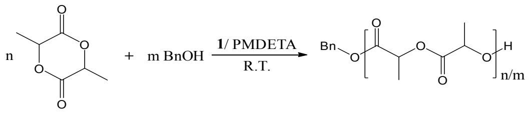
photoresponsive azobenzene-based thiourea catalyst **1** was synthesized and applied in the photoswitchable ROP of *rac*-lactide.

Azobenzene-based thiourea compound **1** was synthesized according to a reported procedure (Chart 1).[17] Compound **1** has *Z* and *E* isomers, which can be mutually transformed easily by appropriate light irradiation. The *E* isomer of compound **1** has an open active site of thiourea group for the coordination of lactide via hydrogen bond interactions (Chart 1). While the thiourea group in *Z* isomer can be blocked by a formation of intramolecular hydrogen bonds with the nitro group. Consequently compound **1** as a catalyst will be deactivated.

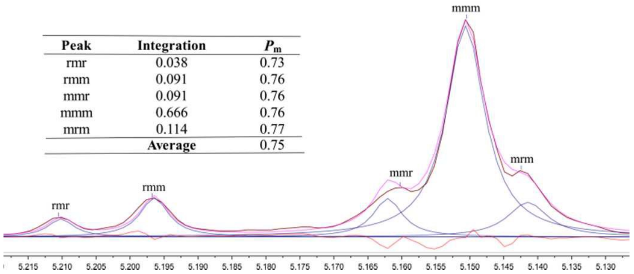
Table 1: Polymerization of lactide catalyzed by **1**/PMDETA[a]



entry	catalyst	monomer	$[LA]_0/[I]_0$	conv.(%)[b]	t (h)	$M_{n,calc}$[c]	$M_{n,obsd}$[d]	PDI	P_m[e]
1	**1**	*L*-LA	50:1	95	24	6900	6200	1.04	1
2	**1**	*L*-LA	100:1	94	48	13600	11000	1.03	1
3	**1**	*L*-LA	150:1	95	72	20600	15100	1.05	1
4	**1**	*L*-LA	200:1	90	120	26000	19000	1.04	1
5	**1**	*rac*-LA	50:1	94	24	6900	6400	1.04	0.75
6	**1**	*rac*-LA	100:1	95	48	13800	10300	1.03	0.74
7	**1**	*rac*-LA	150:1	94	72	20400	14700	1.03	0.73
8	**1**	*rac*-LA	200:1	91	120	26300	18500	1.05	0.74

[a] Conditions (unless special instructions): $[LA]_0$ = 1 M, [**1**] = [PMDETA] = 0.02 M; in $CDCl_3$. [b] Lactide conversion determined by ^1H NMR. [c] g/mol, these values were calculated from $[M_{lactide} \times [LA]_0/[BnOH]_0 \times$ conversion yield $+ M_{BnOH}]$ [d] g/mol, these values were obtained from GPC analysis and calibrated by polystyrene standard and corrected using the Mark-Houwink factor of 0.58.[19] [e] Determined by analysis of all of the tetrad signals in the methine region of the homonuclear-decoupled ^1H NMR spectra.[18]

Based on this hypothesis, the ROP reactions of *L*-LA and *rac*-LA using compound **1** as a catalyst together with N,N,N',N'',N''-pentamethyldiethylenetriamine (PMDETA) as a co-catalyst were tested (Table 1). When a 50:1:1:1 ratio of $[L\text{-}LA]_0/[\mathbf{1}]_0/[PMDETA]_0/[BnOH]_0$ was used with a catalyst concentration of 0.02 M at room temperature (entry 1, Table 1), the polymerization of *L*-LA within 24 h almost be finished, affording a polymer with an expected molecular weight and low polydispersity (PDI). The linear relationships between the molecular weights of the polymers and the monomer-to-initiator ratio indicate the polymerization remains controllable and exhibits characteristics of a "living" polymerization (entries 1-4, Table 1 and Fig. S2). In the **1**/PMDETA catalyzed ROP of *rac*-LA (entries 5-8, Table 1), the azobenzene-based thiourea catalyst shows modest iso-slectivities of P_m = 0.73-0.75 under controllable conditions with a living character at room temperature. The microstructure analysis of a polymer (P_m = 0.75, Fig. 1) via homonuclear decoupled ^1H NMR spectroscopy indicates that the isoselective mechanism for the ROP of *rac*-LA was the chain-end control mechanism because the tetrad probabilities agree well with the Bernoullian statistics.[18]



Peak	Integration	P_m
rmr	0.038	0.73
rmm	0.091	0.76
mmr	0.091	0.76
mmm	0.666	0.76
mrm	0.114	0.77
	Average	0.75

Fig. 1 Homonuclear-decoupled ^1H NMR spectrum of PLA (entry 5, Table 1).

In order to study the effect of irradiation for the rate and isoselectivity of the ROP of *rac*-Lactide, we firstly quantify their photostationary states (PSS) via ^1H NMR. The ratio of *E*-isomer and *Z*-isomer of compound **1** with a concentration of 20 mM in $CDCl_3$ is more than 99/1. After irradiation with UV light (λ = 330-400 nm, λ_{max} = 365 nm) for 3 h, 34% *Z*-**1** isomer was obtained (Fig. S4). Considering *Z*-isomer of compound **1** may be inactive in the ROP of lactide due to the intramolecular hydrogen bonding interactions between thiourea group and one O-atom of nitro group (Chart 1), so the rate of polymerization could be switched by UV/ambient irradiation through the process of *E*-*Z*/*Z*-*E* isomerization. For the polymerization of *rac*-lactide with a 50:1:1:1 ratio of $[rac\text{-}LA]_0/[\mathbf{1}]_0/[PMDETA]_0/[BnOH]_0$ in ambient light, the conversion of reaction reached to 94 % after 24 h. However, only 30 % lactide can be converted for the same reaction under ultraviolet irradiation (Fig. 3a). The vast difference between the reaction rates ($k_{amb} = 2.08\times10^{-3}$ min^{-1} in ambient light *vs* $k_{UV} = 2.08\times10^{-4}$ min^{-1} in UV light, Figure S5, k_{amb}/k_{uv} = 10) shows the light has a great influence on the activity of compound **1** indicating the formation of *Z*-isomer will decrease the whole reaction rate. What is more, the isotaticities of polymers at different conversions in this progress keep similar (P_m = 0.72-0.76, Fig. 2) and are almost same to the reaction in ambient light. Because *Z*-isomer and *E*-isomer should have different isoselectivies unless by chance, this same isoselectivities should result from *E*-isomer which may suggest the *Z*-isomer of compound **1** is non-active for the ROP of lactide.

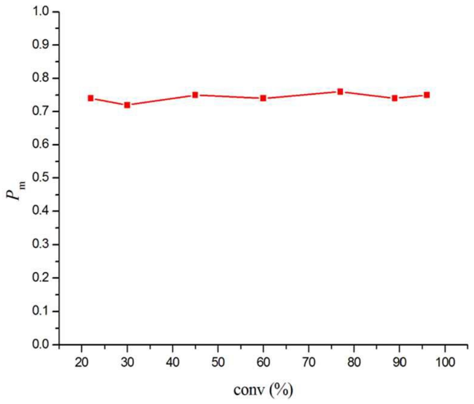


Fig. 2 Plot of P_m of final polymer vs conversion (%) for the ring opening polymerization of lactide catalyzed by **1** ($[rac\text{-}LA]_0/[\mathbf{1}]_0/[PMDETA]_0/[BnOH]_0$ = 50:1:1:1, $[rac\text{-}LA]$ = 1 M).

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Furthermore, compound **1** as a catalyst could be switched from "OFF" state to "ON" state within the course of the polymerization by stopping UV irradiation. After 6 h in the UV light, the rate of polymerization was increased by alternating UV to ambient light compared with the whole reaction in UV light (conversion: 33 % vs 45 % after 28 h, Fig. 3b). On contrast, the reaction rate was decreased when UV irradiation was applied for the reaction in the ambient light after 6 h (conversion: 91 % vs 75 % after 24 h, Fig. 3c). In fact, the difference of activity for "switched off" and "switched on" of this catalyst was not remarkable, which can be ascribed to that the process of *E-Z*/*Z-E* isomerization was not instantaneous and thorough.

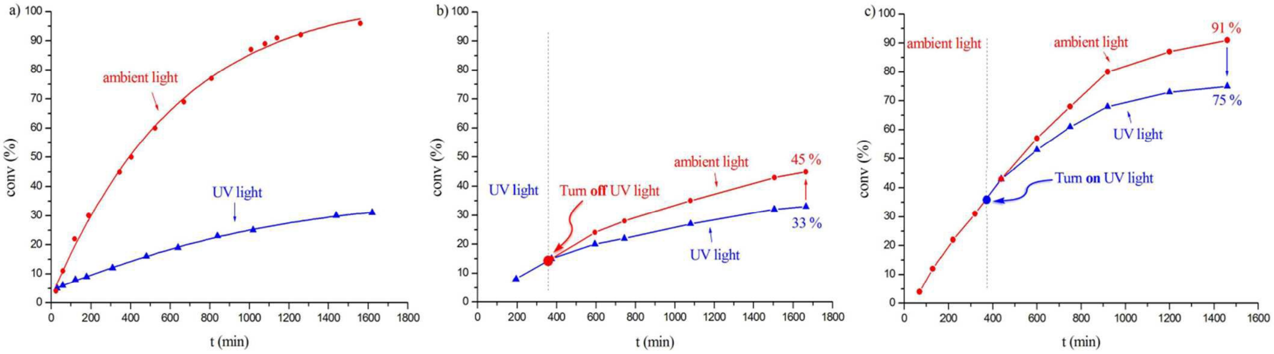

Fig. 3 (a) ROP of *rac*-lactide by **1** in the UV light (blue line) and ambient light (red line); (b) the reaction vessel was exposed to UV light 6 h and then was kept in ambient light (red line); (c) the reaction vessel was exposed to ambient light 6 h and then was kept in UV light (blue line).

In conclusion, an azobenzene-based thiourea compound **1** as a catalyst was successfully used in the ring-opening polymerization of *rac*-lactide giving isotactic enriched polymer with desirable molecular weights and narrow molecular weight distributions. In particularly, the reactivity of this catalytic polymerization system with photoresponsive azobenzene-based thiourea/PMDETA could be switched between slow and fast states by alternating exposure to UV and ambient light.

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