Electronic Supplementary Information

Stereogradient polycaprolactones formed by asymmetric kinetic resolution polymerization of 6-methyl-ε-caprolactone

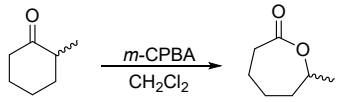
Chengdong Lv,[a,b] Guangqiang Xu,*[a,b] Rulin Yang, [a,b] Li Zhou [a] and Qinggang Wang *[a,b]

a. Qingdao Institute of Bioenergy and Bioprocess Technology, Chinese Academy of Sciences, Qingdao, 266101, China.

b. Center of Materials Science and Optoelectronics Engineering, University of Chinese Academy of Sciences, Beijing, 100049, China.

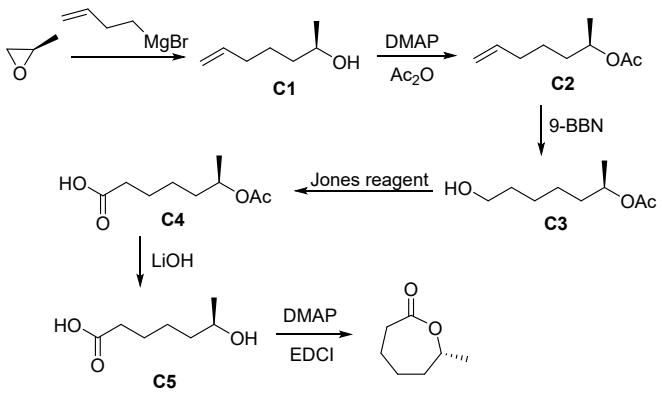
1. Synthesis procedure of the racemic/chiral 6-methyl-ε-caprolactone (6-MeCL)

(a) Racemic 6-methyl-ε-caprolactone (*rac*-6-MeCL)



Rac-6-MeCL was synthesized by using the Baeyer-Villiger reaction. At room temperature, 3-chloroperoxybenzoic acid (*m*-CPBA, 30 g, 174 mmol, 1.1 equiv.) was added to 2-methylcyclohexanone (17.7 g, 158 mmol, 1 equiv.) in 150 mL dichloromethane (DCM). After 12 h, Na_2SO_3 (3 M, 100 mL) and saturated brine (200 mL) was added to the mixture. The reaction mixture was extracted with DCM (200 mL) to obtain oil liquid. The crude product was then purified by flash chromatography (*n*-hexane: ethyl acetate = 20:1) to give a colorless liquid (14.4 g, 71% yield). ^{1}H NMR (400 MHz, Chloroform-*d*) δ: 4.48 – 4.41 (m, 1H), 2.89 – 2.45 (m, 2H), 2.04 – 1.79 (m, 3H), 1.71 – 1.53 (m, 3H), 1.35 (d, *J* = 6.4 Hz, 3H). ^{13}C NMR (100 MHz, Chloroform-*d*) δ: 175.7, 77.0, 36.4, 35.2, 28.5, 23.1, 22.7.

(b) Chiral 6-methyl-ε-caprolactone (*R or S*-6-MeCL)



(*R*) or (*S*)-6-methyl-ε-caprolactone was synthesized by six steps reactions from chiral propylene oxide.

Step 1: Under Ar condition, CuI (3.8 g, 0.03 mol, 0.1 equiv.) was dissolved in dried THF (50 mL) and cooled to - 20 °C, then 3-butenylmagnesium bromide solution (1 M THF, 250 mL, 0.25 mol, 1.25 equiv.) was added. (*S*) or (*R*)-propylene oxide (11.6 g in 50 mL THF, 0.2 mol, 1 equiv.) was added slowly to react for 3 h. After accomplish, NH_4Cl (1 M, 150

mL) was added to the reaction system, and ethyl acetate (100 mL) was used to extract the reaction system, dried to obtain colorless liquid **C1** (18.2 g, 80% yield).

Step 2: Under Ar condition, **C1** compound (18.2 g, 0.16 mol, 1 equiv.) was dissolved in DCM (100 mL), DMAP (1.95 g, 0.016 mol, 0.1 equiv.) and triethylamine (24.1 g, 0.24 mol, 1.5 equiv.) were added at 0 °C. Then acetic anhydride (24.4 g, 0.24 mol, 1.5 equiv.) was added slowly and reacted overnight. After accomplish, reaction mixture was washed with brine (100 mL) for 3 times and dried to obtain **C2** as colorless liquid (22.3 g, 89% yield).

Step 3: Under Ar condition, **C2** compound (22.3 g, 0.143 mol, 1 equiv.) was dissolved in dried THF (100 mL), and 9-BBN (0.5 M in THF, 380 mL, 0.179 mol, 1.25 equiv.) was added to react overnight at 0 °C. Then NaOH (3 M in H_2O, 60 mL, 0.179 mol, 1.25 equiv.) and H_2O_2 (9.8 M in H_2O, 18 mL, 0.179 mol, 1.25 equiv.) were added to react for 4 h. After accomplish, reaction mixture was extracted with ethyl acetate (100 mL) and washed with brine for 3 times, then dried to obtain **C3** as colorless liquid (24.0 g, 96% yield).

Step 4: At - 10 °C (ice salt bath), Jones reagent (2 M CrO_3 in H_2SO_4, 50 mL, 0.1 mol, 2.0 equiv.) was added to **C3** compound (8.94 g, 0.05 mol, 1 equiv.) in 100 mL acetone slowly to react for 3 h. After accomplish, 50 mL isopropanol was added, the mixture was filtered by diatomite (washed with acetone) and washed with saturated $NaHCO_3$ (70 mL). The aqueous phase was adjusted to *p*H = 2 with 1 N HCl solution, then extracted with 50 mL ethyl acetate. The organic phase was washed with brine (50 mL) and dried to obtain **C4** as colorless liquid (5.7 g, 59% yield).

Step 5: At room temperature, **C4** (5.7 g, 0.03 mol, 1 equiv.) was dissolved in the mixture solution (THF:H_2O = 9:1, 50 mL), then LiOH (1 g, 0.045 mol, 1.5 equiv.) was added slowly to react overnight. After accomplish, THF was removed and the aqueous phase was adjusted to pH = 2 with 1 N HCl solution. Reaction mixture was extracted with ethyl acetate and washed with brine for 3 times to obtain light yellow liquid after rotary evaporator, then further purified with flash column chromatography (PE:EA = 3:1) to obtain **C5** (1.5 g, 34% yield). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 3.84 – 3.80 (m, 1H), 2.38 (t, *J* = 7.4 Hz, 2H), 1.80 – 1.36 (m, 6H), 1.20 (d, *J* = 6.2 Hz, 3H). ^{13}C NMR (100 MHz, Chloroform-*d*) δ 178.2, 67.9, 38.8, 33.7, 25.2, 24.6, 23.5.

Step 6: At room temperature, EDCI·HCl (0.34 g, 0.04 mol, 1.3 equiv.) and DMAP (0.25 g, 0.045

mol, 1.5 equiv.) were dissolved in 40 mL DCM, and **C5** (0.2 g, 0.03 mol, 1 equiv.) in 10 mL DCM was added to reaction mixture. After accomplish, DCM was removed and reaction mixture was purified by flash column chromatography (PE:EA = 20:1) to obtain (*S*) or (*R*)-6-MeCL as colorless oil. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 4.48 – 4.41 (m, 1H), 2.89 – 2.45 (m, 2H), 2.04 – 1.79 (m, 3H), 1.71 – 1.53 (m, 3H), 1.35 (d, *J* = 6.4, 3H). ^{13}C NMR (100 MHz, Chloroform-*d*) δ 175.7, 77.0, 36.4, 35.2, 28.5, 23.1, 22.7.

2. Figures

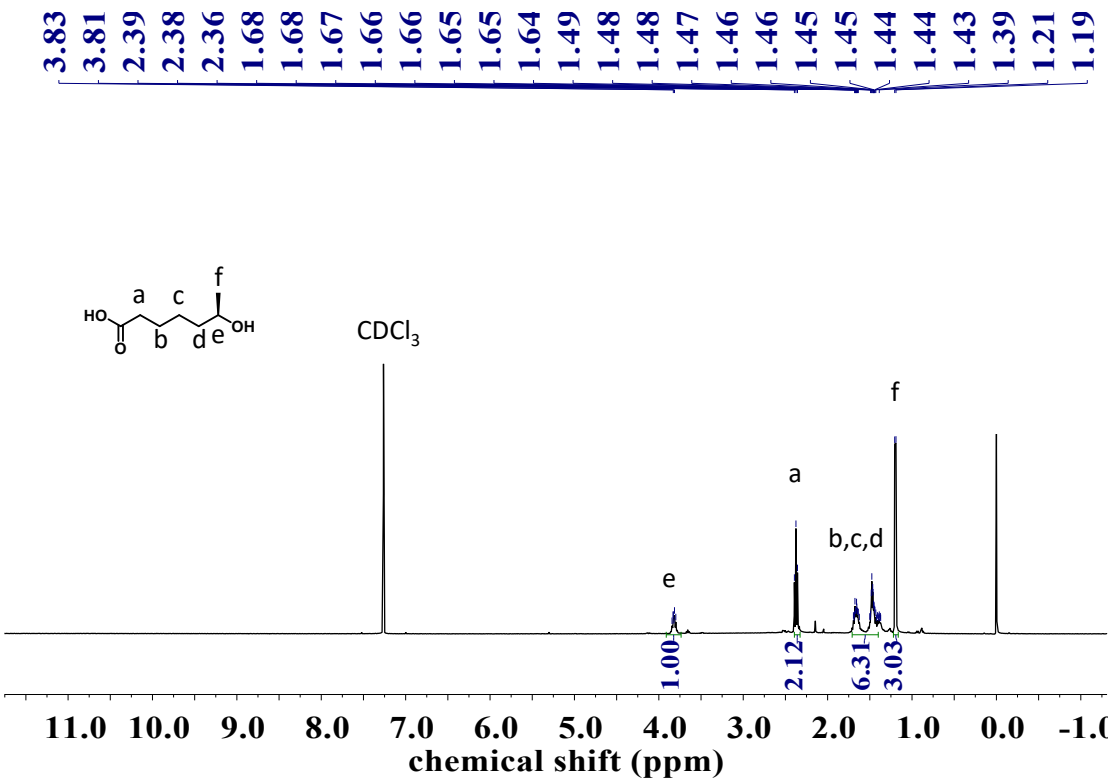


Figure S1. ^{1}H NMR spectrum of **C5** compound (400 MHz, Chloroform-*d*, 298 K).

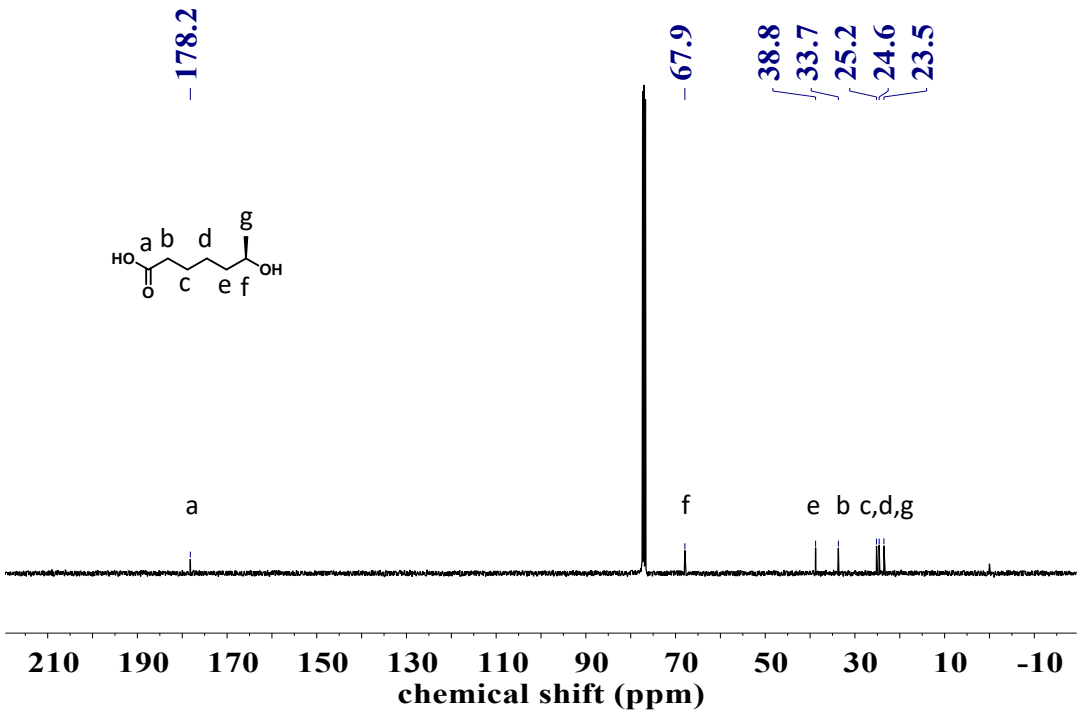


Figure S2. ^{13}C NMR spectrum of **C5** compound (100 MHz, Chloroform-*d*, 298 K).

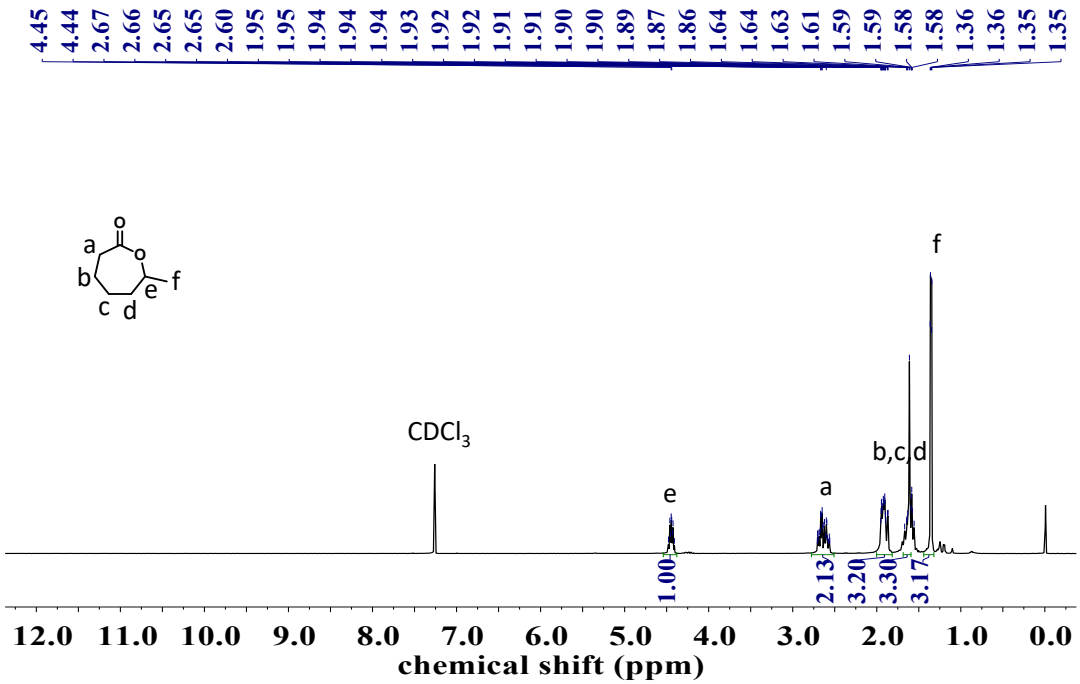


Figure S3. ^{1}H NMR spectrum of 6-MeCL (400 MHz, Chloroform-*d*, 298 K).

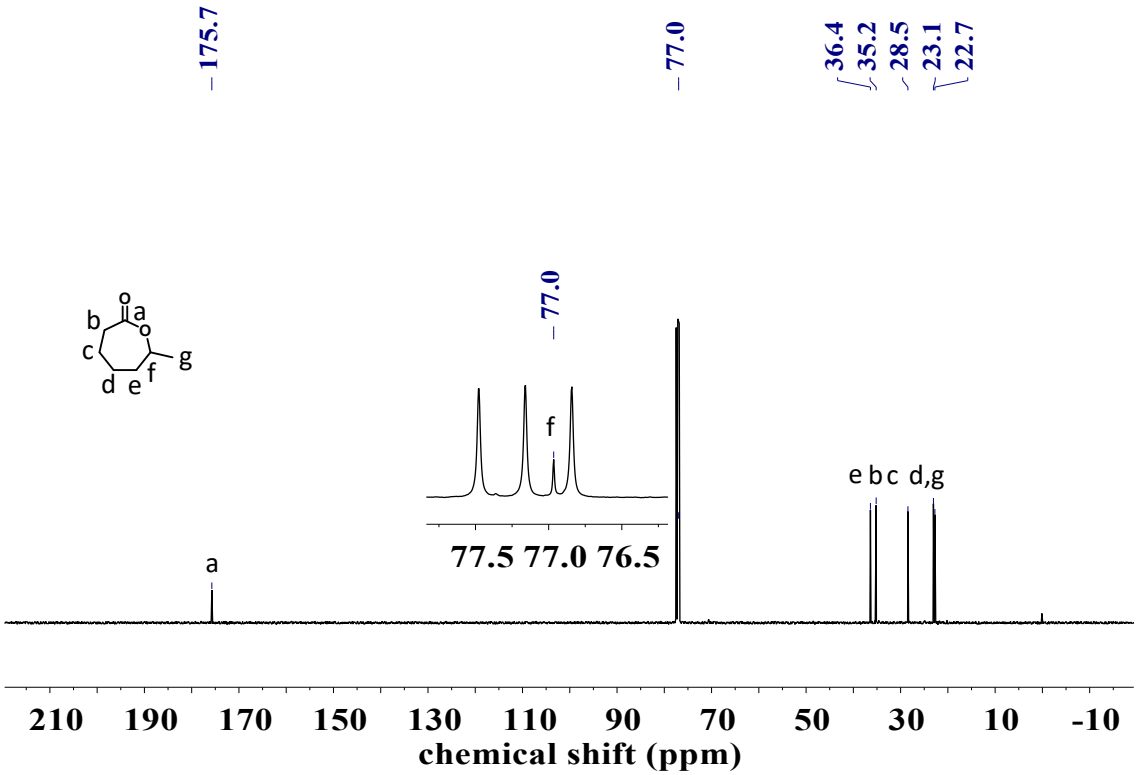


Figure S4. ^{13}C NMR spectrum of 6-MeCL (100 MHz, Chloroform-*d*, 298 K).

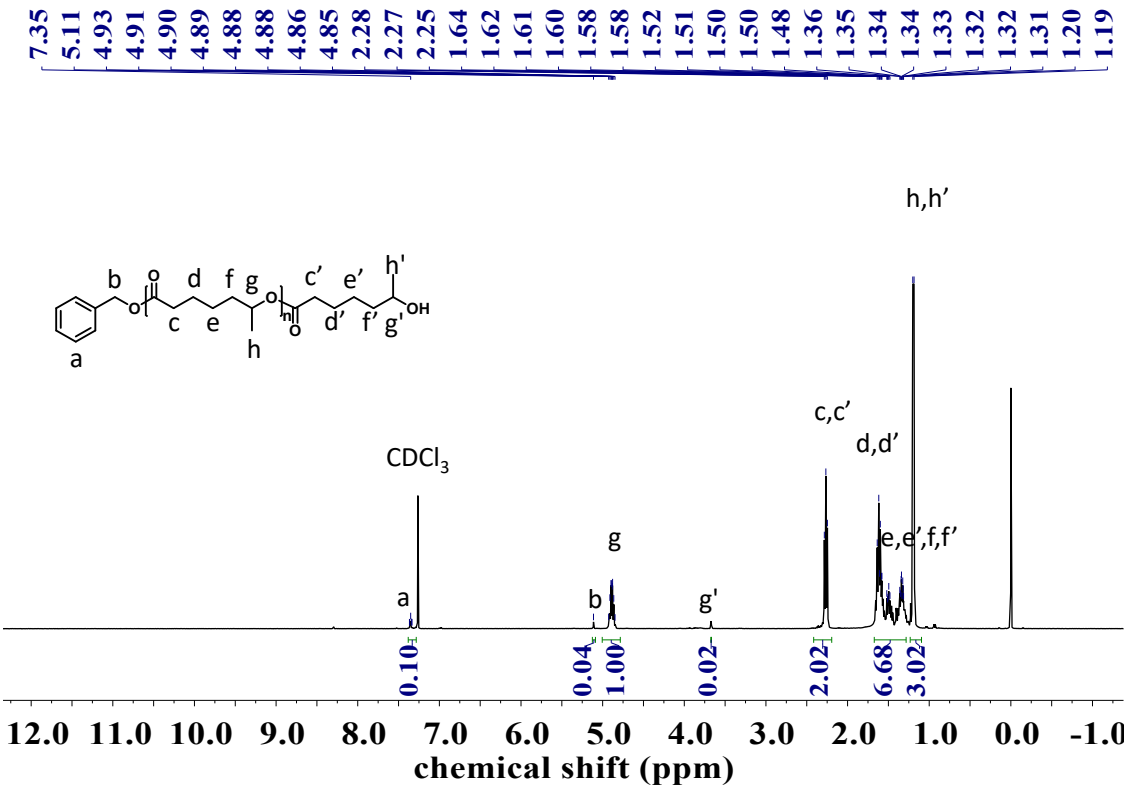


Figure S5. ^{1}H NMR spectrum of P(6-MeCL) (400 MHz, Chloroform-*d*, 298 K).

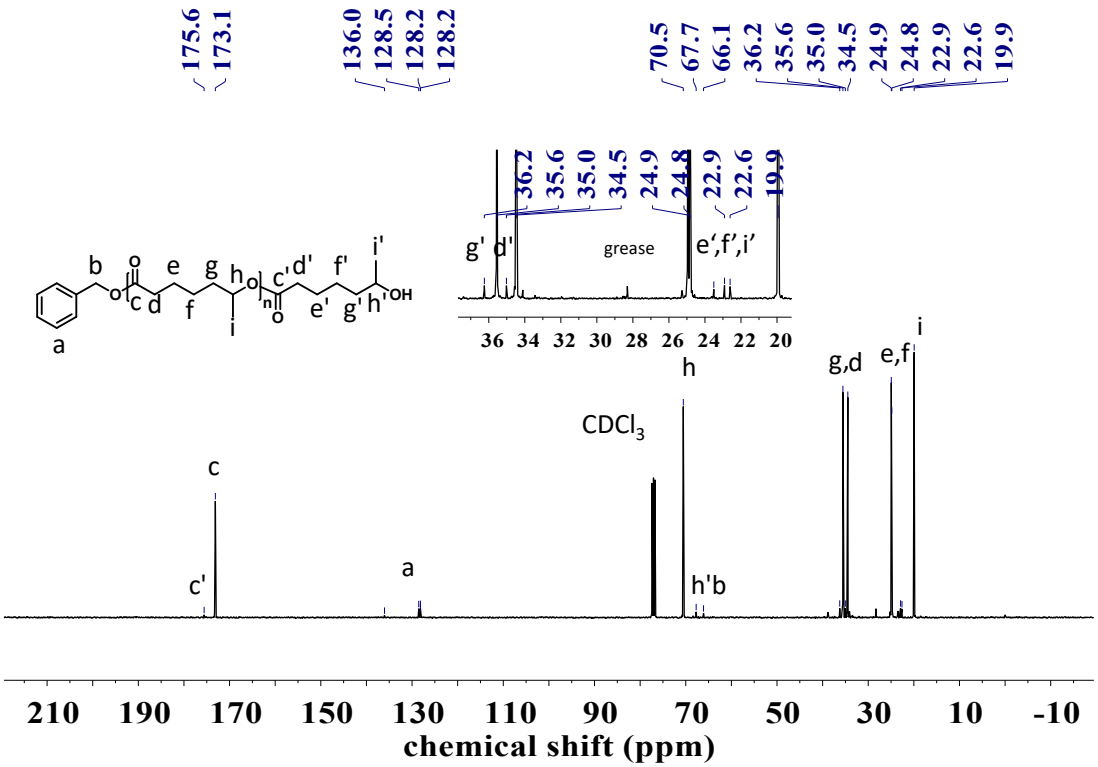


Figure S6. ^{13}C NMR spectrum of P(6-MeCL) (100 MHz, Chloroform-*d*, 298 K).

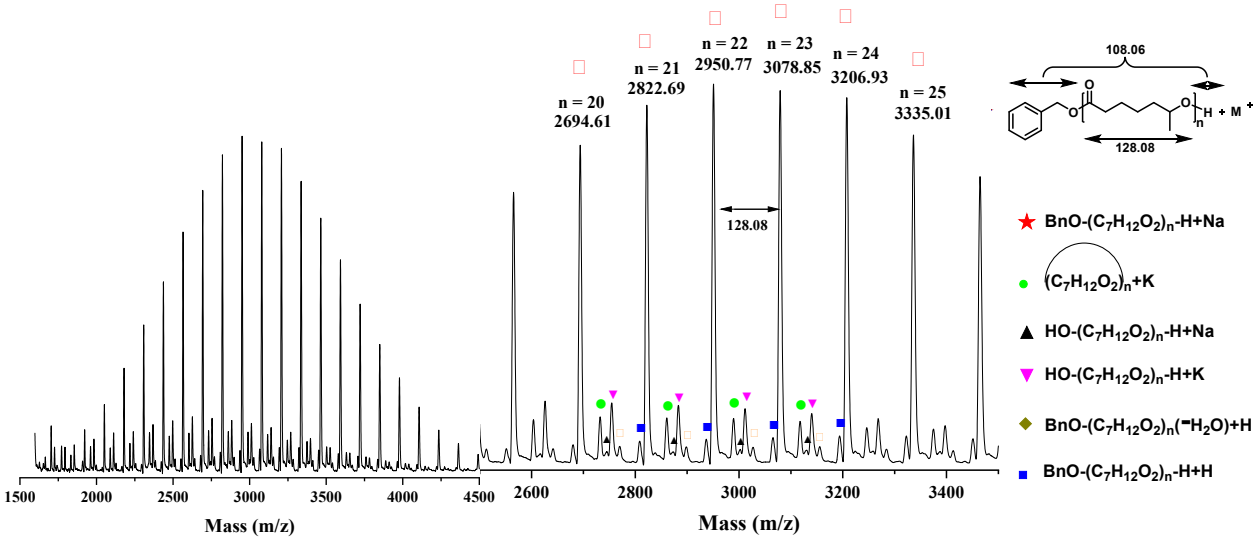


Figure S7. MALDI-TOF MS spectrum of low molecular weight P(6-MeCL).

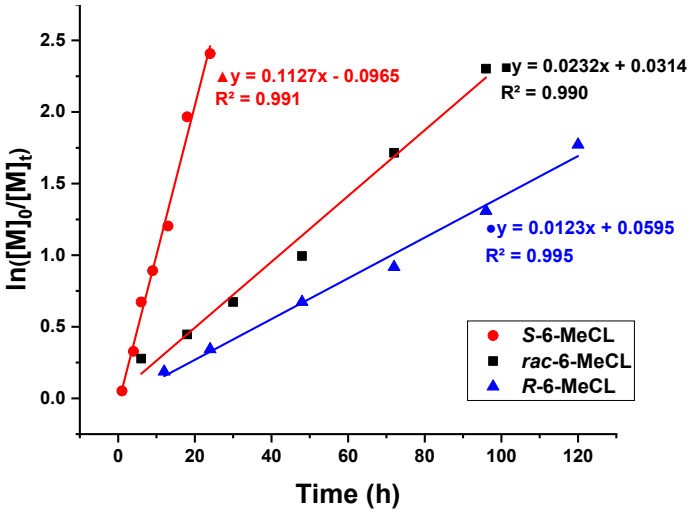


Figure S8. Semilogarithmic plots of ln([6-MeCL]$_0$/[6-MeCL]$_t$) versus time for *rac/R/S*-6-MeCL polymerization catalyzed by (*S*)-CPA-2 at room temperature.

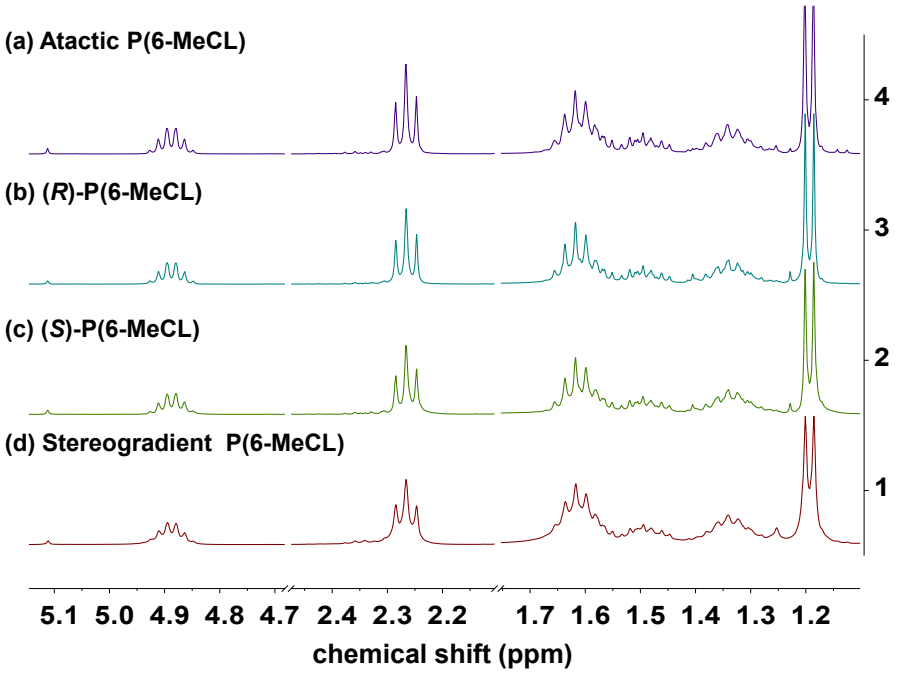


Figure S9. ^{1}H NMR spectra of atactic/isotactic/stereogradient P(6-MeCL)s. (Atactic polymer: Table S1, entry 1; (*R*)/(*S*)-polymer: Table 2, entries 2/3; Stereogradient polymer: Table 2, entry 1.)

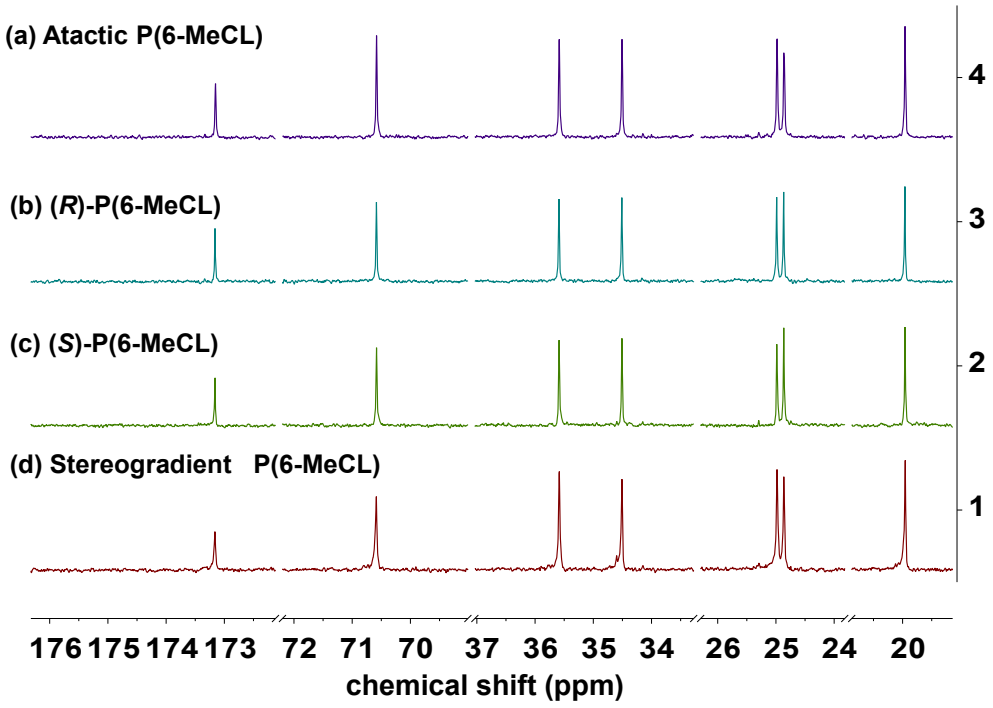


Figure S10. ^{13}C NMR spectra of atactic/isotactic/stereogradient P(6-MeCL)s. (Atactic polymer: Table S1, entry 1; (*R*)/(*S*)-polymer: Table 2, entries 2/3; Stereogradient polymer: Table 2, entry 1.)

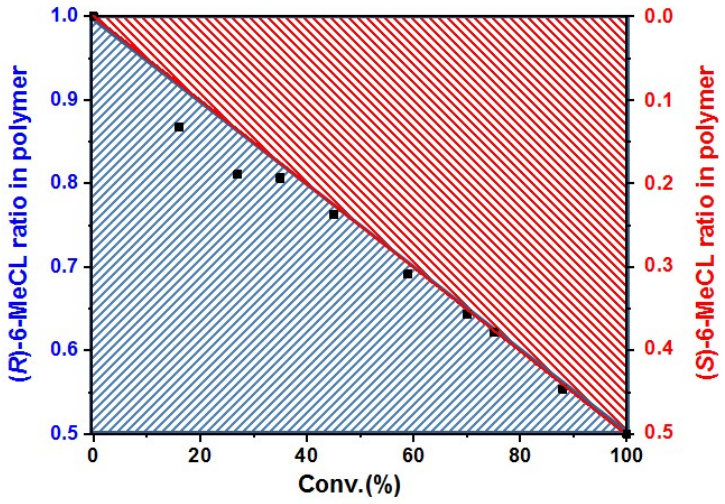


Figure S11. (*R*)/(*S*)-6-MeCL ratios in stereogradient P(6-MeCL) samples from AKRP of *rac*-6-MeCL by (*R*)-CPA-2 according to Table S3.

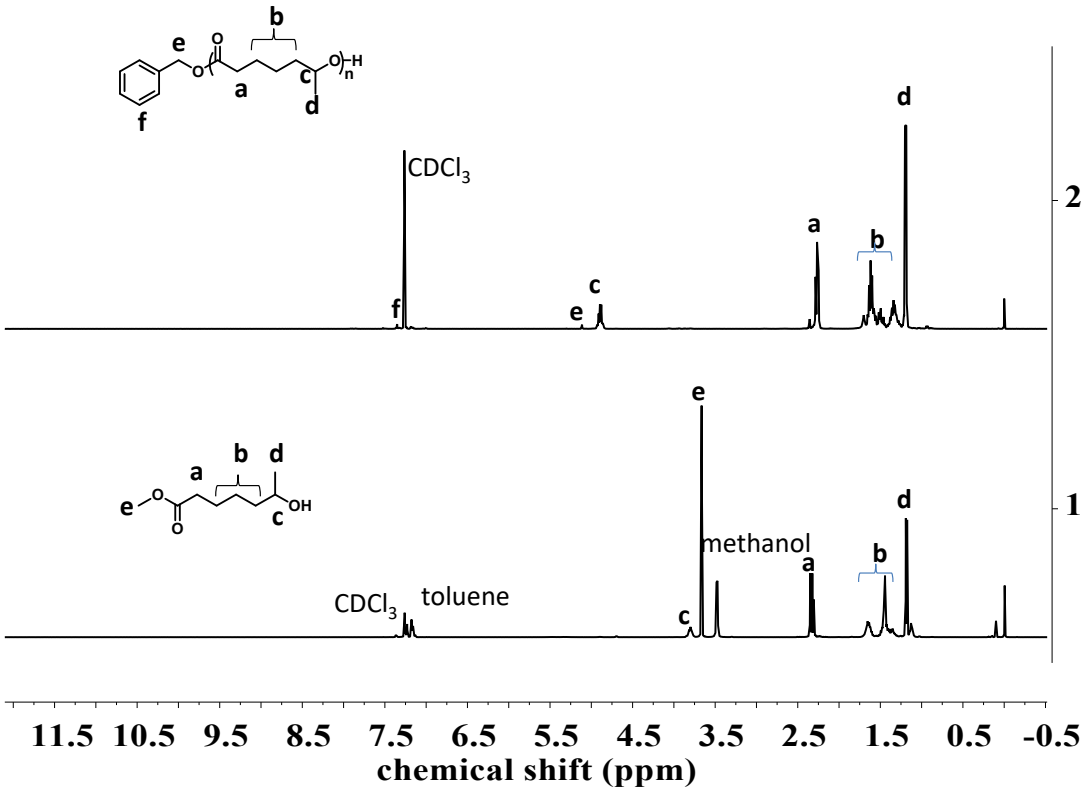
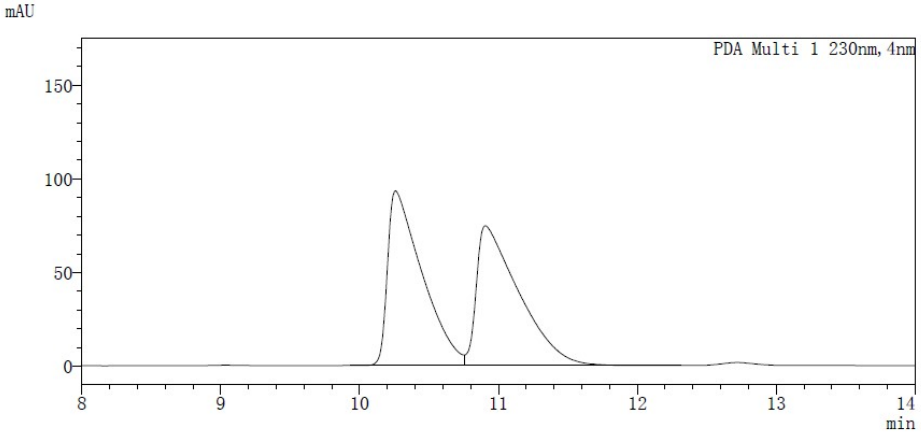
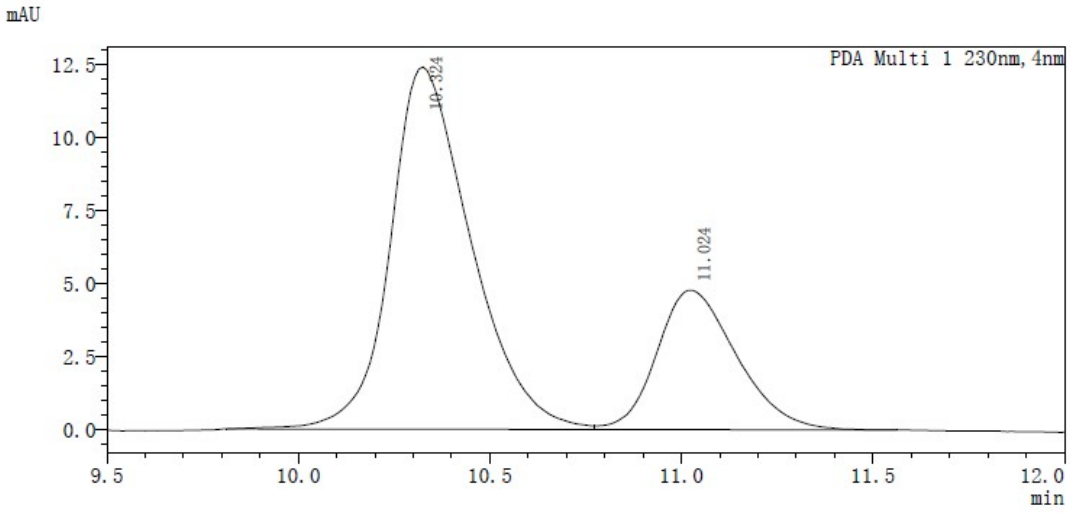


Figure S12. ^{1}H NMR spectrum of the alcoholysis reaction (400 MHz, Chloroform-*d*, 298 K).



Peak	Time	Area	Height	Area(%)
1	10.258	1606664	93413	50.104
2	10.905	1599968	74682	49.896
		3206632	16809	100.000

Figure S13. HPLC chromatogram of the *rac*-6-MeCL. Column, Chiralpak IA-3; flow rate, 1 mL/min; eluent, hexane/isopropanol = 95/5; detector, UV (230 nm).



Peak	Time	Area	Heigh	Area(%)
1	10.324	18219	12395	72.479
2	11.024	69180	4776	27.521
		25136	17171	100.000

Figure S14. HPLC chromatogram of the unreacted 6-MeCL at 48% conversion for AKRP of *rac*-6-MeCL (Table 1, entry 3).

3. Tables

Table S1. Synthesis of atactic P(6-MeCL) [a]

Entry	Cat.	[M]/[Cat.]/[BnOH]	Time (h)	Conv. (%)	$M_{n,NMR}$ [b] (g/mol)	$M_{n,NMR}$ [c] (g/mol)	$M_{n,GPC}$ [d] (g/mol)	PDI [d]
1	Diphenyl phosphat	50:1:1	48	83	5400	5400	5000	1.14

[a] Reactions were carried out in toluene at room temperature; [b] Calculated from $M_{n[6\text{-MeCL}]} \times$ Conv. $\times$ 50 + $M_{n[BnOH]}$ by ^{1}H NMR.· [c] Calculated from $M_{n[6\text{-MeCL}]} \times$ DP + $M_{n[BnOH],}$ DP was the polymerization degree determined by the integral ratio between chain end and main chain by ^{1}H NMR. [d] Determined by GPC at 40 °C in THF against polystyrene standards.

Table S2. Synthesis of gram-scale atactic/stereogradient P(6-MeCL)s for the viscoelasticity test.[a]

Polymer	Monomer	Cat.	[M]/[Cat.]/[BnOH]	Mass (g)	Yield (%)	$M_{n,GPC}$ [b] (g/mol)	PDI [b]
Atactic P(6-MeCL)	*rac*-6-MeCL	Diphenyl phosphat	350:1:7	6	84	14600	1.16
Stereogradient P(6-MeCL)	*rac*-6-MeCL	(*R*)-CPA-2	350:1:7	6	88	15100	1.15

[a] Reactions were carried out in toluene at room temperature; [b] Determined by GPC at 40 °C in THF against polystyrene standards.

Table S3. (*R*)/(*S*)-6-MeCL monomer ratio in unreacted monomer and polymer at different conversion.[a]

Conv.[b] (%)	*ee* [c] (%)	(*S*)-6-MeCL in unreacted monomer	(*R*)-6-MeCL in unreacted monomer	(*S*)-6-MeCL in polymer	(*R*)-6-MeCL in polymer	(*S*)-6-MeCL ratio in polymer (%)	(*R*)-6-MeCL ratio in polymer (%)
17	15	47.725	35.275	2.275	14.725	0.134	0.866
27	23	44.895	28.105	5.105	21.895	0.179	0.811
35	33	43.225	21.775	6.775	28.225	0.194	0.806
45	43	39.325	15.675	10.675	34.325	0.237	0.763
59	55	31.775	9.225	18.225	40.775	0.309	0.691
70	67	25.050	4.950	24.950	45.050	0.356	0.644
75	73	21.625	3.375	28.375	46.625	0.378	0.622
88	79	10.740	1.260	39.260	48.740	0.446	0.554

[a] Reactions were carried out in toluene using (*R*)-CPA-2 as organocatalyst and BnOH as the initiator at room temperature; $[rac\text{-6-MeCL}]_0/[\text{CPA-2}]_0/[\text{BnOH}]_0 = 50:1:1$, $[\text{6-MeCL}]_0 = 0.4$ mol L^{-1}. [b] Monomer conversion was determined and calculated by ^{1}H NMR in $CDCl_3$. [c] Enantiomeric excess of the unreacted monomer was measured by chiral HPLC.