Supporting Information

Selective Polymerization of Epoxides from Hydroxycarboxylic Esters: Expediting Controlled Synthesis of *α*-Carboxyl-*ω*-Hydroxyl Polyethers

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Experimental Section

Materials

Tetrahydrofuran (THF; Guangzhou Chemical Reagent, AR) was successively dried over molecular sieve (4 Å), calcium hydride (CaH_2), and *n*-butyllithium (*n*-BuLi) capped with 1,1-diphenylethylene before vacuum-distilled. Dichloromethane (CH_2Cl_2; Guangzhou Chemical Reagent, AR) and ε-caprolactone (CL; Aladdin, 99%) were dried by CaH_2 and distilled. Ethylene oxide (EO; Aldrich, 99%) was first condensed from a metal cylinder into a Schlenk flask by cooling the flask at 0 °C under vacuum and dried by stirring with sodium hydride (NaH) at 0 °C for 4 h, then vacuum-transferred into a graduated flask pre-charged with *n*-BuLi and stirred at 0 °C for 1 h before finally cryo-distilled into the reaction flask. Propylene oxide (PO; Aldrich, 99%) was stirred with NaH overnight and cryo-distilled into a storage flask. Ethyl 6-hydroxyhexanoate (EH; TCI, 96%) and diethyl 3-hydroxyglutarate (DH; TCI, 99%) were dried by azeotropic distillation of THF prior to use. Magnesium sulfate anhydrous ($MgSO_4$, Aladdin, AR) and aluminum oxide (Al_2O_3, Aladdin, AR) were washed with CH_2Cl_2 and vacuum-dried prior to use. Hydrochloride (HCl; Aladdin, AR), potassium hydroxide (KOH; Aladdin, AR), 1,5,7-triazabicyclo[4.4.0]dec-5-ene (TBD; TCI, 98%), *tert*-butylimino-tris(dimethylamino)phosphorane (*t*-BuP_1; Aldrich, 97%), 1-*tert*-butyl-2,2,4,4,4-pentakis(dimethylamino)-2λ^5,4λ^5- catenadi(phosphazene) (*t*-BuP_2; Aldrich, 2.0 mol L^{-1} in THF) and triethylborane (Et_3B; TCI, 1.0 mol L^{-1} in THF) were used as received.

Instrumentation

NMR spectra were recorded at 25 °C on a Bruker AV400 NMR spectrometer using deuterated chloroform ($CDCl_3$) as the solvent and tetramethylsilane as the internal standard. ^1H NMR

spectra were used to calculate number-average molar mass ($M_{n,NMR}$) by comparing the integrals of signals from end groups and polymer main bodies.

For the relatively high-molar-mass poly(ethylene oxide) PEO samples, size exclusion chromatography (SEC) coupled with a refractive index (RI) detector was conducted in *N*,*N*-dimethylformamide (DMF) with LiBr (0.05 mol L^{-1}) at 50 °C and a flow rate of 1.0 mL min^{-1} using three successively connected Styragel columns (HR2, HR4, HR6). A series of narrowly dispersed PEO standards were used for calibration to obtain the number-average molar mass ($M_{n,SEC}$) and molar mass distribution ($Đ_M$). For polymers that are well-soluble in THF, SEC was conducted in THF at 35 °C using two identical PLgel MIXED-C columns at the same flow rate. Calibration was done with a series of narrowly dispersed PEO standards as well.

Matrix assisted laser desorption/ionization time of flight mass spectrometry (MALDI-TOF MS) measurement was performed on a Bruker Autoflex III Smartbeam MALDI-TOF mass spectrometer (Bruker, Germany). Samples were dissolved in THF (10 mg mL^{-1}) and mixed with a solution of sodium trifluoroacetate in THF (10 mg mL^{-1}) in a volume ratio of 5:1. This solution was then mixed with a solution of matrix, 2,5-dihdroxybenzoic acid in THF (20 mg mL^{-1}), in a volume ratio of 1:20. Then, 0.4 μL of the final solution was spotted on the target plate (dried-droplet method). The reflective positive ion mode was used to acquire the mass spectra of the samples. Calibration was done externally with poly(methyl methacrylate) standards using the nearest neighbor positions.

Polymer Synthesis

(1) α-Carboxylic ester-ω-hydroxyl PEO, initiated by ethyl 6-hydroxyhexanoate (EH)

A typical procedure of entry 1 in Table 1 is as follows. A round-bottom reaction flask was dried with a heat gun on a vacuum line and transferred into a glovebox where purified EH (176.2 mg, 1.1 mmol), THF (2.2 mL), Et_3B (1.0 mol L^{-1}, 170 μL, 0.17 mmol), and *t*-BuP_1 (13 μL, 0.06

mmol) were successively loaded. The flask was then docked back on the vacuum line where purified EO (3.9 mL, 77.0 mmol) was slowly introduced by cryo-distillation at -20 °C. The reaction mixture was gradually warmed up to RT (*ca*. 25 °C). White solids (crystallized PEO) appeared in 25 min. The amount of precipitates increased so quickly that the stirrer stopped spinning in a few minutes, which was considered as the end point of the reaction. A small aliquot was withdrawn and diluted with 0.6 mL of $CDCl_3$ containing one drop of acetic acid for ^{1}H NMR analysis to determine the conversion of EO. The $CDCl_3$ solution was further diluted with THF for SEC measurement to obtain $M_{n,SEC}$ and $Đ_M$. Conv.(EO) = 100%, theoretical number-average molar mass ($M_{n,th}$) = 3.2 kg mol^{-1}. $M_{n,SEC}$(THF) = 3.2 kg mol^{-1}, $Đ_M$ = 1.07. One third of the crude product was dissolved in dichloromethane (DCM) containing a few drops of acetic acid and precipitated in *n*-hexane. The product (a white solid) was then collected and dried in vacuum. ^{1}H NMR (600 MHz, $CDCl_3$): 4.14-4.10 ($CH_3CH_2OCOCH_2CH_2$ $CH_2CH_2CH_2O$−PEO−), 3.73-3.71 (−PEO−CH_2CH_2OH), 3.70-3.59 (−OCH_2CH_2O−), 3.46-3.44 ($CH_3CH_2OCOCH_2CH_2CH_2CH_2CH_2$O−PEO−), 2.31-2.28 ($CH_3CH_2OCOCH_2CH_2CH_2$ CH_2CH_2O−PEO−), 1.67-1.56 ($CH_3CH_2OCOCH_2CH_2CH_2CH_2CH_2O$−PEO−), 1.40-1.35 ($CH_3$ $CH_2OCOCH_2CH_2CH_2CH_2CH_2O$−PEO−), 1.28-1.24 ($CH_3CH_2OCOCH_2CH_2CH_2CH_2CH_2O$− PEO−); $M_{n,NMR}$ = 3.4 kg mol^{-1}.

(2) α-Carboxyl-ω-hydroxyl PEO through hydrolysis of α-carboxylic ester-ω-hydroxyl PEO

To another one third of the crude product described in (1) was added THF (3.0 mL), KOH (0.10 g, 1.8 mmol), and water (0.10 mL, 5.6 mmol). The mixture was stirred at 45 °C for 12 h before a small aliquot was withdrawn for ^{1}H NMR analysis to determine the conversion of carboxylic ester end groups (100%). Then the reaction mixture was acidified by a HCl solution until pH becomes *ca.* 3. The crude product was mixed with DCM and filtered. The filtrate was stirred with neutral alumina, dried by anhydrous $MgSO_4$, and evaporated to dryness to afford *α*-carboxyl-*ω*-hydroxyl PEO as a white solid. $M_{n,SEC}$(THF) = 2.9 kg mol^{-1}, $Đ_M$ = 1.07. ^{1}H NMR

(600 MHz, $CDCl_3$): 3.73-3.71 (−PEO−CH_2CH_2OH), 3.70-3.59 (−OCH_2CH_2O−), 3.45-3.47 (HOOC$CH_2CH_2CH_2CH_2CH_2$O−PEO−), 2.33-2.31 (HOOC$CH_2CH_2CH_2CH_2CH_2$O−PEO−), 1.68-1.57 (HOOC$CH_2CH_2CH_2CH_2CH_2$O−PEO−), 1.45-1.39 (HOOC$CH_2CH_2CH_2CH_2CH_2$O−PEO−); $M_{n,NMR}$ = 2.9 kg mol^{-1}.

(3) α-Amide-ω-hydroxyl PEO through aminolysis of α-carboxylic ester-ω-hydroxyl PEO

To the last one third of the crude product described in (1) was added toluene (2.0 mL), benzylamine (0.40 mL, 3.7 mmol), and TBD (0.051 g, 0.37 mmol). The mixture was stirred at RT for 24 h. Then a small aliquot was withdrawn for ^{1}H NMR analysis to determine the conversion of carboxylic ester end groups (100%). The *α*-amide-*ω*-hydroxyl PEO was afforded as a white solid by precipitation in *n*-hexane and dried in vacuum. $M_{n,SEC}$(THF) = 3.4 kg mol^{-1}, $Đ_M$ = 1.07. ^{1}H NMR (600 MHz, $CDCl_3$): 7.34-7.26 ($C_6H_5CH_2$NHCO−), 4.44 ($C_6H_5CH_2$NHCO−), 3.73-3.71 (−PEO−CH_2CH_2OH), 3.70-3.59 (−OCH_2CH_2O−), 3.46-3.44 (−NHCO$CH_2CH_2CH_2CH_2$O−PEO−), 2.24-2.21 (−NHCO$CH_2CH_2CH_2CH_2CH_2$O−PEO−), 1.71-1.66 (−NHCO$CH_2CH_2CH_2CH_2CH_2$O−PEO−), 1.62-1.57 (−NHCO$CH_2CH_2CH_2CH_2CH_2$O−PEO−), 1.42-1.37 (−NHCO$CH_2CH_2CH_2CH_2CH_2$O−PEO−); $M_{n,NMR}$ = 3.2 kg mol^{-1}.

(4) α-Carboxylic ester-ω-hydroxyl PPO, initiated by EH

A typical procedure of entry 2 in Table 1 is as follows. To a pre-dried reaction flask was successively loaded EH (96.1 mg, 0.60 mmol), PO (2.5 mL, 36.0 mmol), Et_3B (1.0 mol L^{-1}, 90 μL, 0.09 mmol), and *t*-BuP_2 (2.0 mol L^{-1}, 15 μL, 0.03 mmol). The mixture was stirred at RT for 12 h, then a small aliquot was withdrawn for ^{1}H NMR and SEC measurements. Conv.(PO) = 100%, $M_{n,th}$ = 3.6 kg mol^{-1}. $M_{n,SEC}$(THF) = 3.8 kg mol^{-1}, $Đ_M$ = 1.07. Half of the reaction mixture was quenched by a few drops of acetic acid. The crude product was diluted with DCM and stirred with neutral alumina to remove the catalyst residuals. After filtration and evaporation of the solvent, a viscous liquid product was obtained and dried in vacuum. ^{1}H NMR (600 MHz, $CDCl_3$): 4.14-4.10 (CH_3CH_2OCOC$H_2CH_2CH_2CH_2CH_2$O−PPO−), 3.95-3.90

(−PPO−$CH_2CH(CH_3)OH$), 3.70-3.34 (−O$CH_2CH(CH_3)$O−), 3.33-3.30 ($CH_3CH_2OCOCH_2CH_2CH_2CH_2CH_2CH_2O$−PPO−), 2.31-2.27 ($CH_3CH_2OCOCH_2CH_2CH_2CH_2CH_2O$−PPO−), 1.67-1.55 ($CH_3CH_2OCOCH_2CH_2CH_2CH_2CH_2O$−PPO−), 1.40-1.35 ($CH_3CH_2OCOCH_2CH_2CH_2CH_2CH_2CH_2O$−PPO−), 1.27-1.23 ($CH_3CH_2OCOCH_2CH_2CH_2CH_2CH_2O$−PPO−), 1.21-1.08 (−$OCH_2CH(CH_3)$O−); $M_{n,NMR}$ = 3.5 kg mol^{-1}.

(5) α-Carboxyl-ω-hydroxyl PPO through hydrolysis of α-carboxylic ester-ω-hydroxyl PPO

To the other half of the crude product described in (4) was added THF (3.0 mL), KOH (0.09 g, 1.6 mmol), and water (0.10 mL, 5.5 mmol). The mixture was stirred at 45 °C for 12 h before a small aliquot was withdrawn for ^{1}H NMR analysis to determine the conversion of carboxylic ester end groups (100%). Then the reaction mixture was acidified by a HCl solution until pH becomes *ca.* 3. The crude product was diluted with THF and filtered. The filtrate was washed with neutral alumina, dried by anhydrous $MgSO_4$, and evaporated to dryness to afford *α*-carboxyl-*ω*-hydroxyl PPO as a viscous liquid. $M_{n,SEC}$(THF) = 3.7 kg mol^{-1}, $Đ_M$ = 1.06. ^{1}H NMR (600 MHz, $CDCl_3$): 3.95-3.90 (−PPO−$CH_2CH(CH_3)OH$), 3.70-3.34 (−O$CH_2CH(CH_3)$O−), 3.33-3.30 ($HOOCCH_2CH_2CH_2CH_2CH_2O$−PPO−), 2.34-2.30 ($HOOCCH_2CH_2CH_2CH_2CH_2O$−PPO−), 1.69-1.56 ($HOOCCH_2CH_2CH_2CH_2CH_2O$−PPO−), 1.45-1.39 ($HOOCCH_2CH_2CH_2CH_2CH_2O$−PPO−), 1.21-1.08 (−$OCH_2CH(CH_3)$O−); $M_{n,NMR}$ = 3.8 kg mol^{-1}.

Entries 3~4 followed the same ROP and hydrolysis procedures as entry 1 and 2, respectively. Entries 7~8 followed the same ROP procedures as entry 1 and 2, respectively. Entry 7 used TBD instead of KOH to catalyze the hydrolysis of DH-PEO-OH. After the removal of organic solvent, the hydrolyzed crude product was dissolved in Millipore-Q water, stirred with cation-exchange resin (Dowex50WX4) for 3 min, then freeze-dried for 2 days.

(6) α-Carboxyl-ω-hydroxyl PPO/PEO, initiated by oligoCL (CL_8)

To a pre-dried reaction flask was successively loaded CL (1.0 mL, 9.0 mmol), THF (1.2 mL), anhydrous ethanol (66 μL, 1.1 mmol), and *t*-BuP_2 (2.0 mol L^{-1}, 28 μL, 0.056 mmol). The

mixture was stirred at RT for 10 min, then a small aliquot was withdrawn for ^{1}H NMR measurements. Conv.(CL) = 100%, Conv.(ethanol) (initiation efficiency) = 100%. Then Et_3B (1.0 mol L^{-1}, 168 μL, 0.168 mmol) was added to quench the oligomerization of CL.

Subsequently, *ca*. 1.2 mL of the mixture containing 0.55 mmol of oligoCL was withdrawn and transferred to another flask, followed by addition of PO (3.1 mL, 44 mmol). The new reaction mixture was stirred at RT and quenched after 12 h by addition of a few drops of acetic acid. Conv.(PO) = 100%, $M_{n,th}$ = 5.6 kg mol^{-1}. $M_{n,SEC}$(THF) = 5.9 kg mol^{-1}, $Đ_M$ = 1.10. ^{1}H NMR (600 MHz, $CDCl_3$): 4.14-4.11 ($CH_3CH_2O{-}CL_8{-}$), 4.07-4.05 ($-CH_2CH_2CH_2CH_2CH_2OCO-$), 3.95-3.90 ($-PPO-CH_2CH(CH_3)OH$), 3.70-3.34 ($-OCH_2CH(CH_3)O-$), 3.33-3.30 ($-OCOCH_2CH_2CH_2CH_2CH_2O-PPO-$), 2.38-2.26 ($-OCOCH_2CH_2CH_2CH_2CH_2-$), 1.70-1.55 ($-OCOCH_2CH_2CH_2CH_2-$), 1.43-1.34 ($-OCOCH_2CH_2CH_2CH_2CH_2-$), 1.27-1.24 ($CH_3CH_2O{-}CL_8{-}$), 1.21-1.08 ($-OCH_2CH(CH_3)O-$); $M_{n,NMR}$ = 5.6 kg mol^{-1}.

To the rest of the oligoCL solution was added THF (1.0 mL). Then EO (2.0 mL, 39.5 mmol) was cryo-distilled into the flask at -20 °C. The new reaction mixture was slowly warmed up to RT and stirred for another 1.5 h to obtain a white solid. Conv.(EO) = 100%, $M_{n,th}$ = 4.0 kg mol^{-1}. $M_{n,SEC}$(THF) = 3.5 kg mol^{-1}, $Đ_M$ = 1.14. ^{1}H NMR (600 MHz, $CDCl_3$): 4.15-4.11 ($CH_3CH_2O{-}CL_8{-}$), 4.07-4.03 ($-CH_2CH_2CH_2CH_2CH_2OCO-$), 3.74-3.71 ($-PEO-CH_2CH_2OH$), 3.70-3.59 ($-OCH_2CH_2O-$), 3.46-3.43 ($-OCOCH_2CH_2CH_2CH_2CH_2O-PEO-$), 2.32-2.27 ($-OCOCH_2CH_2CH_2CH_2CH_2-$), 1.70-1.55 ($-OCOCH_2CH_2CH_2CH_2CH_2-$), 1.43-1.34 ($-OCOCH_2CH_2CH_2CH_2-$), 1.27-1.24 ($CH_3CH_2O{-}CL_8{-}$); $M_{n,NMR}$ = 4.1 kg mol^{-1}.

Purification and hydrolysis of the crude product of CL_8-PEO and CL_8-PPO followed the same procedure of entry 1 and 2, respectively.

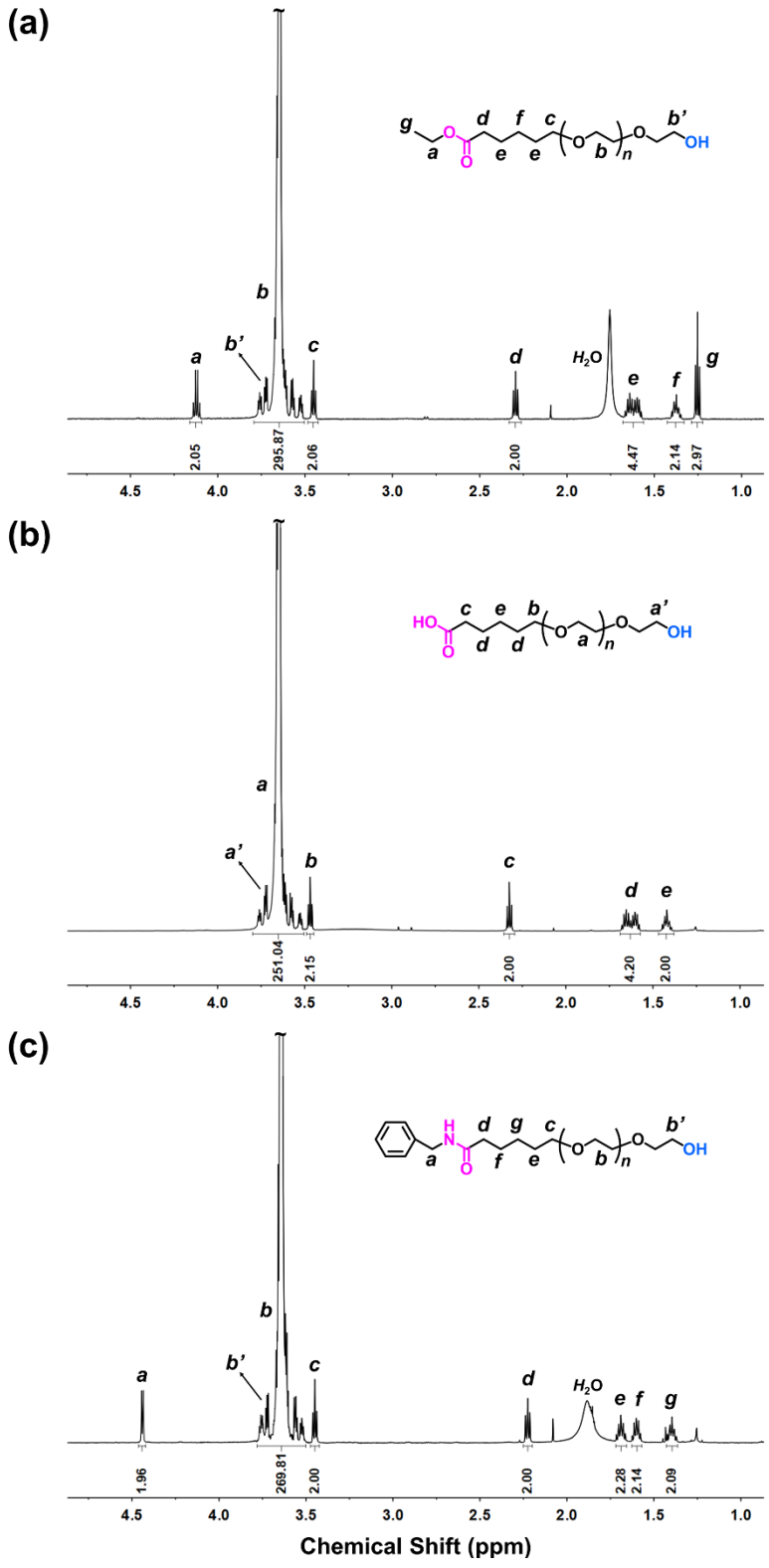

Fig. S1. ^{1}H NMR spectra (isolated products) of EH-initiated α-carboxylic ester-ω-hydroxyl PEO (entry 1 in Table 1) (a), the corresponding α-carboxyl-ω-hydroxyl PEO obtained after hydrolysis (b), and the corresponding α-amide-ω-hydroxyl PEO obtained after aminolysis (c) with integral values noted.

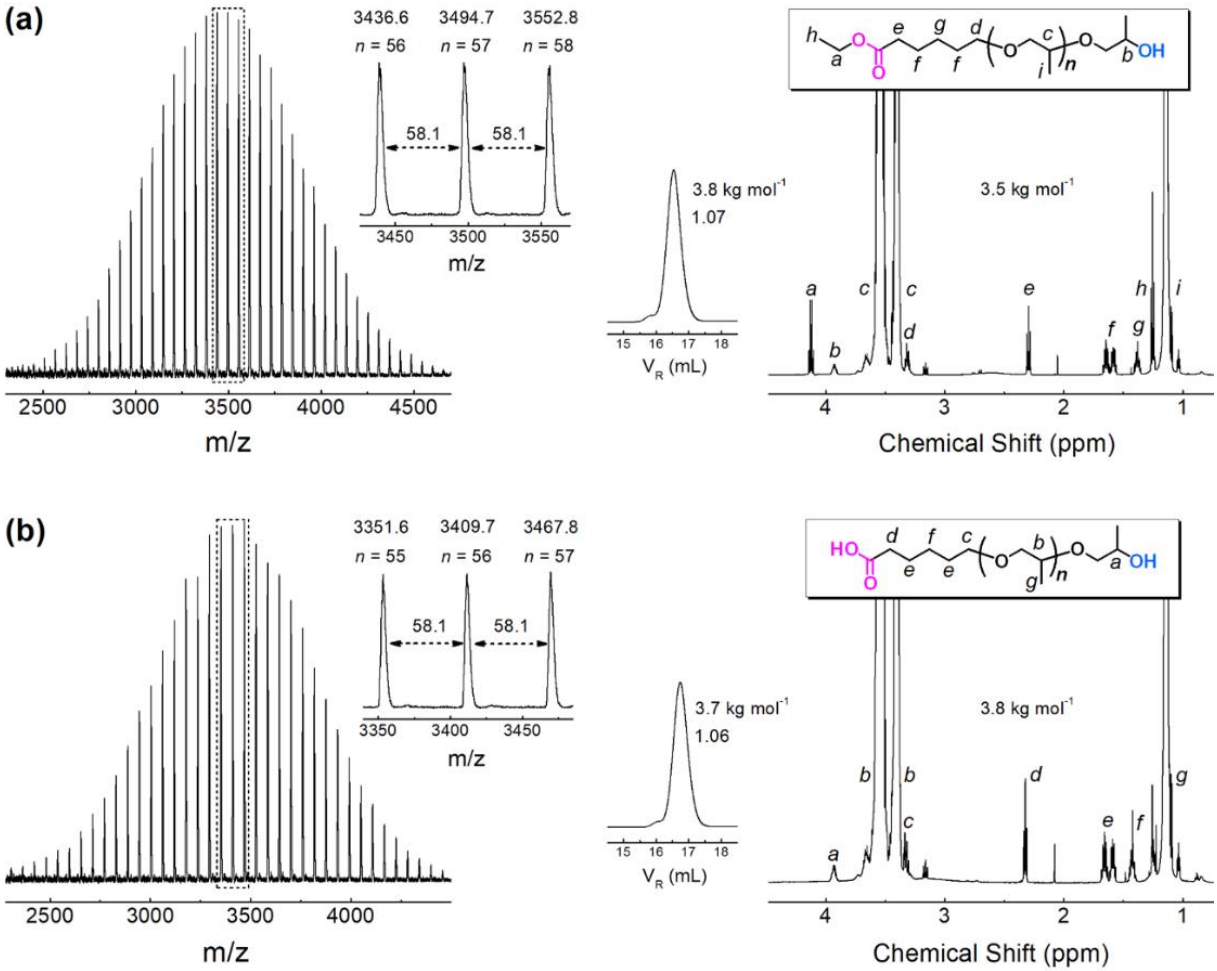

Fig. S2. MALDI-TOF MS spectra (left), SEC traces (middle; RI signals, THF, 35 °C, PEO standards; with $M_{n,SEC}$ and $Đ_M$ noted), and ^{1}H NMR spectra (right; $CDCl_3$; with $M_{n,NMR}$ noted) of EH-initiated α-carboxylic ester-ω-hydroxyl PPO corresponding to entry 2 in Table 1 (a) and the α-carboxyl-ω-hydroxyl PPO obtained after hydrolysis of the carboxylic ester end group (b). Mass signals in the MALDI-TOF MS spectra correspond to PPOs ionized by sodium cations. Calculated masses for $[EH\text{-}PO_{56}]Na^+$ (a) and hydrolyzed $[EH\text{-}PO_{56}]Na^+$ (b) are 3436.8 and 3408.8 Da, respectively.

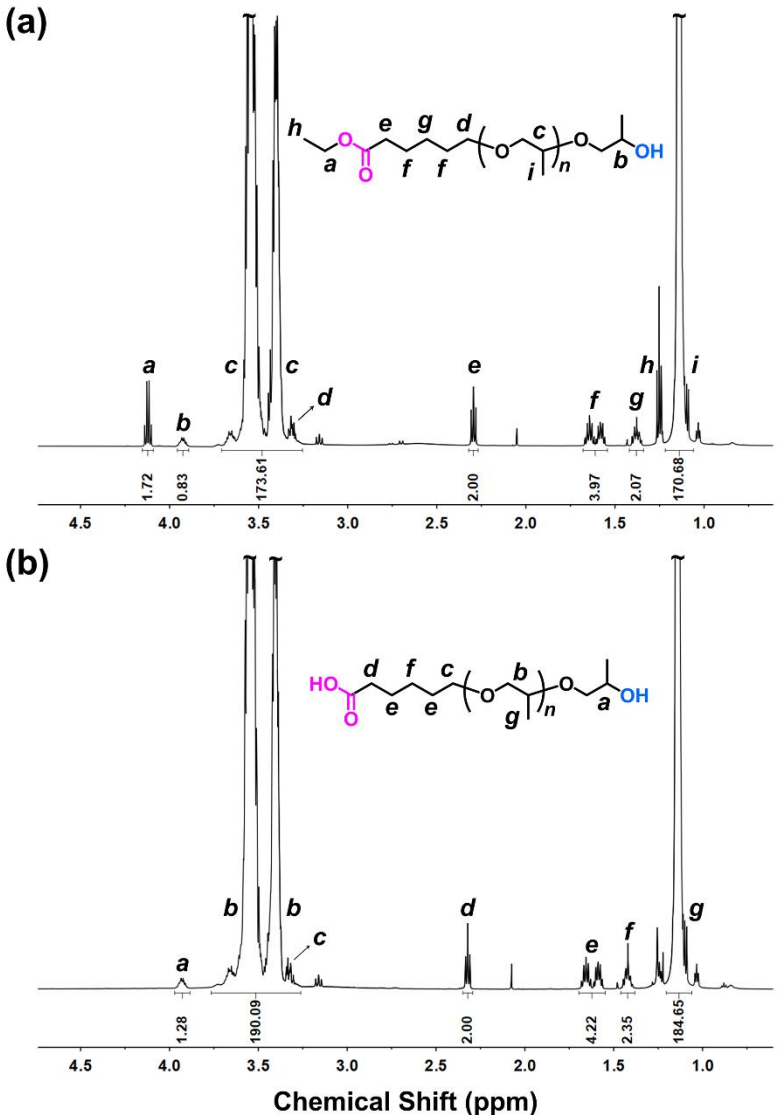

Fig. S3. ^{1}H NMR spectra (isolated products) of EH-initiated α-carboxylic ester-ω-hydroxyl PPO (entry 2 in Table 1) (a) and the corresponding α-carboxyl-ω-hydroxyl PPO obtained after hydrolysis (b) with integral values noted.

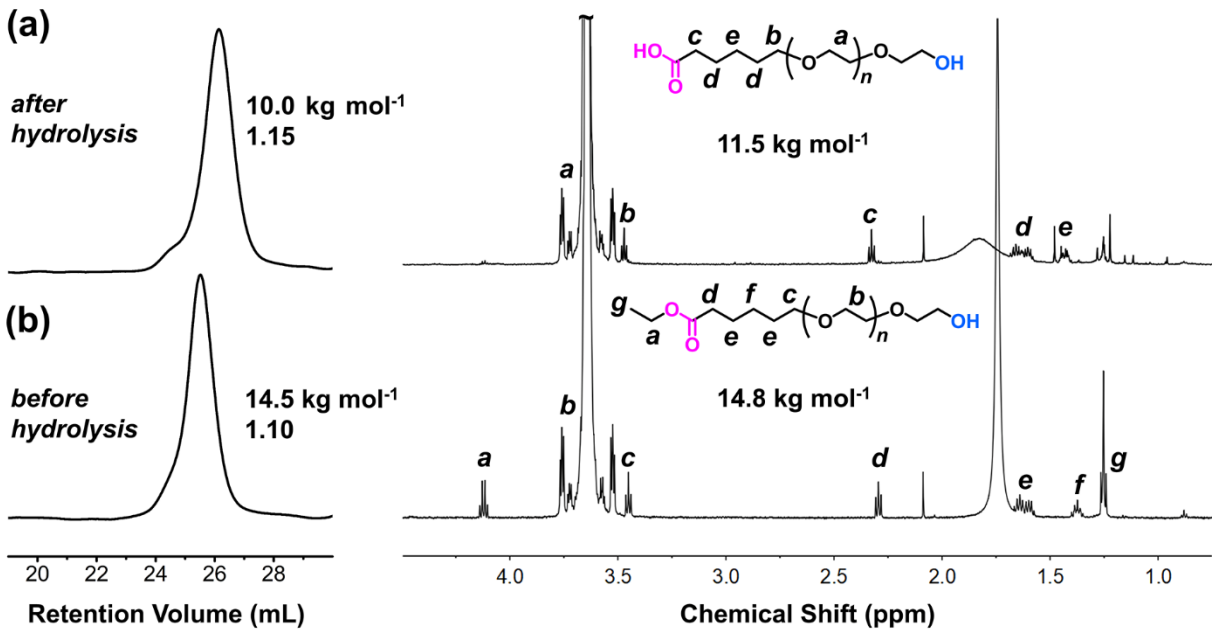

Fig. S4. SEC traces (left; crude products; RI signals; DMF, 50 °C, PEO standards; with $M_{n,SEC}$ and $Đ_M$ noted) and ^{1}H NMR spectra (right; isolated products; $CDCl_3$; with $M_{n,NMR}$ noted) of a relatively high-molar-mass α-carboxyl-ω-hydroxyl PEO (a) and the corresponding EH-initiated α-carboxylic ester-ω-hydroxyl PEO before hydrolysis (entry 3 in Table 1).

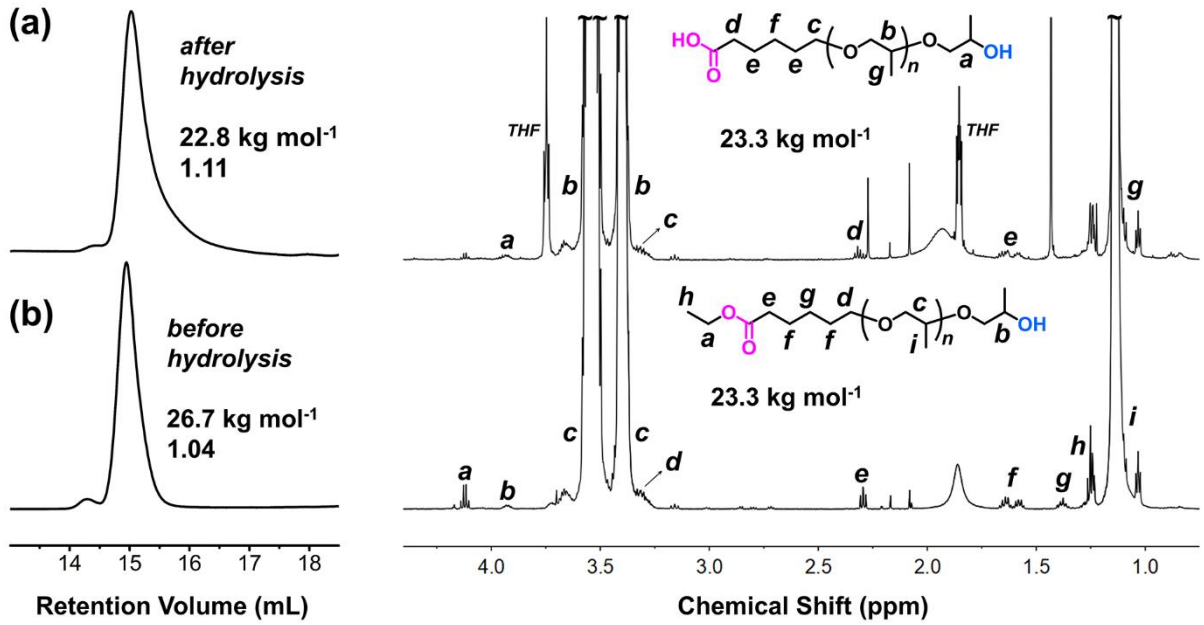

Fig. S5. SEC traces (left; crude products; RI signals; THF, 35 °C, PEO standards; with $M_{n,SEC}$ and $Đ_M$ noted) and ^{1}H NMR spectra (right; isolated products; $CDCl_3$; with $M_{n,NMR}$ noted) of a relatively high-molar-mass α-carboxyl-ω-hydroxyl PPO (a) and the corresponding EH-initiated α-carboxylic ester-ω-hydroxyl PPO before hydrolysis (entry 4 in Table 1).

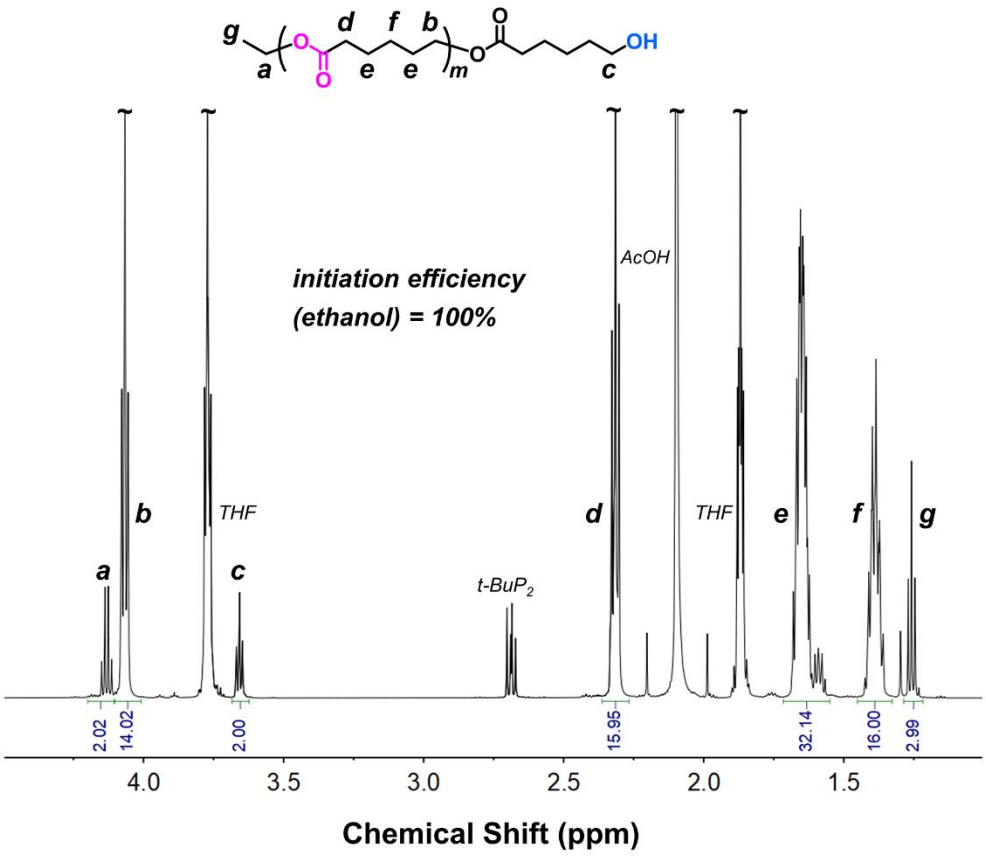

Fig. S6. ^{1}H NMR spectrum (crude product; $CDCl_3$) of the oligoCL (DP = 8) synthesized by ethanol-initiated oligomerization of CL with *t*-BuP_2 as the catalyst ($[CL]_0/[ethanol]_0/[t\text{-}BuP_2]$ = 8/1/0.05) and used as an initiator for the ROP of EO and PO (entries 5 and 6 in Table 1).

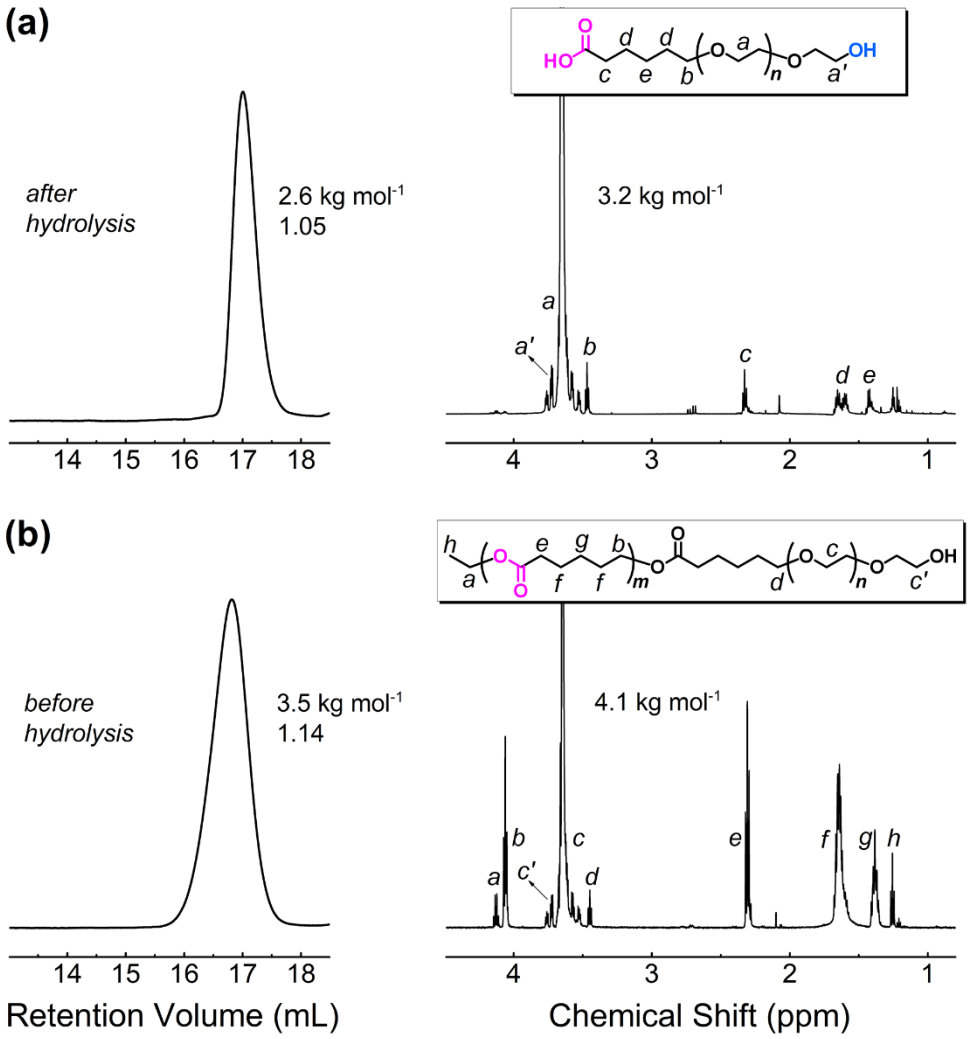

Fig. S7. SEC traces (left; crude products; RI signals; THF, 35 °C, PEO standards; with $M_{n,SEC}$ and $Đ_M$ noted) and ^{1}H NMR spectra (right; isolated products; $CDCl_3$; with $M_{n,NMR}$ noted) of α-carboxyl-ω-hydroxyl PEO (a) and the corresponding oligoCL-initiated PEO (CL_8-PEO) before hydrolysis (b) (entry 5 in Table 1).

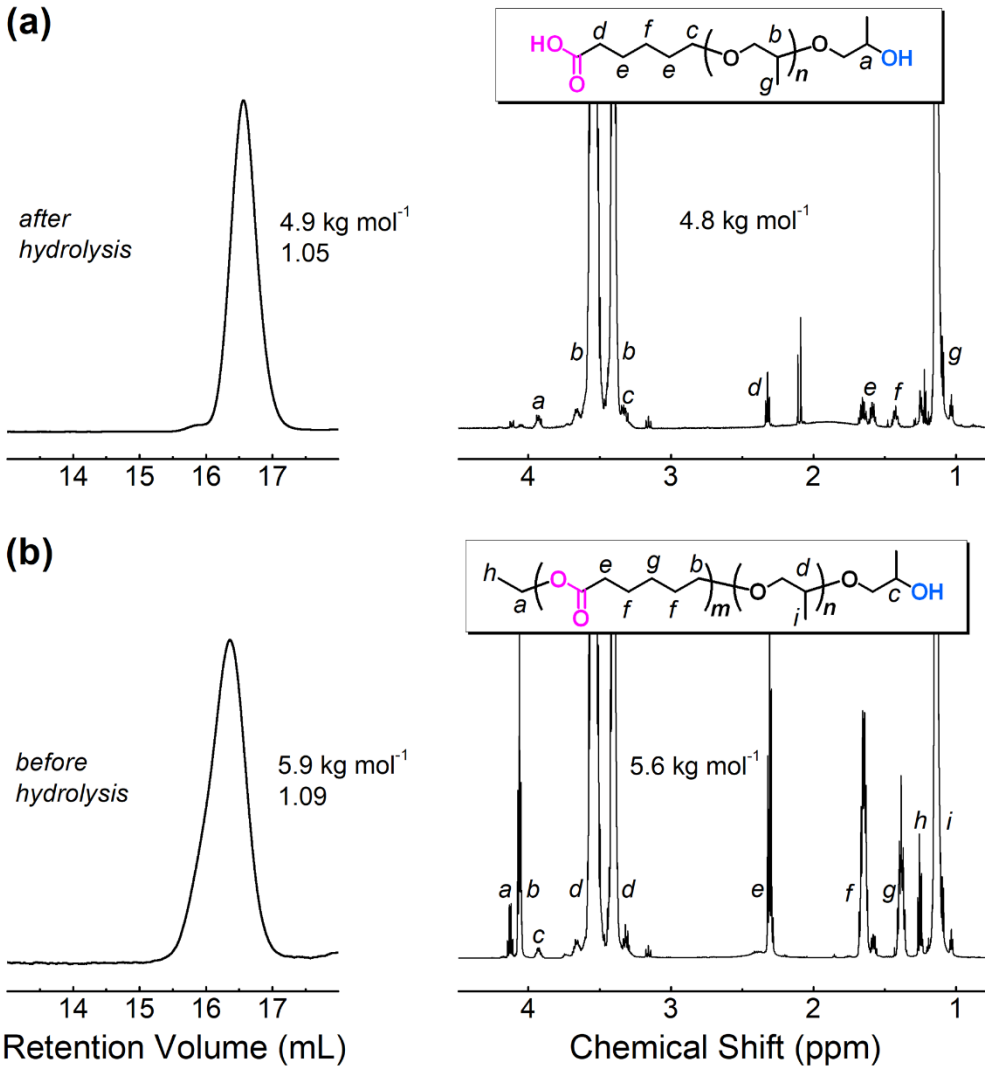

Fig. S8. SEC traces (left; crude products; RI signals; THF, 35 °C, PEO standards; with $M_{n,SEC}$ and $Đ_M$ noted) and ^{1}H NMR spectra (right; isolated products; $CDCl_3$; with $M_{n,NMR}$ noted) of α-carboxyl-ω-hydroxyl PPO (a) and the corresponding oligoCL-initiated PPO (CL_8-PPO) before hydrolysis (b) (entry 6 in Table 1).

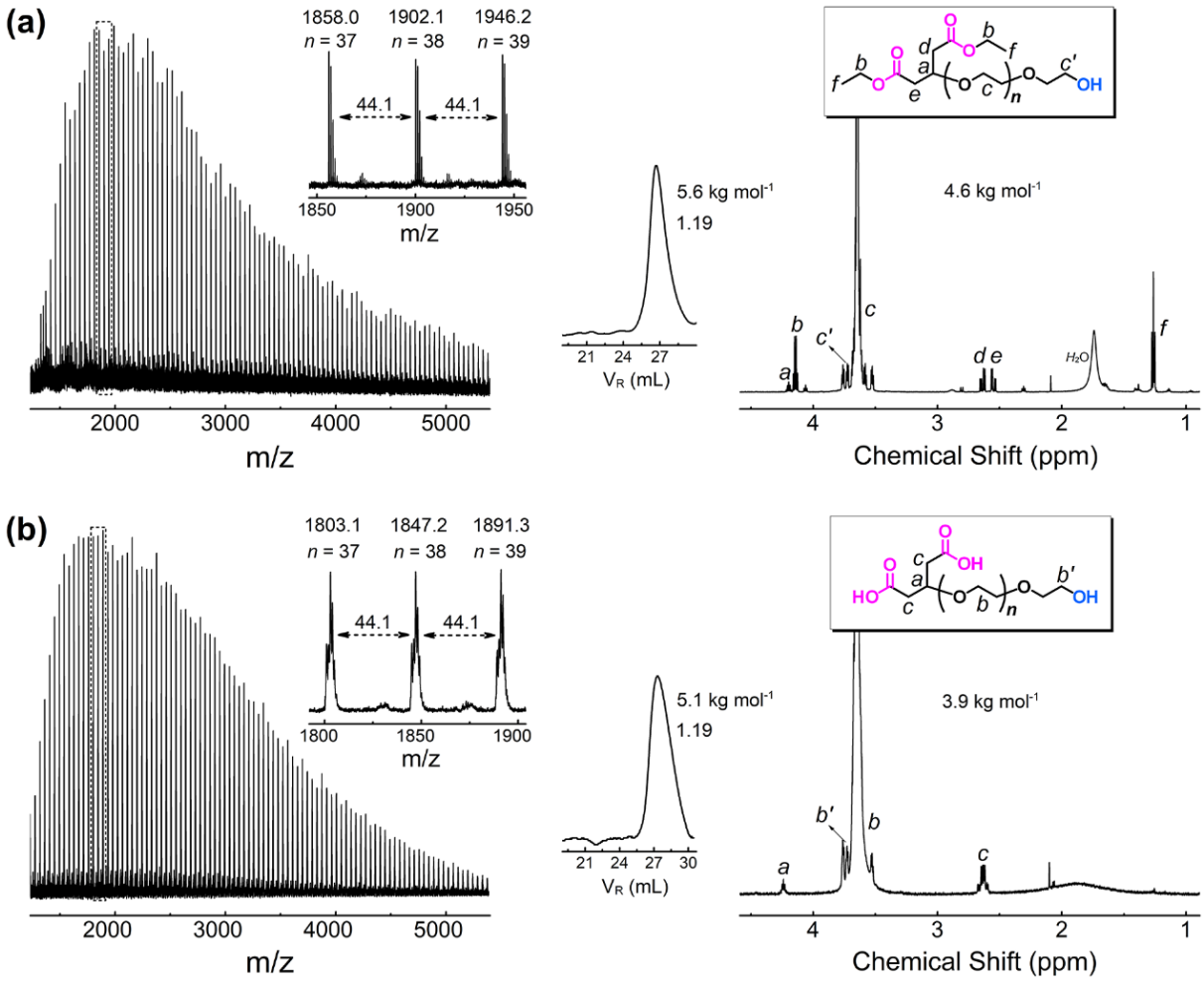

Fig. S9. MALDI-TOF MS spectra (left; isolated products), SEC traces (middle; crude products; RI signals, DMF, 50 °C, PEO standards; with $M_{n,SEC}$ and $Đ_M$ noted), and ^{1}H NMR spectra (right; isolated products; $CDCl_3$; with $M_{n,NMR}$ noted) of DH-initiated α-dicarboxylic ester-ω-hydroxyl PEO corresponding to entry 7 in Table 1 (a) and the α-dicarboxyl-ω-hydroxyl PEO obtained after hydrolysis of the dicarboxylic ester end group (b). Mass signals in the MALDI-TOF MS spectra correspond to PEOs ionized by sodium cations. Calculated masses for [DH-EO_{37}]Na^+ (a) and hydrolyzed [DH-EO_{37}]Na^+ (b) are 1858.9 and 1802.9 Da, respectively.

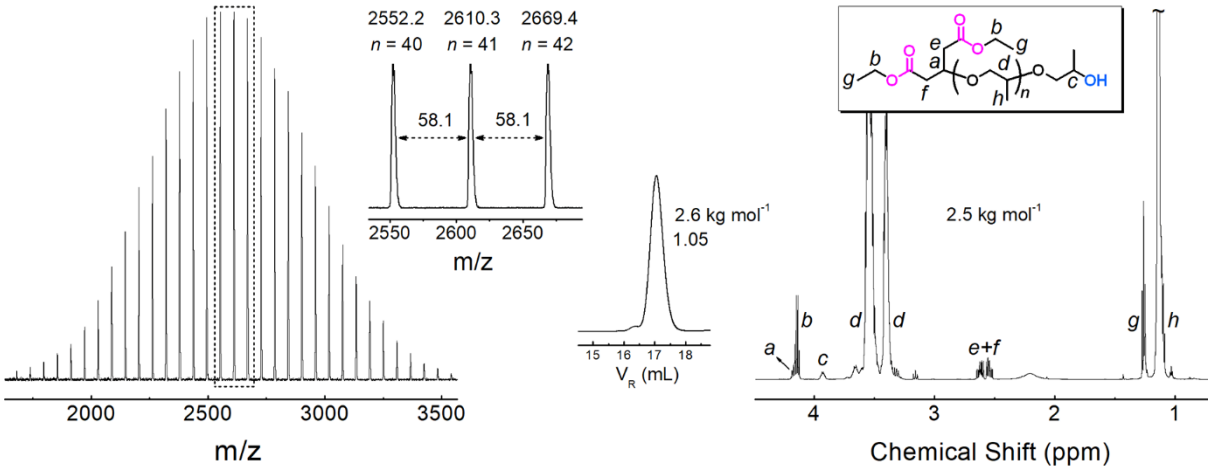

Fig. S10. MALDI-TOF MS spectrum (left; isolated product), SEC traces (middle; crude product; RI signals, THF, 35 °C, PEO standards; with $M_{n,SEC}$ and $Đ_M$ noted), and ^{1}H NMR spectra (right; isolated product; $CDCl_3$; with $M_{n,NMR}$ noted) of DH-initiated α-dicarboxylic ester-ω-hydroxyl PPO corresponding to entry 8 in Table 1. Mass signals in the MALDI-TOF MS spectrum correspond to PPOs ionized by sodium cations. Calculated masses for [DH-PO_{40}]Na^+ is 2551.2 Da.