Organocatalytic Ring-Opening Polymerization toward Poly(γ-amide-ε-caprolactone)s with Tunable LCSTs

Supporting Information

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1. Experimental detail

1.1 Materials

Ethyl 2-cyclohexanonecarboxylate (98%), concentrated sulfuric acid (70wt%), 3-(3-dimethylaminopropyl)-1-ethylcarbodiimide hydrochloride (EDC) (98%), *N*-hydroxysuccinimide (NHS) (98%), 1-propanamine (99%), isopropylamine (99%), diethylamine(99%), pyrrolidine(99%), aminocyclopropan, benzyl alcohol (BnOH,99%), 3-Chloroperoxybenzoic Acid (m-CPBA), 1,5,7-triazabicyclo[4.4.0]Dec-5-Ene (TBD) (97%), 1,8-diazabicyclo[5.4.0]-7-undecene (DBU) (99%), *S*-1-dodecyl-*S*′-(*α*′,*α*″-dimethyl-*α*‴-acetic acid) trithiocarbonate, azodiisobutyronitrile (AIBN), *N*-isopropylacrylamide, tannous octoate ($Sn(Oct)_2$)(99%), trifluoroacetic Acid (99%) and 4-oxopiperidinium chloride (97%) were purchased from Adamas. 3,3′,5,5′-tetramethylbenzidine(TMB) (99%) and trinitrobenzene sulfonic acid (TNBS) (99%) were purchased Sigma-Aldrich, other reagents were purchased from Greagent. Unless otherwise noted, all commercial reagents and solvents were directly used.

Thiourea (TU)were prepared according to the literature.[1]

TMB-A solution: 13.6g sodium acetate, 1.6g citric acid, 0.3ml 30% hydrogen peroxide, and 500ml distilled water.

TMB-B solution: 0.2g disodium ethylenediamine tetraacetate, 0.95g citric acid 0.95g, glycerol 50ml, 0.15g TMB and 500ml distilled water

10mM phosphate buffer (PBS) solution: 8g sodium chloride, 0.2g potassium chloride, 1.44g disodium hydrogen phosphate 0.24g mono potassium phosphate and 800ml distilled water. Then,

pH of solution was adjusted to 7.4 with HCl solution. Finally, volume was adjusted to 1L with additional distilled water.

1.2 Instruments and measurements

^{1}H NMR and ^{13}C NMR spectrum were measured on a Bruker AVANCE III 400 MHz (^{1}H NMR) or 150MHz (^{13}C NMR) instrument at room temperature with $CDCl_3$ as the solvent. Molecular weight and molecular weight distribution of the polymers were estimated by an Agilent Technologies 1260 Infinity containing a refractive index detector, and the flow rate was 1.0 mL/min. the columns for DMF (containing 0.01 M LiBr) as an eluent included 10 μm MIXED-BLS, 5μm MIXED-C, and 5μm MIXED-D. The temperature for DMF was 50°C. Matrix-assisted laser desorption/ionization time-of-flight mass spectrometry (MALDI-TOF-MS) was carried out using a Bruker Ultraflextreme spectrometer in which 9-Nitroanthracene was used as the matrix, and NaI was used as the cationic reagent in the linear positive model. Glass transition temperatures (T_g) of polymer were determined using a TA Q2000 DSC with a liquid N_2 cooling unit and a heating/cooling rate of 10 °C/min. Transmittance measurement was measured on a vis-UV chromatogram analyzer (Shanghai Zhetu science apparatus company limited) with a thermostat sample holder, and the heating rate was 1°C/min. Sample has a 5wt% or 1wt% concentration in D_2O or deionized water. Temperature-variable ^{1}H NMR spectra were recorded on Varian Mercury plus (600 MHz) spectrometer using D_2O as solvent (concentration=5wt%) with an increment of 5°C. The sample of polymer solution (concentration=5wt% in D_2O) for FT-IR measurements was prepared by being sealed between two CaF_2 tablets. All time-resolved FT-IR spectra at different temperatures were recorded on a Nicolet Nexus 470 spectrometer with a resolution of 4 cm^{-1}, and 32 scans were available for an acceptable signal-to-noise ratio. Temperatures were manually controlled with an electronic cell holder at rates of ca. 0.3°C/min with an increment of 0.9°C. Raw spectra were baseline-corrected by the software Omnic, ver. 6.1a. Calorimetric measurements of polymer solution (concentration=5wt% in D_2O) were performed on a Mettler-Toledo differential scanning calorimeter (DSC) thermal analyzer with varying scanning rates from 0 to 50°C.

1.3 Procedure of monomer preparation

Preparation of 4-oxocyclohexane-1-carboxylic acid

4-Oxocyclohexane-1-carboxylic acid was synthesized according to the literature procedure.[2] A solution of ethyl 4-ketocyclohexanecarboxylate (100g, 70mmol) in 2wt% H_2SO_4 was heated to 105ºC for 4 h. The cooled solution was extracted with ethyl ether, and the organic

layer was separated, dried over magnesium sulfate, filtered, concentrated. A white solid was obtained (5.1g, 71% yield, white solid).

4-oxocyclohexane-1-carboxylic acid:

^{1}H NMR (400 MHz, $CDCl_3$) δ=11.6(s, 1H), 2.89–2.78 (m, 1H), 2.60-2.46 (m, 2H), 2.46–2.34 (m, 2H), 2.32-2.19 (m, 2H), 2.15-1.96 (m, 2H).

Preparation of 4-oxo-*N*-propylcyclohexane-1-carboxamide

4-Oxocyclohexane-1-carboxylic acid (20g) was dissolved in 400ml CH_2Cl_2. Then EDC and NHS were added into solution in room temperature. after 3h. 10ml 1-Propanamine was dropwise added with continuous stirring for 24h. the mixture were filtered and the solvent was removed under reduced pressure. Purification by column chromatography on silica gel using pure ethyl acetate (R_f=4,0) as the eluant afforded 17.6g (68% yield) of the white powder:

N-isopropyl-4-oxocyclohexane-1-carboxamide (16.5g, 63% yield, white powder), *N*, *N*-diethyl-4-oxocyclohexane-1-carboxamide (16.2g ,57% yield, white powder), 4-(pyrrolidine-1-carbonyl) cyclohexan-1-one (16.0g, 59% yield, white powder) were synthesized using the similar steps above.

4-oxo-*N*-propylcyclohexane-1-carboxamide:

^{1}H NMR (400 MHz, $CDCl_3$) δ =5.67(s, 1H), 3.31–3.14 (q, *J*=8Hz, 2H), 2.58–2.45 (m, 3H), 2.39–2.25 (m, 2H), 2.22-2.01 (m, 2H), 2.05–1.91 (m, 2H), 1.62–1.41 (m, 2H), 0.92 (t, *J*= 8Hz, 3H).

N-isopropyl-4-oxocyclohexane-1-carboxamide:

^{1}H NMR (400 MHz, $CDCl_3$) δ=5.39(s, 1H), 4.23–4.03 (m, 1H), 2.70–2.45 (m, 3H), 2.44–2.28 (m, 2H), 2.26-2.11 (m, 2H), 2.10-1.97 (m, 2H), 1.40-1.03 (d, *J*= 8Hz, 6H).

N, N-diethyl-4-oxocyclohexane-1-carboxamide:

^{1}H NMR (400 MHz, $CDCl_3$) δ=3.42-3.19 (m, 4H), 2.89-2.71 (m, 1H), 2.54–2.19 (m, 4H), 2.06–1.87 (m, 4H), 1.20-0.97 (m, 6H).

4-(pyrrolidine-1-carbonyl) cyclohexan-1-one:

^{1}H NMR (400 MHz, $CDCl_3$) δ=3.51 (s, 4H), 2.88-2.71 (m, 1H), 2.63-2.50(m, 2H), 2.41-2.24 (m, 2H), 2.14–1.80 (m, 8H).

Preparation of 7-oxo-*N*-propyloxepane-4-carboxamide (NNCL)

4-Oxo-*N*-propylcyclohexane-1-carboxamide (10g) was dropwise added into the CH_2Cl_2 solution of 20g m-CPBA in the ice-water bath. Then the reaction was stirred for another 48h in room temperature. The mixture was filtered and the solvent was removed under reduced pressure. The residue was participated in 100ml anhydrous ether three times repeatedly to collect 9.6g (84% yield) NNCL of the white powder.

N-isopropyl-7-oxooxepane-4-carboxamide (NICL) (8.9g, 82% yield, white powder), *N*, *N*-diethyl-7-oxooxepane-4-carboxamide (DECL) (7.4g, 81% yield, Crystal solid), 5-(pyrrolidine-1-carbonyl)oxepan-2-one(VPyCL) (7.7g, 83% yield, white powder) were synthesized using the similar steps above.

7-oxo-*N*-propyloxepane-4-carboxamide(NNCL):

^{1}H NMR (400 MHz, $CDCl_3$) δ=5.72(s, 1H), 4.60-4.42 (m, 1H), 4.26-4.10(m, 1H), 4.26–3.90 (m, 1H), 3.27–3.14 (q, *J*=8Hz, 2H), 2.99–2.83 (m, 1H), 2.68-2.54 (m, 1H), 2.50–2.37 (m, 1H), 2.19–1.87 (m, 4H), 1.60–1.43 (m, 2H),0.92 (t, *J*= 4Hz, 6H).

^{13}C NMR (150MHz, $CDCl_3$): δ=175.56(O***C***OCH_2), 173.77(CH***C***ONH), 67.02(O***C***H_2CH_2), 45.92(CH_2***C***H(CO)CH_2), 41.15(NH***C***H_2CH_2), 32.27(CO***C***H_2CH_2), 32.18(CH_2***C***H_2CH), 25.78(CH_2***C***H_2CH), 22.74(CH_2***C***H_2CH_3), 11.32(CH_2***C***H_3).

FT-IR (ν, cm^{-1}): 1733.86 (C=O of ester bond), 1633.10, (C=O of amide bond).

EI-MS: m/z =199.1.

DSC: T_m= 89.74°C.

Solubility: Dichloromethane (CH_2Cl_2), ethyl acetate, methanol, H_2O and *et al.*

Morphology: White power.

N-isopropyl-7-oxooxepane-4-carboxamide(NICL):

^{1}H NMR (400 MHz, $CDCl_3$) δ=5.72(s, 1H), 4.51-4.40 (m, 1H), 4.22-4.10(m, 1H), 4.07–3.90 (m, 1H), 2.94–2.80 (m, 1H), 2.64–2.50 (m, 1H), 2.46-2.33 (m, 1H), 2.08–1.76 (m, 4H), 1.19-0.99 (d, *J*= 4Hz, 6H).

^{13}C NMR (150MHz, $CDCl_3$): δ=175.61(O***C***OCH_2), 172.88(CH***C***ONH), 67.04(O***C***H_2CH_2), 46.07(CH_2***C***H(CO)CH_2), 41.23(NH***C***$(CH_3)_2$), 32.28(CO***C***H_2CH_2), 32.14(CH_2***C***H_2CH), 25.72(CH_2***C***H_2CH), 22.58(C(***C***$H_3)_2$).

FT-IR (ν, cm^{-1}): 1739.63 (C=O of ester bond), 1632.08, (C=O of amide bond).

ESI-MS: m/z =199.1

DSC: T_m= 158.22°C

Solubility: CH_2Cl_2, ethyl acetate, methanol, H_2O and *et al.*

Morphology: White power.

N, *N*-diethyl-7-oxooxepane-4-carboxamide (DECL):

^{1}H NMR (400 MHz, $CDCl_3$) δ=4.68-4.42 (m, 1H), 4.30-4.12 (m, 1H), 3.35 (s, 4H), 3.01-2.88 (m, 1H), 2.87-2.75 (m, 1H), 2.69-2.54 (m, 1H), 2.19 – 1.89 (m, 4H), 1.26-1.05 (m, 6H).

^{13}C NMR (150MHz, $CDCl_3$): δ=175.38(O***C***OCH_2), 173.10(CH***C***ON), 67.01(O***C***H_2CH_2), 41.99(CH_2***C***H(CO)CH_2), 40.95(N(***C***$H_2CH_3)_2$), 32.19(CO***C***H_2CH_2), 25.68(CH_2***C***H_2CH), 15.09(CH_2***C***H_2CH), 13.03(CH_2***C***H_3).

FT-IR (ν, cm^{-1}): 1719.58 (C=O of ester bond), 1627.38, (C=O of amide bond).

EI-MS: m/z =213.1

DSC: T_m= 75.01°C

Solubility: CH_2Cl_2, ethyl acetate, methanol, H_2O and *et al.*

Morphology: Crystal solid.

5-(pyrrolidine-1-carbonyl)oxepan-2-one(VPyCL):

^{1}H NMR (400 MHz, $CDCl_3$) δ= 4.63-4.46 (m, 1H), 4.27-4.11 (m, 1H), 3.46 (t, J = 8 Hz, 4H), 3.04–2.89 (m, 1H), 2.80-2.70 (m, 1H), 2.67 – 2.51 (m, 1H), 2.20 – 1.76 (m, 8H).

^{13}C NMR (150MHz, $CDCl_3$): δ=175.43(O***C***OCH_2), 172.38(CH***C***ON), 66.87(O***C***H_2CH_2), 46.54,45.91(N(***C***$H_2CH_2)_2$), 42.78(CH_2***C***H(CO)CH_2), 32.22(CO***C***H_2CH_2), 31.57(CH_2***C***H_2CH), 24.99(CH_2***C***H_2CH), 24.11(N(CH_2***C***$H_2)_2$).

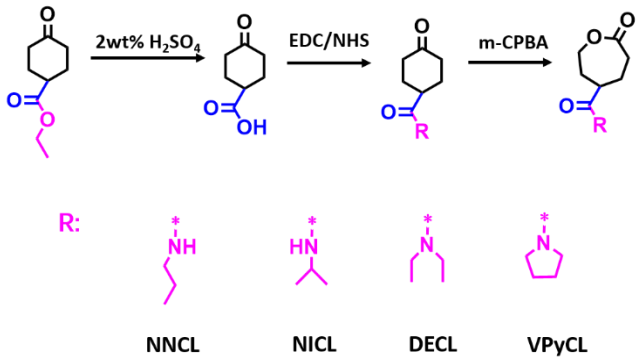
FT-IR (ν, cm^{-1}): 1724.01 (C=O of ester bond), 1627.29 (C=O of amide bond).

EI-MS: m/z =211.1

DSC: T_m= 124.01°C

Solubility: CH_2Cl_2, ethyl acetate, methanol, H_2O and *et al.*

Morphology: White power.



Scheme S1. The synthesized route of *γ*-amide-*ε*-caprolactones.

Preparation of ethyl 7-oxooxepane-4-carboxylate (EMCL):

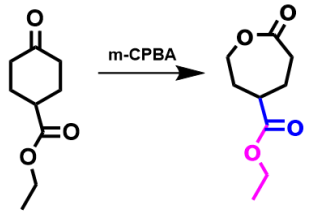
Ethyl 4-ketocyclohexanecarboxylate (10g) was dropwise added into the CH_2Cl_2 solution of 17g m-CPBA in the ice-water bath. Then the reaction was stirred for another 24 h in room temperature. The mixture was filtered and the solvent was washed successively with saturated $Na_2S_2O_3$ solution (three times), $NaHCO_3$ solution (three times) and NaCl solution (three times). The organic extraction was dried with anhydrous $MgSO_4$, filtered and purified by column chromatography (silica gel, R_f=2,0, petroleum ether (PE): ethyl acetate (Et_2O) = 1:1). The resulting product is transparent crystal (6.3g, 58%yield, transparent crystal).

Ethyl 7-oxooxepane-4-carboxylate (EMCL):

^{1}H NMR (400 MHz, $CDCl_3$) δ= 4.45-4.31 (m, 1H), 4.27-4.07 (m, 3H), 2.88-2.59(m, 3H), 2.27–1.88 (m, 4H), 1.35–1.19 (t, *J*=, 4Hz, 3H).

Solubility: CH_2Cl_2, ethyl acetate, methanol and *et al.*

Morphology: Transparent crystal.



Scheme S2. The synthesized route of ethyl 7-oxooxepane-4-carboxylate (EMCL).

Preparation of tert-butyl 7-oxo-1,4-oxazepane-4-carboxylate (Boc-NIPIL)：

4-Oxopiperidinium chloride(10g) and NaOH(3g) were added into 100ml water. Then reaction was stirred until the solid was completely dissolved. Di-tert-butyl dicarbonate (7.2g, dissolved in 20ml THF) was dropwise to the above solution at 0°C. After 8h, the mixture was extracted using dichloromethane three times and the organic layer was separated. Organic extraction was washed with saturated NaCl solution (three times). After organic extraction was dried with anhydrous $MgSO_4$, filtered organic solution was concentrated to obtain preliminary intermediate (12.5g, 87% yield). Intermediate was directly reacted without further purification.

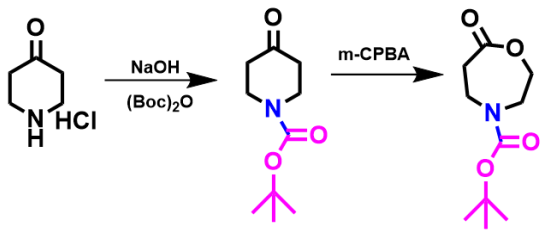
Above intermediate (5g) was dropwise added into the CH_2Cl_2 solution of 6g m-CPBA in the ice-water bath. Then the reaction was stirred for another 24 h in room temperature. The mixture was filtered and the solvent was washed successively with saturated $Na_2S_2O_3$ solution (three times), $NaHCO_3$ solution (three times) and NaCl solution (three times). The organic extraction was dried with anhydrous $MgSO_4$, filtered and concentrated to obtain the crude product. Crude product was further purified by recrystallizing twice using THF and n-Hexane as solvent. The resulting product was white granular crystal (3.8g, 71%yield, white granular crystal).

Tert-butyl 7-oxo-1,4-oxazepane-4-carboxylate (Boc-NIPIL)：

^{1}H NMR (400 MHz, $CDCl_3$) δ= 4.36-4.18 (m, 2H), 3.81-3.60 (m, 4H), 2.90-2.74 (m, 2H), 1.48 (s, 9H).

Solubility: CH_2Cl_2, ethyl acetate, methanol and *et al.*

Morphology: White granular crystal.



Scheme S3. The synthesized route of ethyl 7-oxooxepane-4-carboxylate (EMCL)

1.4 General procedure for homo-polymerization

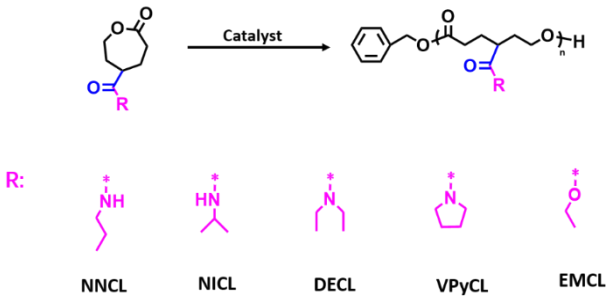
Organic catalyst such as TBD to catalyze the polymerization: NNCL (100mg, 502umol) was add into 10ml flame-dried Schlenk flask containing a magnetic stir bar and vacuumized 3h in the 50ºC oil pot. Then benzyl alcohol solution (13.2uL, benzyl alcohol was dissolved in the methylbenzene with a 0.1028g/ul concentration) and dry CH_2Cl_2 (0.5mL) was added into the flash. To this solution, TBD (3.4mg, 25.1umol, relative to the monomer molar mass) was added to initiate polymerization. The reaction mixture was allowed to stir at room temperature in an argon protective atmosphere. After reaching the predetermined time, about 20 ul of acetic acid was added into the flash to quenched reaction. Slight crude products were taken out from the system to dry in vacuum. Monomer conversion and the molecular weight of those rude products were determined by ^{1}H NMR spectroscopy and GPC, respectively. Residual products were precipitated in anhydrous ether third times and dried in vacuum to further characterize.

Poly(*N*-isopropyl-4-oxocyclohexane-1-carboxamide) (PNICL), Poly(*N*, *N*-diethyl-7-oxooxepane-4-carboxamide) (PDECL), Poly(5-(pyrrolidine-1-carbonyl)oxepan-2-one) (VPyCL), Poly(ethyl 7-oxooxepane-4-carboxylate)(PEMCL), with TBD catalyzing, were prepared followed by the above procedure.

Organic metal catalyst $Sn(Oct)_2$ to catalyze the polymerization: NNCL (100mg, 502μmol), benzyl alcohol (13.2μL, benzyl alcohol was dissolved in the methylbenzene with a 0.1028g/ul concentration) was added in the a 10ml flame-dried Schlenk flask containing a magnetic stir bar, vacuumized 3h in the 50ºC oil pot, Then $Sn(Oct)_2$ solution (9.6uL, $Sn(Oct)_2$ was dissolved in the methylbenzene with a 0.1028g/ul concentration, relative to the monomer weight) was added into the flash. The reaction mixture was allowed to stir at 130ºC in an argon protective atmosphere. After 24h, reaction was cooled and in 0.5 ml CH_2Cl_2 and precipitated in ether twice. Slight crude products were taken out from the system to dry in vacuum. Monomer conversion and the molecular weight of those rude products were determined by ^{1}H NMR spectroscopy and GPC, respectively.

Residual products were dissolved in 0.5 ml CH_2Cl_2 and precipitated in anhydrous ether third times and dried in vacuum to further characterize.

Poly(*N*-isopropyl-4-oxocyclohexane-1-carboxamide) (PNICL), Poly(*N*, *N*-diethyl-7-oxooxepane-4-carboxamide) (PDECL), Poly(5-(pyrrolidine-1-carbonyl)oxepan-2-one) (VPyCL) with $Sn(Oct)_2$ catalyzing were prepared followed by the above procedure.



Scheme S4. ROP of *γ*-amide- and *γ*-ester-*ε*-caprolactones

Poly(*N*-isopropyl-4-oxocyclohexane-1-carboxamide)(PNICL) (DP:40)

^{1}H NMR (400 MHz, $CDCl_3$) (DP:40) δ=6.90-6.20(s, 33H), 4.24-3.95(m, 117H), 2.51-1.17(m, 117H), 2.06-1.86(m, 77H), 1.84-1.65(m, 80H), 1.20-1.06(m, 238H).

MALDI-tof-MS: PNICL had a precise structure with a benzyl group and an OH group at two terminals. For example, the observed value, m/z =2123.1, agrees with the theory value of PNICL with degree of polymerization of 10 [108.1($M_{initiator}$) + 199.1($M_{monomer}$) ×10+ 23.0(M_{Na+}) = 2123.1].

Poly(*N*, *N*-diethyl-7-oxooxepane-4-carboxamide) (PDECL) (DP:40)

^{1}H NMR (400 MHz, $CDCl_3$) (DP:40) δ=4.29-3.85(m, 82H), 3.49-3.25(m, 168H), 2.88-2.71(m, 40H), 2.43-2.17(m, 88H), 2.10-1.87(m, 88H), 1.87-1.68(m, 83H), 1.24-1.01(m, 252H).

MALDI-tof-MS: PDECL had a precise structure with a benzyl group and an OH group at two terminals. For example, the observed value, m/z =2262.1, agrees with the theory value of PNICL with degree of polymerization of 10 [108.1($M_{initiator}$) + 213.1($M_{monomer}$) ×10 + 23.0(M_{Na+}) = 2262.1].

Poly(5-(pyrrolidine-1-carbonyl)oxepan-2-one) (VPyCL) (DP:40)

^{1}H NMR (400 MHz, $CDCl_3$) δ=4.14-3.92(m, 69H), 3.54-3.36(m, 156H), 2.81-2.61(m, 39H), 2.49-2.16(m, 92H), 2.07-1.60(m, 349H).

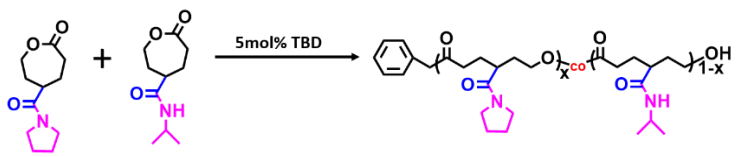
MALDI-tof-MS: PVPyCL had a precise structure with a benzyl group and an OH group at two terminals. For example, the observed value, m/z =2242.1, agrees with the theory value of PNICL with degree of polymerization of 10 [108.1($M_{initiator}$) + 211.1($M_{monomer}$) ×10 + 23.0(M_{Na+}) =2242.1].

1.5 Kinetics of Polymerization

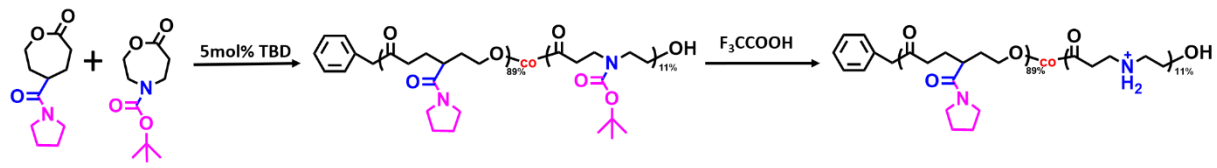
NICL (100 mg, 502μmol) was add in the a 10ml flame-dried Schlenk flask containing a magnetic stir bar and vacuumized 3h in the 50°C oil pot. Then benzyl alcohol solution (13.2μL, benzyl alcohol was dissolved in the methylbenzene with a 0.1028g/ul concentration) and dry CH_2Cl_2 (0.5mL) was added into the flash. Then TBD (3.4 mg, 25.1μmol, relative to the monomer molar mass) was added to initiate polymerization. The reaction mixture was allowed to stir continuously at room temperature in an argon protective atmosphere. An 50ul solution was taken out from flask at a predetermined time interval in a continuous argon condition. Sample was quenched by acetic acid for ^{1}H NMR spectroscopy analysis and GPC analysis. Residual solution would continue to react in an argon protective atmosphere until next sampling.

Other TBD-catalyzed ROP kinetic studies of DECL and VPyCL were carried out in a similar manner.

1.6 General procedure for co-polymerization



Scheme S5. Preparation of P(VPyCL$_X$-*co*-NICL$_{1-X}$)$_{20}$



Scheme S6. Preparation of P(VPyCL$_{89\%}$-*co*- PIL$_{11\%}$)$_{20}$

VPyCL (100mg, 502umol) and NICL (106mg, 502umol) were add into 10ml flame-dried Schlenk flask containing a magnetic stir bar and vacuumized 3h in the 50°C oil pot. Then benzyl alcohol solution (52.7uL, benzyl alcohol was dissolved in the methylbenzene with a 0.1028g/ul concentration) and dry CH_2Cl_2 (1.0mL) was added into the flash. To this solution, TBD (7.0mg, 50.3umol, relative to the monomer molar mass) was added to initiate polymerization. The reaction mixture was allowed to stir at room temperature. After reaching the predetermined time, about 40ul of acetic acid was added into the flash to quenched reaction. Crude products were precipitated in anhydrous ether third times and dried in vacuum to further characterize.

Other copolymers including P(VPyCL$_x$-*co*-NICL$_{1-x}$)$_{20}$ and P(VPyCL$_{90\%}$-*co*-Boc-NIPIL$_{10\%}$)$_{20}$ were carried out in a similar manner.

1.7 Deprotection of co-polymer

P(VPyCL$_{90\%}$-*co*-Boc-NIPIL$_{10\%}$)$_{20}$ (100mg) was added into 10ml flame-dried Schlenk flask containing a magnetic stir bar. Then dry CH_2Cl_2 (1.0mL) was added into the flash to dissolved copolymer. In addition, trifluoroacetic acid (1ml) was added to remove the protecting group of copolymer. After stirring at room temperature for 1hour, solution was precipitated in anhydrous ether third times and dried in vacuum to further characterize.

1.8 Preparation of PNIPAM-NHS

Preparation of PNIPAM-NHS was divided into two steps. First step was the preparation of PNIPAM. NIPAM (500mg) was added into 10ml flame-dried Schlenk flask containing a magnetic stir bar. Then dry THF (1.0mL) was added into the flash to dissolved monomer. Then the RAFT chain transfer agent *S*-1-dodecyl-*S*′-(*α*′,*α*″-dimethyl-*α*‴-acetic acid) trithiocarbonate (DDAT) and initiator ANIBN were added into the flash. After the mixture was degassed by three freeze-evacuate-thaw cycles, the reaction mixture was allowed to stir at 70°C under argon atmosphere.

After stirring for 24 hours, solution was precipitated in anhydrous ether third times and precipitation was dried in vacuum to further characterize.

Second step was the preparation of PNIPAM-NHS. Prepared PNIPAM (100mg) was added into 10ml Schlenk flask containing a magnetic stir bar. Then dry CH_2Cl_2 (1.0 mL) was added into the flash to dissolved monomer. Then EDC (100mg) and NHS (100mg) was added into the flash. After the reaction mixture was stirred at room temperature under argon atmosphere for 12h, solution was precipitated in anhydrous ether third times and precipitation was dried in vacuum without further characterization.

1.9 Preparation of P(VPyCL$_{89\%}$-*co*- PIL$_{11\%}$)$_{20}$-NHS

Preparation of P(VPyCL$_{89\%}$-*co*- PIL$_{11\%}$)$_{20}$-NHS was divided into two steps. First step was the preparation of P(VPyCL$_{89\%}$-*co*- Boc-NIPIL$_{11\%}$)$_{20}$-COOH. Dry P(VPyCL$_{89\%}$-*co*- Boc-NIPIL$_{11\%}$)$_{20}$ (370mg), succinic anhydride (10mg), pyridine (0.1ml) and chloroform (5ml) were added into 10ml Schlenk flask containing a magnetic stir bar. After stirred at 60^{o}C under argon atmosphere for 12h, solution was precipitated in anhydrous ether third times and was dried in vacuum. Dry precipitation P(VPyCL$_{89\%}$-*co*- Boc-NIPIL$_{11\%}$)$_{20}$ was deprotected according to the procedure in S1.7 to gain P(VPyCL$_{89\%}$-*co*-PIL$_{11\%}$)$_{20}$-COOH. The deprotected crude product was precipitated in anhydrous ether third times and precipitation was dried in vacuum without further characterization.

The preparation of P(VPyCL$_{89\%}$-*co*-PIL$_{11\%}$)$_{20}$-NHS was prepared according to the prepared procedure of PNIPAM-NHS. Result product was dried in vacuum without further characterization.

1.10 Thermal Properties of polymers

To evaluate thermal properties of those poly(*γ*-amide-*ε*-caprolactone)s, differential scanning calorimetry (DSC) and the thermogravimetric analysis (TGA) were respectively employed to measure the glass transition temperature (T_g) and decomposition temperature (T_d) of poly(*γ*-amide-*ε*-caprolactone)s (Figure S34-S35). T_g of those polymers was higher than that of PCL owning to the destroy of steric regularity from the introduction of amide groups into PCL. However, the observed T_g among different poly(*γ*-amide-*ε*-caprolactone)s from DSC curve exhibited difference but was not regular (Figure S34). T_d of those polymers measured ranged from 300^{o}C to 345^{o}C, lower than the reported PCL value (350^{o}C) (Figure S35), suggesting that the introduce of amide groups in the side chain of PCL would lower thermal stabilities. It was observed that T_d of PDECL$_{10}$ and PVPyCL$_{10}$ at near 350^{o}C was higher than that of PNICL$_{10}$ at 300^{o}C. It was likely

that heat resistance of $PNICL_{10}$, relative to $PDECL_{10}$ and $PVPyCL_{10}$, showed inferior owing to the exist of the secondary amide substituent.

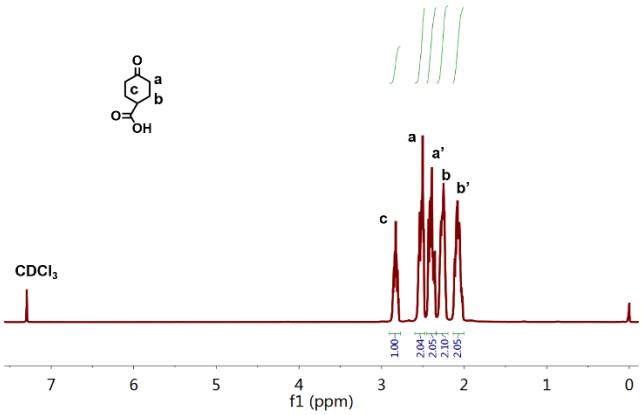


Figure S1. ^{1}H NMR spectrum of 4-oxocyclohexane-1-carboxylic acid

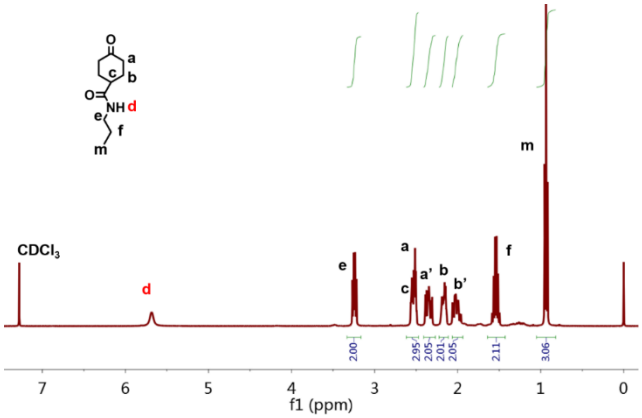


Figure S2. ^{1}H NMR spectrum of 4-oxo-*N*-propylcyclohexane-1-carboxamide

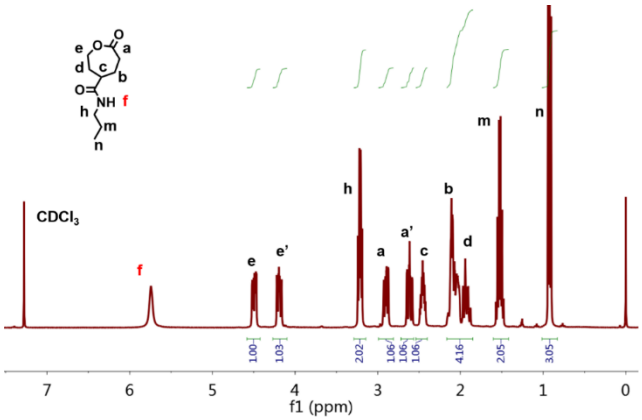


Figure S3. ^{1}H NMR spectrum of 7-oxo-*N*-propyloxepane-4-carboxamide (NNCL)

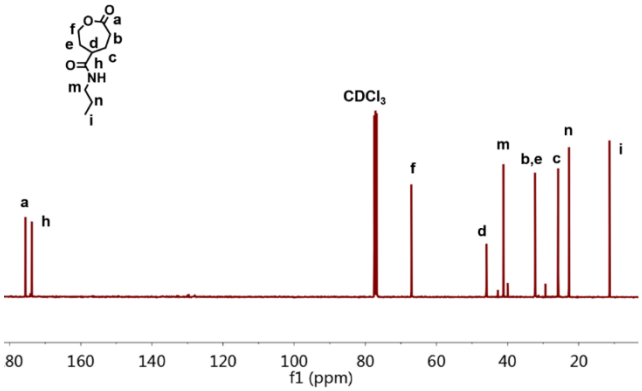


Figure S4. ^{13}C NMR spectrum of 7-oxo-*N*-propyloxepane-4-carboxamide (NNCL)

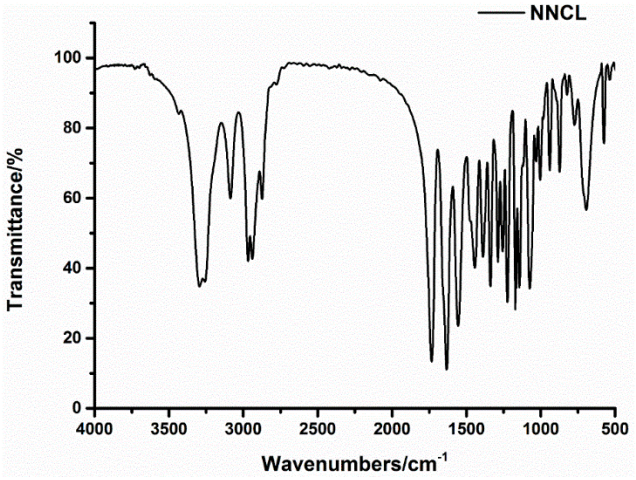


Figure S5. FT-IR spectrum of 7-oxo-*N*-propyloxepane-4-carboxamide (NNCL)

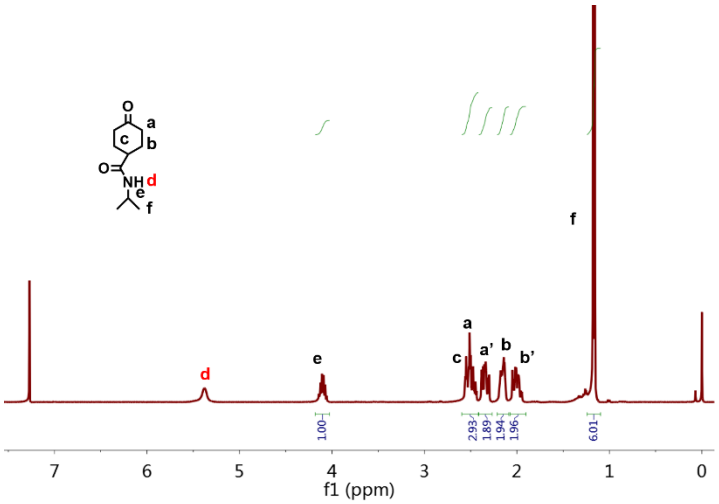


Figure S6. [1]H NMR spectrum of 4-oxo-*N*-propylcyclohexane-1-carboxamide

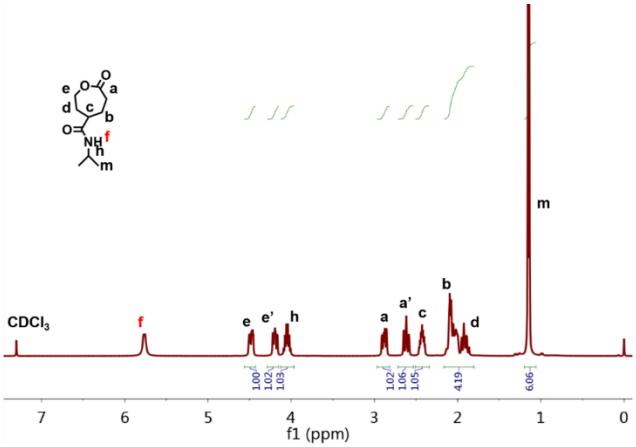


Figure S7. [1]H NMR spectrum of *N*-isopropyl-7-oxooxepane-4-carboxamide (NICL)

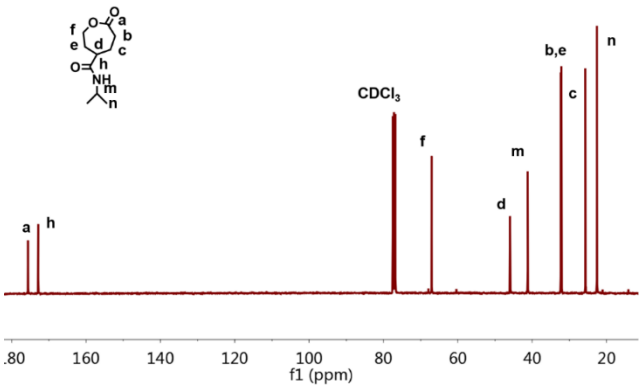


Figure S8. [13]C NMR spectrum of *N*-isopropyl-7-oxooxepane-4-carboxamide (NICL)

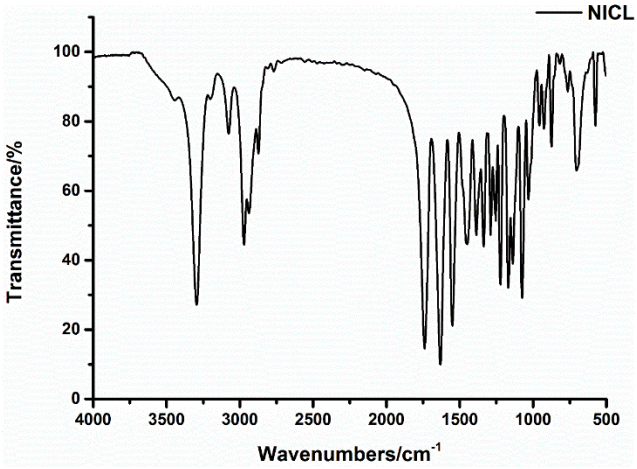


Figure S9. FT-IR spectrum of *N*-isopropyl-7-oxooxepane-4-carboxamide (NICL)

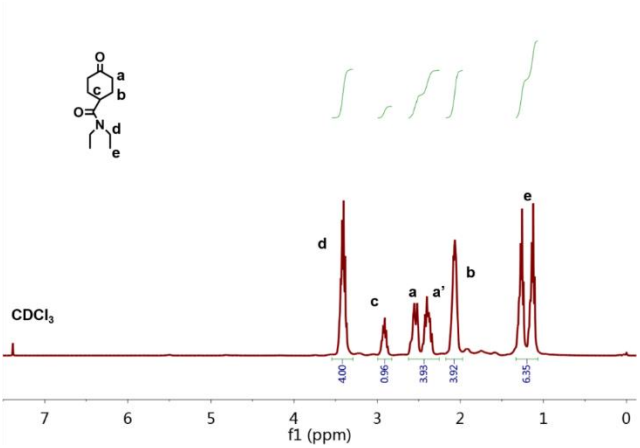


Figure S10. ^{1}H NMR spectrum of *N*-cyclopropyl-4-oxocyclohexane-1-carboxamide

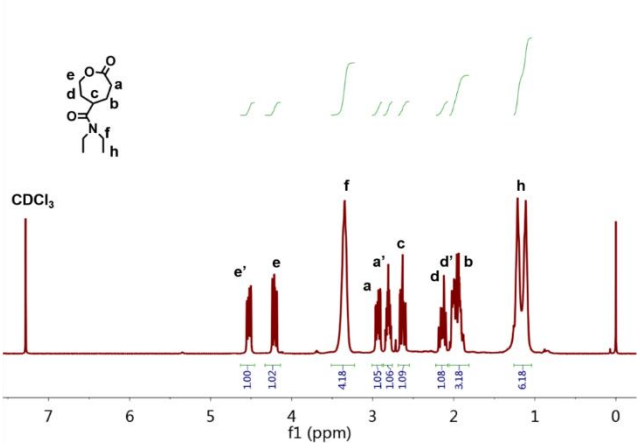


Figure S11. ^{1}H NMR spectrum of *N*, *N*-diethyl-7-oxooxepane-4-carboxamide (DECL)

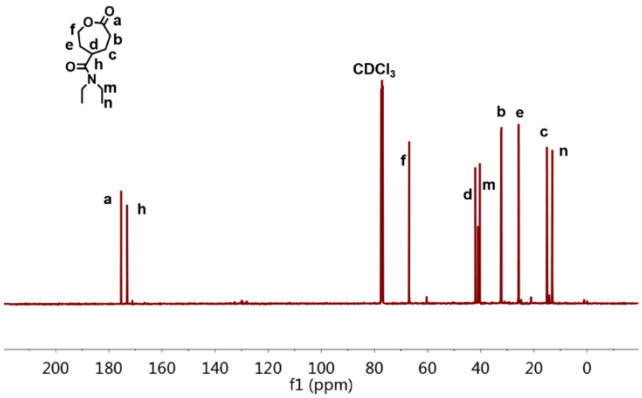


Figure S12. ^{13}C NMR spectrum of *N*, *N*-diethyl-7-oxooxepane-4-carboxamide (DECL)

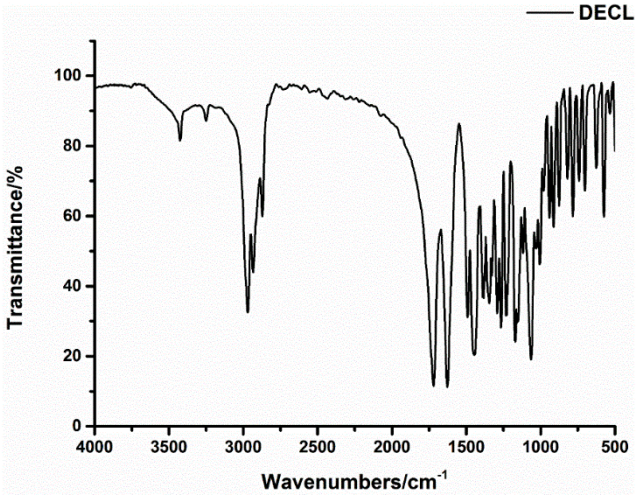


Figure S13. FT-IR spectrum of *N*, *N*-diethyl-7-oxooxepane-4-carboxamide (DECL)

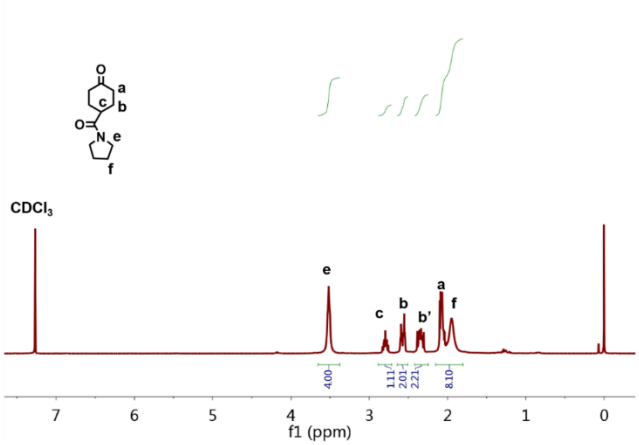


Figure S14. ^{1}H NMR spectrum of 4-(pyrrolidine-1-carbonyl) cyclohexan-1-one

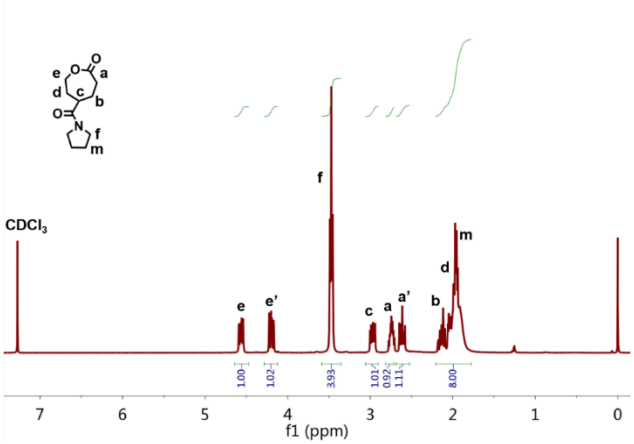


Figure S15. ^{1}H NMR spectrum of 5-(pyrrolidine-1-carbonyl)oxepan-2-one(VPyCL)

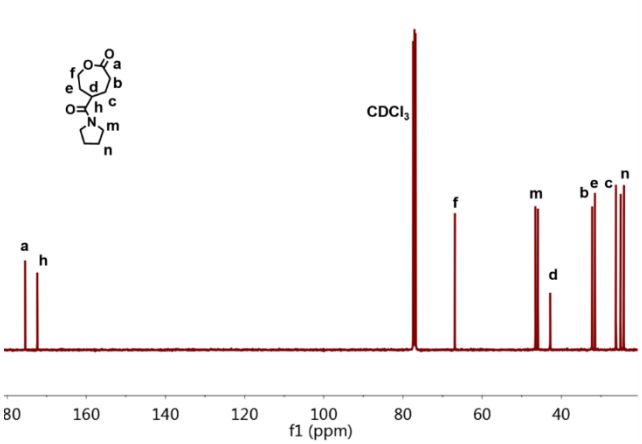


Figure S16. ^{13}C NMR spectrum of 5-(pyrrolidine-1-carbonyl)oxepan-2-one(VPyCL)

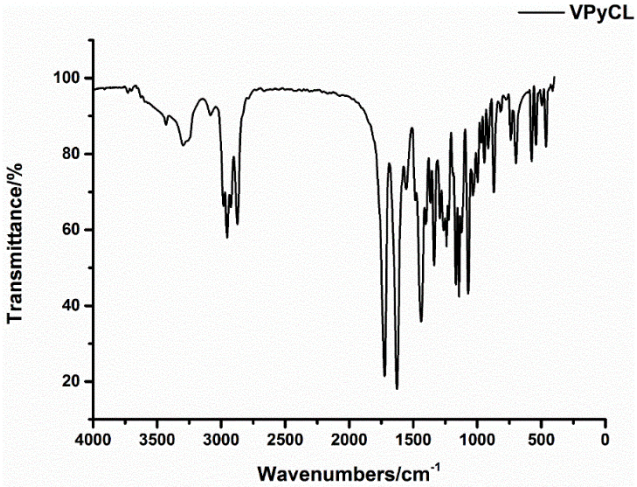


Figure S17. FT-IR spectrum of 5-(pyrrolidine-1-carbonyl)oxepan-2-one(VPyCL)

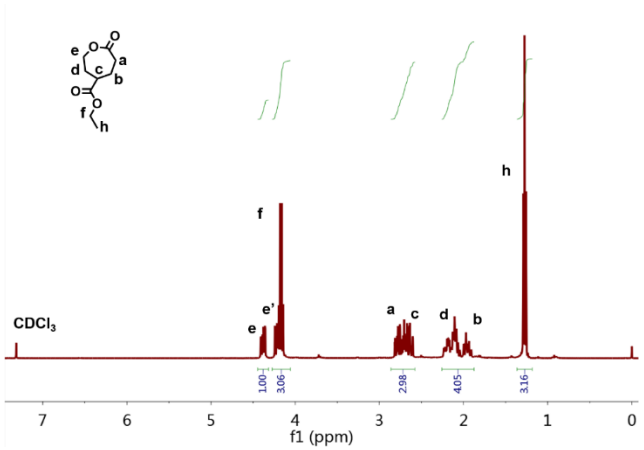


Figure S18. ^{1}H NMR spectrum of ethyl 7-oxooxepane-4-carboxylate(EMCL)

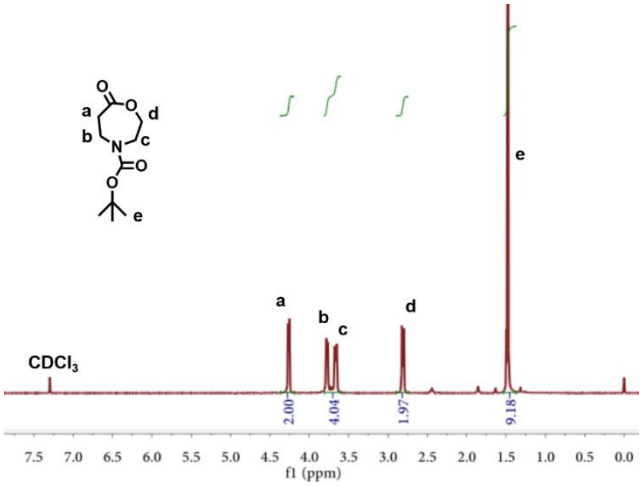


Figure S19. ^{1}H NMR spectrum of tert-butyl 7-oxo-1,4-oxazepane-4-carboxylate(Boc-NIPIL)

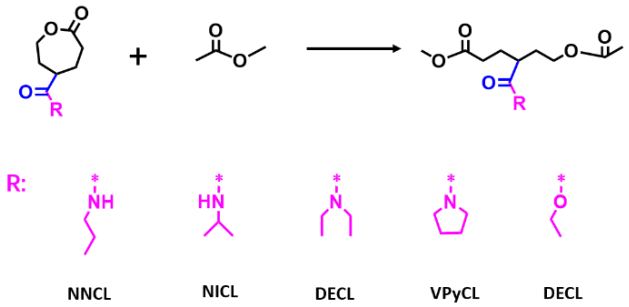
2 Computer simulation

All the geometries were fully optimized by means of the hybrid M06-2x[1] functional with the triple-zeta, polarized and diffuse 6-311+G(d,p) basis set.[2] No symmetry or geometry constraint was imposed during the optimizations. All the optimized geometries were corroborated to be factual minima on the potential energy surface via frequency calculations at the same theoretical level. All of these calculations were carried out with the Gaussian 09 suite of programs. All calculations were performed with the SMD solvent model in dichloromethane and the enthalpies were obtained from the frequency calculations at 298.15K and 1 atm. The independent gradient

model (IGM)[3] analysis was performed with the Multiwfn[4] program and visualized by using the VMD package[5].

2.1 The enthalpies of ring opening

The enthalpies of ring opening were evaluated as ΔHro ($\Delta Hro = H_{ring} - H_{C3H6O2} - H_{chain}$), where H_{ring}, H_{C3H6O2} and H_{chain} are the thermal enthalpies of optimized γ-substituted ε-caprolactones, methyl acetate, and methyl acetate-(γ-substituted ε-caprolactone) adduct. [6]



Scheme S7. A model of ring-opening reaction between functional ε-caprolactone and methyl acetate

2.2 The independent gradient model (IGM) analysis

The independent gradient model (IGM) was developed by Lefebvre and coworkers[3] to identify and isolate the interaction between user-defined fragments. They used $\delta_g = |\rho IGM| - |\rho|$ to describe the interactions. In this work, we applied the δg analysis to 5 different substituted monomers. Figure S20 shows the 3D real space RGB-colored function isosurfaces and 2D scatter plot of δginter *vs* sign$(\lambda_2)\rho$, where $(\lambda_2)\rho$ is the second eigenvalue of the electron-density Hessian matrix. Blue indicates strong attractive interaction, red the steric repulsion, and green the van der Waals (vdW) interaction.

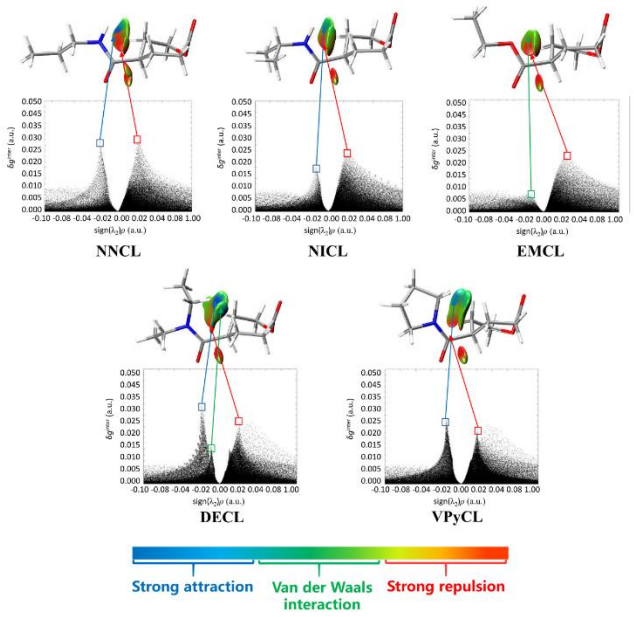


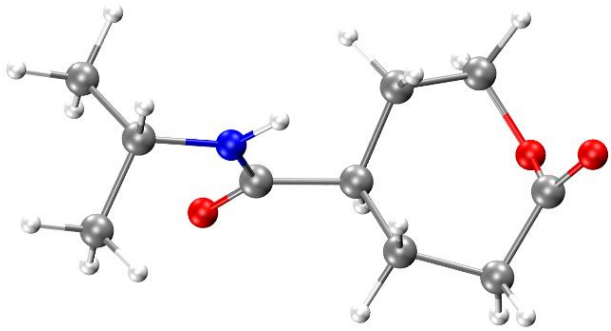
Figure S20. The independent gradient model (IGM) analysis of intramolecular interactions between substituted group and ring.

Table S1 The Result of Computer Simulation

Entry	Monomer	Attraction/a.u[a]	Repellant/a.u[a]	*ΔHro*[a]/kcal/mol[b]
1	NNCL	0.030	0.033	-16.0
2	NICL	0.020	0.025	-17.6
3	DECL	0.035	0.025	-16.6
4	VPyCL	0.027	0.023	-17.4
5	EMCL	0.010	0.023	-14.7

[a]Attraction and repellant were calculated through independent gradient model (IGM) analysis from Figure S20. [b]Δ*Hro* was calculated through a model of ring opening reaction in Figure S20.

NICL



Center Number	Atomic Type	Coordinates (Angstroms) X	Y	Z
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2	C	-0.883294	-1.320254	0.141400
3	C	-2.389532	-1.593912	0.354613
4	C	-0.918972	1.219309	-0.328490
5	C	-3.135747	-0.435038	-0.233065
6	C	-2.292608	1.728357	0.106018
7	H	-0.691213	0.265278	1.608655
8	H	-0.651895	-1.459915	-0.919683
9	H	-2.608927	-1.656365	1.421722
10	H	-0.961072	0.869463	-1.366098
11	H	-2.809917	2.232611	-0.713015
12	H	-0.328340	-2.080920	0.696529
13	H	-2.673549	-2.521100	-0.141740
14	H	-0.232346	2.069970	-0.309531
15	H	-2.209083	2.410165	0.951351
16	O	-3.622388	-0.380001	-1.328736
17	O	-3.094182	0.638561	0.603581
18	C	1.136817	0.059276	0.608504
19	O	1.751549	0.074024	1.668886
20	N	1.743894	0.001186	-0.597254
21	H	1.157343	-0.007048	-1.419896
22	C	3.197271	-0.048635	-0.808099
23	H	3.315756	-0.092459	-1.893186
24	C	3.811567	-1.311397	-0.207695
25	H	3.725728	-1.301704	0.879809
26	H	3.313882	-2.204704	-0.592476
27	H	4.870354	-1.366890	-0.472488
28	C	3.883217	1.218177	-0.301321
29	H	4.942383	1.195873	-0.569604
30	H	3.433561	2.107091	-0.750073
31	H	3.801694	1.292798	0.784197

Zero-point correction= 0.269303 (Hartree/Particle)
Thermal correction to Energy= 0.283870
Thermal correction to Enthalpy= 0.284815
Thermal correction to Gibbs Free Energy= 0.227042
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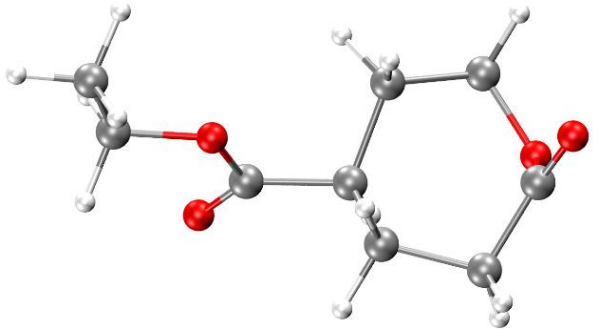
Sum of electronic and thermal Energies= -671.394848
Sum of electronic and thermal Enthalpies= -671.393904
Sum of electronic and thermal Free Energies= -671.451677

EMCL



Center Number	Atomic Type	Coordinates (Angstroms) X	Y	Z
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3	C	2.045269	0.627187	1.503601
4	C	0.534197	-0.455195	-1.160506
5	C	2.734419	0.582436	0.172878
6	C	1.956999	-0.936533	-1.439425
7	H	0.539571	-1.607283	0.687537
8	H	0.159123	1.426902	0.807255
9	H	2.392598	-0.209773	2.112014
10	H	0.431959	0.605992	-1.405759
11	H	2.377786	-0.450090	-2.322105
12	H	0.038301	0.369606	2.212442
13	H	2.254241	1.569140	2.009242
14	H	-0.136570	-0.999911	-1.830421
15	H	1.988347	-2.016726	-1.575870
16	O	3.103557	1.522852	-0.474063
17	O	2.796441	-0.696477	-0.292714
18	C	-1.384293	-0.833230	0.403740
19	O	-1.949101	-1.785497	0.884641
20	O	-2.029395	0.217006	-0.109989
21	C	-3.471186	0.172094	-0.080724
22	H	-3.795624	0.070195	0.956908
23	H	-3.801406	-0.709552	-0.634041
24	C	-3.975407	1.450085	-0.705831
25	H	-5.067291	1.446182	-0.708588
26	H	-3.634903	2.319799	-0.140407
27	H	-3.627610	1.540992	-1.736713

Zero-point correction= 0.228938 (Hartree/Particle)
Thermal correction to Energy= 0.241958

Thermal correction to Enthalpy= 0.242902
Thermal correction to Gibbs Free Energy= 0.187946
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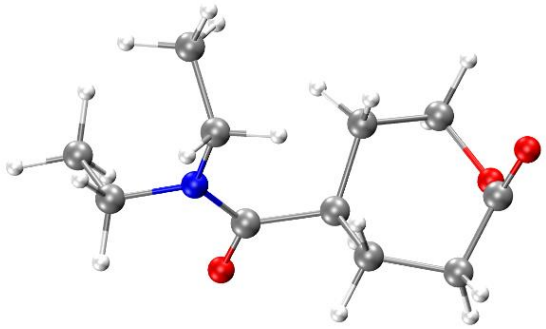
Sum of electronic and thermal Free Energies= -652.050560

DECL



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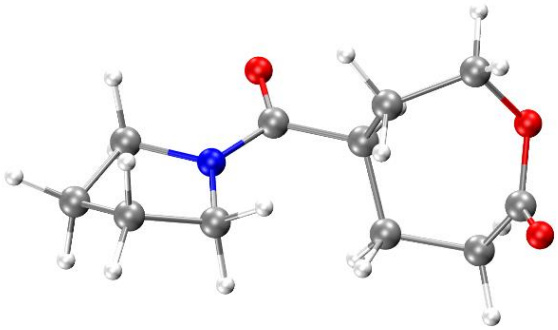
4	C	-0.778702	0.624636	0.925126
5	C	-3.197669	0.067234	-0.245883
6	C	-2.038073	0.435556	1.769067
7	H	-0.797278	-1.509595	0.702093
8	H	-0.900823	0.180073	-1.834346
9	H	-2.869297	-1.938065	-0.859472
10	H	-0.928441	1.472763	0.251350
11	H	-2.470743	1.395050	2.060964
12	H	-0.680949	-1.566947	-1.823196
13	H	-3.069523	-0.779798	-2.205995
14	H	0.040274	0.893676	1.597602
15	H	-1.832715	-0.153913	2.662069
16	O	-3.662914	1.139804	-0.516519
17	O	-3.008546	-0.344732	1.039373
18	C	1.065479	-0.968070	0.023678
19	O	1.450436	-2.081847	0.379428
20	N	1.947438	-0.053670	-0.451288
21	C	4.011120	-0.384021	0.908396
22	H	5.066140	-0.660314	0.836528

23	H	3.946954	0.618822	1.336385
24	H	3.518479	-1.085279	1.583496
25	C	1.625415	1.266622	-0.988322
26	H	2.043320	1.325032	-1.998733
27	H	0.550493	1.362075	-1.090592
28	C	2.173108	2.408013	-0.139806
29	H	1.876406	3.364618	-0.576729
30	H	1.784967	2.357223	0.880131
31	H	3.264377	2.383006	-0.096673
32	C	3.364720	-0.432872	-0.471288
33	H	3.869112	0.254675	-1.153111
34	H	3.447249	-1.439090	-0.886193

Zero-point correction= 0.298970 (Hartree/Particle)
Thermal correction to Energy= 0.314359
Thermal correction to Enthalpy= 0.315303
Thermal correction to Gibbs Free Energy= 0.256692
Sum of electronic and zero-point Energies= -710.670308
Sum of electronic and thermal Energies= -710.654919
Sum of electronic and thermal Enthalpies= -710.653975
Sum of electronic and thermal Free Energies= -710.712586

VPyCL

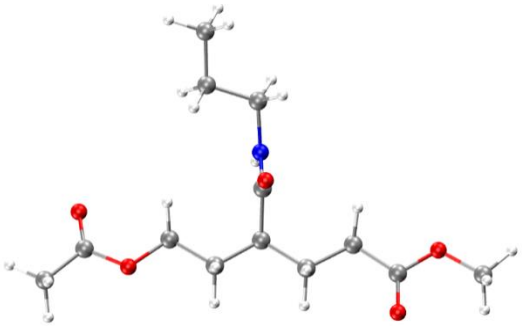


Center Number	Atomic Type	Coordinates (Angstroms) X	Y	Z
1	C	-0.529083	0.700134	0.229446
2	C	-0.876286	-0.394597	1.261699
3	C	-2.385893	-0.500384	1.581625
4	C	-0.980150	0.343364	-1.210408
5	C	-3.111584	-0.591522	0.271287
6	C	-2.410989	0.804362	-1.489043
7	H	-1.052399	1.613891	0.523466

8	H	-0.539833	-1.368774	0.900975
9	H	-2.717806	0.393405	2.112710
10	H	-0.914040	-0.737190	-1.365484
11	H	-2.849528	0.261305	-2.329190
12	H	-0.351136	-0.192081	2.198757
13	H	-2.580643	-1.388017	2.182449
14	H	-0.326738	0.813191	-1.950749
15	H	-2.448776	1.873958	-1.692029
16	O	-3.468639	-1.598393	-0.275434
17	O	-3.225931	0.635288	-0.310486
18	C	0.937488	1.126470	0.281133
19	O	1.211745	2.314831	0.455706
20	C	1.817637	-1.222661	-0.163595
21	C	4.118538	-0.638210	0.036423
22	C	3.182187	-1.538783	-0.771935
23	H	0.992982	-1.433683	-0.841490
24	H	1.672699	-1.791171	0.760714
25	H	5.086552	-0.480892	-0.439061
26	H	4.286681	-1.073746	1.025343
27	H	3.193361	-1.244600	-1.825393
28	H	3.427391	-2.598610	-0.701671
29	N	1.920115	0.214793	0.130568
30	C	3.322942	0.660499	0.165358
31	H	3.524844	1.204408	1.089198
32	H	3.509339	1.339214	-0.672752

Zero-point correction= 0.278608 (Hartree/Particle)
Thermal correction to Energy= 0.292344
Thermal correction to Enthalpy= 0.293288
Thermal correction to Gibbs Free Energy= 0.237662
Sum of electronic and zero-point Energies= -709.492889
Sum of electronic and thermal Energies= -709.479153
Sum of electronic and thermal Enthalpies= -709.478209
Sum of electronic and thermal Free Energies= -709.533835

Ring opened NNCL

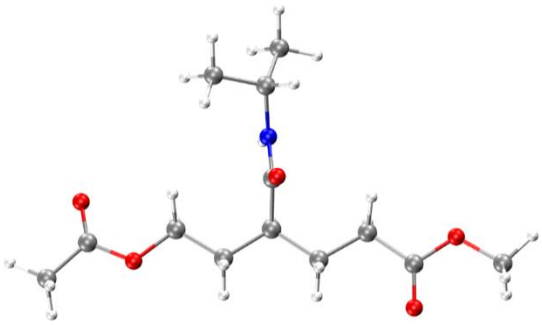


Center Number	Atomic Type	Coordinates (Angstroms) X	Y	Z
1	C	6.514454	-0.426702	-0.074363
2	H	6.734720	-1.361509	-0.591461
3	H	7.166906	0.365712	-0.433297
4	H	6.641392	-0.563463	1.000171
5	O	5.180156	0.004521	-0.368879
6	C	4.198324	-0.827699	-0.002823
7	O	4.402702	-1.880688	0.548032
8	C	2.845744	-0.280409	-0.374409
9	H	2.777981	0.733958	0.032124
10	H	2.825189	-0.176709	-1.465079
11	C	1.701535	-1.157296	0.115500
12	H	1.830800	-2.175522	-0.259925
13	H	1.716353	-1.209573	1.207400
14	C	0.336017	-0.635952	-0.340075
15	H	0.316204	-0.599298	-1.435527
16	C	-0.788075	-1.556169	0.149957
17	H	-0.612695	-2.565844	-0.231744
18	H	-0.765751	-1.599594	1.242733
19	C	-2.149163	-1.076116	-0.310577
20	H	-2.203433	-1.010931	-1.401167
21	H	-2.396756	-0.095353	0.105353
22	O	-3.120656	-2.030110	0.149915
23	C	-4.400023	-1.772462	-0.150438
24	C	-5.317017	-2.822079	0.400957
25	H	-6.344092	-2.594189	0.125773
26	H	-5.030556	-3.800397	0.010778
27	H	-5.218957	-2.853418	1.487863
28	O	-4.740939	-0.805444	-0.786717
29	C	0.109102	0.769669	0.208648
30	O	0.147755	0.998722	1.412333
31	N	-0.132807	1.730381	-0.708647
32	H	-0.210479	1.459910	-1.678509

33	C	-0.462827	3.097902	-0.334169
34	H	-0.207928	3.744430	-1.176751
35	H	0.171241	3.378404	0.510126
36	C	-1.933373	3.267675	0.040819
37	H	-2.553731	2.966246	-0.809496
38	H	-2.162784	2.589387	0.867974
39	C	-2.243400	4.707198	0.437292
40	H	-2.017924	5.396358	-0.381785
41	H	-3.297416	4.827899	0.695773
42	H	-1.648566	5.009467	1.303815

Zero-point correction= 0.361409 (Hartree/Particle)
Thermal correction to Energy= 0.384168
Thermal correction to Enthalpy= 0.385112
Thermal correction to Gibbs Free Energy= 0.304053
Sum of electronic and zero-point Energies= -939.705802
Sum of electronic and thermal Energies= -939.683042
Sum of electronic and thermal Enthalpies= -939.682098
Sum of electronic and thermal Free Energies= -939.763157

Ring opened NICL

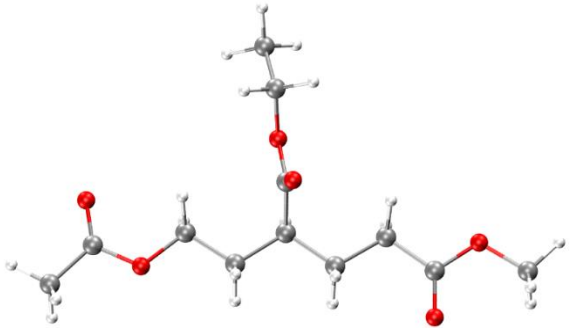


Center Number	Atomic Type	Coordinates (Angstroms) X	Y	Z
1	C	6.350386	-0.861436	-0.069547
2	H	6.518342	-1.676360	-0.774649
3	H	7.062372	-0.058636	-0.244972
4	H	6.444598	-1.234037	0.950931
5	O	5.054546	-0.284766	-0.273135
6	C	4.011675	-1.103274	-0.090843
7	O	4.133939	-2.259206	0.229825
8	C	2.705992	-0.398590	-0.348178
9	H	2.727268	0.550250	0.196402

10	H	2.683642	-0.143749	-1.414082
11	C	1.498383	-1.241469	0.039580
12	H	1.538945	-2.203266	-0.477466
13	H	1.522305	-1.448177	1.112974
14	C	0.174373	-0.554976	-0.305097
15	H	0.139627	-0.368743	-1.384563
16	C	-1.013116	-1.441947	0.086925
17	H	-0.913938	-2.408503	-0.415122
18	H	-0.988506	-1.619834	1.165895
19	C	-2.338840	-0.815789	-0.294173
20	H	-2.391251	-0.611267	-1.367450
21	H	-2.520820	0.119391	0.243171
22	O	-3.370592	-1.754123	0.054099
23	C	-4.629833	-1.386018	-0.214675
24	C	-5.611587	-2.439674	0.200930
25	H	-6.622319	-2.112923	-0.031716
26	H	-5.388882	-3.371632	-0.322142
27	H	-5.514316	-2.625350	1.272249
28	O	-4.907466	-0.330721	-0.729480
29	C	0.072839	0.777404	0.431163
30	O	0.185485	0.843000	1.650707
31	N	-0.147535	1.861758	-0.340376
32	H	-0.276472	1.728463	-1.334593
33	C	-0.346855	3.202472	0.211209
34	H	0.389444	3.324346	1.009511
35	C	-0.087066	4.225756	-0.885135
36	H	-0.803064	4.098574	-1.703448
37	H	-0.203500	5.236320	-0.489239
38	H	0.923814	4.124810	-1.286747
39	C	-1.747982	3.340933	0.801159
40	H	-1.875828	4.330529	1.247281
41	H	-2.502170	3.213998	0.018567
42	H	-1.914054	2.589655	1.575808

Zero-point correction= 0.360763 (Hartree/Particle)
Thermal correction to Energy= 0.383526
Thermal correction to Enthalpy= 0.384470
Thermal correction to Gibbs Free Energy= 0.304048
Sum of electronic and zero-point Energies= -939.709612
Sum of electronic and thermal Energies= -939.686849
Sum of electronic and thermal Enthalpies= -939.685905
Sum of electronic and thermal Free Energies= -939.766327

Ring opened EMCL

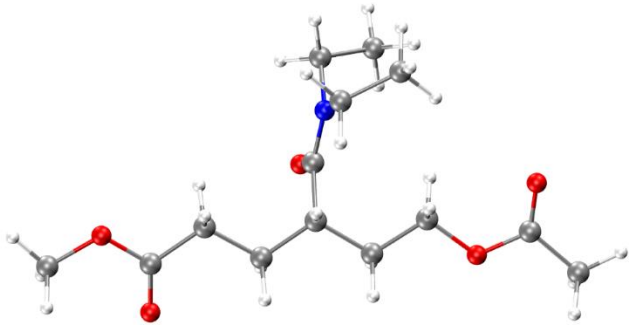


Center Number	Atomic Type	Coordinates (Angstroms) X	Y	Z
1	C	6.292044	-0.744815	-0.141251
2	H	6.431415	-1.543325	-0.870861
3	H	7.015326	0.049475	-0.308769
4	H	6.398120	-1.146367	0.866997
5	O	5.003423	-0.139460	-0.304849
6	C	3.949813	-0.944462	-0.128555
7	O	4.055223	-2.110065	0.161414
8	C	2.652764	-0.212343	-0.350808
9	H	2.692236	0.716680	0.226761
10	H	2.624752	0.080385	-1.406474
11	C	1.436737	-1.053203	0.015031
12	H	1.455255	-1.990782	-0.545256
13	H	1.466849	-1.309473	1.077643
14	C	0.121630	-0.333548	-0.291907
15	H	0.085351	-0.066397	-1.351848
16	C	-1.081277	-1.224161	0.049771
17	H	-1.001648	-2.151536	-0.523535
18	H	-1.049796	-1.481938	1.112719
19	C	-2.400434	-0.550061	-0.270011
20	H	-2.464332	-0.272631	-1.325767
21	H	-2.559423	0.350146	0.331082
22	O	-3.441083	-1.493432	0.032804
23	C	-4.700067	-1.074020	-0.151545
24	C	-5.692511	-2.146139	0.183068
25	H	-6.701700	-1.748842	0.104328
26	H	-5.566840	-2.978746	-0.512458
27	H	-5.509791	-2.520287	1.191529
28	O	-4.968870	0.033364	-0.546916
29	C	0.024987	0.946434	0.515796
30	O	0.184046	1.007987	1.711144
31	O	-0.284034	2.002656	-0.238381
32	C	-0.461223	3.259318	0.450467

33	H	-1.243796	3.134137	1.201930
34	H	0.471176	3.509503	0.960785
35	C	-0.833811	4.291902	-0.585163
36	H	-1.760966	4.015933	-1.091314
37	H	-0.980645	5.258063	-0.098062
38	H	-0.043087	4.398191	-1.330513

Zero-point correction= 0.320791 (Hartree/Particle)
Thermal correction to Energy= 0.341842
Thermal correction to Enthalpy= 0.342786
Thermal correction to Gibbs Free Energy= 0.266462
Sum of electronic and zero-point Energies= -920.304958
Sum of electronic and thermal Energies= -920.283908
Sum of electronic and thermal Enthalpies= -920.282963
Sum of electronic and thermal Free Energies= -920.359287

Ring opened DECL

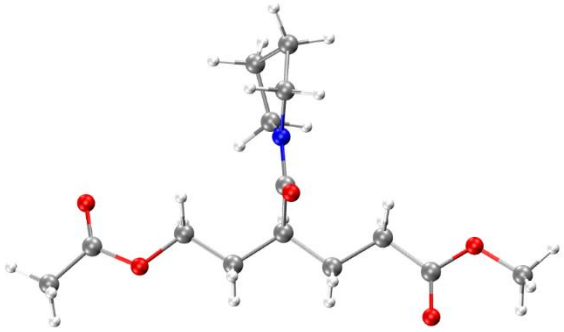


Center Number	Atomic Type	Coordinates (Angstroms) X	Y	Z
1	0	-6.529620	-0.585574	0.216445
2	0	-6.696228	-1.511631	0.768022
3	0	-7.198315	0.192761	0.576320
4	0	-6.690138	-0.759494	-0.848246
5	0	-5.202965	-0.096461	0.447084
6	0	-4.203708	-0.905693	0.074834
7	0	-4.388580	-1.992042	-0.415027
8	0	-2.860430	-0.282668	0.346124
9	0	-2.832441	0.671554	-0.190686
10	0	-2.818853	-0.039741	1.413387
11	0	-1.700337	-1.178870	-0.064776
12	0	-1.774446	-2.138112	0.454407
13	0	-1.751016	-1.380821	-1.136633
14	0	-0.344216	-0.550041	0.268399

15	0	-0.306314	-0.394040	1.346085
16	0	0.797360	-1.495270	-0.133506
17	0	0.665040	-2.448723	0.385526
18	0	0.742957	-1.688092	-1.208995
19	0	2.157263	-0.923812	0.209775
20	0	2.242637	-0.702320	1.278112
21	0	2.368276	-0.007801	-0.349340
22	0	3.140762	-1.911636	-0.141118
23	0	4.419879	-1.579248	0.074404
24	0	5.352148	-2.676733	-0.342052
25	0	6.379452	-2.383810	-0.138636
26	0	5.107057	-3.590631	0.202232
27	0	5.223632	-2.876600	-1.407621
28	0	4.749230	-0.518259	0.545688
29	0	-0.192859	0.762908	-0.504166
30	0	-0.481502	0.770240	-1.700873
31	0	0.263876	1.885837	0.105484
32	0	1.585024	3.102188	-1.628600
33	0	1.603277	4.020001	-2.221970
34	0	2.508075	3.051473	-1.047646
35	0	1.553282	2.252862	-2.312712
36	0	0.359211	3.095175	-0.721347
37	0	0.378512	3.948964	-0.041064
38	0	-0.547425	3.166178	-1.324444
39	0	0.652584	2.037018	1.509920
40	0	-0.012712	2.778649	1.965105
41	0	0.496011	1.100019	2.034542
42	0	2.102972	2.474982	1.685987
43	0	2.283142	3.459945	1.249964
44	0	2.330839	2.536944	2.752892
45	0	2.791388	1.760701	1.228340

Zero-point correction= 0.390001 (Hartree/Particle)
Thermal correction to Energy= 0.413715
Thermal correction to Enthalpy= 0.414659
Thermal correction to Gibbs Free Energy= 0.333214
Sum of electronic and zero-point Energies= -978.969020
Sum of electronic and thermal Energies= -978.945306
Sum of electronic and thermal Enthalpies= -978.944362
Sum of electronic and thermal Free Energies= -979.025808

Ring opened VPyCL

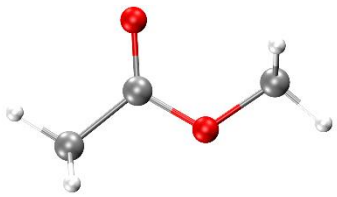


Center Number	Atomic Type	Coordinates (Angstroms) X	Y	Z
1	C	6.296222	-1.055846	-0.396577
2	H	6.337697	-1.941847	-1.031056
3	H	7.003742	-0.307927	-0.746540
4	H	6.517354	-1.332802	0.634976
5	O	5.004936	-0.440554	-0.482547
6	C	3.965297	-1.202557	-0.121825
7	O	4.087205	-2.341259	0.255240
8	C	2.663684	-0.456978	-0.250397
9	H	2.715373	0.400151	0.430666
10	H	2.615736	-0.045355	-1.263824
11	C	1.453939	-1.331961	0.048804
12	H	1.468093	-2.210900	-0.601198
13	H	1.498787	-1.688757	1.080475
14	C	0.134023	-0.585470	-0.167886
15	H	0.097387	-0.243598	-1.205425
16	C	-1.058523	-1.512876	0.097615
17	H	-0.946375	-2.419454	-0.503802
18	H	-1.055776	-1.806547	1.151374
19	C	-2.377477	-0.850968	-0.243851
20	H	-2.431144	-0.592417	-1.304787
21	H	-2.544927	0.058426	0.342009
22	O	-3.421659	-1.791834	0.058267
23	C	-4.673878	-1.403535	-0.213962
24	C	-5.669816	-2.463778	0.147402
25	H	-6.673344	-2.124594	-0.098158
26	H	-5.439498	-3.381490	-0.396982
27	H	-5.598126	-2.680478	1.214953
28	O	-4.936260	-0.326792	-0.691340
29	C	0.069277	0.606841	0.785452
30	O	0.231161	0.437704	1.994215
31	C	-0.461242	2.181563	-1.126027
32	C	-0.212409	4.178465	0.173545

33	C	-0.997246	3.609144	-1.010151
34	H	-1.195378	1.498703	-1.553970
35	H	0.448978	2.150524	-1.733859
36	H	-0.670165	5.066932	0.608196
37	H	0.804853	4.430660	-0.138814
38	H	-2.063737	3.580850	-0.769945
39	H	-0.864153	4.171462	-1.934276
40	N	-0.155929	1.831134	0.272514
41	C	-0.178640	3.007431	1.153333
42	H	0.696598	3.004391	1.803833
43	H	-1.072790	2.981156	1.785028

Zero-point correction= 0.369901 (Hartree/Particle)
Thermal correction to Energy= 0.391913
Thermal correction to Enthalpy= 0.392857
Thermal correction to Gibbs Free Energy= 0.315026
Sum of electronic and zero-point Energies= -977.792852
Sum of electronic and thermal Energies= -977.770840
Sum of electronic and thermal Enthalpies= -977.769895
Sum of electronic and thermal Free Energies= -977.847726

Methyl acetate



Center Number	Atomic Type	Coordinates (Angstroms) X	Y	Z
1	C	1.866895	-0.161842	0.000129
2	H	2.541379	-1.014646	0.000270
3	H	2.025507	0.446057	-0.891175
4	H	2.025414	0.446279	0.891300
5	O	0.544351	-0.712263	0.000129
6	C	-0.461452	0.171100	-0.000053
7	O	-0.283171	1.364221	-0.000209
8	C	-1.794989	-0.513011	-0.000027
9	H	-1.877616	-1.150450	-0.882247
10	H	-1.877739	-1.150130	0.882413
11	H	-2.589113	0.229737	-0.000215

Zero-point correction= 0.090311 (Hartree/Particle)
Thermal correction to Energy= 0.096468
Thermal correction to Enthalpy= 0.097412
Thermal correction to Gibbs Free Energy= 0.059269
Sum of electronic and zero-point Energies= -268.271015
Sum of electronic and thermal Energies= -268.264858
Sum of electronic and thermal Enthalpies= -268.263913
Sum of electronic and thermal Free Energies= -268.302057

Table S2. Results for ROP of γ-amide-ε-caprolactones[a]

Entry	Monomer	Catalyst[b]	$[M]_0/[I]_0$	Time/h	Reaction temperature/°C	Conversion/%[c]	M_n/Da[c]	M_n/Da[d]	$Đ$[d]
1	NNCL	$Sn(Oct)_2$	40	24	130	30	2500	3400	—[e]
2	NNCL	DBU/TU	40	48	25	9	700	—	—
3	NICL	$Sn(Oct)_2$	40	24	165	49	5200	2400	—[e]
4	NICL	DBU/TU	40	48	25	17	1500	—	—
5	DECL	$Sn(Oct)_2$	40	24	130	20	1800	2200	—[e]
6	DECL	DBU/TU	40	48	25	15	1400	—	—
7	VPyCL	$Sn(Oct)_2$	40	24	130	51	4400	1800	—[e]
8	VPyCL	DBU/TU	40	48	25	16	1500	—	—

[a]All reactions used benzyl alcohol (BnOH) as the initiator. [b]$Sn(Oct)_2$:5wt%(relative to the monomer weight), DBU/TU:10mol% (relative to the monomer mole mass). [c]Conversion and number average molecular weight (M_n)were calculated by ^1H NMR. [d]M_n and dispersity ($Đ$) were measured by GPC in DMF using polymethyl methacrylate (PMMA) standards as calibration. [e]The GPC curves showed multiple peaks.

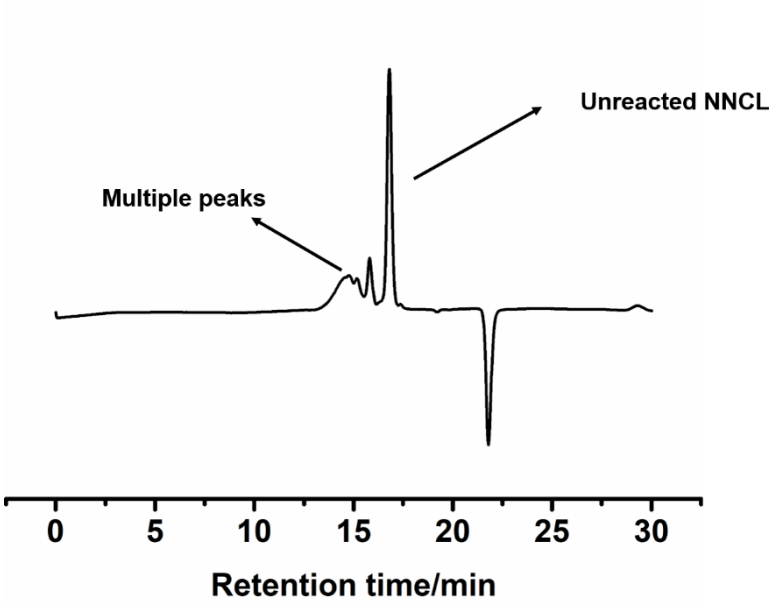


Figure S21. GPC curve of crude $PNNCL_{40}$ after reaction for 3.5h.

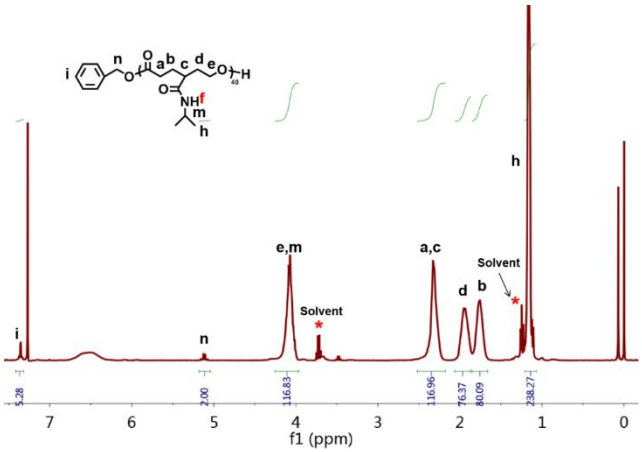


Figure S22. ^{1}H NMR spectrum of poly(*N*-isopropyl-4-oxocyclohexane-1-carboxamide)$_{40}$ ($PNICL_{40}$)

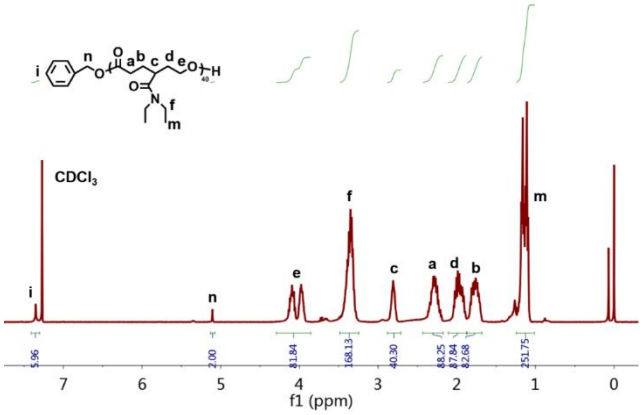


Figure S23. ^{1}H NMR spectrum of poly(*N*, *N*-diethyl-7-oxooxepane-4-carboxamide)$_{40}$ (PDECL)$_{40}$

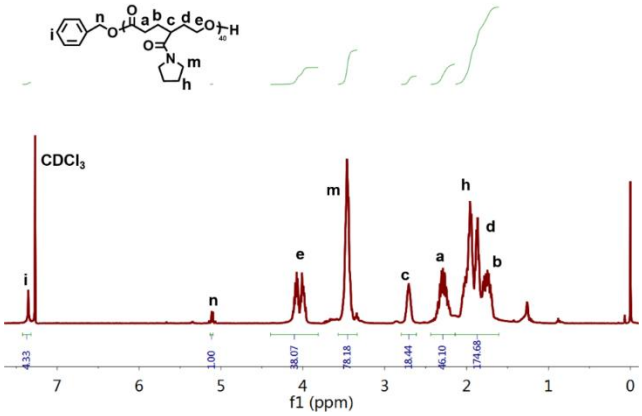
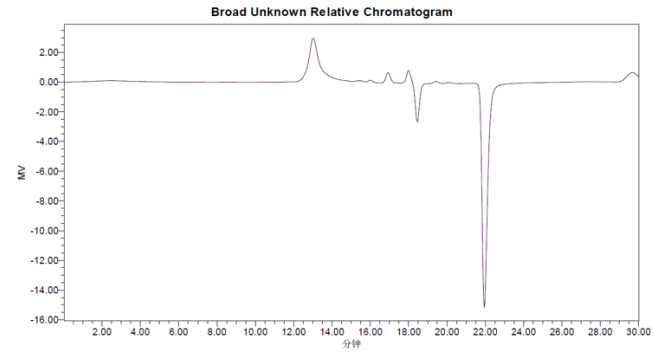


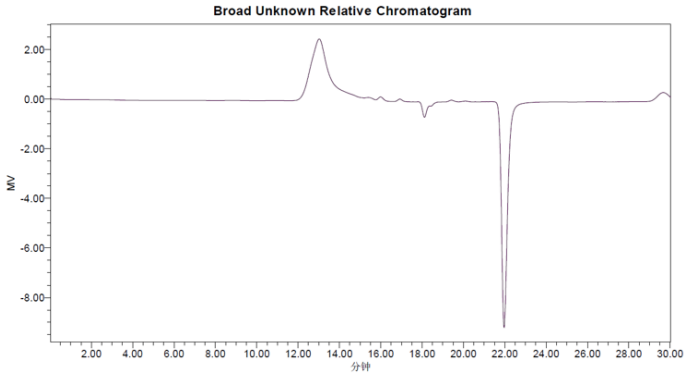
Figure S24. ^{1}H NMR spectrum of poly(5-(pyrrolidine-1-carbonyl)oxepan-2-one)$_{40}$ (PVPyCL)$_{40}$



Broad Unknown Relative Peak Table

	Distribution Name	Mn (Daltons)	Mw (Daltons)	MP (Daltons)	Mz (Daltons)	Mz+1 (Daltons)	Polydispersity	Mz/Mw	Mz+1/Mw
1		8216	9157	8685	10214	11375	1.114528	1.115399	1.242167

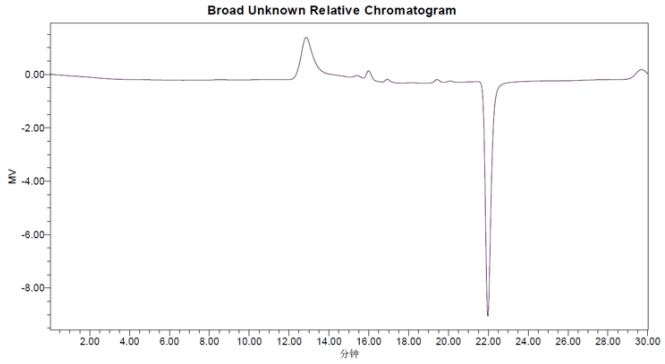
Figure S25. GPC curve of crude PNICL$_{40}$. M_n=8216, $Đ$=1.14528



Broad Unknown Relative Peak Table

	Distribution Name	Mn (Daltons)	Mw (Daltons)	MP (Daltons)	Mz (Daltons)	Mz+1 (Daltons)	Polydispersity	Mz/Mw	Mz+1/Mw
1		8128	9361	8681	10708	12055	1.151792	1.143859	1.287728

Figure S26. GPC curve of crude PDECL$_{40}$. M_n=8128, $Đ$ =1.1517



Broad Unknown Relative Peak Table

	Distribution Name	Mn (Daltons)	Mw (Daltons)	MP (Daltons)	Mz (Daltons)	Mz+1 (Daltons)	Polydispersity	Mz/Mw	Mz+1/Mw
1		8159	9365	8423	10696	12038	1.147729	1.142113	1.285511

Figure S27. GPC curve of crude PVPyCL$_{40}$. M_n=8159, $Đ$ =1.1477

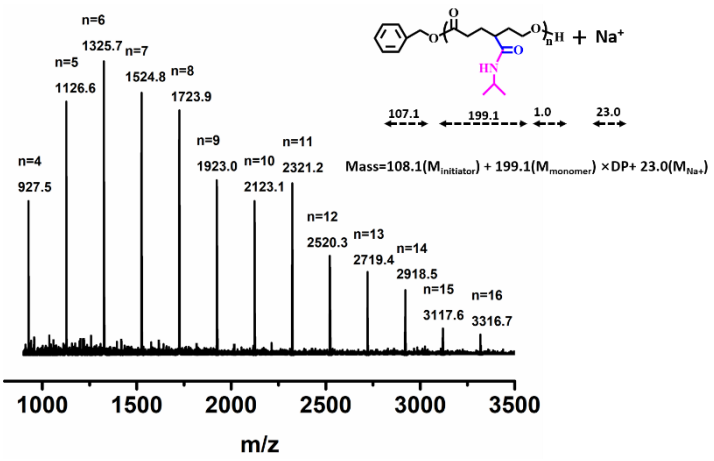


Figure S28. MALDI-tof-MS of $PNICL_{10}$ initiated by BnOH.

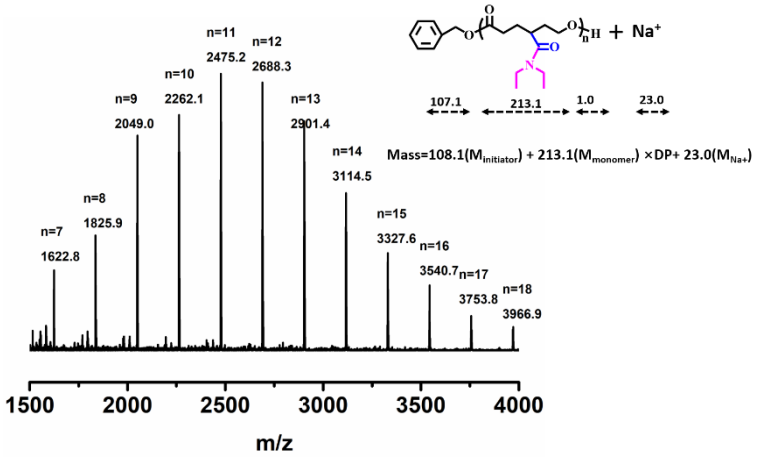


Figure S29. MALDI-tof-MS of $PDECL_{10}$ initiated by BnOH.

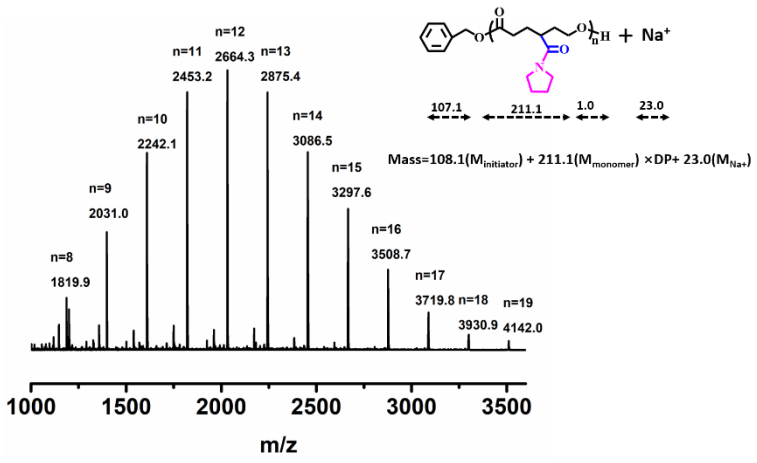


Figure S30. MALDI-tof-MS of $PVPyCL_{10}$ initiated by BnOH

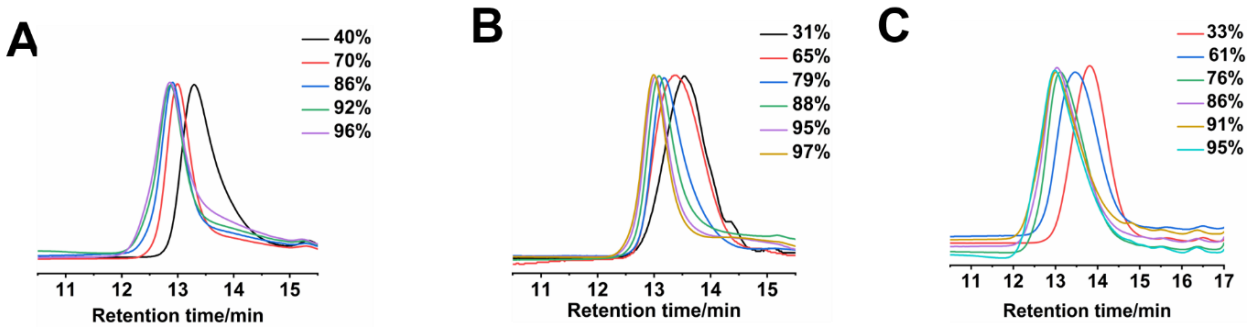


Figure S31. GPC curve of (A) $PNICL_{40}$, (B) $PDECL_{40}$ and (C) $PVPyCL_{40}$ at different monomer conversion

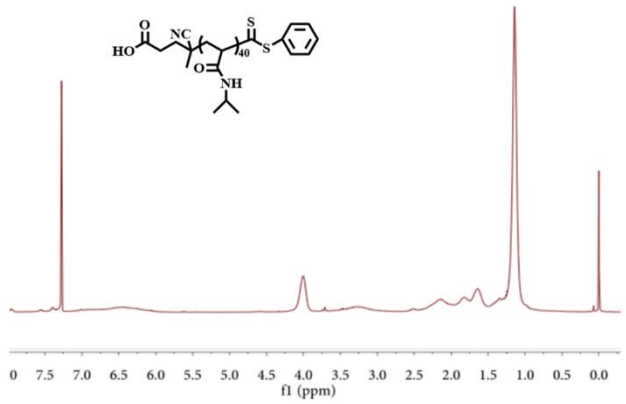


Figure S32. ^1H NMR spectrum of $PNIPAM_{40}$-COOH

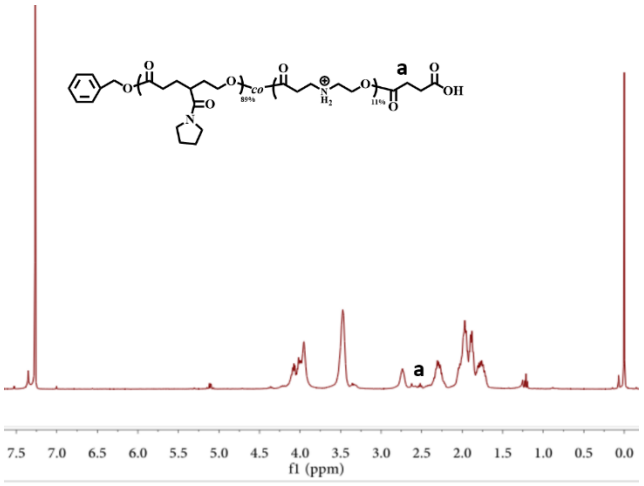


Figure S33. ^1H NMR spectrum of $P(VPyCL_{89\%}$-*co*-$PIL_{89\%})_{20}$-COOH

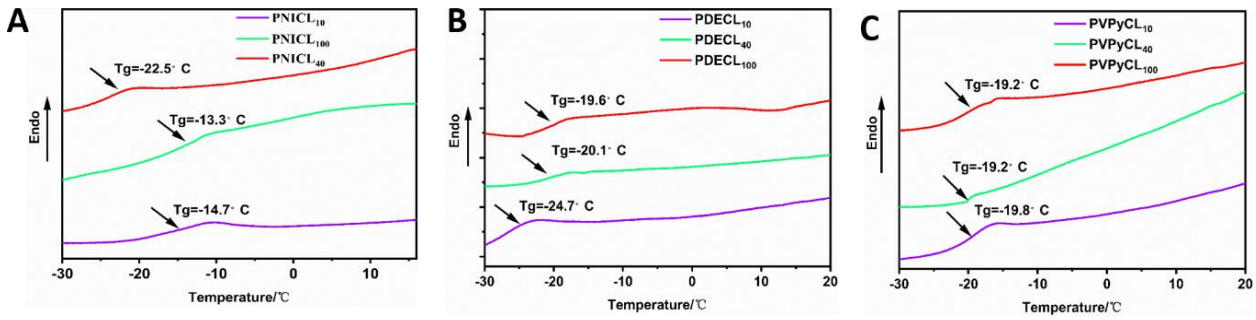


Figure S34. DSC of PNICL, PDECL and PVPyCL

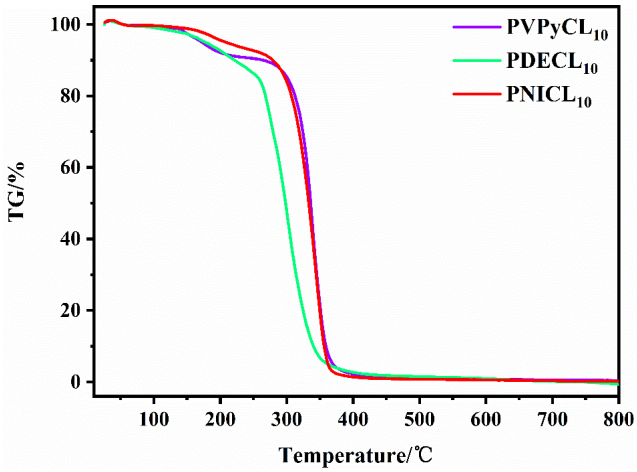


Figure S35. TGA of $PNICL_{10}$, $PDECL_{10}$, $PVPyCL_{10}$

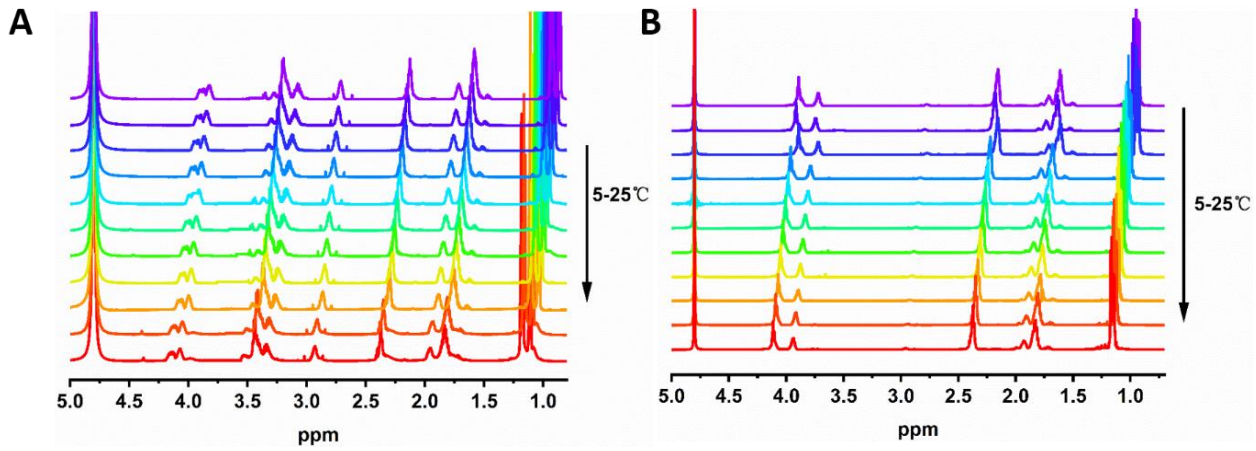


Figure S36. Variable temperature ^1H NMR of (A) $PNICL_{10}$ and (B) $PDECL_{10}$ in D_2O, concentration=5wt%

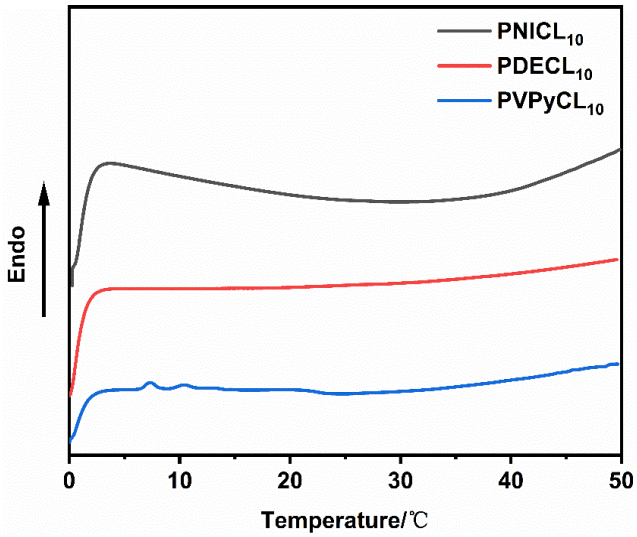


Figure S37. DSC of $PNICL_{10}$, $PDECL_{10}$, $PVPyCL_{10}$ in D_2O, concentration=5wt%

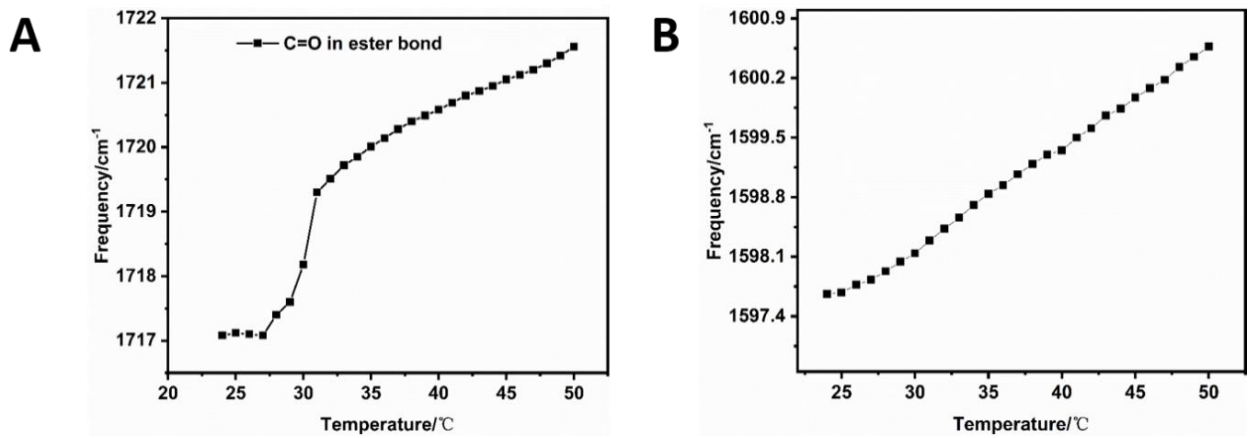


Figure S38. Quantitative analysis of the wavenumber changes of the V(C=O) of (A) ester bond and (B) amide bond, with temperature, $PVPyCL_{10}$ in D_2O, concentration=5wt%

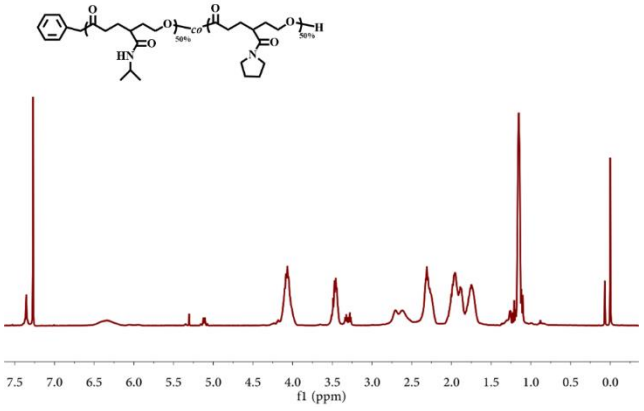


Figure S39. ^{1}H NMR spectrum of P(VPyCL$_{50\%}$-*co*-NICL$_{50\%}$)$_{20}$

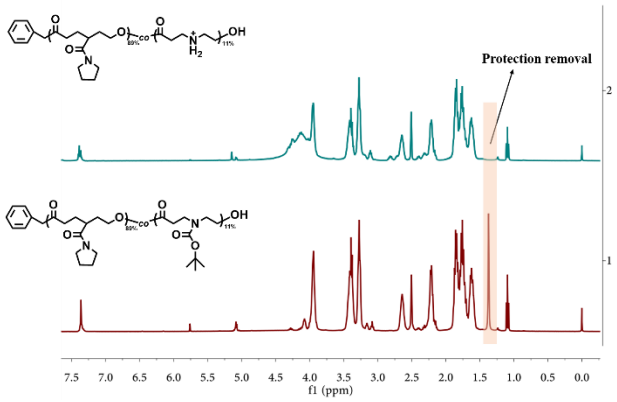


Figure S40. ^{1}H NMR spectrum of P(VPyCL$_{90\%}$-*co*-Boc-NIPIL$_{10\%}$)$_{20}$ and deprotection product

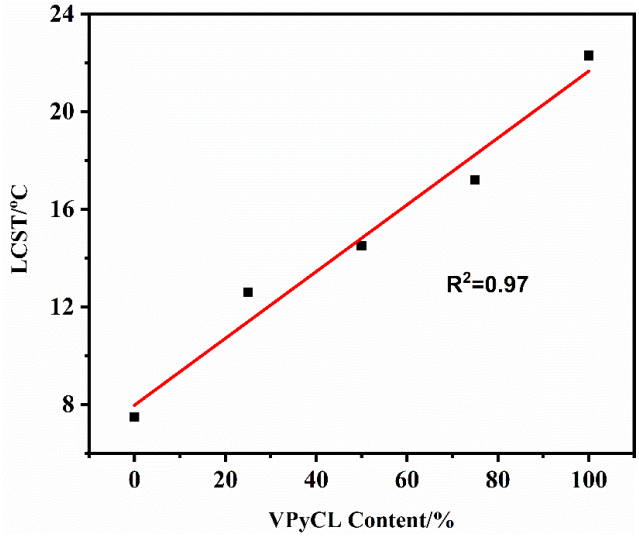


Figure S41. Temperature-dependent transmittance of P(VPyCL$_{x}$-*co*-NICL$_{1-x}$)$_{20}$ Solutions

3 The degradation experiments of poly(*γ*-amide-*ε*-caprolactone)s

The degradation experiment was carried out under Lipase immobilized from *Candida Antarctica* in phosphate buffer solution (PBS, pH = 7.4) according to literature.[7] In brief, 500mg P(VPyCL$_{89\%}$-*co*-PIL$_{11\%}$)$_{20}$ was dispersed in 50ml PBS solution.100mg native enzyme was added into solution and stirred at 37°C. In order to ensure high activities of the enzyme throughout the experiment, native enzyme was replaced in 24h. 5ml solution was taken at pre-determined time to measure LCST of degraded polymer solution. Residual polymer solution was lyophilized to measure GPC curve in DMF.

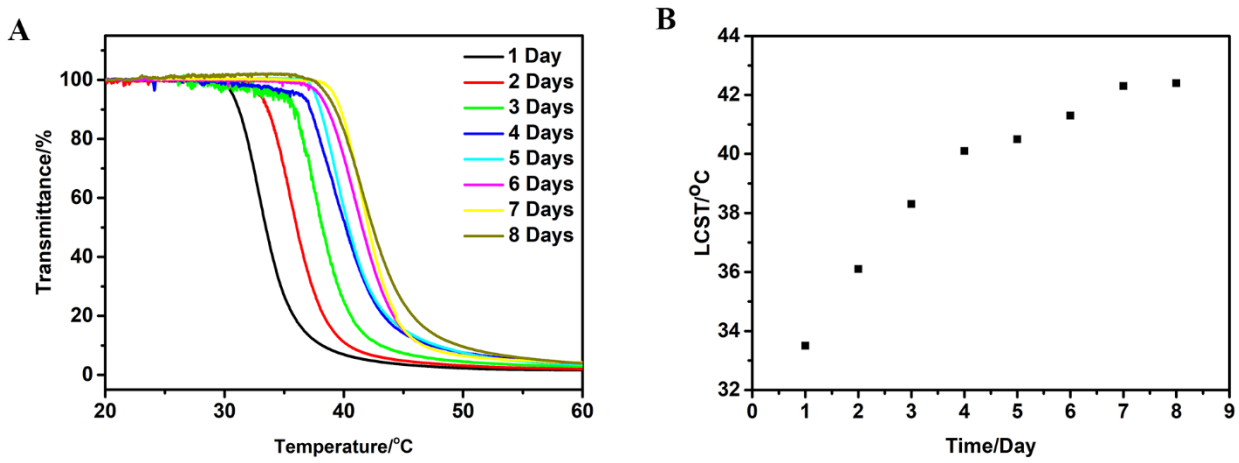


Figure S42. (A) Transmittance versus temperature of P(VPyCL$_{89\%}$-*co*-PIL$_{11\%}$)$_{20}$ under enzymatic conditions in different time. (B) LCST versus time of P(VPyCL$_{89\%}$-*co*-PIL$_{11\%}$)$_{20}$ under enzymatic conditions

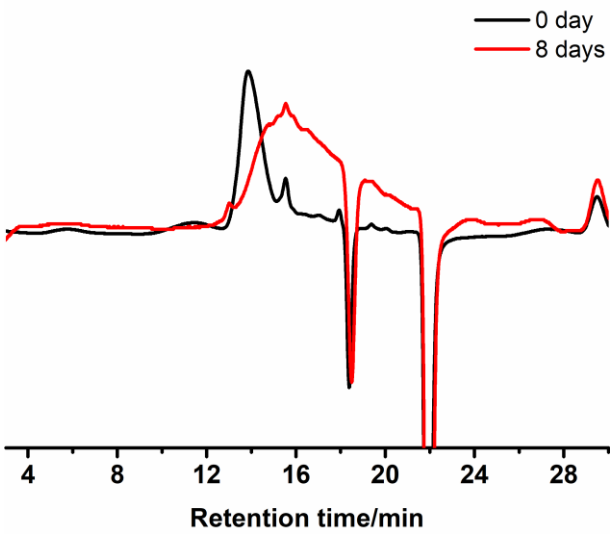


Figure S43. GPC curve of P(VPyCL$_{89\%}$-*co*-PIL$_{11\%}$)$_{20}$ under enzymatic conditions for 0 day and 8 days

4 Cell viability experiments of poly(*γ*-amide-*ε*-caprolactone)s

Cell viability of PVPyCL$_{20}$, P(VPyCL$_{89\%}$-*co*-PIL$_{11\%}$)$_{20}$ as well as its degraded product (degraded product was gained after P(VPyCL$_{89\%}$-*co*-PIL$_{11\%}$)$_{20}$ degraded in enzyme solution for 8 days) was measured through MTT assay toward bone mesenchymal stem cells (MSCs). Before

cell viability experiments, all samples were dissolved in PBS solution with 10mg/ml concentration and sterilized by ultraviolet light for 30 min. Then MSCs were left to adhere and proliferate on the wells for 24 h, then incubated with a concentration range (from 0 to 1000 ug/mL) of $PVPyCL_{20}$, $P(VPyCL_{89\%}\text{-}co\text{-}PIL_{11\%})_{20}$ as well as its degraded product. After incubation for 24h or 96h, MTT solution was added to culture for an additional 4h, and the average optical density (OD) were measured by Universal Microplate Spectrophotometer. Cell viability was calculated according to the following formula: *Cell viability (%) = (ODsample)/(ODcontrol) × 100%*. Experiments were performed in triplicate.

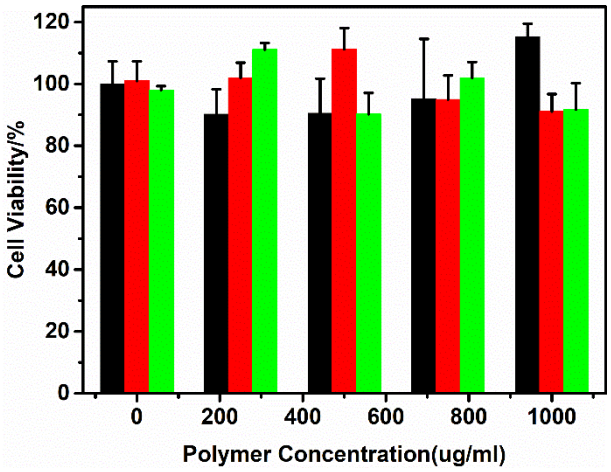


Figure S44. Cell viability versus polymer concentration of $PVPyCL_{20}$ (black line) and $P(VPyCL_{89\%}\text{-}co\text{-}PIL_{11\%})_{20}$ (red line) and degraded product of $P(VPyCL_{89\%}\text{-}co\text{-}PIL_{11\%})_{20}$ (green line) and incubation for 24h, *n=3*

5 Poly(γ-amide-ε-caprolactone)s/enzyme bioconjugation

5.1 Preparation of modified HRP

10mg HRP was mixed with 100mg $P(VPyCL_{89\%}\text{-}co\text{-}PIL_{11\%})_{20}$-NHS and 100mg PNIPAM-NHS ($P(VPyCL_{89\%}\text{-}co\text{-}PIL_{11\%})_{20}$-NHS and PNIPAM-NHS were prepared in section S1.8 and S1.9). 2ml PBS solution (PH=7.4, 10mM) was add into the flash to dissolve solid. After stirring at room temperature for 24h, reaction was terminated through dialysis (*Mco=14000*) in deionized water for 24h. Purified product was collected and stored in 4°C refrigerator (HRP modified with $P(VPyCL_{89\%}\text{-}co\text{-}PIL_{11\%})_{20}$ was denoted as HRP-1, HRP modified with PNIPAM was denoted as HRP-2).

5.2 Measurement of modified degree

Modified degree of HRP was determined through trinitrobenzene sulfonic acid (TNBS) experiment. Before measuring modified degree, an important reminder was that concentration of purified product was prior to be determined through with UV-vis spectroscopy at 405nm by using a standard curve method. Concentration of modified HRP was respectively 570ug/ml and 470ug/ml. native HRP, modified HRP-1 and HRP-2 were sufficiently mixed with 20ul TNBS solution. After reacting at 40^{o}C for 2h, absorbance of solution was measured through with UV-vis spectroscopy at 420nm. Absorbance of native HRP, modified HRP-1 and HRP-2 was denoted as ΔA_{HRP}, ΔA_{HRP-1}, ΔA_{HRP-2}. Modified degree (E%) of HRP was determined according to the formula: $E\%=[(\Delta A_{HRP}/C_{HRP}-\Delta A_{sample}/C_{sample})/(\Delta A_{HRP}/C_{HRP})]*100\%$.

5.3 Measurement of enzyme activity

Enzyme activity was determined through 3,3′,5,5′-tetramethylbenzidine (TMB) liquid substrate system. In detail, native HRP, modified HRP-1 and HRP-2 were placed at 50^{o}C water bath at different time. Then, these HRP samples were taken out to be mixed with TMB solution (TMB solution was prepared through equal mixture of TMB-A solution and TMB-B solution). After reacting at room temperature for 30min, 1M H_2SO_4 solution was added into the system to terminate reaction. Absorbance of solution was measured through with UV-vis spectroscopy at 450nm. Experiments were performed in triplicate.

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