Highly controlled immortal polymerization of β-butyrolactone by a dinuclear indium catalyst

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Contents

A. Experimental section

General Considerations. All the air and moisture sensitive operations were done in an MBraun glove box or using a standard Schlenk line. A Bruker Avance 300 MHz or 400 MHz spectrometer was used to record spectra. For determination of polymer tacticity, a Bruker Avance 600 MHz spectrometer was used to run inverse gated ^{13}C{^{1}H} spectra for poly(hydroxybutyrate). ^{1}H NMR chemical shifts are given in ppm versus residual protons in deuterated solvents as follows: δ 7.27 $CDCl_3$, δ 5.34 CD_2Cl_2, δ 3.58 THF-d_8 (O-CH_2), δ 1.94 CD_3CN. ^{13}C NMR chemical shifts are given in ppm versus residual ^{13}C in solvents as follows: δ 77.23 $CDCl_3$. Molecular weights and polydispersity indices were

determined by triple detection gel permeation chromatography using a Waters liquid chromatograph equipped with a Waters 515 HPLC pump, a Waters 717 plus autosampler, Waters Styragel columns (4.6 × 300 mm) HR5E, HR4 and HR2, a Waters 2410 differential refractometer, a Wyatt tristar miniDAWN laser light scattering detector and a Wyatt ViscoStar viscometer. A flow rate of 0.5 mL/min was used and samples were dissolved in THF (*ca.* 2 mg/mL). The measurements were carried out at laser wavelength of 690 nm, at 25 °C. The data were processed using the Astra software provided by Wyatt Technology Corp with a polystyrene standard calibration curve via the Mark–Houwink equation in THF at 25 °C ($[\eta] = KM^a$ while [η] = intrinsic viscosity, M = molecular weight, and K and a are Mark–Houwink parameters, $K = 1.832 \times 10^{-4}$ dl/g and $a = 0.69$. The dn/dc values for poly(hydroxybutyrate) used for GPC were 0.044 mL/g and 0.067 mL/g, respectively. The dn/dc value used for mPEG-*co*-PHB was 0.063 mL/g.

The temperatures of the NMR monitoring experiments were calibrated using the reagents and formulae in Table S1.

Table S1. Formulae for calibrating temperatures

Standard	Temperature	Formula
4% MeOH in MeOH-d_4	270–300 K	$(4.109-\Delta\delta)/0.008708$[a]
80% Ethylene Glycol in DMSO-d_6	300–400 K	$(4.218-\Delta\delta)/0.009132$[b]

[a]Δδ is the shift difference (ppm) between C*H*$_3$ and O*H* peaks of MeOH. [b]Δδ is the shift difference (ppm) between C*H*$_2$ and O*H* peaks of ethylene glycol.

Materials. Toluene and THF were taken from an IT Inc. solvent purification system with activated alumina columns and degassed before use. CH_2Cl_2 and CH_3CN were refluxed with CaH_2 and distilled under N_2 and degassed before use. Ethanol, methanol, $CDCl_3$, CD_2Cl_2 and CD_3CN were dried over CaH_2, transferred under vacuum and degassed by several freeze-pump-thaw cycles before use. THF-d_8 was dried over Na/benzophenone, transferred under vacuum and degassed through several freeze-pump-thaw cycles before use. Poly(ethylene glycol) monomethyl ether (mPEG) (molecular weights 350 g/mol) was purchased from Sigma-Aldrich and dried by adding dry toluene and pumping down to dryness for 2 cycles. β-Butyrolactone, purchased from Aldrich, was stirred in CaH_2 for

48 hours, collected by vacuum distillation, degassed by three freeze-pump-thaw cycles and kept in the freezer at −30 °C. The internal standard for *in situ* NMR spectroscopic studies, 1,3,5-trimethoxybenzene (TMB), was purchased from Sigma-Aldrich and used without any further purification. The catalyst $[(NNO)InCl]_2(\mu\text{-}OEt)(\mu\text{-}Cl)$ (**1**) was prepared by previously published procedures.[1]

NMR scale polymerization of BBL with 1. A teflon sealed NMR tube was calibrated to have a 1.00 mL mark with CD_3CN by a 1.00 mL syringe. Complex **1** (5.0 mg, 0.0045 mmol) and an internal standard 1,3,5-trimethoxybenzene (5.0 mg, 0.0030 mmol) were dissolved in CD_3CN and transferred to the tube. Then BBL (74.1 μL, 0.909 mmol) was added to the tube. CD_3CN was added until the total volume of the solution reached 1.00 mL. The reaction mixture was immediately cooled in liquid nitrogen. On a NMR spectrometer, the target temperature was set at 60 °C. 80% Ethylene glycol in $(CD_3)_2SO$ was used to calibrate the temperature of the spectrometer prior to a sample loading. The solution thawed, mixed and warmed up to room temperature before the NMR tube was inserted into the NMR spectrometer set at 60 °C. The polymerization was monitored by ^1H NMR spectroscopy to over 90% conversion.

Large-scale polymerization of BBL with 1. In a 20 mL scintillation vial, 5.0 mg (0.0045 mmol) of **1** was dissolved in 1.00 mL THF. BBL (74.1 μL, 0.909 mmol) was slowly added to the stirring solution of **1**. The reaction mixture was stirred for 16 h and then quenched with an HCl solution (0.5 mL of 1.5 M HCl in Et_2O). The resulting clear solution was concentrated to dryness. A sample of the residue was dissolved in $CDCl_3$ to be analyzed by ^1H NMR spectroscopy to determine conversion. The residue was dissolved in a minimum amount of CH_2Cl_2 (~ 0.5 mL). Cold methanol (0 °C) was added to the solution. The polymer precipitated, and the supernatant was decanted off. The polymer was then washed with cold methanol (1 × 3 mL) and dried under vacuum overnight.

Large-scale immortal polymerization of BBL with 1 in the presence of ethanol. A 20 mL scintillation vial was charged with a 0.90 mL stock solution of **1** and an internal

standard in THF (**1**, 0.00305 M, 0.00275 mmol; TMB, 0.0346 M, 0.0311 mmol). A 32.1 μL stock solution of ethanol in THF (0.171 M, 0.00550 mmol) using a micro syringe was added to the stirring catalyst solution. Subsequently, BBL (224 μL, 2.75 mmol) using a micro syringe was slowly added to the stirring solution. The reaction mixture was stirred overnight and then quenched with an HCl solution (0.5 mL of 1.5 M HCl in Et_2O). The resulting clear solution was concentrated to dryness. A sample of the residue was dissolved in $CDCl_3$ to be analyzed by ^1H NMR spectroscopy to determine conversion. The residue was dissolved in a minimum amount of CH_2Cl_2 (~ 0.5 mL). Cold methanol (0 °C) was added to the solution and the polymer precipitated. The solution was quickly immersed in liquid nitrogen for a few seconds to harden the polymer. Then, the supernatant was decanted off. The resulting polymer was then washed with cold methanol (1 × 3 mL) and dried under vacuum overnight.

Large-scale immortal polymerization of BBL with 1 in the presence of mPEG. A 20 mL scintillation vial vas charged with a 0.90 mL stock solution of **1** and TMB in THF (**1**, 0.00304 M, 0.00273 mmol; TMB, 0.0357 M, 0.0321 mmol). A 43.9 μL stock solution of mPEG in THF (0.0622 M, 0.0027 mmol) using a micro syringe was added to the stirring catalyst solution. Subsequently, BBL (223 μL, 2.73 mmol) using a micro syringe was slowly added in to the stirring solution. The reaction mixture was stirred overnight and then quenched with an acidic solution (0.5 mL of 1.5 M HCl in Et_2O). The resulting clear solution was concentrated to dryness. A sample of the residue was dissolved in $CDCl_3$ to be analyzed by ^1H NMR spectroscopy to determine conversion. The residue was dissolved in a minimum amount of CH_2Cl_2 (~ 0.5 mL). Cold methanol (0 °C) was added to the solution and the polymer precipitated. The solution was quickly immersed in liquid nitrogen for a few seconds to harden the polymer. Then, the supernatant was decanted off. The resulting polymer was then washed with cold methanol (1 × 3 mL) and dried under vacuum overnight.

Procedure for *in situ* reactivity of 1 with 2 and 10 equivalents of ethanol. ^1H NMR spectroscopy (400 MHz NMR spectrometer, $CDCl_3$ at room temperature) was used to monitor the reactivity of **1** with ethanol. Representative sample preparation with **1** was

described with 2 equivalents of ethanol. In a glovebox, a 0.25 mL stock solution of **1** in $CDCl_3$ (0.25 mL, 0.0023 M) was loaded to a teflon-sealed NMR tube and made up to 0.9 mL with a 0.65 mL solution of $CDCl_3$, and the solution was mixed and frozen in the glovebox using a liquid N_2 cold wall (–90 °C). A 0.1 mL stock solution of ethanol in $CDCl_3$ (0.1 mL, 0.0045 M) was added to the frozen solution of **1** and frozen again, forming a bilayer. The NMR tube was sealed and quickly evacuated by vacuum to remove N_2 gas from the NMR tube. Two solutions were thawed and quickly mixed before the NMR tube was loaded into the NMR spectrometer.

Procedure for reactivity of 1 with neat methanol. A 20 mL scintillation vial was charged with **1** (5.0 mg, 0.0045 mmol), and an approximately 5 mL methanol was added to the vial. The mixture was stirred for 16 hours at room temperature. The solvent was removed under vacuum to dryness. The resulting white solid was washed with hexane and further dried *in vacuo* for a few hours. The resulting product was analyzed by ^1H NMR spectroscopy (400 MHz NMR spectrometer, $CDCl_3$ at room temperature).

B. Solvent effects

a) Large-scale polymerization of BBL with 1

Table S2. Solvent dependence of BBL polymerization by complex **1**.

Entry	Solvent	Temp (°C)[a]	Time (h)	Conv. (%)[b]
1	Toluene	25	8.4	89
2	Toluene	60	4.0	> 99
3	CH_2Cl_2	25	8.5	98
4	CH_2Cl_2	60	0.8	> 99
5	CH_3CN	25	8.5	98
6	CH_3CN	60	0.5	98
7	THF	25	1.0	97

[a]The temperature indicated was the oil bath temperature. [b]Determined by ^{1}H NMR spectroscopy (400 MHz, $CDCl_3$, 25 °C).

b) *In situ* studies of the polymerization of BBL with 1 in different solvents

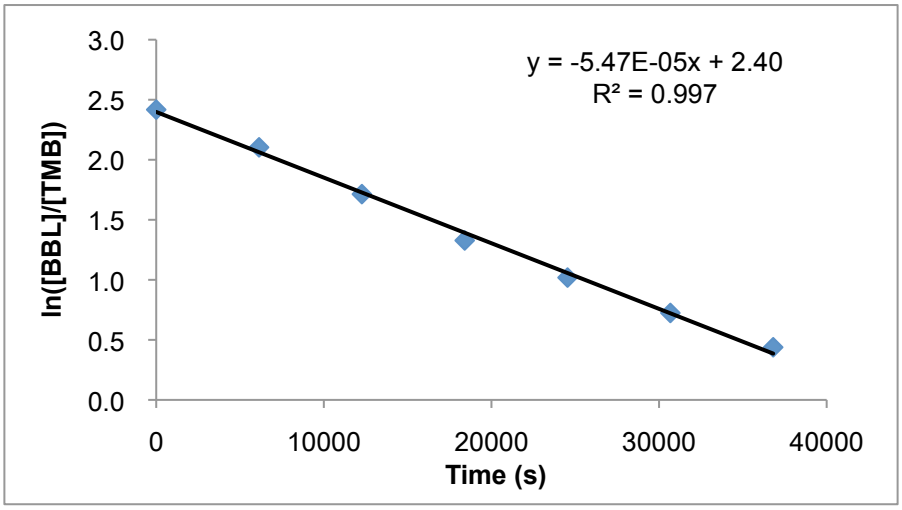

Figure S1. Plot of ln[BBL] vs time for polymerization of BBL in CD_3CN (400 MHz, 25 °C). [**1**] = 0.0045 M, [BBL]/[**1**] = 200.

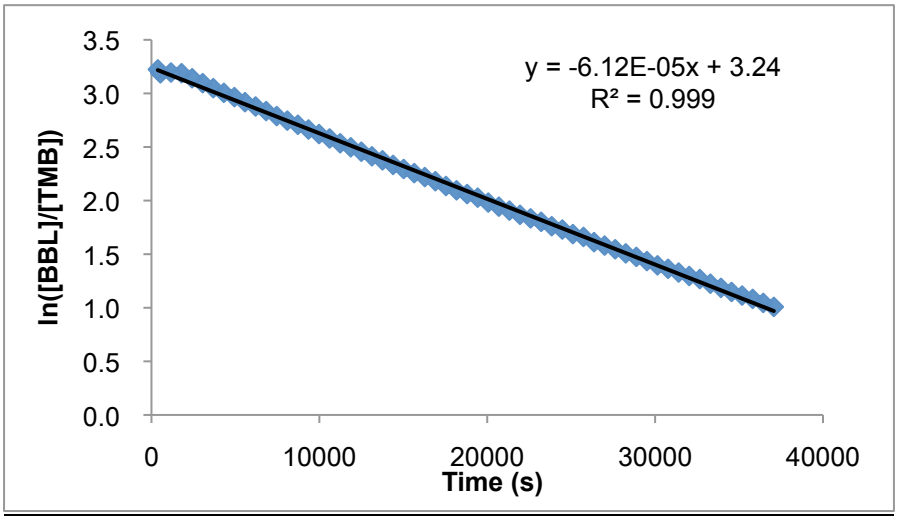

Figure S2. Plot of ln[BBL] vs time for polymerization of BBL in CD_2Cl_2 (400 MHz, 25 °C). [**1**] = 0.0045 M, [BBL]/[**1**] = 200.

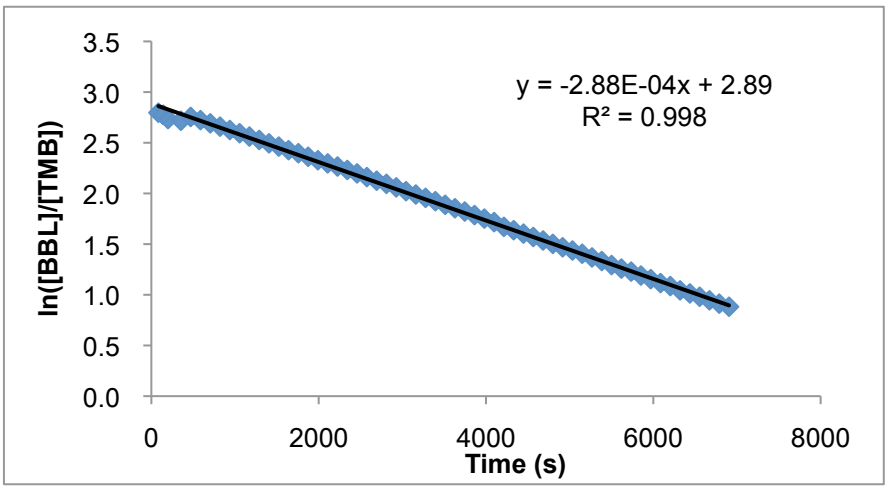

Figure S3. Plot of ln[BBL] vs time for polymerization of BBL in THF-d_8 (400 MHz, 25 °C). [**1**] = 0.0045 M, [BBL]/[**1**] = 200.

C. *In situ* studies of polymerization of BBL with variable concentrations of 1

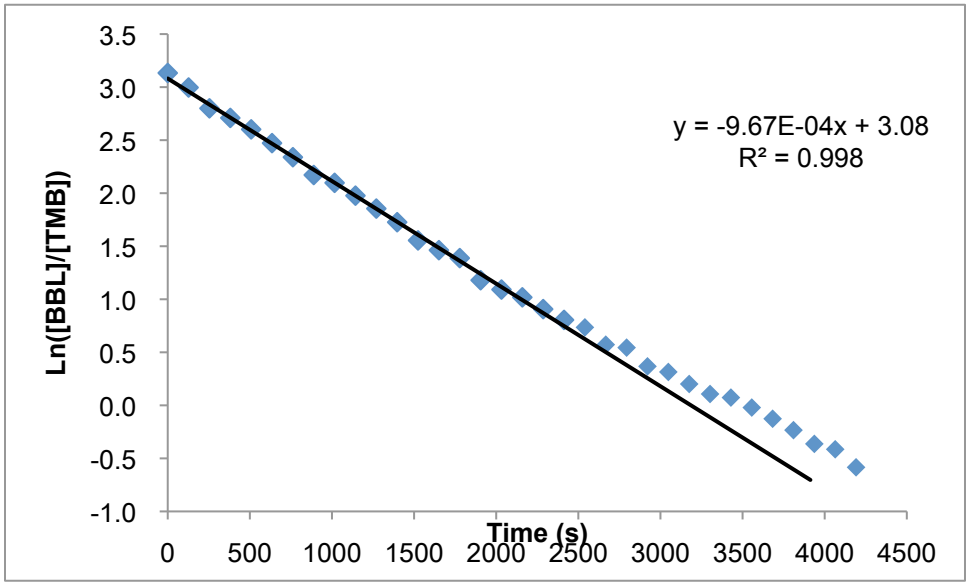

Figure S4. Plot of ln[BBL] vs time for polymerization of BBL in CD_3CN (400 MHz, 60.6 °C). [**1**] = 0.0045 M, [BBL]/[**1**] = 200. (Linear regression used only early part of plot)

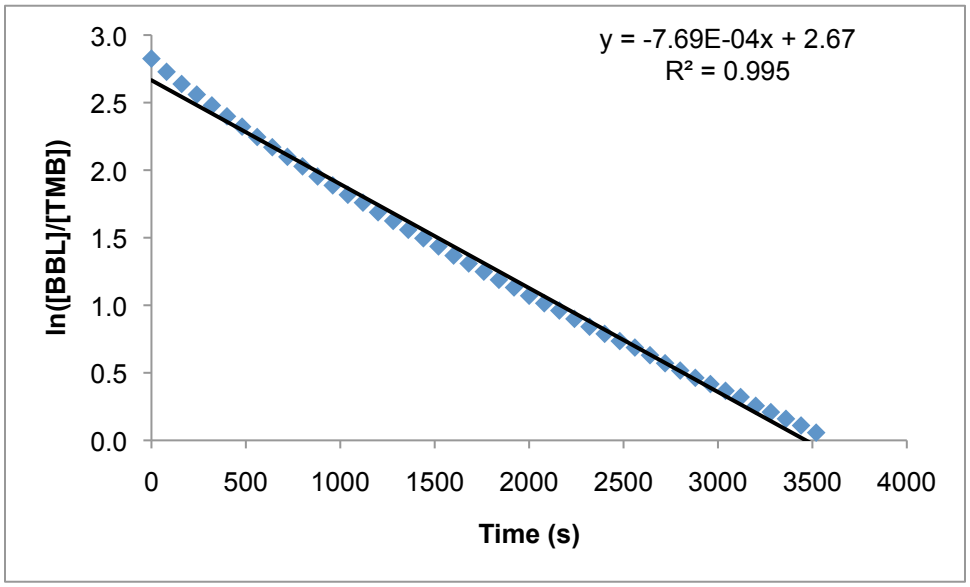

Figure S5. Plot of ln[BBL] vs time for polymerization of BBL in CD_3CN (400 MHz, 60.6 °C). [**1**] = 0.0037 M, [BBL]/[**1**] = 200.

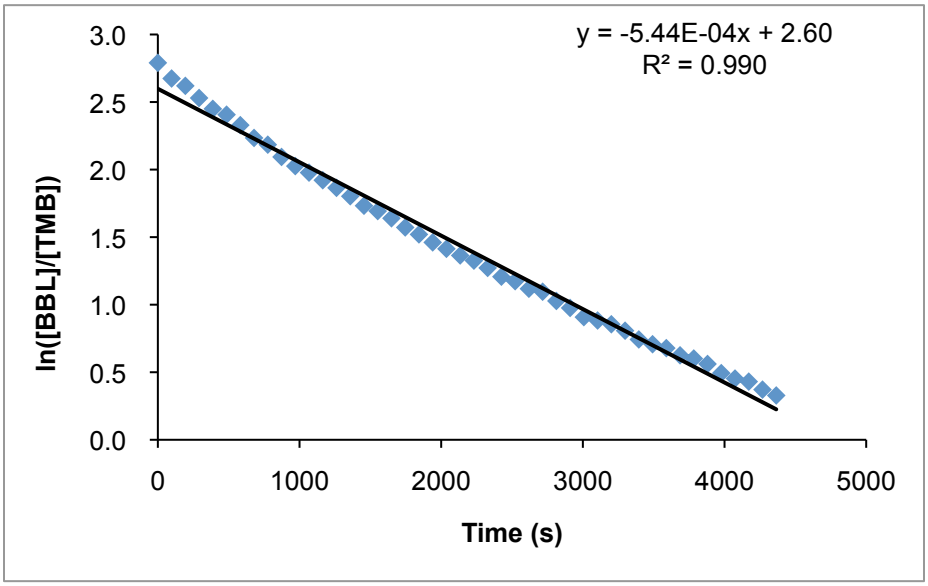

Figure S6. Plot of ln[BBL] vs time for polymerization of BBL in CD_3CN (400 MHz, 60.6 °C). [**1**] = 0.0030 M, [BBL]/[**1**] = 200.

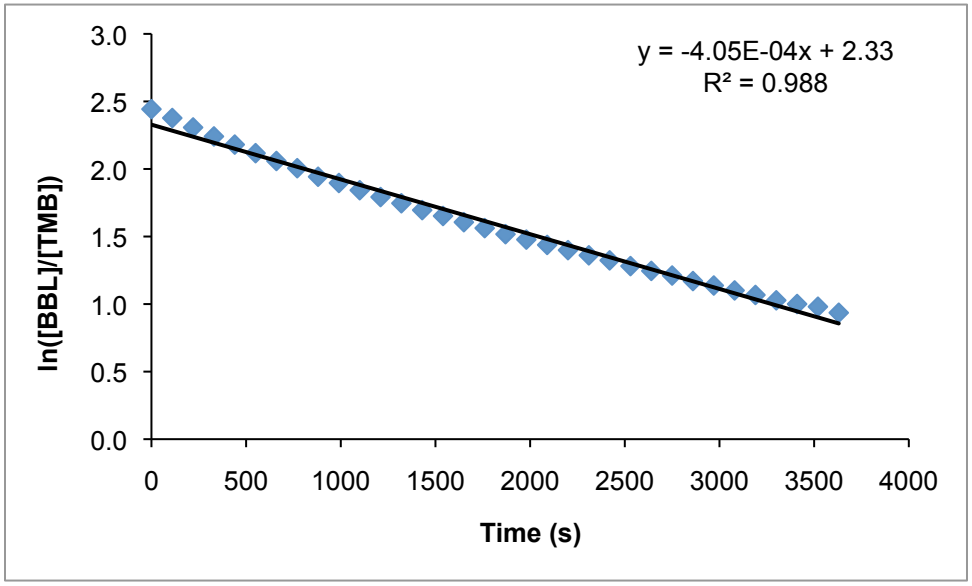

Figure S7. Plot of ln[BBL] vs time for polymerization of BBL in CD_3CN (400 MHz, 60.6 °C). [**1**] = 0.0023 M, [BBL]/[**1**] = 200.

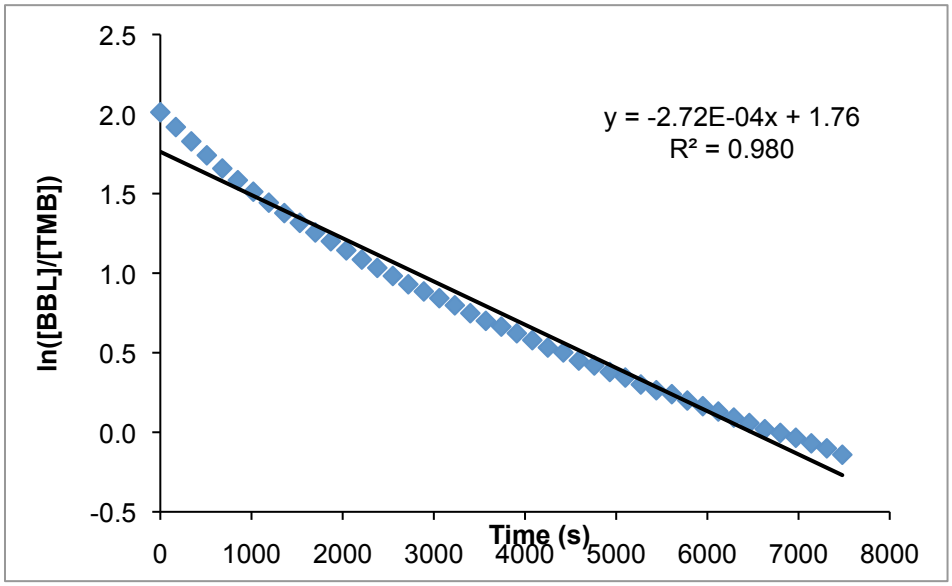

Figure S8. Plot of ln[BBL] vs time for polymerization of BBL in CD_3CN (400 MHz, 60.6 °C). [**1**] = 0.0016 M, [BBL]/[**1**] = 200.

Table S3. Observed rate constants for the polymerization of BBL with different concentration of **1**[a]

Entry	[1] (mol/L)	k_{obs} ($\times 10^{-5}$ s^{-1})
1	0.0045	96.7
2	0.0037	76.9
3	0.0030	54.4
4	0.0023	40.5
5	0.0016	27.2

[a]All the experiments were run in CD_3CN at 60.6 °C, monitored *in situ* with ^1H NMR spectroscopy, [BBL]/[**1**] = 200.

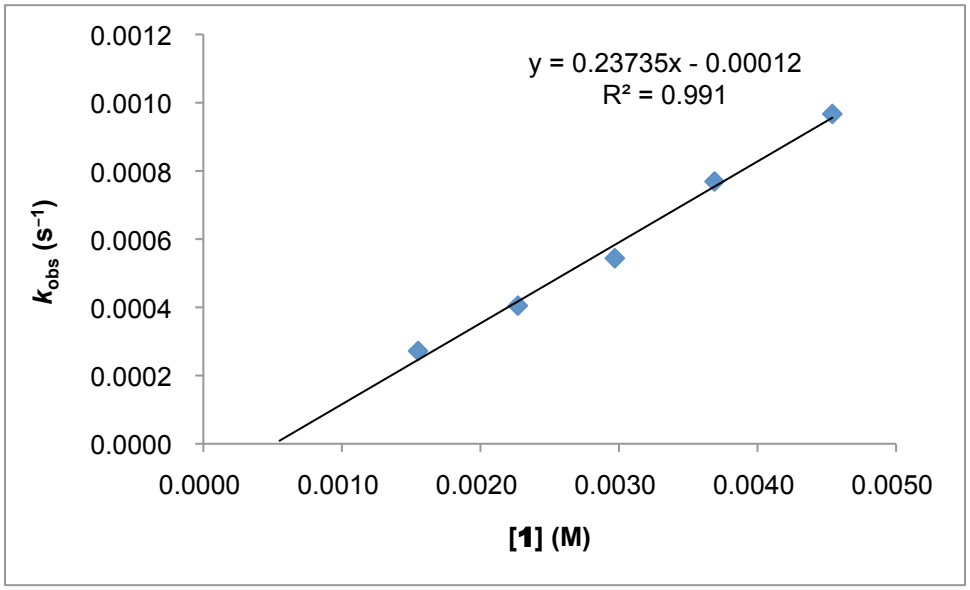

Figure S9. Plot of k_{obs} vs [**1**]. The polymerization of BBL was monitored *in situ* by ^{1}H NMR spectroscopy (300 MHz or 400 MHz, CD_3CN). The temperature was calibrated to be at 60.6 °C using 80% ethylene glycol in DMSO-d_6. [BBL]/[**1**] = 200.

These data show that the polymerization is first order in concentration of **1**. Since the rate is also first order in [BBL], we can propose an overall rate equation during propagation:

$$\text{rate} = k \times [\text{BBL}] \times [\mathbf{1}] \quad \text{(S1)}$$

in which

$$k \times [\mathbf{1}] = k_{obs} \quad \text{(S2)}$$

The rate constant k was calculated from the slope of Figure S9 to be 0.24(±0.13) $M^{-1}s^{-1}$

D. Activation parameters for the polymerization of BBL with 1

Table S1. k_{obs} and k at variable temperatures[a].

Entry	Temp (°C)	1/T (K^{-1})	k_{obs} ($*10^{-5}$ s^{-1})	k (M^{-1} s^{-1}) [b]	ln(k_{obs}/T)	ln(k/T)
1	22.4	0.003384	5.5	0.0120	−15.497	−10.115
2	29.2	0.003307	11.3	0.0246	−14.800	−9.418
3	40.2	0.003191	24.9	0.0541	−14.045	−8.664
4	51.2	0.003083	71.9	0.156	−13.019	−7.638
5	60.6	0.002996	76.9	0.167	−12.981	−7.599
6	72.2	0.002896	215.4	0.468	−11.985	−6.603

[a]All the experiments were run in CD_3CN, monitored *in situ* by ^1H NMR spectroscopy, [**1**] = 0.0046 M, [BBL]/[**1**] = 200. [b]The rate constant k is calculated as: $k = k_{obs}/[\mathbf{1}]$.

According to transition state theory, the Eyring equation (Equation S3) was used to obtain the thermodynamic parameters, enthalpy ($\Delta H^{\ddagger}$) and entropy ($\Delta S^{\ddagger}$) of activation of polymerization:

$$\ln\frac{k}{T} = -\frac{\Delta H^{\neq}}{R}\times\frac{1}{T} + \ln\frac{k_b}{h} + \frac{\Delta S^{\neq}}{R} \qquad \text{(S3)}$$

By plotting the natural logarithm of the observed rate over temperature against the inverse of the temperature, $\Delta H^{\neq}$ and $\Delta S^{\neq}$ during polymerization can be calculated from the slope and the *y*-intercept of the line. Usually the observed rate k_{obs} is used to plot ln(k_{obs}/T) vs 1/T. However, since k_{obs} is affected by the concentration of the catalyst **1**, which leads to a large change in $\Delta S^{\neq}$ from different concentration of the catalyst, we also use the rate constant k to plot ln(k/T) vs 1/T as a comparison. The activation parameters from Figure S11 are reported in the paper.

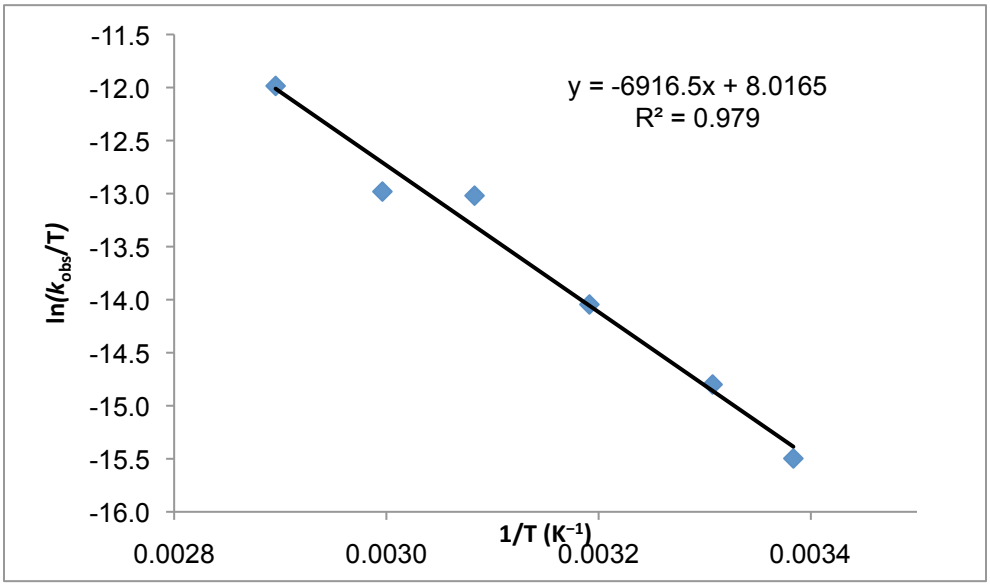

Figure S10. Plot of ln(k_{obs}/T) vs 1/T for polymerization of BBL with **1**in CD_3CN. Activation parameters for the polymerization were obtained as: $\Delta H^{\ddagger}$ = 58(4) kJ mol^{-1} $\Delta S^{\ddagger}$ = –131(13) J $mol^{-1}K^{-1}$ ([**1**] = 0.0046 mol/L, [BBL]/[**1**] = 200).

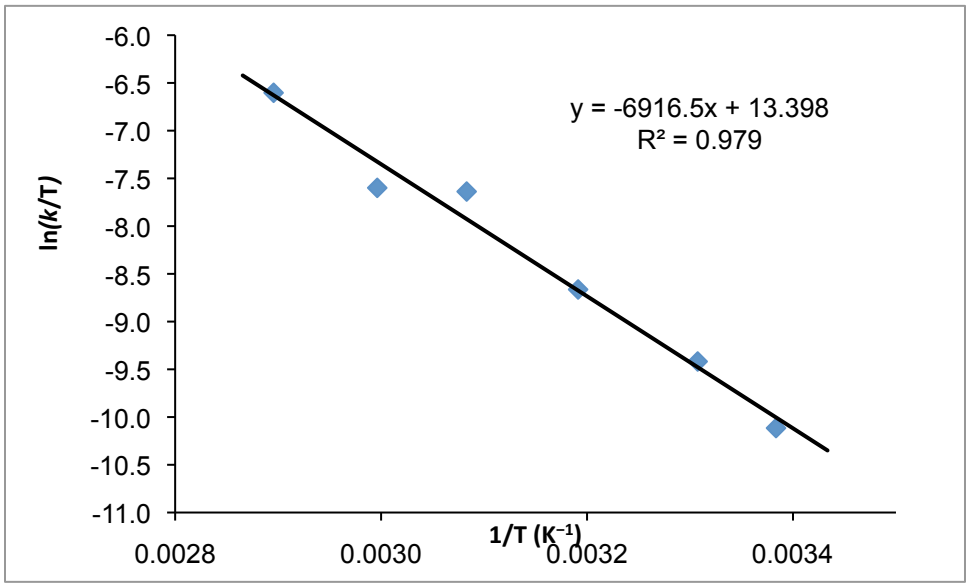

Figure S11. Plot of ln(k/T) vs 1/T for polymerization of BBL with **1** in CD_3CN. If this plot was used to obtain the activation parameters, $\Delta H^{\ddagger}$ would be the same as the above. However, $\Delta S^{\ddagger}$ would be –86(13) J $mol^{-1}K^{-1}$ instead. ([**1**] = 0.0046 mol/L, [BBL]/[**1**] = 200).

E. ^{1}H NMR and inverse gated ^{13}C{^{1}H} NMR spectra of PHB

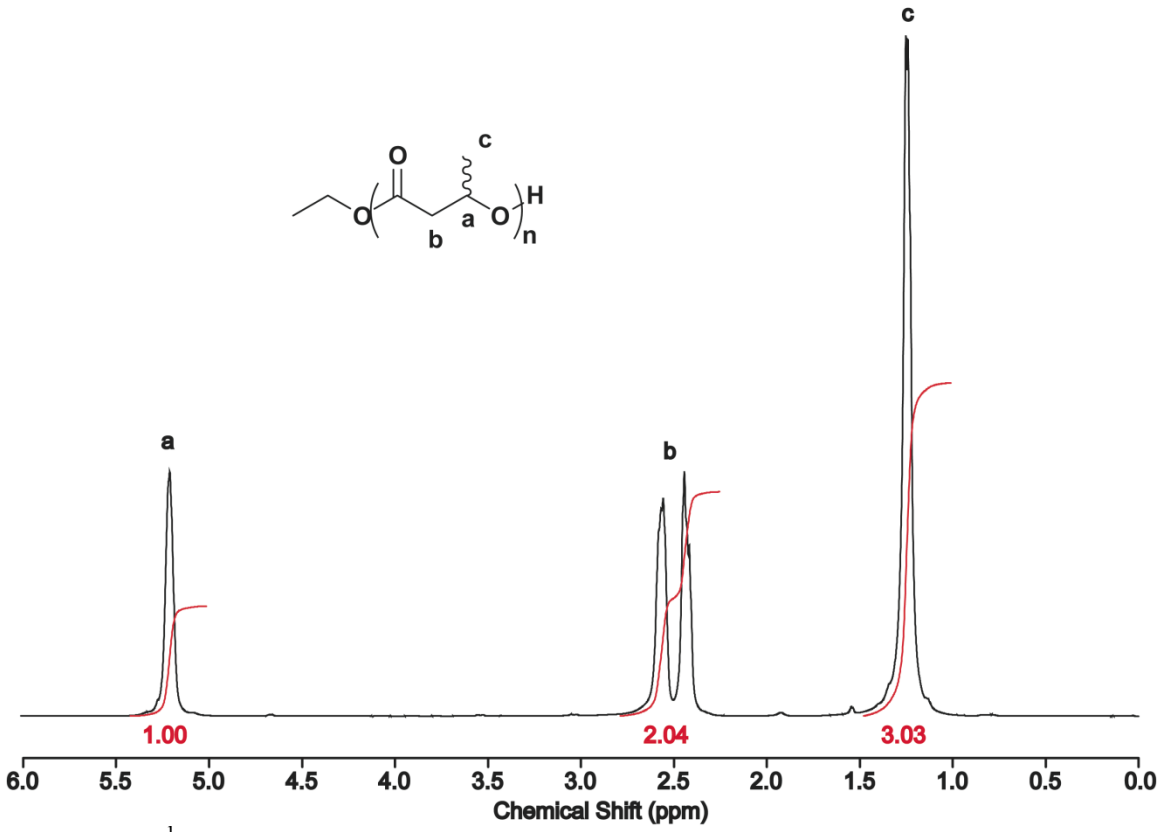

Figure S12. ^{1}H NMR spectrum of PHB in $CDCl_3$ (600 MHz, 298 K). The polymerization 1000 equivalents of [BBL]/[**1**] was performed in CH_3CN at 60 °C.

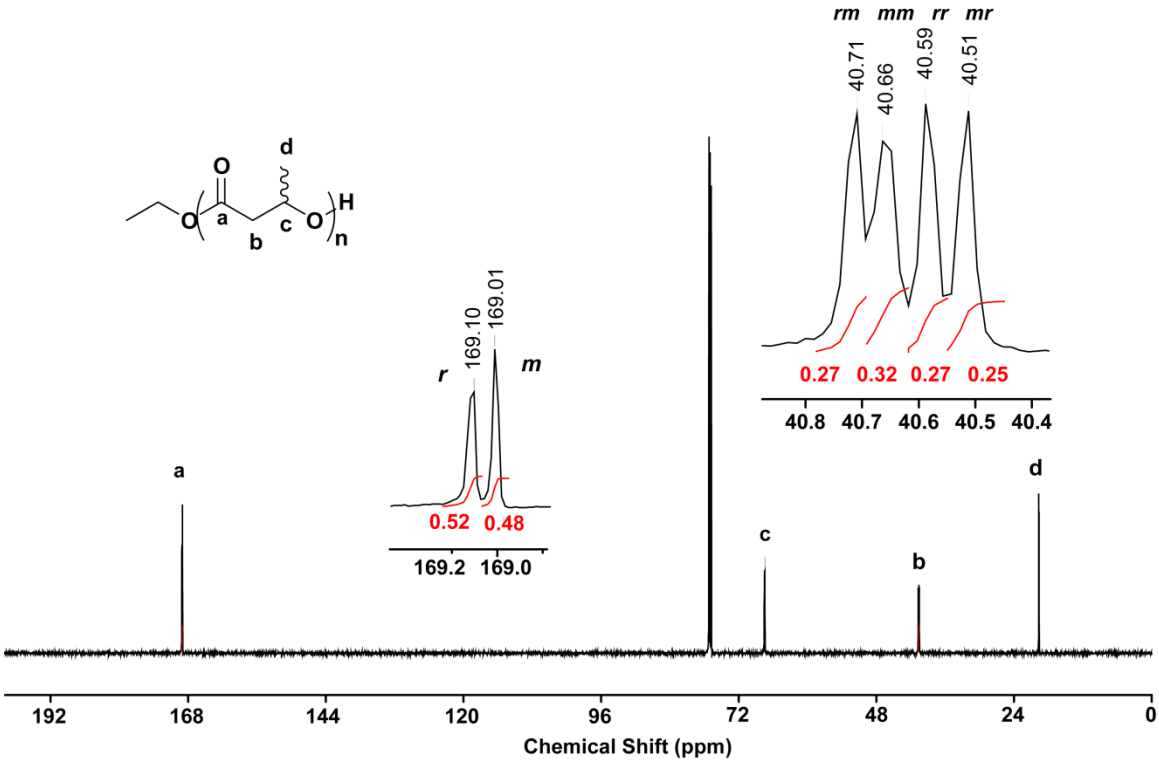

Figure S13. Inverse gated $^{13}C\{^{1}H\}$ NMR spectrum of PHB in $CDCl_3$ (150 MHz, 298 K). The polymerization of 1000 equivalents of [BBL]/[**1**] was performed in CH_3CN at 60 °C.

According to literature, the upfield and downfield signals in the carbonyl region correspond to the meso (*m*) dyad sequences and the racemic (*r*) dyad sequences respectively. So P_m is calculated from the relative integration of the upfield signal to the total carbonyl region[2]:

$$P_m = \frac{I_m}{I_m + I_r} = \frac{0.48}{0.48 + 0.52} = 0.48$$

F. Exchange with added alcohols

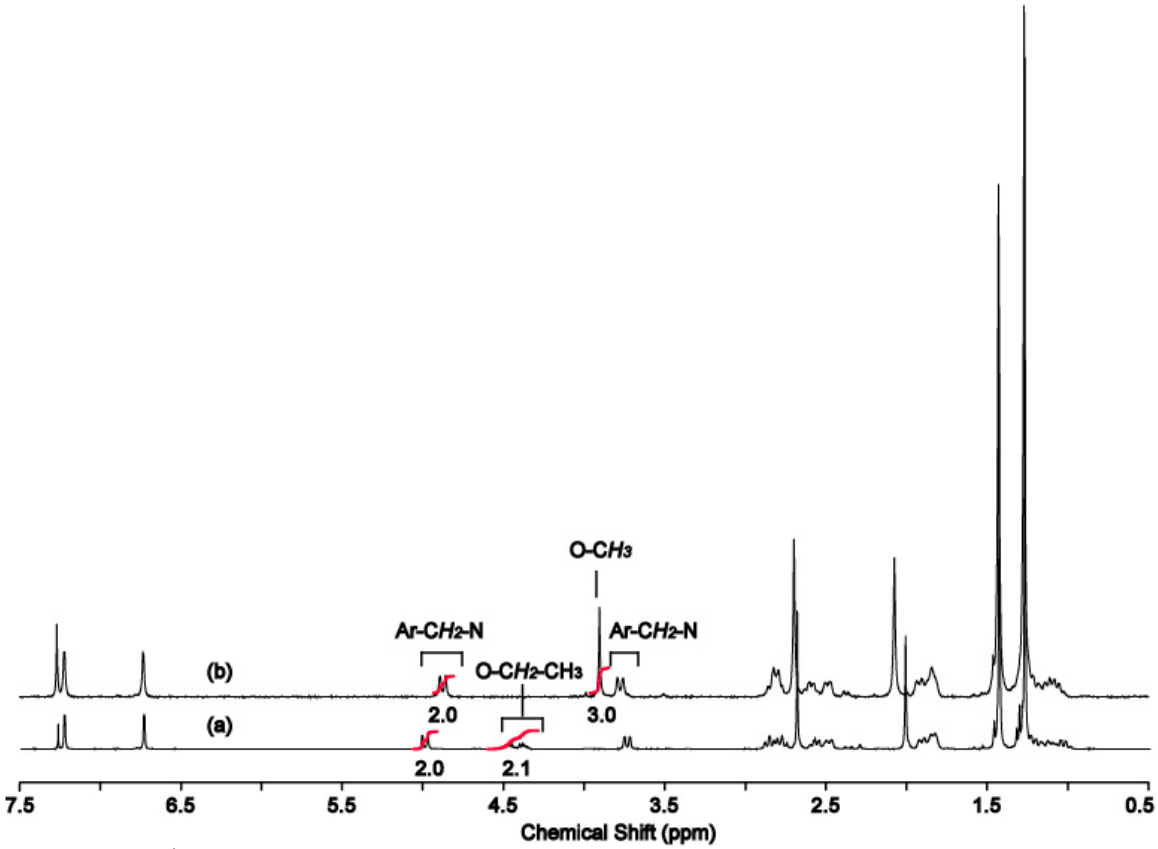

Figure S14. ^{1}H NMR spectra of (a) $[(NNO)InCl]_2(\mu\text{-}Cl)(\mu\text{-}OEt)$ **1** and (b) complex **1** reacted with dried neat MeOH for 16 hr at room temperature.

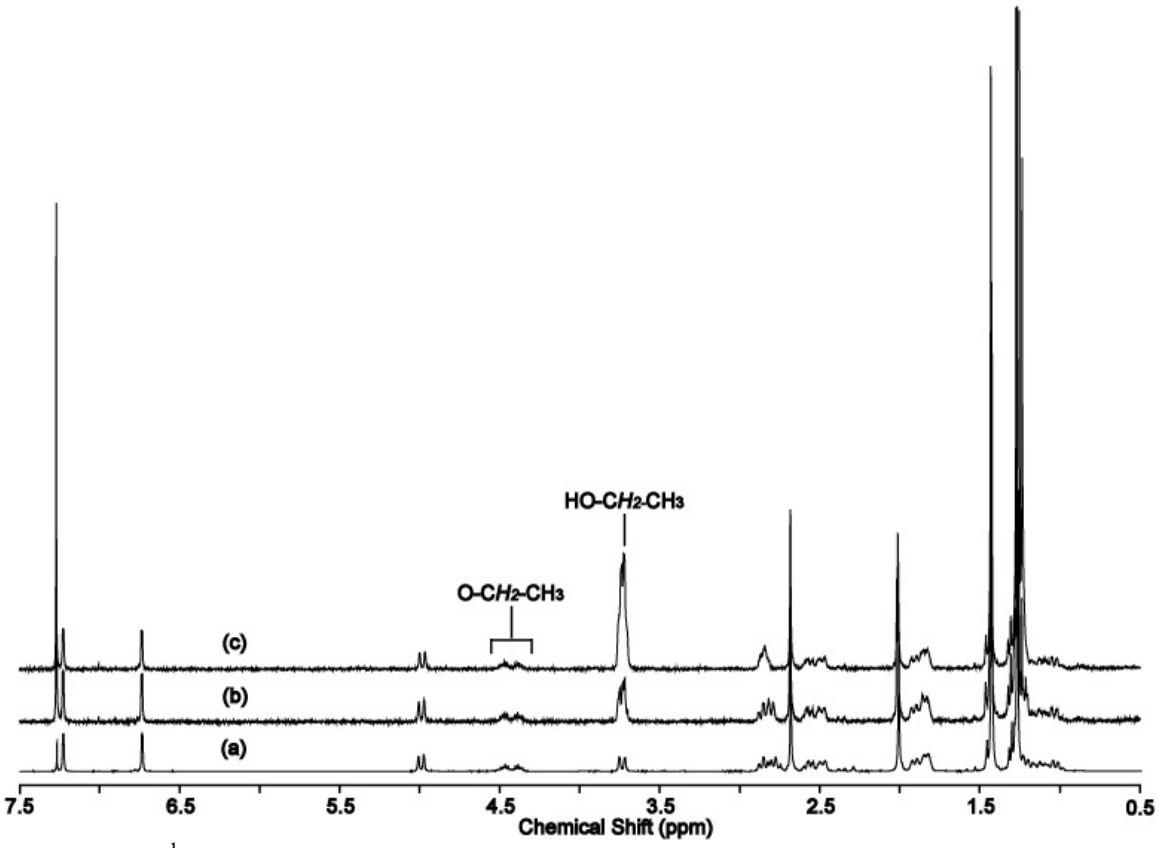

Figure S15. ^{1}H NMR spectra of (a) $[(NNO)InCl]_2(\mu\text{-}Cl)(\mu\text{-}OEt)$ **1,** and complex **1** with (b) 2 equivalents and (c) 10 equivalents of EtOH after 24 hr in $CDCl_3$ at 25 °C.

G. Gel permeation Chromatographic studies of PHB resulted from immortal polymerization of BBL in the presence of EtOH

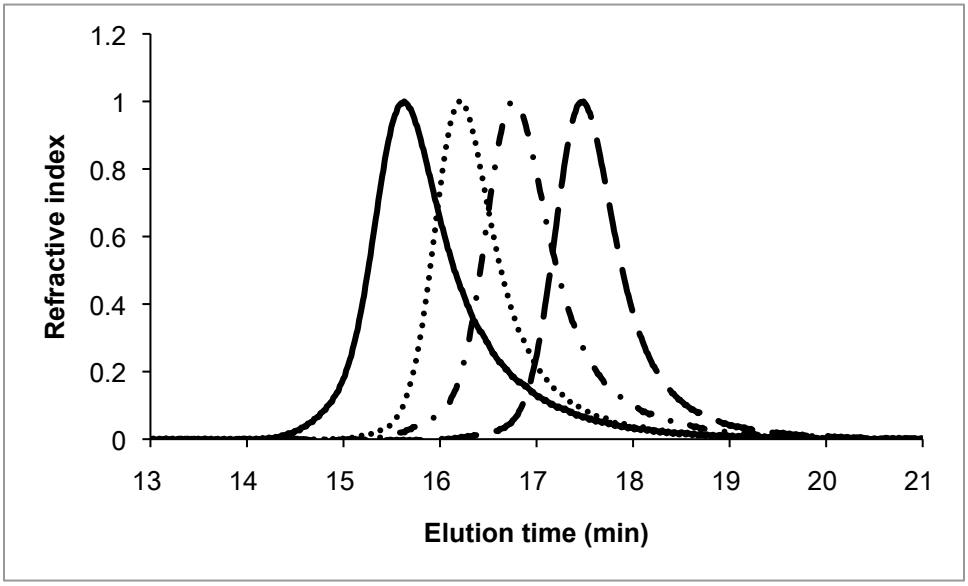

Figure S16. GPC traces of the polymers produced by iROP of BBL with ethanol by **1**. Solid line: [BBL]/[ROH]/[**1**] = 1000/0/1 (M_n = 82.89 kDa, *PDI* = 1.07); dot line): [BBL]/[ROH]/[**1**] = 4000/10/1 (M_n = 44.02 kDa, *PDI* = 1.01); dot and dash line: [BBL]/[ROH]/[**1**] = 1000/2/1 (M_n = 28.34 kDa, *PDI* = 1.01); dash line: [BBL]/[ROH]/ [**1**] = 1000/4/1 (M_n = 16.77 kDa, *PDI* = 1.01).

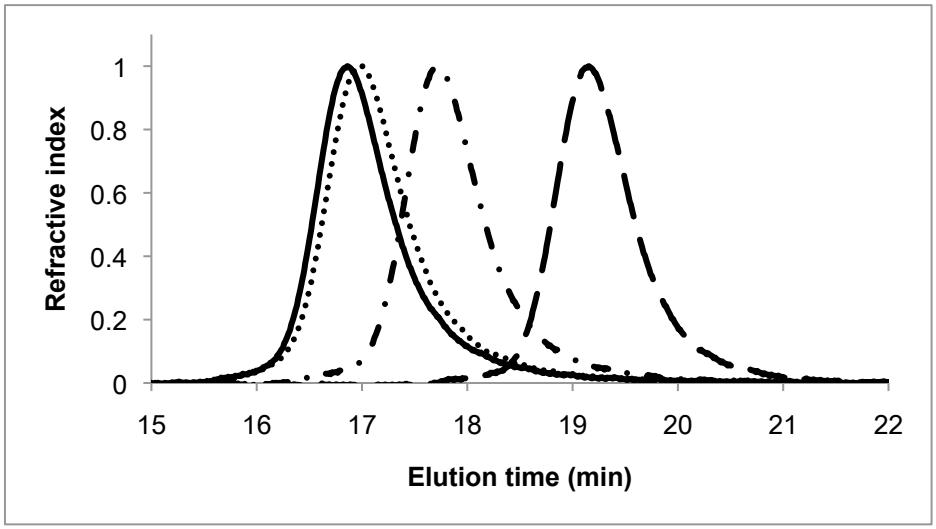

Figure S17. GPC traces of the polymers produced by iROP of BBL with mPEG 350 by **1**. Solid line: [BBL]/[ROH]/[**1**] = 10000/20/1 (M_n = 36.09 kDa, *PDI* = 1.01); dot line): [BBL]/[ROH]/[**1**] = 1000/2/1 (M_n = 27.97 kDa, *PDI* = 1.01); dot and dash line: [BBL]/[ROH]/[**1**] = 1000/4/1 (M_n = 17.07 kDa, *PDI* = 1.02); dash line: [BBL]/[ROH]/ [**1**] = 10000/100/1 (M_n = 7.569 kDa, *PDI* = 1.03).

H. References

1. Douglas, A. F.; Patrick, B. O.; Mehrkhodavandi, P. *Angew. Chem. Int. Ed.,* 2008, **47**, 2290-2293.

2. (a) Amgoune, A.; Thomas, C. M.; Ilinca, S.; Roisnel, T.; Carpentier, J.-F. *Angew. Chem. Int. Ed.,* 2006, **45**, 2782-2784; (b) Kemnitzer, J. E.; Mccarthy, S. P.; Gross, R. A. *Macromolecules,* 1993, **26**, 1221-1229.