

Supporting Information

One-pot Synthesis of Optically Active Polymer via Concurrent Cooperation of Enzymatic Resolution and Living Radical Polymerization

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Experimental Section

1. Materials

Ethyl 2-bromoisobutyrate (EBiB, J&K Chemical, 98%), copper bromide (CuBr, J&K Chemical, 98%), 4-nitrophenyl acetate (4-NPA, J&K Chemical, 97%), triethylamine (TEA, J&K Chemical, 99.5%), (±)-2-octanol (Aladding Reagent, 98%), R-(-)-2-octanol (Beijing Lyra Material-Tech Co., Ltd, 99.5%), methacryloyl chloride (J&K Chemical, 97%) and immobilized *Candida Antarctica* lipase B (Novozym 435, Beijing Cliscent Science and Technology Co., LTD) were used as purchased. 2,2,2-Trifluoroethyl methacrylate (TFEMA, J&K Chemical, 98%) was passed through a basic aluminum oxide column prior to use.

2. Instrumental Analysis

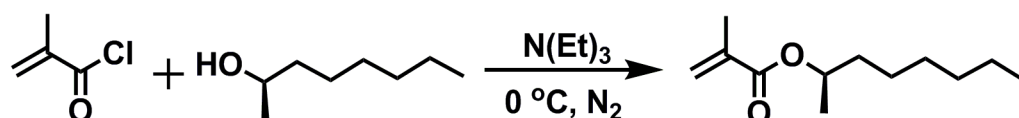
Gel permeation chromatography (GPC) analyses of polymers were performed using tetrahydrofuran (THF) as the eluent. The GPC system was a Shimadzu LC-20AD pump system comprising an auto injector, a MZ-Gel SDplus 10.0 μm guard column (50 \times 8.0 mm, 10² Å) followed by three MZ-Gel SDplus 10.0 μm bead-size columns (10⁵, 10³, and 10² Å) and a differential refractive index (dRI) detector. The system was calibrated with narrow molecular weight distribution polystyrene standards ranging from 200 to 10⁶ g mol⁻¹.

¹H NMR spectra were obtained using a JEOL JNM-ECA400 (400MHz) spectrometer for all samples. The specific rotation of the polymers was measured on an SGW-3 Autopolarizer in acetone (concentration=10 mg/mL) at 25 °C with λ =589.3 nm. Differential scanning calorimetry (DSC) was recorded on DSC Q2000 (TA

Instrument). The e. e. value was determined by GC (Astec Chiraldex β -PM, 50m*0.25mm*0.12 μ m, 70 $^{\circ}$ C, He, 1.0773 mL/min). The ESI-MS data were collected using a MicroTOF-QII Bruker. The FT-IR spectra were obtained in a transmission mode on a Perkin-Elmer Spectrum 100 spectrometer (Waltham, MA, USA).

3. Method

3.1. Synthesis of (R)-2-octyl methacrylate or (\pm)-2-octyl methacrylate



Methacryloyl chloride (2.0 g, 19.1 mmol), (R)-2-octanol (2.0 g, 15.4 mmol), triethylamine (2.0 g, 19.9 mmol) were dissolved in dry THF (25 mL). The system was stirred at 0 $^{\circ}$ C under nitrogen atmosphere for 12h. After removing the white solid by filtration, the filtrate was concentrated by rotation evaporation and the obtained crude product was purified by column chromatography on silica gel, eluting with petroleum ether to yield the target products.

1 H NMR (400 MHz, CDCl₃)/ppm: 6.07 (s, 1H, CH₂=C(CH₃)CO), 5.51 (s, 1H, CH₂=C(CH₃)CO), 4.95 (m, 1H, COOCH(CH₃)CH₂), 1.93 (s, 3H, CH₂=C(CH₃)), 1.40~1.20 (m, 13H, CH(CH₃)(CH₂)₅CH₃), 0.87 (t, J = 6.4 Hz, 3H, CH(CH₂)₅CH₃).

13 C NMR (100 MHz, CDCl₃)/ppm: 167.27, 137.05, 124.86, 71.43, 36.05, 31.83, 29.22, 25.44, 22.66, 20.02, 18.43, 14.14.

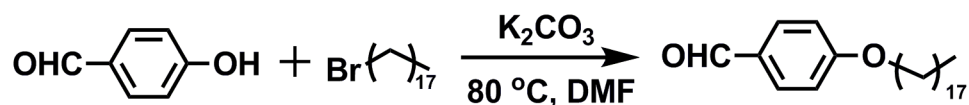
IR(ν /cm⁻¹): 2957, 2929, 2859, 1716, 1638, 1452, 1402, 1378, 1354, 1317, 1295, 1168, 1121, 1306, 1009, 936, 857, 813, 725.

ESI-MS: M+Na⁺ expected (observed): 221.1512 (221.1514).

The racemic monomer was synthesized by the same procedure.

3.2. Synthesis of 4'-(4-(octadecyloxy)phenyl)-2,2':6',2''-terpyridine (tpy)

3.2.1 Synthesis of 4-(octadecyloxy)benzaldehyde



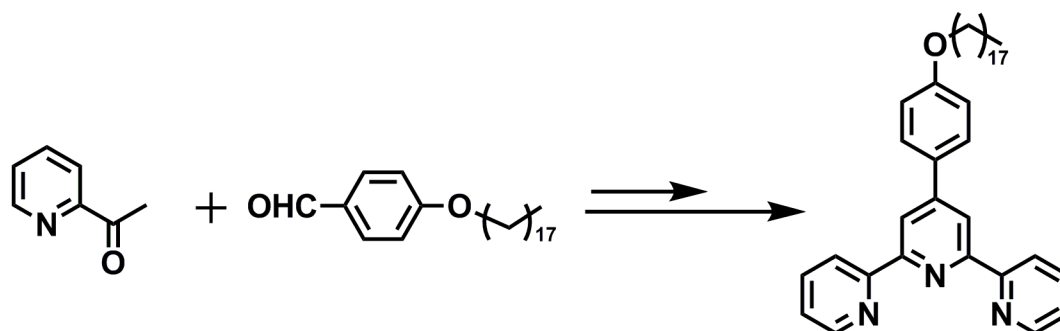
Bromooctadecane (6.67 g, 20 mmol), potassium carbonate (5.52 g, 40 mmol) and 4-hydroxybenzaldehyde (3.66 g, 30 mmol) were dissolved in DMF (100 mL) and reacted at 80 °C for 12 h. After cooling, the solution was poured into NaOH aqueous solution (50 mL, 5%), the precipitate was collected by filtration and recrystallized from ethanol. After drying under reduced pressure for 24 h, 5.95 g (15.9 mmol, 79.5%) of 4-(octadecyloxy)benzaldehyde was obtained as a pale powder:

¹H NMR (400 MHz, CDCl₃)/ppm: 9.86 (s, 1H, CHO); 7.81 (d, *J* = 8.7 Hz, 2H, ArH), 6.97 (d, *J* = 8.7 Hz, 2H, ArH), 4.03 (t, 2H, *J* = 6.7 Hz, OCH₂), 1.80 (m, 2H, OCH₂CH₂), 1.45 (m, 2H, OCH₂CH₂CH₂), 1.25 (m, 28H, AlkylH), 0.87 (t, 3H, *J* = 6.4 Hz, CH₃). ¹³C NMR (100 MHz, CDCl₃)/ppm: 190.93, 164.35, 132.08, 129.82, 114.83, 68.52, 32.01, 29.78-29.13 (13C), 26.04, 22.78, 14.22.

IR(ν/cm⁻¹): 2915, 2848, 2733, 1692, 1601, 1578, 1508, 1470, 1429, 1396, 1311, 1253, 1215, 1167, 1109, 1053, 1035, 1022, 1008, 858, 832, 812, 718.

ESI-MS: M+H⁺ expected (observed): 375.3258 (375.3253).

3.2.2 Synthesis of 4'-(4-(octadecyloxy)phenyl)-2,2':6',2''-terpyridine (tpy)



2-Acetylpyridine (3.63g, 30 mmol) and 4-(octadecyloxy)benzaldehyde (3.74 g, 10 mmol) were dissolved in mixed solution (methanol/THF = 1/1, 150 mL) by stirring for 5 min at 50 °C to get a clear solution, followed by addition of KOH aqueous solution (60 mL, 15%) and $\text{NH}_3\cdot\text{H}_2\text{O}$ (10 mL). The mixture was allowed to stand at 70 °C for 12 h. The reaction solution was concentrated by rotary evaporation to remove volatiles. Then the mixture was extracted by toluene. The extract was concentrated by rotary evaporation to a dark green solid. The solid was collected by vacuum filtration and rinsed with cold diethylether. After drying, a pale green solid was obtained as final product:

^1H NMR (400 MHz, CDCl_3)/ppm: 8.73 (d, $J = 4.5$ Hz, 2H, 3-H, 3''-H), 8.71 (s, 2H, 3'-H, 5'-H), 8.67 (d, $J = 7.8$ Hz, 2H, 6-H, 6''-H), 7.88 (m, 2H, 4-H, 4''-H), 7.87 (d, $J = 9.2$ Hz, 2H, ArH), 7.35 (m, 2H, 5-H, 5''-H), 7.02 (d, $J = 9.2$ Hz, 2H, ArH), 4.03 (t, $J = 6.7$ Hz, 2H, OCH_2), 1.80 (m, 2H, OCH_2CH_2), 1.45 (m, 2H, $\text{OCH}_2\text{CH}_2\text{CH}_2$), 1.25 (m, 28H, AlkylH), 0.87 (t, $J = 6.4$ Hz, 3H, CH_3). ^{13}C NMR (400 MHz, CDCl_3)/ppm: 160.22, 156.48, 155.85, 149.92, 149.12, 137.03, 130.45, 128.54, 123.87, 121.56, 118.36, 114.96, 68.23, 32.01, 29.78-29.13 (Alkyl-C), 26.04, 22.78, 14.22. ESI-MS: IR(v/cm^{-1}): 2915, 2850, 1659, 1633, 1609, 1585, 1567, 1517, 1442, 1421, 1391, 1297, 1258, 1229, 1185, 1114, 1039, 990, 913, 846, 826, 788, 733, 660.

ESI-MS: $M+H^+$ expected (observed): 578.4105 (578.4105).

3.2. Model enzymatic resolution reaction

A model enzymatic resolution reaction between TFEMA and (\pm)-2-octanol was conducted as follow. To schlenk tube A were charged TFEMA (1.00 g, 6.0 mmol), (\pm)-2-octanol (1.55 g, 12.0 mmol), TEA (0.60 g, 6.0 mmol) and toluene (6.0 mL). The resulting solution was then degassed through three freeze-pump-thaw cycles. In the mean time, Novozym 435 (0.5 g) were added into another schlenk tube B equipped with a magnetic stir bar followed by evacuated and backfilled with nitrogen for three times. Then the thawed solution in tube A was cannulated into tube B under nitrogen atmosphere. The final reaction mixture was put into an oil bath maintained at 55 °C. Samples were withdrawn periodically for 1H NMR and chiral GC analyses to characterize conversion and resolution efficiency, respectively.

3.3. One-pot synthesis of optically active polymer

A typical procedure for the one-pot synthesis of optically active polymer is as follows. To schlenk tube A were charged TFEMA (1.00 g, 6.0 mmol), (\pm)-2-octanol (1.55 g, 12.0 mmol), TEA (0.60 g, 6.0 mmol), EBiB (14.6 mg, 0.075 mmol), anisole (10.0 mg, 0.092 mmol) and toluene (6.0 mL). The resulting solution was then degassed through three freeze-pump-thaw cycles. In the mean time, CuBr (1.5 mg, 0.01 mmol), tpy (18.0 mg, 0.03 mmol) and Novozym 435 (0.5 g) were added into another schlenk tube B equipped with a magnetic stir bar followed by evacuated and backfilled with nitrogen for three times. Then the thawed solution in tube A was cannulated into tube B under nitrogen atmosphere. The final reaction mixture was put into an oil bath

maintained at 55 °C. Samples were withdrawn periodically for ¹H NMR and GPC analyses for conversion and molecular weight determination, respectively. At the end of the polymerization, the mixture was centrifuged to remove immobilized enzyme, then passed through a short neutral alumina column prior to further purification. The purified polymer was obtained via precipitation from THF to methanol for three times, and then dried under vacuum for further characterization. All polymers obtained through one-pot combination of enzymatic resolution reaction and ATRP are prepared with the same approach and all other control polymers were prepared in the similar manner as that described above.

3.4. Transesterification of poly(TFEMA)

Poly(TFEMA) (0.1 g, Mn=8800, synthesized by ATRP), (±)-2-octanol (0.155 g), TEA (0.06 g), Novozym (0.05 g), toluene (1 mL) and Chloroform-d (1 mL) were mixed together and placed at 55 °C. After 40 hours, the mixture was centrifuged to remove the enzyme and the liquor was subjected to ¹H NMR characterization.

3.5. Enzyme activity test

The Novozym 435 after polymerization was collected by centrifugation and washed using toluene to remove copper salts until the washing liquor turned from light green to colorless. Subsequently the enzyme was dried under vacuum until constant weight for next activity test using 4-NPA as substrate. The typical procedure is as follow.

A toluene solution (1.0 mL) containing 4-NPA (20.0 mg, 0.11 mmol) and methanol (7.0 mg, 0.22 mmol) was added into a 1.5 mL vial containing 6.0 mg of recycled Novozym 435. The assay reactions were carried out at 35 °C (450 rpm). Samples were

withdrawn periodically for enzyme activity analysis. The produced 4-nitrophenol (4-NP) in the reaction was determined by UV/Vis at the λ_{max} (304 nm). The enzyme activity was defined as the the formation rate of 4-NP catalyzed by enzyme. The activity of pristine enzyme was tested with the same fashion and defined as a control (100%) to calculate the retained activity of enzyme samples after polymerization. The test was repeated 3 times and the result was expressed as mean \pm SD.

Supporting Data

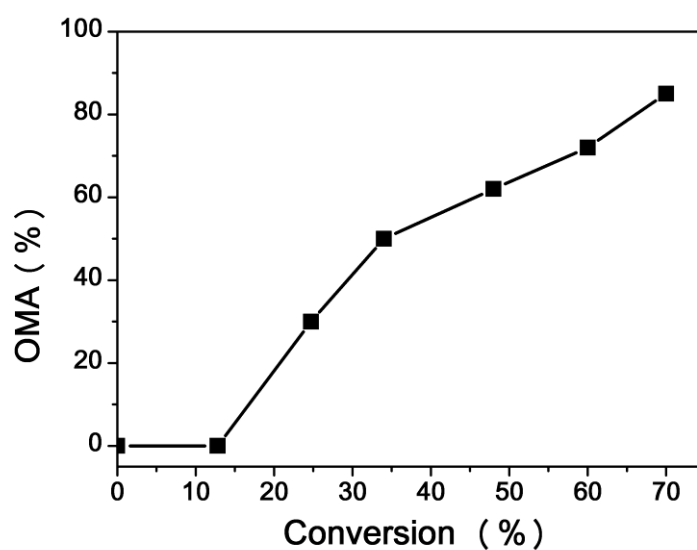


Figure S1. The proportion of OMA in poly(TFEMA)-*co*-poly(OMA) *versus* polymerization conversion.

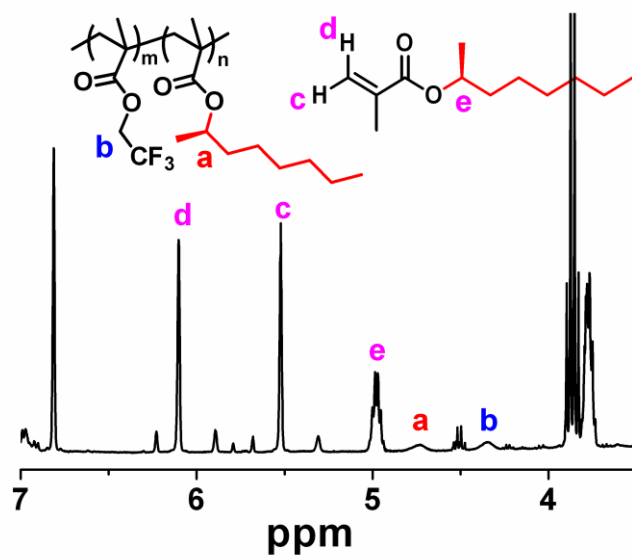


Figure S2. The ^1H NMR (CDCl_3) analysis of the reaction mixture for the one-pot synthesis of optically active polymer at 10 hours.

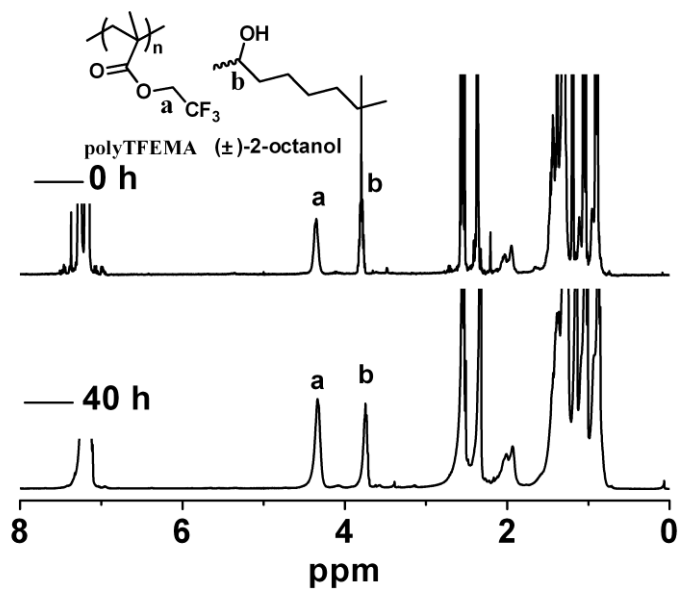


Figure S3. Transesterification experiment of poly(TFEMA) and racemic 2-octanol.

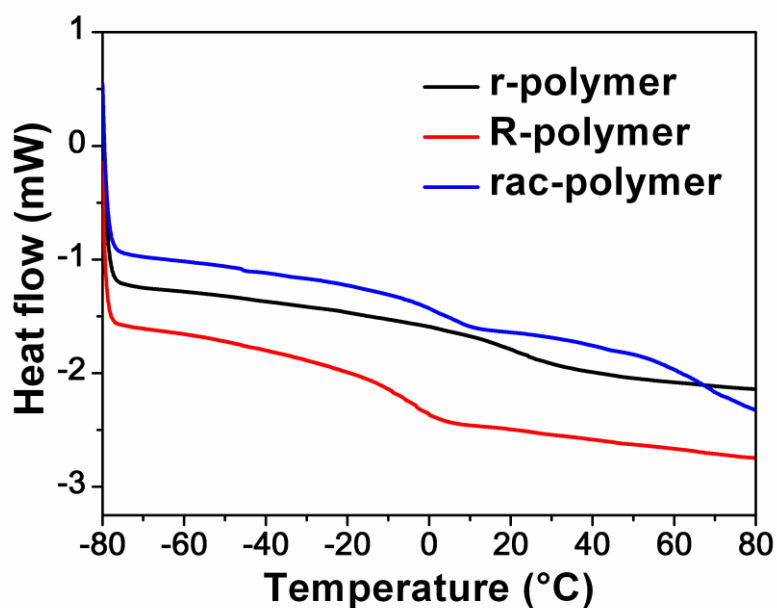


Figure S4. DSC analysis of the obtained polymers: *r*-polymer-prepared by the one-pot enzymatic resolution ATRP; *R*-polymer-prepared by direct ATRP of (*R*)-2-octyl methacrylate; *rac*-polymer-prepared by direct ATRP of racemic 2-octyl methacrylate.

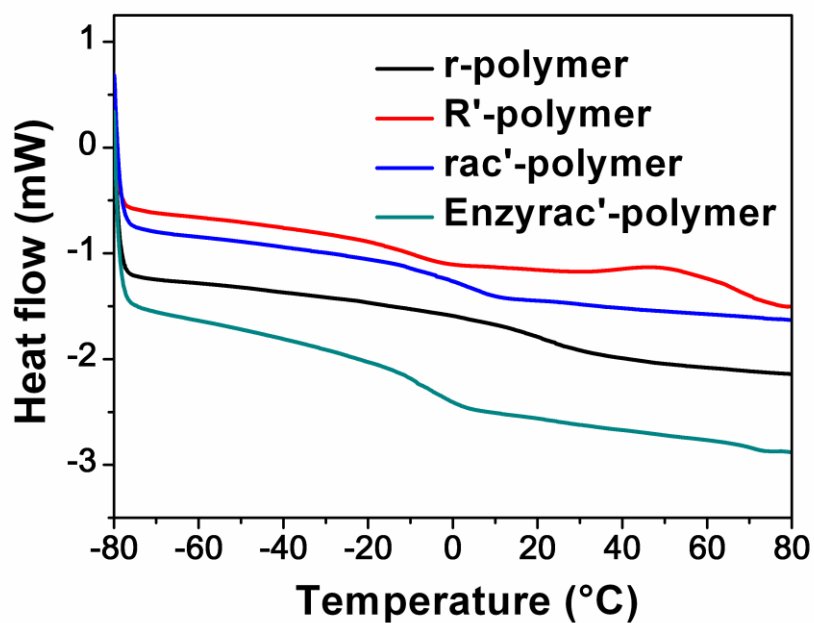


Figure S5. DSC analyses of the obtained polymers: *r*-polymer--prepared by the

one-pot enzymatic resolution ATRP; *R'*-polymer-prepared by direct ATRP of (*R*)-2-octyl methacrylate in the presence of TFE; *rac'*-polymer-prepared by direct ATRP of racemic 2-octyl methacrylate in the presence of TFE; *Enzyrac'*-polymer-prepared by direct ATRP of racemic 2-octyl methacrylate in the presence of TFE and Novozym 435.

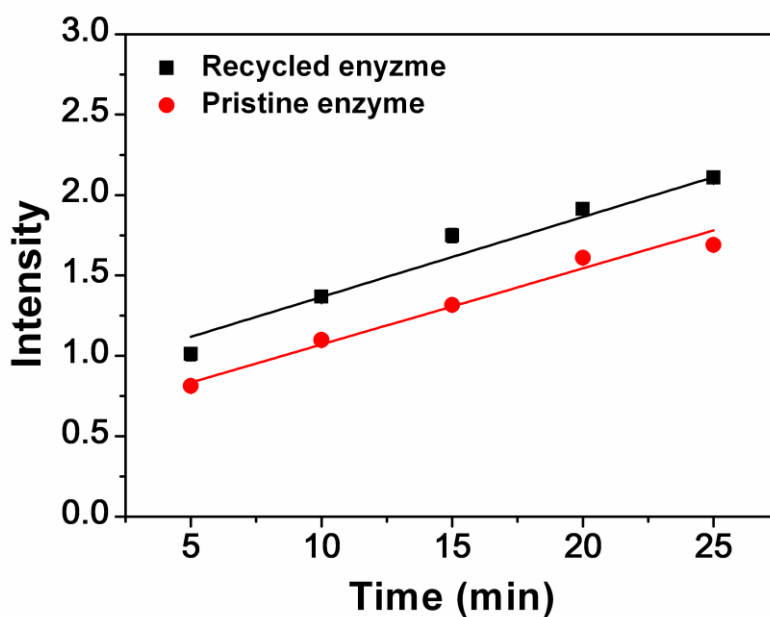


Figure S6. The enzyme activity was tested through enzymatic transesterification of 4-nitrophenyl acetate (4-NPA) with methanol. Values were expressed as group mean \pm SD.