Electronic Supplementary Information for:

Oil Gels with Chemically Cross-linked Copolymer of Trimethylene Carbonate Derivative and L-Lactide: Preparation and Stereocomplex Formation within Gels

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1. Experimental procedure

1-1.) Materials

L-lactide (Musashino Chemical Laboratory, Ltd., Japan) and D-lactide (Musashino Chemical Laboratory, Ltd., Japan) were recrystallized from ethyl acetate. Benzyl alcohol (Wako Pure Chemical Industries, Ltd., Japan) was distilled with molecular sieves 4A. Stannous 2-ethylhexanoate ($Sn(Oct)_2$), toluene, dimethyl sulfoxide (DMSO), Tetrahydrofuran (THF), chloroform, palladium-Activated Carbon (Pd 10%, Pd/C), dichloromethane were obtained from Wako Pure Chemical Industries, Ltd. and used without further purification. Dimethyl carbonate (DMC), dimethyl succinate (DMS), palladium hydroxide 20% on Carbon ($Pd(OH)_2/C$), 1,2-bis(2-aminoethoxy)ethane, ethyl chloroformate, triethylamine were purchased from Tokyo Chemical Industry Co., Ltd. and used as received. Ethanol was obtained from Japan Alcohol Trading Co., Ltd. and used without further purification.

1-2.) Measurements.

The molecular weight of polymer was determined by Gel Permeation Chromatography (GPC). A JASCO Chem NAV system was used with poly(methyl methacrylate) standards at 40 ºC, equipped with PU-2089, AS-2055, CO-2065, and RI-2031. Two commercial columns (TSKgel SuperH3000 and TSKgel SuperH7000 for DMSO, TSKgel Super HM-M and TSKgel GMH_{XL} for $CHCl_3$) were connected in series and DMSO or $CHCl_3$ were used as eluents. ^1H NMR spectra were measured with a NMR spectrometer (JEOL FX400) at 400 MHz. The morphology was observed under a scanning electron microscope (SEM, JEOL JSM-6701) under OsO_4 coating. Analysis of X-ray diffraction (XRD) was carried out in Rigaku RINT InPlane/ultraX 18 SAXS-IP.

1-3.) Synthesis of poly(2-methyl-2- benzyloxycarbonyltrimethylene-*co*- L-lactide)

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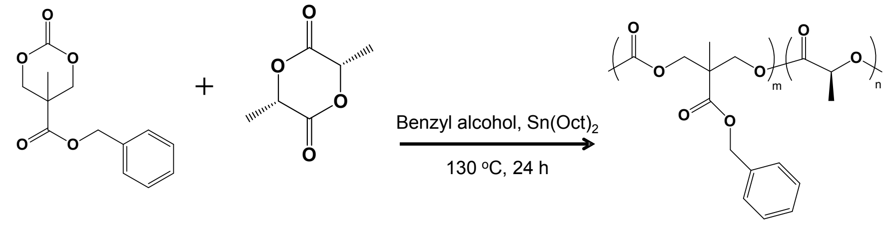


5-Methyl-5-benzyloxycarbonyl-1,3-dioxane-2-one (MBC)

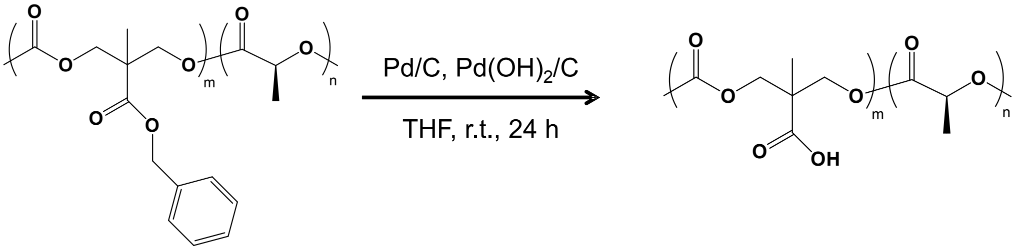
L-Lactide

Poly(2-methyl-2-benzyloxycarbonyltrimethylene-*co*- L-lactide)

5-Methyl-5-benzyloxycarbonyl-1,3-dioxane-2-one (MBC) was synthesized according to the previous literature.[S1] MBC (21.9 g, 87.5 mmol) was copolymerized with L-lactide (25.2 g, 175 mmol) in a bulk melt in the presence of stannous 2-ethylhexanoate ($Sn(Oct)_2$)/toluene (0.1 g mL^{-1}, 0.65 mL, 0.160 mmol of $Sn(Oct)_2$) at 120 °C for 24 hours. The resulting product was dissolved in chloroform and precipitated with ether/hexane = 1/1 and methanol. After drying the product in a vacuum oven (4 hours at room temperature and overnight at 40 °C), poly(2-methyl-2-benzyloxycarbonyltrimethylene-*co*-L-lactide) was collected (40.2 g, 85%).

The number average molecular weight, M_n = 40000, the weight average molecular weight, M_w = 73000 (eluent : DMSO). From the result of molecular weight, it is calculated that one polymer chain have 86 units of MBC and 258 units of lactic acid (75 mol% of lactic acid were contained in copolymer). If reactivity of MBC and L-lactide were equal, 80 mol% of lactic acid were contained in theory. Therefore, the content of lactic acid in copolymer was low than theoretical value. It is suggested that block sequence of lactic acid were formed in the latter half of this reaction.

1-4.) Synthesis of poly(2-methyl-2-carboxy trimethylene carbonate-*co*-L-lactide)



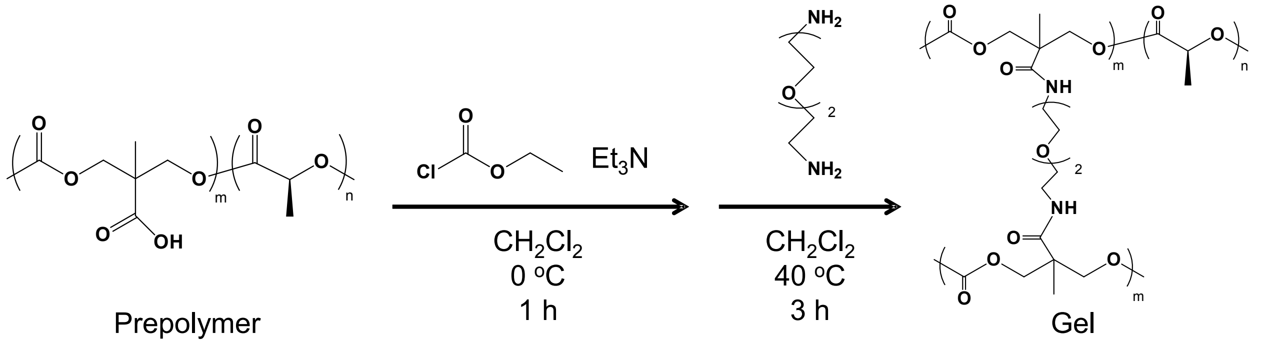
Poly(2-methyl-2-benzyloxycarbonyltri-methylene-*co*- L-lactide)

Poly(2-methyl-2- carboxy-trimethylene carbonate-*co*-L-lactide)

Poly(2-methyl-2-benzyloxycarbonyltrimethylene-*co*-L-lactide) (28.8 g) was dissolved in THF and the benzyl protecting groups removed under hydrogen (H_2) in the presence of Pd/C (10 wt%, 4.8 g) and $Pd(OH)_2/C$ (20 wt%, 4.8 g) for 24 hours at room temperature. The resulting polymer was then filtered and evaporated. and dried *in vacuo* at 30 °C . After drying the product *in vacuo* overnight at 30 °C, poly(2-methyl-2-carboxy trimethylene carbonate-*co*-L-lactide) was collected (23.5 g, 98%).

M_n = 26000, M_w = 37000 (eluent : DMSO).

1-5.) Cross-linking reaction of copolymers by using 1,2-bis(2-aminoethoxy)ethane.



Poly(2-methyl-2-carboxy trimethylene carbonate-*co*-L-lactide) was used as prepolymer of preparing oil gel. Prepolymer (m : n = 25 : 75, the number average molecular weight, M_n = 26000, 0.803 mmol of carboxy group are contained, the weight average molecular weight, M_w = 37000, 300 mg) was dissolved in dichloromethane (0.68 mL). Then, ethyl chloroformate (0.11 mL, 1.16 mmol) and triethylamine (0.12 mL, 0.883 mmol) were added with ice bath. After 1 hour, a given amount of 1,2-bis(2-aminoethoxy)ethane was added and the reaction mixture was warmed at 40 °C for 3 hours. After the reaction, an excess of chloroform ($CHCl_3$) was added to remove unreacted compounds, and oil gel in $CHCl_3$ was obtained.

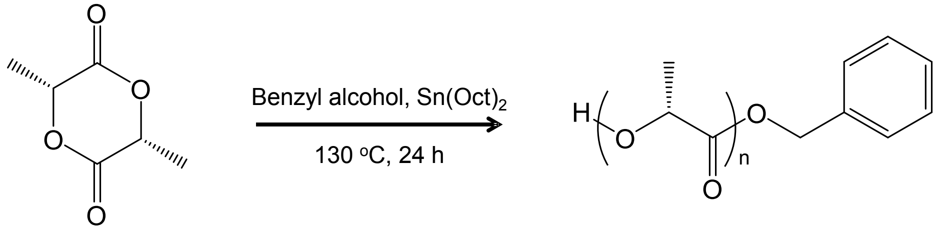
In order to identify the presence of graft copolymer as by-product, $CHCl_3$ was evaporated to get viscous fluid. $CHCl_3$ (100 mL) was added and washed with ultra pure water (100 mL) 5 times. The organic layer was collected and evaporated. We confirmed the presence of graft copolymer by ^{1}H NMR measurement (Figure S4b and Figure S5).

The oil gels used to investigate the morphology under a Scanning Electron Microscope (SEM) and make stereocomplexes inside the gels are prepared as below; poly(2-methyl-2-carboxy trimethylene carbonate-*co*-L-lactide) was used as prepolymer of preparing oil gel. Prepolymer (m : n = 24 : 76, the number average molecular weight, M_n = 13000, 1.55 mmol of carboxy group are contained, the weight average molecular weight, M_w = 19000, 600 mg) was dissolved in dichloromethane (1.37 mL). Then, ethyl chloroformate (0.22 mL, 2.3 mmol) and triethylamine (0.24 mL, 1.7 mmol) were added with ice bath. After 1 hour, 1,2-bis(2-aminoethoxy)ethane (0.77 mmol) was added and the reaction mixture was warmed at room temperature for 3 hours. After the reaction, an excess of chloroform (CHCl3) was added to remove unreacted compounds, and oil gel in $CHCl_3$ was obtained. Oil gels in $CHCl_3$ was dried and immersed into DMC over 2 days to get oil gels used in this experience.

1-6.) Measurement of swelling ratios of oil gels in various solvents.

At first, the weight of dry gel was measured. After that, the dry gel was immersed into various organic solvents until the constant weight. Then, the weight of oil gel was measured. Swelling ratios of oil gels were calculated by the use of the following equation : $(W_s - W_d)/W_d$, where W_s is the weight of the swollen oil gel at room temperature and W_d is the weight of the dry gel.

1-8.) Synthesis of poly(D-lactide) (PDLA)



D-Lactide (4.99 g, 34.7 mmol) and benzyl alcohol (0.13 mL, 1.25 mmol) was heated under N_2 atmosphere around 90 °C to melt. Next, $Sn(Oct)_2$/toluene (0.1 g mL^{-1}, 0.5 mL, 0.1 mmol of $Sn(Oct)_2$) was added to the reaction mixture and heated to 130 °C. After 24 hours, the reaction mixture was dissolved in chloroform and precipitated with methanol. After drying the product in a vacuum oven at 50 °C for 3 hours, PDLA was collected (4.17 g, 81%).

$M_n = 4300$, $M_w = 9700$ (eluent : $CHCl_3$).

1-9.) PLA Stereocomplexation inside oil gels

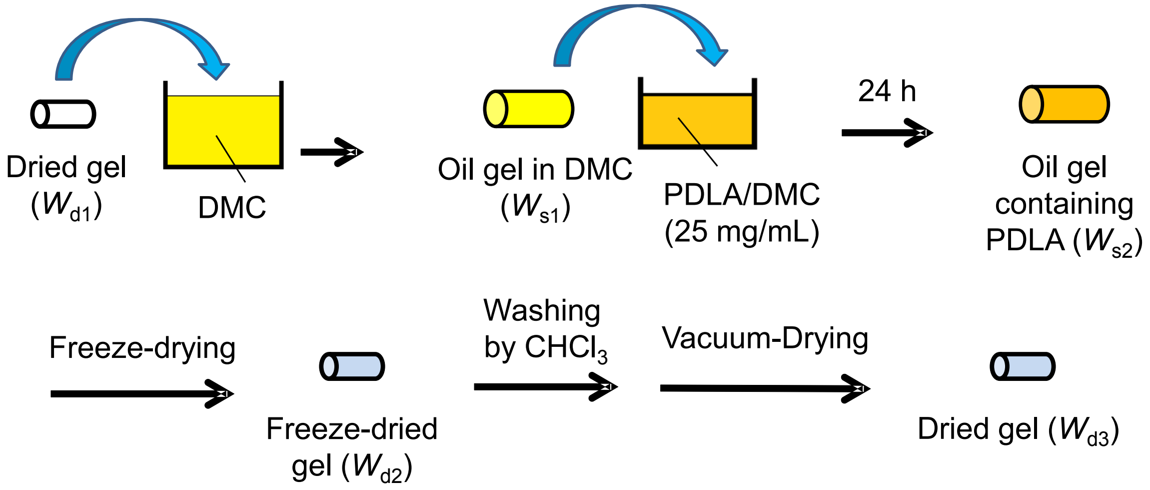


Figure S1. Schematic illustration of the experimental procedure.

Dried-gels (W_{d1}) were immersed into DMC to prepare oil gels in DMC (W_{s1}) The oil gel in DMC was immersed into the DMC dissolving PDLA (PDLA1 or PDLA2[S2], M_{n} of PDLA2 = 8300, M_{w} of PDLA2 = 9900). The concentration of PDLA were 5 mg mL^{-1}, 25 mg mL^{-1} and 50 mg mL^{-1}. After 24 hours, the oil gels (W_{s2}) were freeze-dried and XRD measurements were conducted.

As for the gels inside of which stereocomplexation was vertified, the amount of introduced PDLA was calculated as below; first, freeze-dried gels (weight : W_{d2}) were immersed into $CHCl_3$ over 24 hours to remove PDLA inside gels. Then the oil gels were vacuum-dried at 40 °C for 9 hours to get vacuum-dried gels (weight : W_{d3}). The amount of PDLA was calculated as follows: $W_{\mathrm{d2}} - W_{\mathrm{d3}}$. And we tried to check the decrease of swelling ratio by calculating the swelling ratio as bellows;

$$\text{Swelling ratio 1 (SR1)} = (W_{s1} - W_{d3})/\,W_{d3}$$

$$\text{Swelling ratio 2 (SR2)} = (W_{s2} - W_{d2})/\,W_{d2}$$

Table S1. The amount of gels.

	Weight (mg)
W_{s1}	10.3±3.8
W_{s2}	12.5±2.5
W_{d2}	1.8±0.4
W_{d3}	0.9±0.3

2. ^{1}H NMR spectra

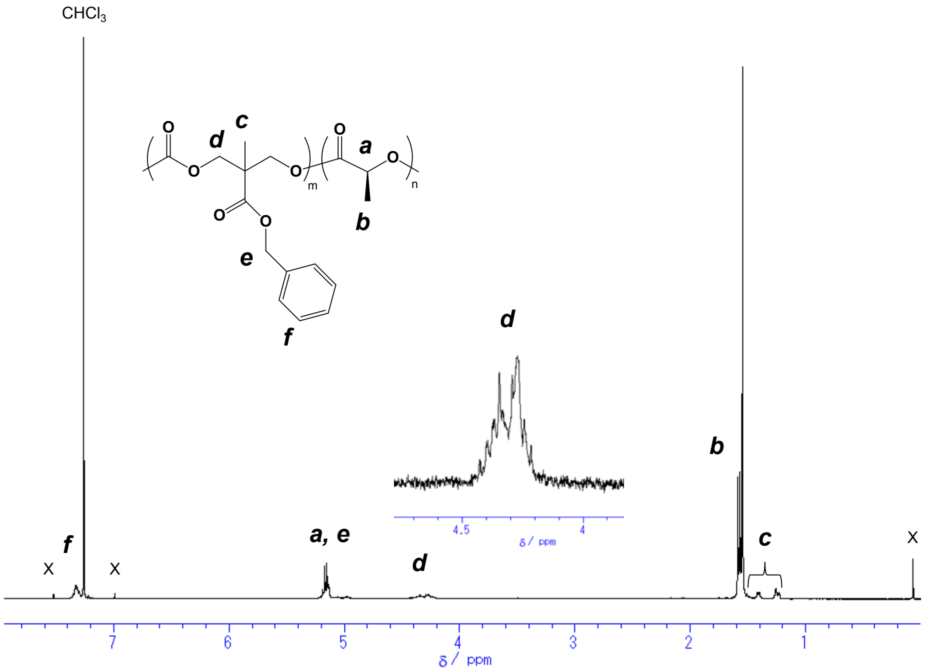


Figure S2. ^{1}H NMR spectrum of poly(2-methyl-2- benzyloxycarbonyltrimethylene-*co*-L-lactide) in DMSO-d_6 at r.t. (400 MHz).

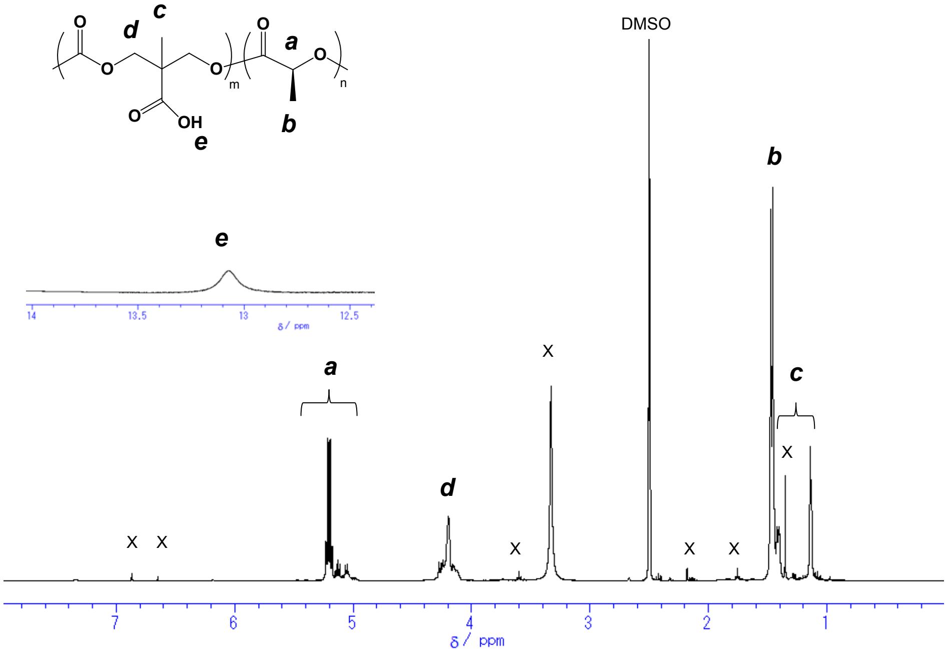


Figure S3. ^{1}H NMR spectrum of poly(2-methyl-2- carboxy trimethylene carbonate - *co*- L-lactide) in DMSO-d_6 at r.t. (400 MHz).

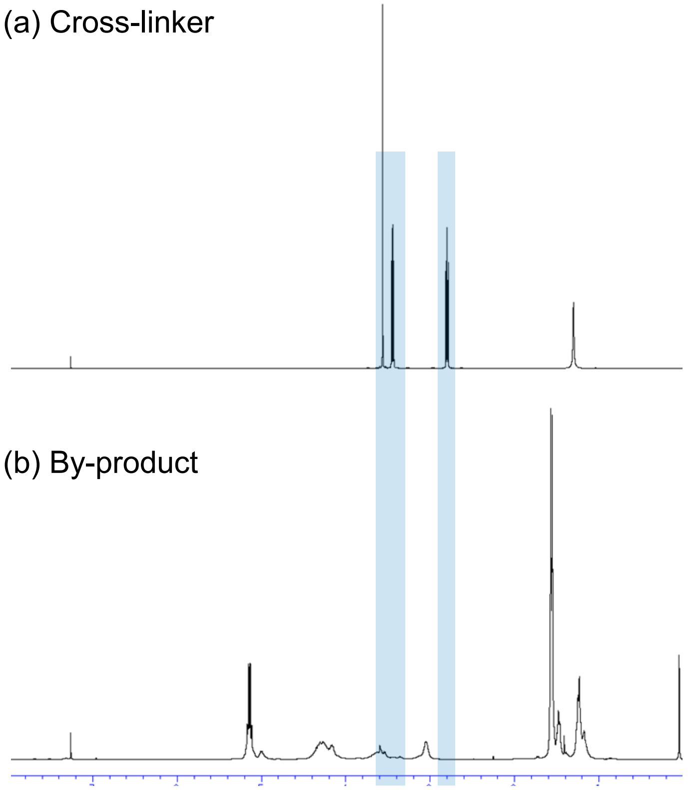


Figure S4. ^{1}H NMR spectra of (a) 1,2-bis(2-aminoethoxy)ethane as a cross-linker and (b) by-product in $CDCl_3$ at r.t. (400 MHz).

In the spectrum of Figure S4b, no peaks are shown derived from 1,2-bis(2-aminoethoxy)ethane. Therefore, 1,2-bis(2-aminoethoxy)ethane are not contained the by-product after washing. And peaks around 3.0 ppm and 3.6 ppm are appeared, those are not shown in the spectrum of prepolymer (Figure S3) and 1,2-bis(2-aminoethoxy)ethane (Figure S4a). Other compounds used for the preparation of oil gels, such as triethylamine, ethyl chloroformate and dichloromethane, don't show peaks around 3.0 ppm and 3.6 ppm. It is suggested that these two peaks in Figure S5 are from the presence of graft polymer.

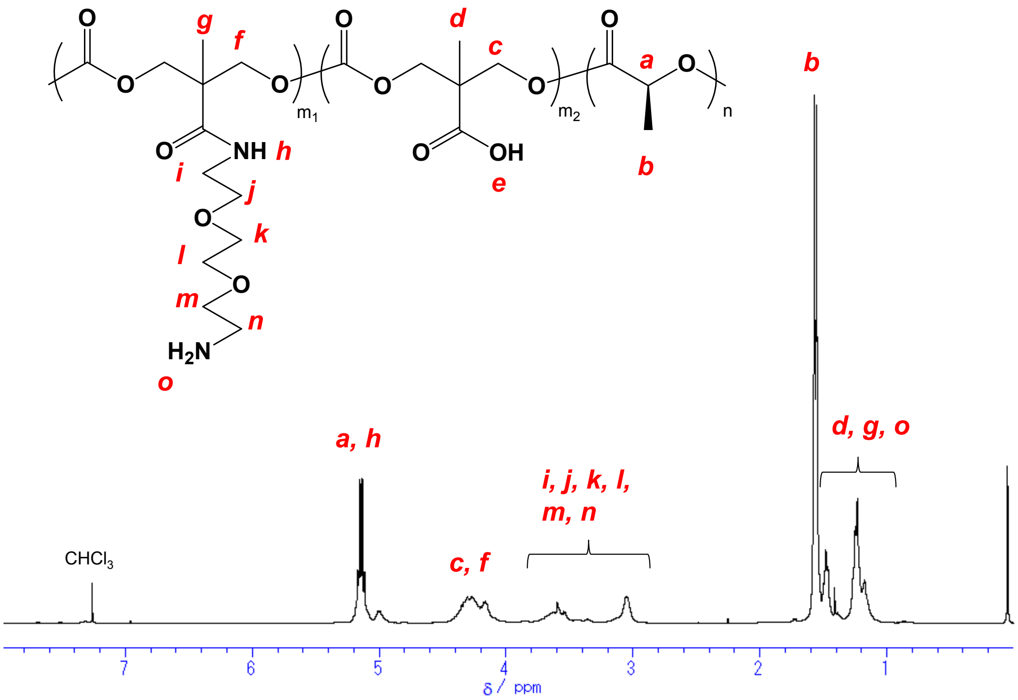


Figure S5. ^{1}H NMR spectrum of by-product in $CDCl_3$ at r.t. (400 MHz).

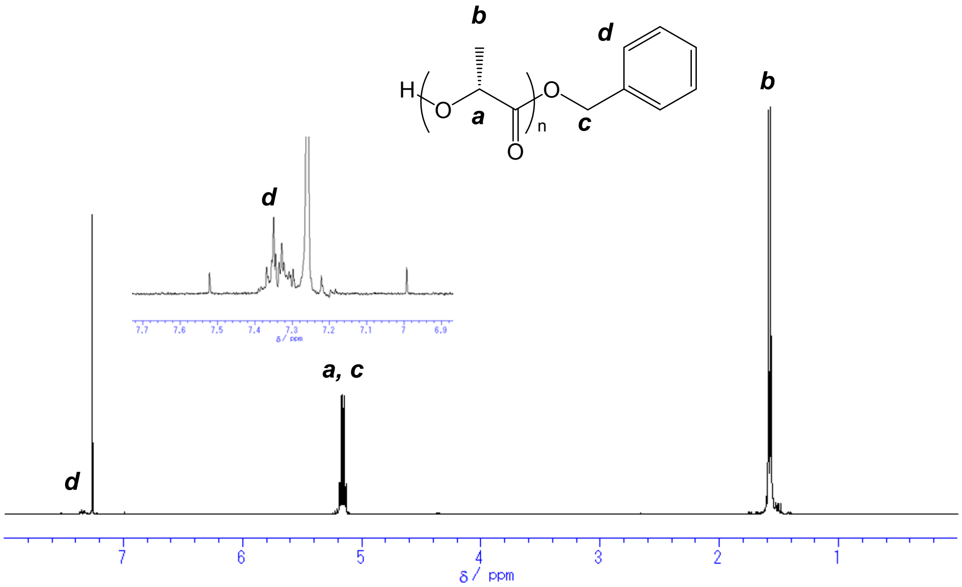


Figure S6. ^{1}H NMR spectrum of PDLA1 in $CDCl_3$ at r.t. (400 MHz).

3. FT-IR/ATR spectra

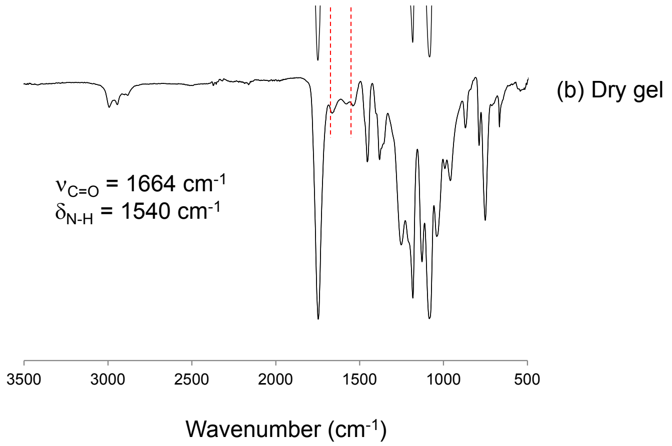
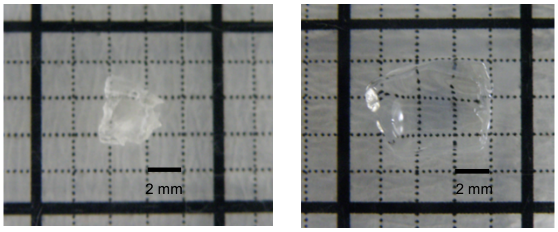


Figure S7. FT-IR/ATR spectra of (a) prepolymer and (b) dry gel.

4. Photographs of oil gels

(a) In Ethanol (b) In DMSO



(c) In DMS (d) In $CHCl_3$ (e) In DMC

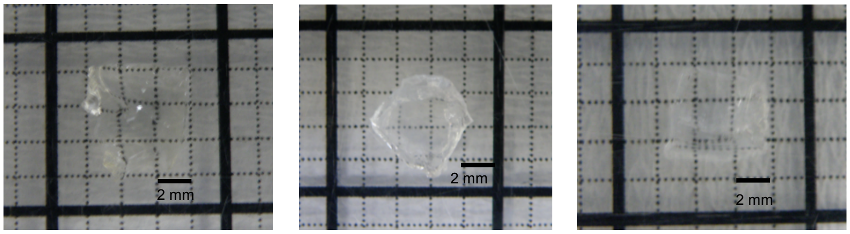


Figure S8. Photographs of oil gels in (a) ethanol, (b) DMSO, (c) DMS, (d) $CHCl_3$ and (e) DMC.

5. XRD patterns

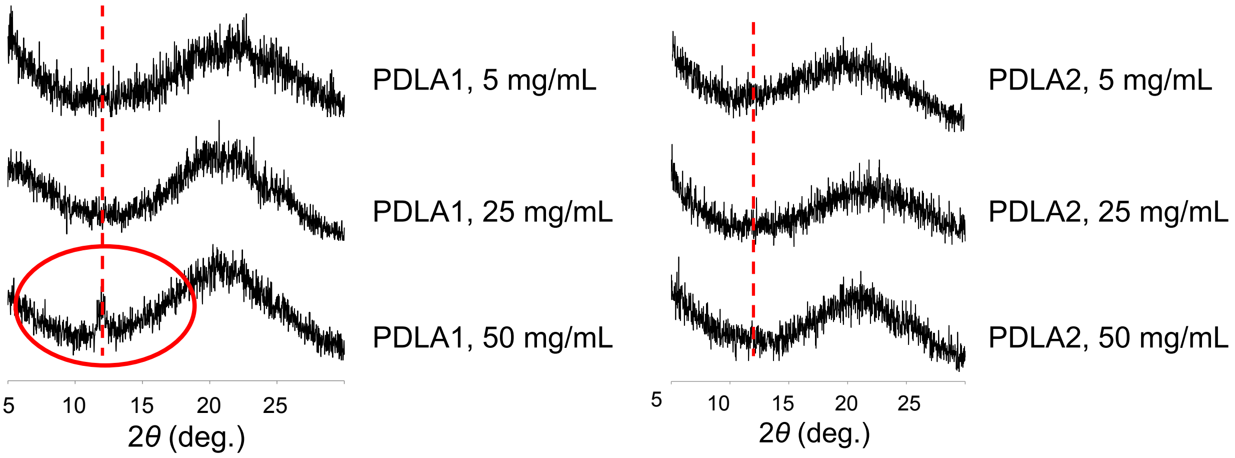


Figure S9. XRD patterns of oil gels after freeze-drying.

The strong peak at $2\theta = 12$ °, which indicates the formation of PLA stereocomplex, was identified only when the oil gel was immersed into the DMC containing PDLA1 (50 mg mL^{-1}). Although oil gels were immersed into the DMC dissolving PDLA2, strong peaks are not shown. And even if PDLA1 were used, it was not sufficient that the concentration was 25 mg mL^{-1}. From these results, molecular weight and the concentration of PDLA is important for the stereocomplexation.

6. The change of swelling ratio by stereocomplexation

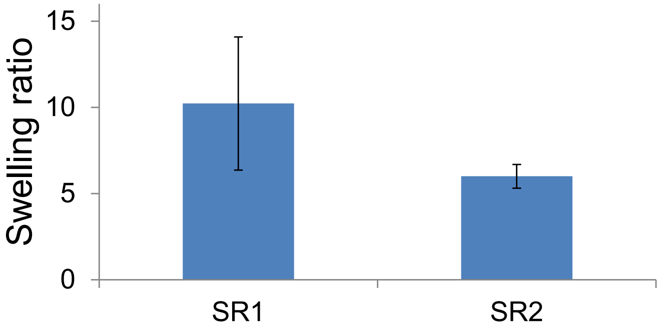


Figure S10. The change of swelling ratio by stereocomplexation.

As for the gels inside of which stereocomplexation was vertified, we calculated the swelling ratio to check the shrinking of oil gels (Figure S10). As a result of significance test ($p<0.05$), there were no significant differences between SR1 and SR2.

7. The effect of reaction time on the yields of oil gels

Prepolymer (m : n = 24 : 76, M_n = 16000, 0.26 mmol of carboxy group are contained, M_w = 26000, 100 mg) was dissolved in dichloromethane (0.23 mL). Then, ethyl chloroformate (36 µL, 0.38 mmol) and triethylamine (40 µL, 0.29 mmol) were added with ice bath. After 1 hour, 1,2-bis(2-aminoethoxy)ethane (0.13 mmol) was added and the reaction mixture was warmed at room temperature for 3 or 24 hours. After the reaction, an excess of $CHCl_3$ was added to remove unreacted compounds, and oil gel in $CHCl_3$ was obtained. Oil gels in $CHCl_3$ was dried and the weight of dried gels was measured.

Table S2. The yields of reactions.

Run	$[NH_2]/[COOH]^a$	Temperature (°C)	Time (h)	Yield (%)
1	1	r.t.	3	22.1
2		r.t.	24	16.7
3		40	3	19.0
4		40	24	12.2

[a] Molar ratio of amino groups of cross-linkers to TMC derivatives

From the results, the longer reaction time resulted in the lower yields, which implied the hydrolysis of ester groups in PLA under alkaline condition.

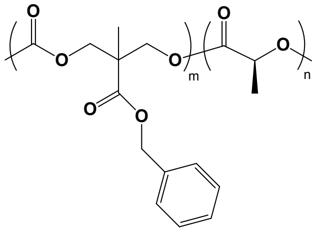
8. Solubility parameters

Table S3. Solubility parameters of various compounds.

Compound	Solubility parameter
Prepolymer	12.5
Ethanol	12.6
Chloroform	11.3
DMSO	8.8
DMS	9.6
DMC	8.5

9. XRD pattern of stereocomplexation with prepolymers

We investigated the stereocomplexation of random copolymer (Figure S11, 12 and Table S4). Here, stereocomplexation of poly(5-methyl-5-benzyloxycarbonyl-1,3-dioxane-2-one-co-L-lactide) (poly(MBC-co-L-lactide), called as copolymer here) and PDLA were studied. We dissolved copolymer and PDLA in chloroform (5 mg/mL) and these solutions (1 mL) are mixed. The mixed solutions was vacuum dried for 3 hours at room temperature and stereocomplexation was confirmed by X-ray diffraction (XRD) measurements. From this results, copolymers with >15% PTMC derivatives incorporated would be able to undergo stereocomplexation



Scheme S1. Chemical structure of poly(MBC-*co*-L-lactide).

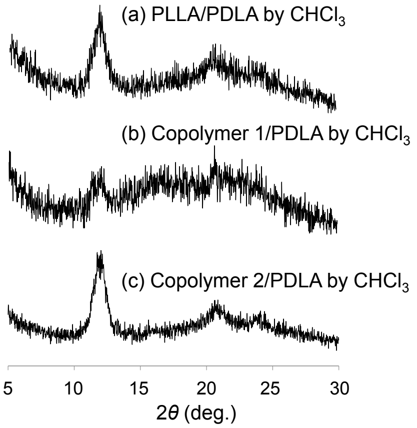


Figure S11. XRD patterns of PLLA/PDLA (a), copolymer 1/PDLA (b) and copolymer 2/PDLA (c) by $CHCl_3$.

Table S4. Data of copolymer.

	MBC content ^{a} (%)	M_n ^{b}	M_w ^{b}	PDI ^{c}
PLLA		9,000	15,000	1.69
Copolymer 1	5.9	6,000	16,000	2.64
Copolymer 2	24	13,000	18,000	1.42
PDLA		7,000	11,000	1.59

[a] Determined by ^1H NMR in dimethyl sulfoxide at r.t. (400 MHz).

[b] Determined by GPC by poly(methyl methacrylate) standards.

[c] Polydispersity (PDI) = M_w/M_n.

Reference

[S1] M. Danquah, T. Fujiwara and R. I. Mahato *Biomaterials* 2010, **31,** 2358-2370.

[S2] H. Ajiro, Y. J. Hisao, H. T. Tran §, T Fujiwara and M. Akashi *Macromolecules* 2013, **46**, 5150-5156.