Facile Synthesis of Fluorescent Dye Labeled Biocompatible Polymers via Immortal Ring-Opening Polymerization

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General Methods. All reactions were carried out under a dry and oxygen-free argon atmosphere by using Schlenk techniques or under a nitrogen atmosphere in an MBraun glovebox. Solvents were purified by an MBraun SPS system. Ligands were synthesized according to modified literature procedures.¹ The phenols and amines were purchased from Aldrich or Fluka. All liquids were dried over 4 Å molecular sieves for a week and distilled before use, and solid materials were used without purification. The synthesis of Salan lutetium complex 1 and Salen aluminium complex 2 followed the established method.² D,L-Lactide (Aldrich) was recrystallized three times with dry ethylacetate. Fluorescent dye **A** was synthesized according the literature³ and dried over anhydrous magnesium sulfate in THF prior to using for polymerization.

Instruments and Measurements. Organometallic samples for NMR spectroscopic measurements were prepared in a glove box by use of NMR tubes and then sealed by paraffin film. ¹H, ¹³C NMR spectra were recorded on a Bruker AV400 (FT, 400 MHz for ¹H; 100 MHz for ¹³C) spectrometer. NMR assignments were confirmed by ¹H-¹H (COSY), ¹H-¹³C (HMQC), and ¹³C NMR (DEPT) experiments when necessary. Polymer characterizations were carried out at 25 °C using a Waters 515 GPC system. The system included a Styragel HMW6E column, a 515 HPLC pump, an IR OPTILAB DSP detector, and a DAWN EOS multiangle laser-light scattering (MALLS) detector (Wyatt Technology). The eluent was THF at a flow rate of 0.35 mL min⁻¹.

Experiments

Synthesis of fluorescent dye A. Rhodamine 6G (5.0 g, 10.4 mmol) was dissolved in 100 mL acetonitrile. To this deep red solution was added monoethanolamine (1.9g, 31.3 mmol). The reaction mixture became gradually heterogeneous and lost color. After refluxing of 1 h, most of the solvent was evaporated under reduced pressure to obtain a concentrated solution and the mixture was filtered. The solid was washed thoroughly with water and dried under vacuum till a constant weight to give 4.1 g off-white product A (86 %). ¹H NMR (300 MHz, CDCl3) $\delta_{\rm H}$ 7.93 (1H, m, C₆H₄), 7.46 (2H, m, C₆H₄), 7.03 (1H, m, C₆H₄), 6.35 (2H, s, C₆H₂), 6.28 (2H, s, C₆H₂), 4.22 (1H, t, *J*_{HH} = 5.7 Hz, NCH₂CH₂OH), 3.53 (2H, s, CH₃CH₂NH), 3.43(2H, m, NCH₂CH₂OH), 3.23 (6H, m, NCH₂CH₂OH+ CH₃CH₂NH), 1.92 (6H, s, ArCH₃), 1.32 (6H, t, *J*_{HH} = 7.1 Hz, CH₃CH₂NH).



Scheme S1 Synthesis of fluorescent dye A



Figure S1. ¹H NMR spectrum of fluorescent dye A (300 MHz, CDCl₃, 25 °C).

Synthesis of Complex 3. To a THF (2.5ml) solution of complex **1** (0.2g, 0.23 mmol) was dropwise added equivalent fluorescent dye **A** (0.11g, 0.23 mmol, in 2.5ml of THF) slowly. The reaction mixture was stirred at 25 °C for 10 minutes, and then volatiles were then removed *in vacuo* to give complex **3** in a quantitative yield (0.26g). ¹H NMR (300 MHz, CDCl₃, 25 °C) $\delta_{\rm H}$ 7.82 (0.5 H, d, $J_{\rm HH}$ = 7.4, C₆H₄), 7.51–7.28 (2 H, m, C₆H₄), 7.16 (2 H, d, $J_{\rm HH}$ = 3, C₆H₂), 7.07 (0.5 H, d, $J_{\rm HH}$ = 7.4, C₆H₄), 7.02(1 H, m), 6.93 (2 H, d, $J_{\rm HH}$ = 3, C₆H₂), 6.37 (1 H, s, C₆H₄), 6.34 (2 H, s, C₆H₄), 6.08 (1 H, s, C₆H₄), 4.40 (1 H, d, $J_{\rm HH}$ = 12.4, CH₃CH₂N*H*), 4.24 (1 H, brs, N(CH₂)₂N), 3.92 (1 H, d, $J_{\rm HH}$ = 12.4, CH₃CH₂N*H*), 3.75 (2 H, brs, NCH₂CH₂O), 3.64–3.45 (4 H, m, ArCH₂N), 3.35 (2 H, brs, NCH₂CH₂O), 3.22 (4 H, m, CH₃CH₂NH), 2.62 (2 H, brs, N(CH₂)₂N), 2.51 (1 H, brs, N(CH₂)₂N), 1.98–1.86 (12 H, m, N(CH₃)₂+ArCH₃), 1.36 (9 H, s, ArC(CH₃)₃), 1.35–1.31 (6 H, m, CH₃CH₂NH) 1.28 (9 H, s, ArC(CH₃)₃), 1.27 (9 H, s, ArC(CH₃)₃), 1.14 (9 H, s, ArC(CH₃)₃).

Synthesis of Complex 4. To a THF (2.5ml) solution of complex 2 (0.2g, 0.35 mmol) was dropwise added equivalent fluorescent dye A (0.16g, 0.35 mmol, in 2.5ml of THF) slowly. The reaction mixture was stirred at 25 °C for 120 minutes, and then volatiles were then removed *in vacuo* to give complex 4 in a quantitative yield (0.35g). ¹H NMR (300 MHz, CDCl₃, 25 °C) $\delta_{\rm H}$ 8.07 (2 H, s, NCH), 7.79 (1 H, m, C₆H₄), 7.41 (2 H, d, *J*=2.3, C₆H₂), 7.32 (2 H, m, C₆H₄), 7.00 (2 H, d, *J* 2.3, C₆H₂), 6.95 (1 H, m, C₆H₄), 6.23 (2 H, s, C₆H₂), 6.06 (2 H, s, C₆H₂), 3.60 (1 H, s, CH₃CH₂N*H*), 3.56 (1 H, s, CH₃CH₂N*H*), 3.40 (1 H, t, *J*=5.0, OCH₂CH₂N), 3.22–3.13 (6 H, m, OCH₂CH₂N + CH₃CH₂NH), 3.04 (4 H, s, CH₂(CH₃)₂CCH₂), 1.77 (6 H, s, ArCH₃), 1.43–1.22 (42 H, m, ArC(CH₃)₃ + CH₃CH₂NH), 1.16 (3 H, s, CH₂(CH₃)₂CCH₂), 0.99 (3 H, s, CH₂(CH₃)₂CCH₂).



Figure S2.¹H NMR spectrum of complex **4** at 25°C (300 MHz, CDCl₃).

Typical Polymerization of *rac*-lactide in the presence of fluorescent dye A. A typical procedure for polymerization of *rac*-LA in the presence of fluorescent dye A was performed in a 25 mL round flask under an N₂ atmosphere. To a vigorously stirred solution of complex 1 in 3 mL of THF was added fluorescent dye A in 2 ml of THF. After 10 minutes, *rac*-LA was added quickly. The polymerization took place immediately at room temperature. After a specified polymerization time, an aliquot was withdrawn and quenched quickly with 1.0 mL of HCl/CH3OH/CHCl3 (0.1/10/60 v/v) solution, and then 1.0 mL of THF was added to obtain a clear solution. Several drops of the quenched solution was taken, removed volatiles and subjected to monomer conversion determination which was monitored by integration of monomer vs polymer methane or methyl resonances in ¹HNMR (CDCl₃). The residue solution was quenched by an excess amount of ethanol, filtered, washed with ethanol, and then dried at 40°C for 24 h *in vacuo* to give polymer product. The molecular weight and the molecular weight distribution of the resulting polymer were determined by GPC. The tacticity of the PLA was calculated according to the methine region homonuclear decoupling ¹H NMR spectrum.

Fluorescent behaviors study of dye A and dye A-labeled PLA. The fluorescent behaviors of study of dye A and dye A-labeled PLA were investigated. It is observed that both of their fluorescence were pH-dependant and acid condition was favorable. In a typical procedure, dye **A** or dye **A**-labeled PLA was dissolved in THF (10^{-6} mol/L). A 2 mL aliquot was removed after measuring the pH using a calibrated pH meter. The pH was then slowly decreased to 2.0 using HCl concentrations of 0.001 M. A PC-controlled Fluoromax-4 spectrofluorimeter (Horiba Jobin Yvon Inc., France) was used for obtaining fluorescence spectra under the following conditions: excitation wavelength (467 nm for dye A and 514nm for dye **A**-labeled PLA), emission scans from 500 to 700 nm at 240 nm/min, an excitation slit width of 5 nm and an emission slit width of 5 nm.



Figure S3. ¹H NMR spectrum of complex **1** at 25°C (300 MHz, Tol-*d*₈).



Figure S4. ¹H NMR spectrum of complex 2 at 25°C (300 MHz, CDCl₃).



Figure S5. ¹H-¹H COSY (400 MHz, CDCl₃, 25°C) spectrum of fluorescent dye-labeled oligomer of PLA. (*: LA). Conditions: $[LA]_0 = 0.69M$, $[LA]_0:[Lu]_0:[A]_0 = 20:1:1$, THF, 97% conversion, $T_p = 25$ °C.



Figure S6. Fluorescence behaviors study of Dye **A** and Dye **A**–labeled PLA ((a) Excitation spectra of dye **A** and dye **A**-labeled PLA. (b) Emission spectra of dye **A** and dye **A**-labeled PLA.)



Figure S7. Coordination-insertion mechanism for lactide ROP initiated by dye-labeled rare-earth metal catalyst (**A**O-[Lu]).

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