Supporting Information for

Photo-Crosslinked Polymer Cubosomes as Recyclable Nanoreactor in Organic Solvents

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CONTENTS

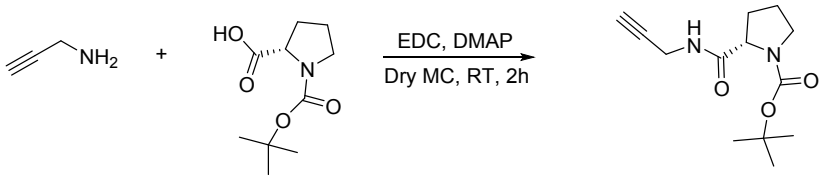
1. Materials and Methods

Materials. Unless otherwise noted, all reagents and chemicals were purchased from Sigma Aldrich, Alfa Aesar, and TCI and used as received. Styrene and 2,3,4,5,6-Pentafluorostyrene were purified by passing through a basic alumina column before polymerization. Dimethylformamide (DMF) and dichloromethane (CH_2Cl_2) were distilled over CaH_2 under N_2. Tetrahydrofuran (THF) was refluxed over a mixture of Na and benzophenone under N_2 atmosphere and distilled before use. All reactions were performed in an inert atmosphere unless otherwise noted.

Methods. 1H NMR, 13C NMR, 19F NMR and 1H- 13C HMBC NMR spectra were recorded by Agilent 400-MR DD2 Magnetic Resonance System and Varian/Oxford As-500 using CD2Cl2 and CDCl3 as solvents and internal standards. Molecular weights and polydispersity indices of polymers and block copolymers were measured by Agilent 1260 Infinity gel permeation chromatography (GPC) system equipped with a PL gel 5μm MiniMIX-D column (Agilent Technologies) and differential refractive index detectors. THF was used as an eluent with a flow rate of 0.3 mL min-1 at 35 °C. A PS standard kit (Agilent Technologies) was used for calibration. Differential scanning calorimetry (DSC) was carried out under N2 gas at a scan rate of 15 °C min-1 with TA Instruments Q10. Transmission electron microscopy (TEM) was performed on a Hitachi 7600 operating at 100 kV and JEOL JEM-2100 operating at 200 kV. Specimens were prepared by placing a drop of the solution on a carbon-coated Cu grid (200 mesh, EM science). After 30 min, remaining solution on a grid was removed with a filter paper, and the grid was dried overnight. Scanning electron microscopy (SEM) was performed on a Hitachi S-4300 operating at 15 kV. Suspension was cast and dried on a slide glass, and coated with Pt by using a Hitachi E-1030 ion sputter. UV-Vis spectrometry (UV-Vis) was measured on a Jasco V-630 spectrophotometer. Synchrotron small-angle X-ray scattering (SAXS) data were obtained on the SAXS beamline

(PLS-II 6D, 11.18 keV, 6.5 m) at Pohang Accelerator Laboratory. The concentrated suspension of the polymer cubosome was dried for a day in a freeze-dryer. Ti-SBA standard was used. UV light sources were Vilber VL-6.LC (254 nm/365 nm, 6 W), and Sankyo G40T10E compact UV-B lamp (output 20 W).

2. Synthesis of basic material



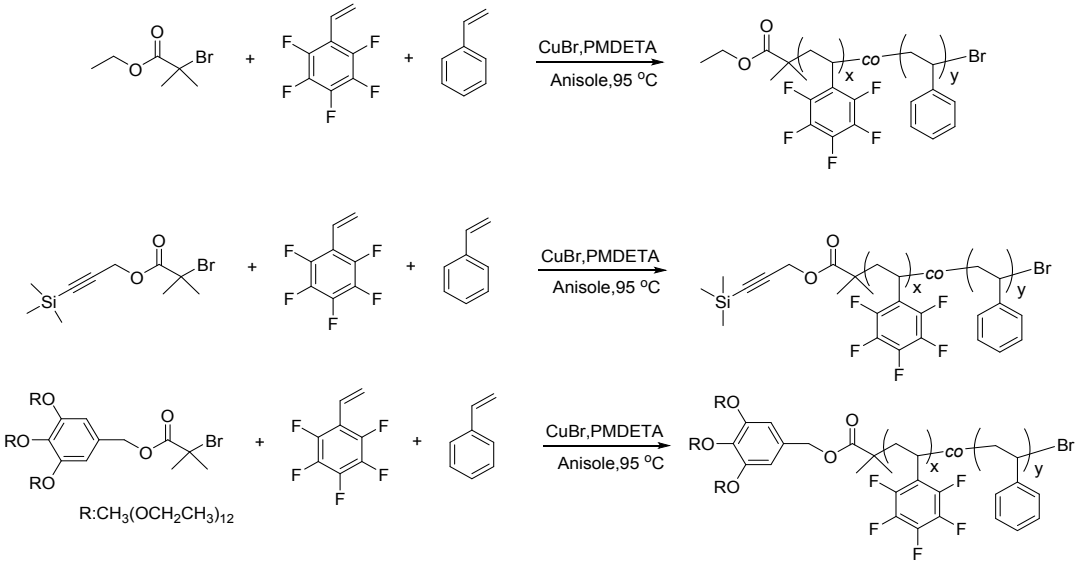
Scheme S1. Synthetic scheme of tert-butyl (S)-2-(prop-2-yn-1-ylcarbamoyl)pyrrolidine-1-carboxylate.

Synthesis of proline with alkyne linker (p-alkyne).

N-(tert-Butoxycarbonyl)-L-proline (4.3 g, 20 mmol), propargylamine (1.32 g, 1.54 ml, 24 mmol) 4-Dimethylaminopyridine (367 mg, 3 mmol) were dissolved in dry CH_2Cl_2 (100 mL) in a Schlenk flask (250 mL) and stirred under 0°C condition. 1-Ethyl-3-(3-dimethylaminopropyl) carbodiimide (4.98 g, 26 mmol) dissolved in dry CH_2Cl_2 (25 mL) was transferred to first solution mixture with cannula. After 15 h, reaction was quenched by adding water (50 mL) and product extracted with CH_2Cl_2 (50 mL × 3 times). The collected organic phases were dried over $MgSO_4$, and evaporated under reduced pressure. The mixture was purified by column chromatography with mixture of hexane and EA (1:1). The first fraction was collected and dried at a reduced pressure. Recrystallization in hexane at 20 ˚C to afford the white solid.[1] The molecule is characterized with ^{1}H NMR and ^{13}C NMR. δH ($CDCl_3$) 7.26 and 6.27 (s, 0.5H and s, 0.5H, NH), 4.24 (m, 1H, CH), 3.98 (m, 2H, $CH_2C\equiv$), 3.43 (m, 2H, CH_2N), 2.21 (m, 1H, C*H*HCHN), 2.19 (s, 1H, HC≡), 1.85

(br s, 3H, CH*H*CHN, C*H*$_2$CH$_2$CHN), 1.44 (m, 9H, (CH$_3$)$_3$); δC (CDCl$_3$) 172.42 and 171.85 (*C*ONHCH$_2$), 156.12 and 154.73 (CO Boc), 80.84 (*C*(CH$_3$)$_3$), 79.59 (HC≡), 71.85 and 71.42 (*C*≡CH), 61.25 and 59.89 (CHN), 47.22 (CH$_2$N), 31.05 and 27.94 (*C*H$_2$CHN), 29.14 (*C*H2C≡), 28.46 (C(*C*H$_3$)$_3$), 23.93 and 24.68 (*C*H$_2$CH$_2$N).

3. Synthesis of polymer materials



Scheme S2. Synthetic scheme of P(pFS-*co*-Sty) with different initiators.

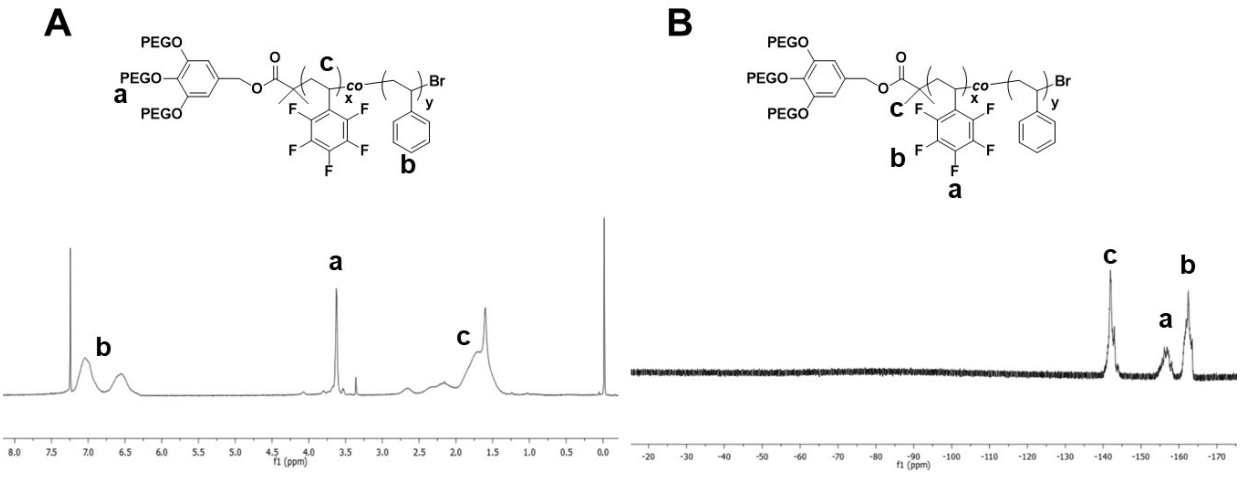


Fig. S1 ^{1}H NMR and ^{19}F NMR of (PEG550)$_3$-P(pFS-*co*-Sty) (5:5 mol/mol).

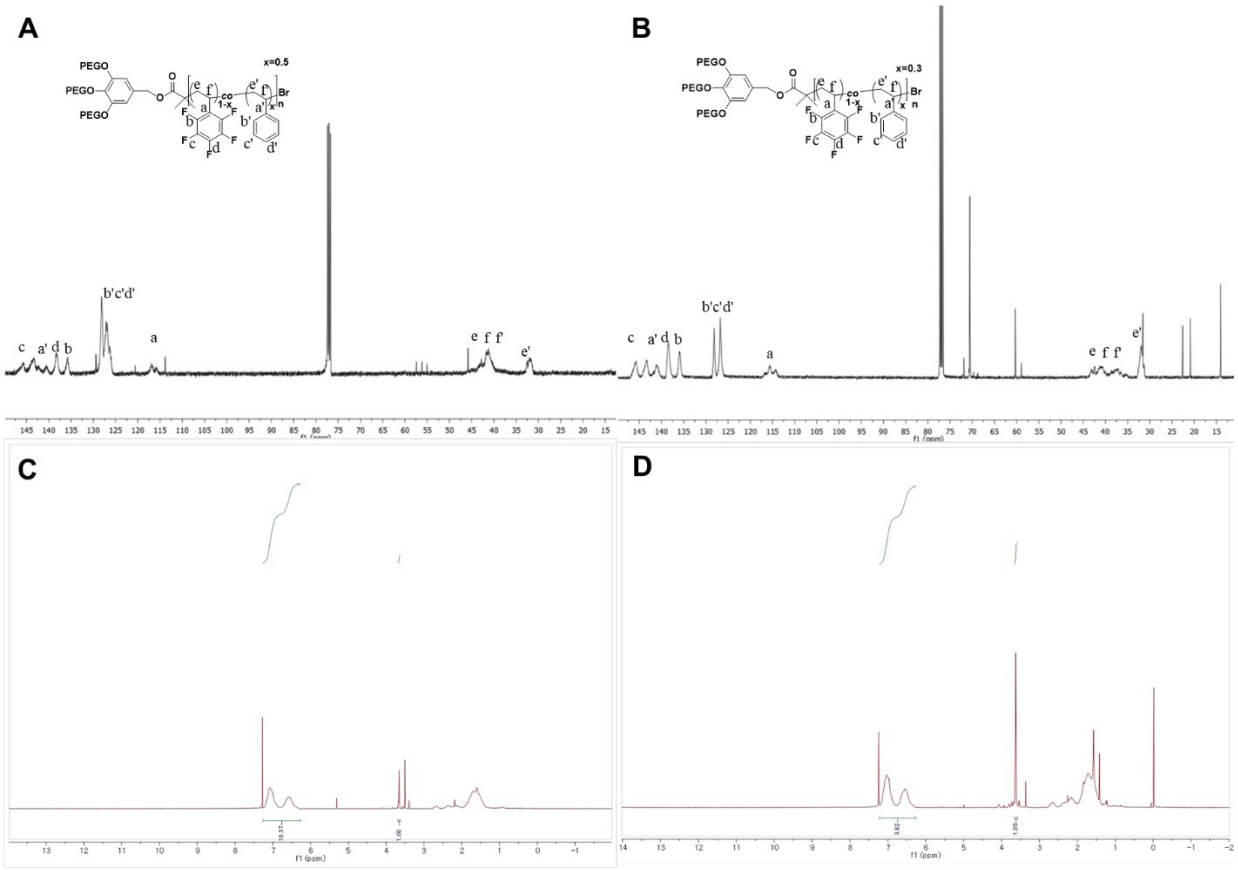


Fig. S2 ^{13}C NMR (A and B) and ^{1}H NMR (C and D) of $(PEG550)_3$-P(pFS-*co*-Sty) (5:5 mol/mol) (A and C) and $(PEG550)_3$-P(pFS-*co*-Sty) (7:3 mol/mol) (B and D).

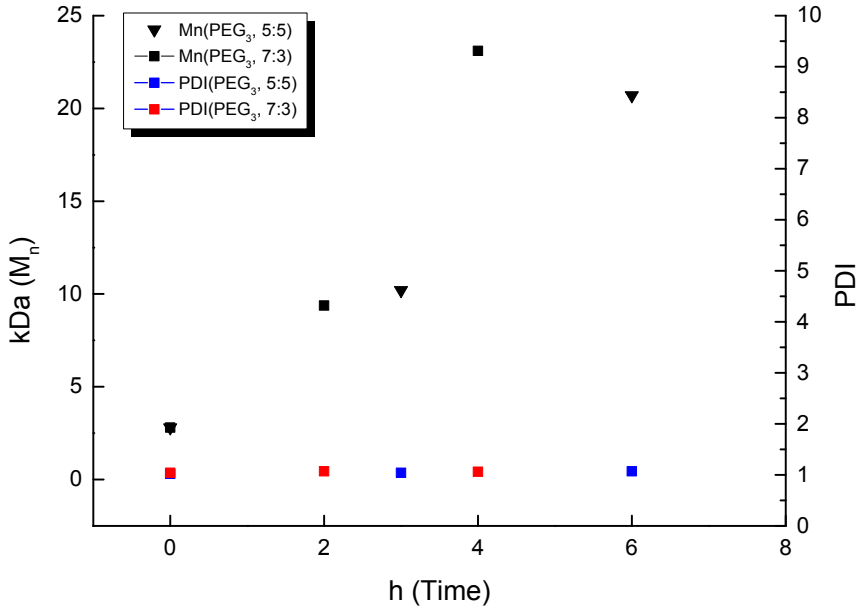


Fig. S3 Molecular weight (M_n) and molecular weight distribution (PDI) of the BCPs determined by GPC during the course of polymerization.

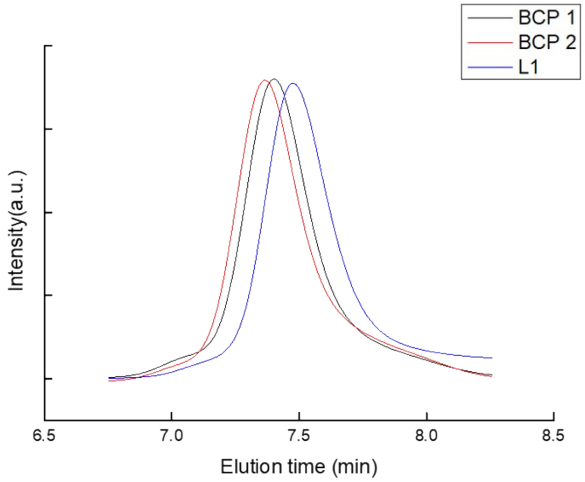


Fig. S4 GPC traces of the polymers **BCP 1** (black), **BCP 2** (red), **L1** (blue).

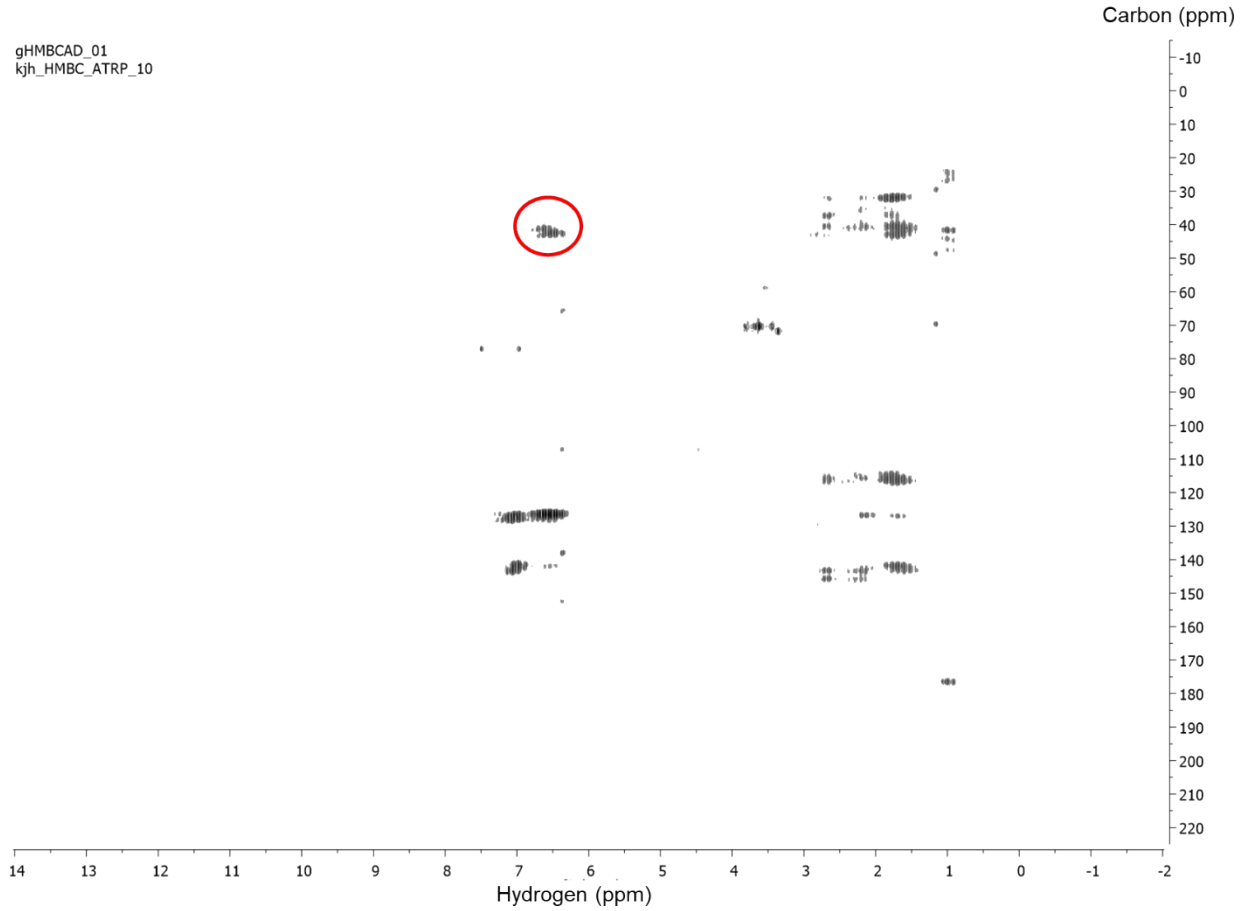
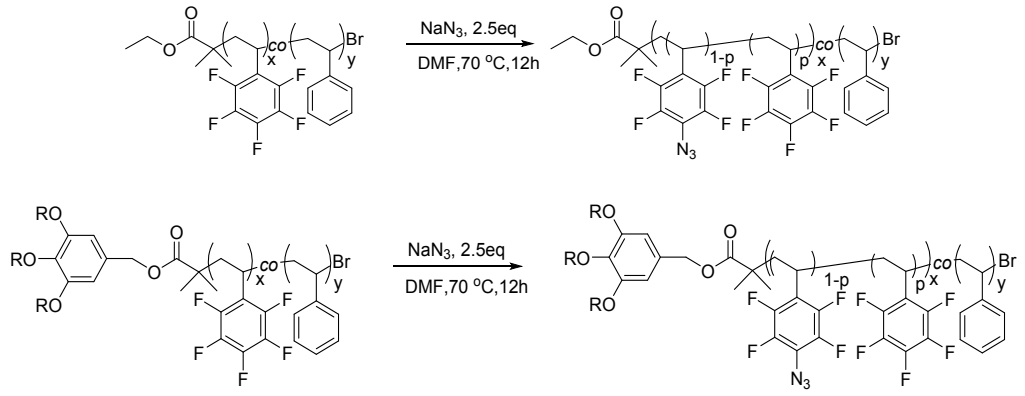


Fig. S5 Entire image of ^{1}H-^{13}C heteronuclear multiple bond correlation (HMBC) data and red circle is enlarged image represented in Fig. 2B



Scheme S3. Preparation of azide-substituted P(pFS-*co*-Sty) and $(PEG550)_3$-P(pFS-*co*-Sty)

Table S1. Characterization of prepared polymers

Sample	Initiator	DP_n (Sty)[b]	DP_n (pFS)[b]	f_{PEG} (%)	M_n (kg mol^{-1}) GPC	M_w (kg mol^{-1}) GPC	$Đ$ GPC
H1	EBIB[a]	71	71	-	14.2	17.4[b]	1.22

[a]EBIB = ethyl α-bromoisobutyrate. [b]Degree of polymerization (DP_n).

4. Basic analysis of polymer material's physical property

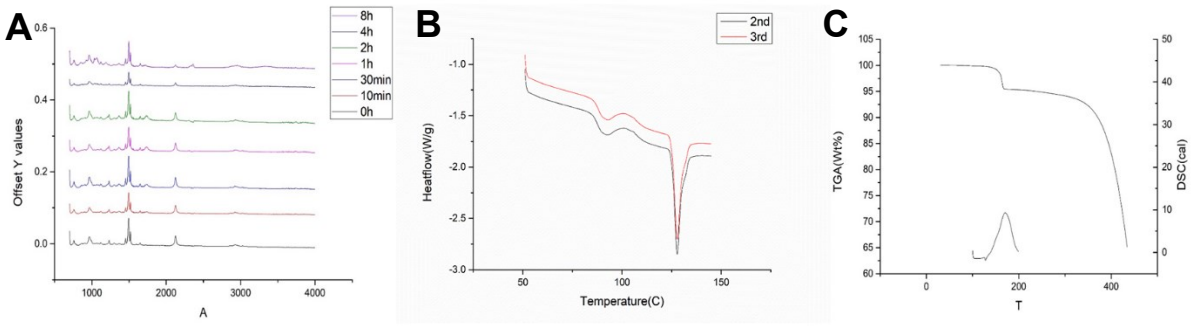
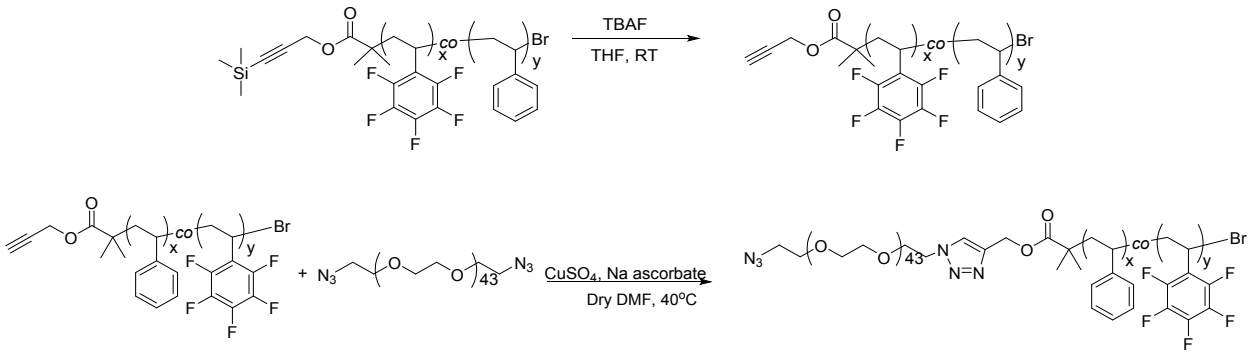


Fig. S6 (A) FT-IR spectra of **H1** in THF (0.01 mg mL^{-1}) with irradiation of short-wavelength UV light (λ = 280 nm) for increasing exposure times. (B) Differential scanning calorimetry (DSC) and (C) Thermo Gravimetric Analysis (TGA) spectra of **H1** and **H1-**N_3.

After azide modification of **H1**, DSC and TGA both showed thermal degradation of pendant azide group in pentafluorostyrene moiety. The photo-degradation of the azide pendant groups of the polymer chains under UV irradiation (= ~280nm) was studied in solution. The photo-degradation of the pendant azide groups of P(pFS-*co*-Sty) (**H1-** N_3) in THF (0.01 mg mL^{-1}) was observed by IR spectroscopy after UV light irradiation (λ = ~280 nm, 20 W). There was a sequential decrease of the azide peaks in IR spectrum that degradation of N≡N bond expose under the UV light (λ = ~280 nm, 20 W) (Fig. S5A). We also investigated the thermal property of **H1** before and after azide substitution. Differential

scanning calorimetry (DSC) of **H1** before azidification showed the glass transition temperature (T_g) at 89 °C with the sharp endothermic peak at 125 °C. The result was explained with π-π stacking between styrene group and 2,3,4,5,6-pentaflurorostyrene group (Fig. S5B).[2] After azide modification, DSC and Thermo Gravimetric Analysis (TGA) both showed thermal degradation of pendant azide group in pentafluorostyrene moiety (Fig. S5C).[3]

5. Synthesis of telechelic functionalized linear block copolymer with click reaction

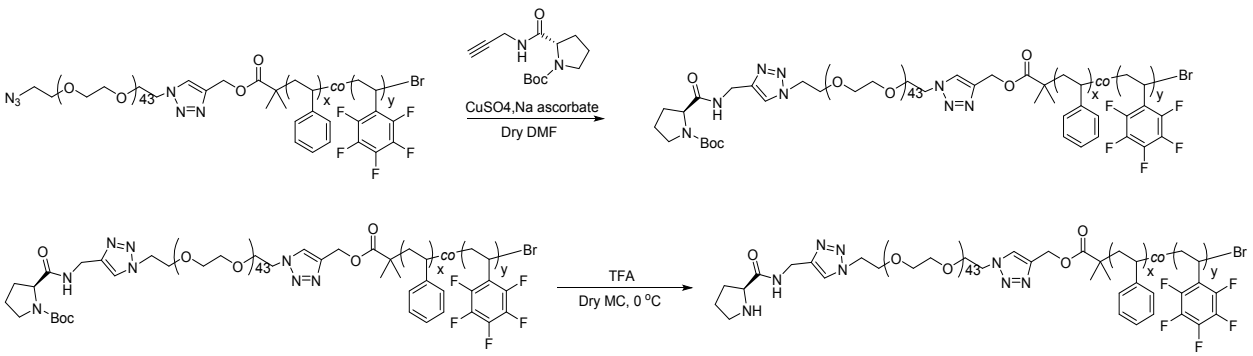


Scheme S4. (A) TMS deprotection of TMS-alkyne-P(pFS-*co*-Sty). (B) Coupling of bis-azide PEG and alkyne-P(pFS-*co*-Sty) via CuAAC reaction.

TMS deprotection of linear polymer and CuAAC reaction between bis-azide (PEG2000).

The TMS-alkyne-P(pFS-*co*-Sty) solution in THF (5 mL) was prepared in a 20 mL glass vial and excess amount of tetra-*n*-butyl ammonium fluoride (TBAF) added into the TMS-alkyne-P(pFS-*co*-Sty) solution and stirred for 5 h at room temperature. After the reaction completed, the alkyne-P(pFS-*co*-Sty) solution with TBAF precipitated in MeOH (50 mL). The white powder was collected by vacuum filtration and dried. For the click reaction, $CuSO_4$ (40 mg) and Sodium ascorbate (30 mg) was completely dried in vacuum for 15 min. Dry DMF (1.5 mL) was added into the vial. The resulting mixture was stirred under N_2

condition for 15 min. To this solution, a solution of the hydrophilic bis-azide (PEG2000) block and collected alkyne-P(pFS-*co*-Sty) hydrophobic part polymer (10 eq. to the hydrophilic module) in DMF (5 mL) was added into the prepared solution containing the reagents of click reaction. The mixture was degassed by bubbling N_2 gas for 15 min. After degassing, the click reaction was proceeded at 40 °C until reaction completion. The extent of the reaction was monitored by GPC. The reaction was quenched by exposing the solution to air, followed by dilution with chloroform. The cooled solution was filtered through aluminum oxide (basic) with $CHCl_3$ to remove the Cu catalyst. The filtered solution was precipitated in cold MeOH (50 mL) to afford white powdery product. If necessary, the resulting block copolymer was purified by preparatory size exclusion chromatography.



Scheme S5. (A) CuAAC reaction between azide-(PEG2000)-P(pFS-*co*-Sty) and boc protected L-proline-alkyne. (B) Boc deprotection of proline telechelic block copolymer.

CuAAC reaction between alkyne terminal boc-protected proline group, followed by boc deprotection for activating functional group in the telechelic part of the polymer.

For the click reaction, $CuSO_4$ (40 mg) and Sodium ascorbate (30 mg) was completely dried in vacuum for 15 min. Dry DMF (1.5 mL) was added into the vial. The resulting mixture was stirred under N_2 condition for 15 min. To this solution, a solution of the (S)-2-(prop-2-

yn-1-ylcarbamoyl) pyrrolidine-1-carboxylate and collected azide-(PEG2000)-P(pFS-*co*-Sty) amphiphilic block copolymer (10 eq. to the boc-protected catalyst module) in DMF (5 mL) was added into the prepared solution containing the reagents of click reaction. The mixture was degassed by bubbling N_2 gas for 15 min. After degassing, the click reaction was proceeded at 40 °C until reaction completion. The extent of the reaction was monitored by GPC. The reaction was quenched by exposing the solution to air, followed by dilution with chloroform. The cooled solution was filtered through aluminum oxide (basic) with $CHCl_3$ to remove the Cu catalyst. The filtered solution was precipitated in cold MeOH (50 mL) to afford white powdery product. The boc-proline-(PEG2000)-P(pFS-*co*-Sty) solution in CH_2Cl_2 (2 mL) was prepared in a 20 mL glass vial trifluoroacetic acid (TFA, 1 mL) added in to the boc-proline-(PEG2000)-P(pFS-*co*-Sty) solution and stirred for 2 hr in 0 °C condition. After 2 hours, proline-(PEG2000)-P(pFS-*co*-Sty) solution with TFA precipitated in MeOH (50 ml). The white powder was collected by vacuum filtration.

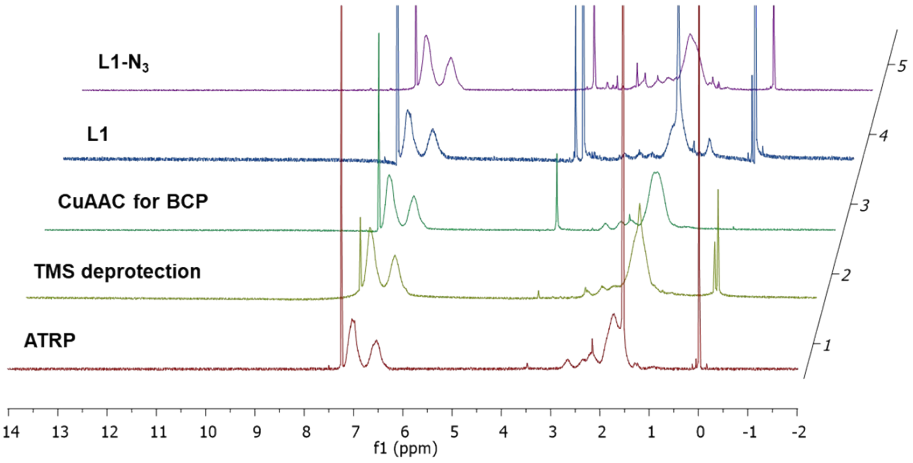


Fig. S7 Entire ^{1}H-NMR data of L1-N_3 resulting polymer and their intermediates.

6. Photo-crosslinking of the self-assembled structures of BCPs

Self-assembly of block copolymers and photo-crosslinking of self-assembled structures.

The prepared polymer (10 mg) was dissolved in 1,4-dioxane or THF (2 mL) in a 20 mL capped vial with a magnetic bar. The solution was stirred for 1 h at room temperature (800 rpm). A syringe pump was calibrated to deliver water at a speed of 0.5 mL h^{-1}. The vial cap was replaced by a rubber septum and water was added to the polymer solution for 4 h using a syringe pump with a 6-mL syringe equipped with a steel needle. The resulting suspension was subjected to dialysis (molecular weight cutoff ~12 to 14 kDA (SpectraPor)) against water for 72 h (with frequent changes). The dialyzed suspension (1 mL) was transferred to 4-mL capped vial with a magnetic bar.

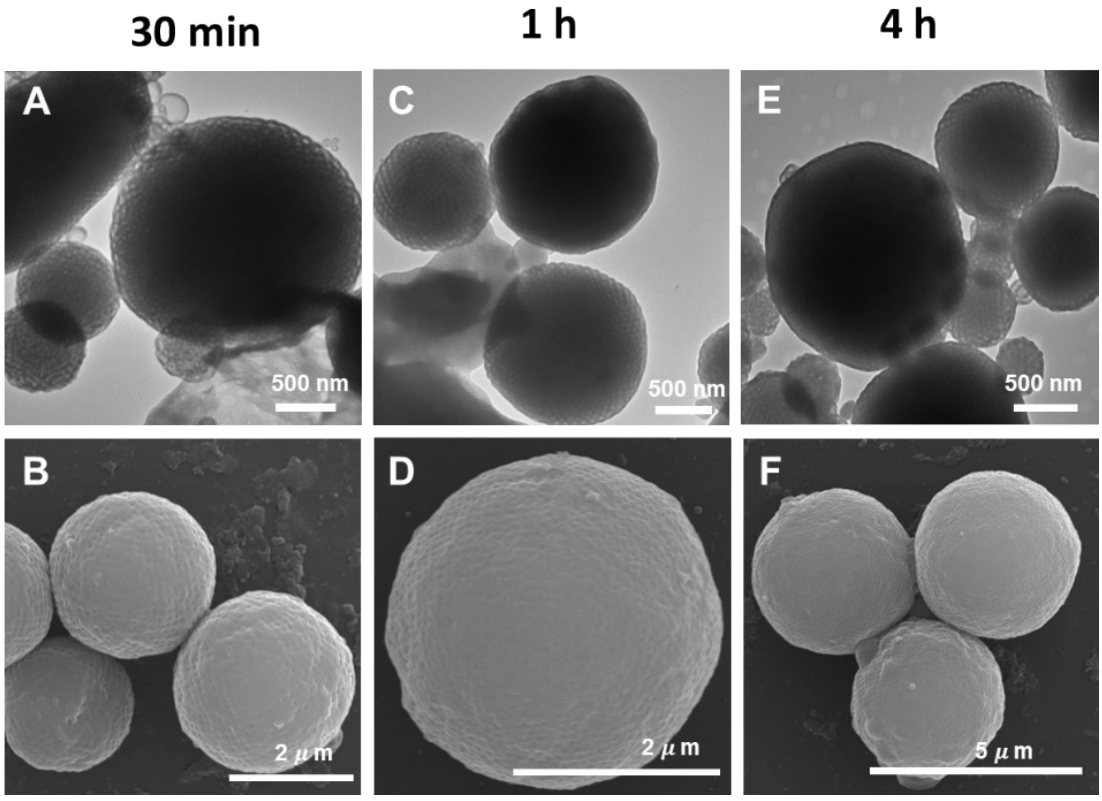


Fig. S8 (A, C and E) TEM and (B, D and F) SEM images of the self-assembled and inner structure of **BCP1** as a function of the water-injection time: (Time of water addition (t) = 30 min for A and B) polymer cubosomes; (t = 1 h for C and D) polymer cubosomes ; and (t = 4 h for E and F) polymer cubosomes.

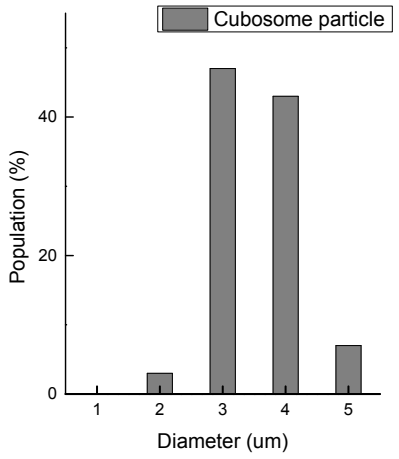


Fig. S9 Average size (3.03μm) and distribution of the polymer cubosome particles. The particle size distribution of polymer cubosomes was measured by analyzing SEM images of polymer cubosomes with ImageJ software. 50 particles were selected for the image analysis from SEM images taken from 5-10 different positions.

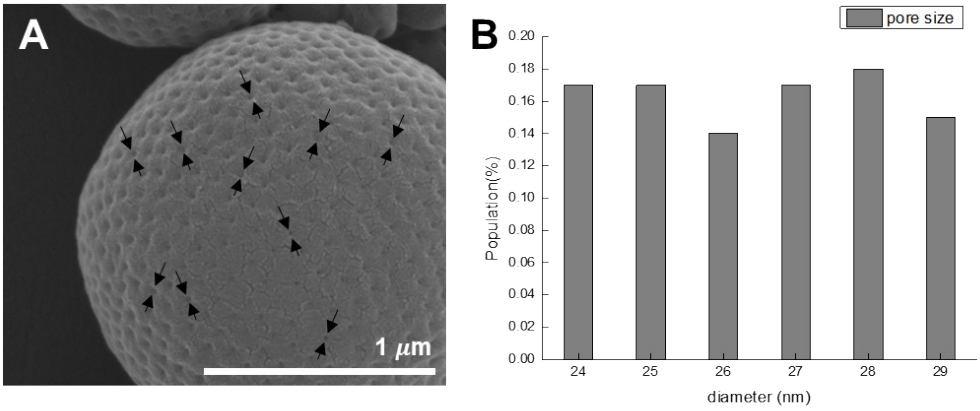


Fig. S10 The average pore size at the circumference of polymer cubosomes was determined by analyzing SEM images of polymer cubosomes with ImageJ software. 10 pores were selected for the image analysis from SEM images taken from 10 different particles. (A) Example of selected pore in cubosome particle (B) Distribution of the pore size.

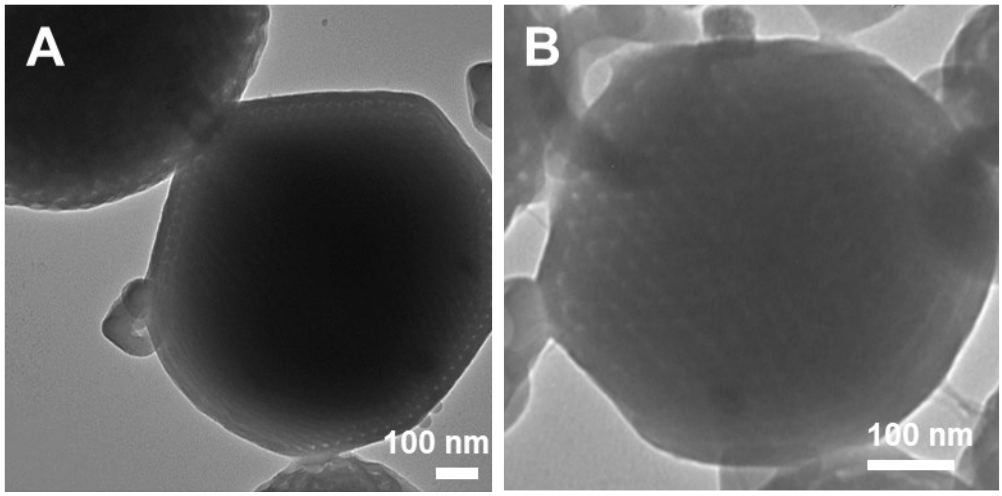


Fig. S11 TEM image of the photo-crosslinked polymer cubosome sustain their complex inner structure in organic solvent (A) DMSO, (B) Dioxane.

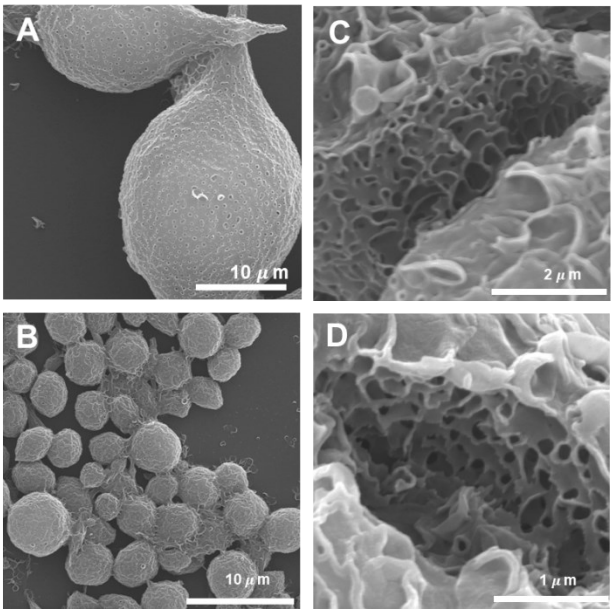
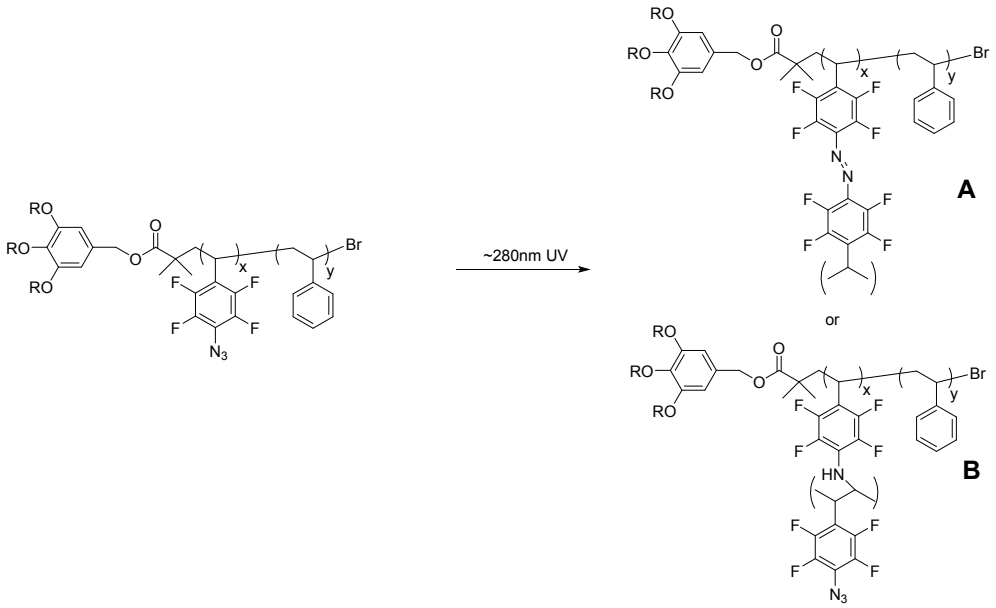


Fig. S12 (A, B, C and D) SEM images of the self-assembled and inner structure of **BCP2** as a function of the water-injection time: (Time of water addition (t) = 1 h for A and C) fibroblast shaped sponge phase particles and inner structure; (t = 30 min for B and D) Spherical shaped sponge phase particles and inner structure.

Photo-crosslinking of self-assembled structure.



Scheme S6. Scheme of photo-crosslinking between hydrophobic blocks of the **BCP1-**N_3 under UV (~280 nm) irradiation.

The solution (1 mL, 1 mg mL^{-1}) containing the self-assembled structure of BCPs in a 3 mL of vial was exposed to short-wavelength UV light (λ = ~280 nm, 20 W) for 8 h with air-blowing (for temperature control) located 1 cm away from the vial. After 8 h, the solution was transferred to the mixture (H_2O : THF = 1 to 10 ratio) to test the physical stability of the cross-linked nanoparticles in chemically harsh condition.

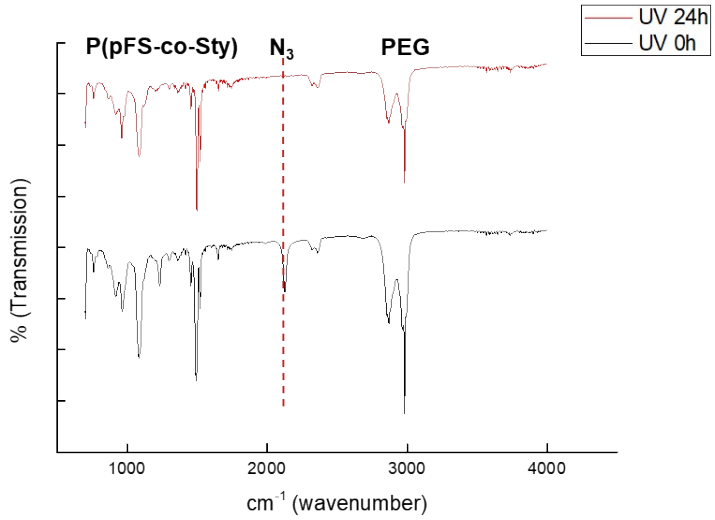
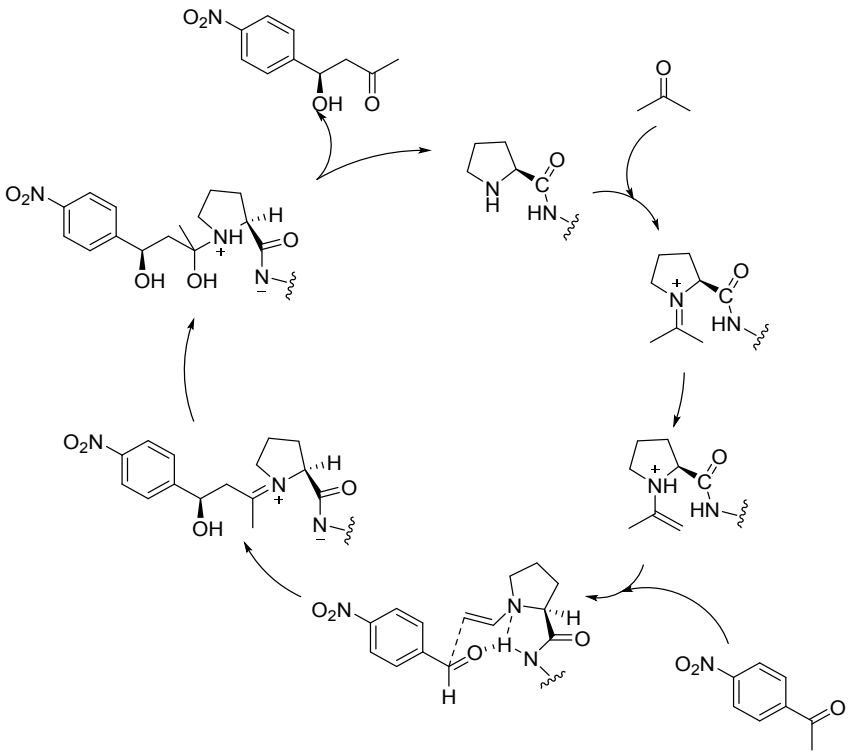


Fig. S13 FT-IR spectra of the self-assembled polymer cubosome before UV irradiation (black), after UV irradiation 24h (red).

7. Asymmetric aldol reaction on cubosome reactor and chiral stationary phase HPLC



Scheme S7. Catalytic cycle for asymmetric aldol reaction in the presence of telechelic L-proline.

Asymmetric aldol reaction with proline-tethered cubosome based structure.

The cross-linked polymer cubosomes of **BCP1-** N_3**/ L1-** N_3 (9:1) (50 mg) in the mixture of THF (1.8 mL) and water (0.2 mL) was prepared in a capped vial, followed by addition of 4-Nitrobenzaldehyde (3.6 mg, 15 μmol) and acetone (200 μL) in the vial. After the reaction was stirred for 72 h, the mixture was quenched by adding saturated NH_4Cl solution and polymer particles were separated from solution by centrifuge (14,000 rpm, 10 min). The product in supernatant was extracted with CH_2Cl_2 (1 mL × 3 times), dried over $MgSO_4$, and evaporated under reduced pressure. The collected polymer cubosome particles are redispersed in the same solution condition (THF (1.8 mL) and water (0.2 mL). The asymmetric aldol reaction were repeatedly proceeded to perform the reusability test (6 times).

Comparing reaction conversion rate between proline functionalized cubosome based structure and L-proline in homogeneous state.

The amount of L-proline (15 μg, 0.13 μmol) was calculated by molecular amount of **L1-**N_3 (M_w = 41k g mol^{-1}, insertion weight 5 mg in polymer cubosome 50 mg). To the mixture of THF (1 mL) and water (1 mL) (to prevent proline solubility issue), 4-Nitrobenzaldehyde (3.6 mg, 15 μmol) and acetone (200 μL) were added. During the reaction, a small amount of mixture was extracted and quenched by adding saturated NH_4Cl solution and the reaction mixture in solution extracted with CH_2Cl_2 (1 mL × 3 times). The organic phases were collected, dried over $MgSO_4$, and evaporated under reduced pressure. For comparative group, The **BCP1-** N_3**/L1-** N_3 (9:1) polymer cubosome (50 mg) solution in THF (1 mL) and water (1 mL), was prepared in a capped vial and mixed with 4-Nitrobenzaldehyde (3.6 mg, 15 μmol) and acetone (200 μL) for 72 h with stirring. During the

reaction, a small amount of mixture was extracted and quenched by adding saturated NH_4Cl solution and polymer particles were separated from solution by centrifuge (14,000 rpm, 10 min). The product in supernatant was extracted with CH_2Cl_2 (1 mL × 3 times), dried over $MgSO_4$, and evaporated under reduced pressure.

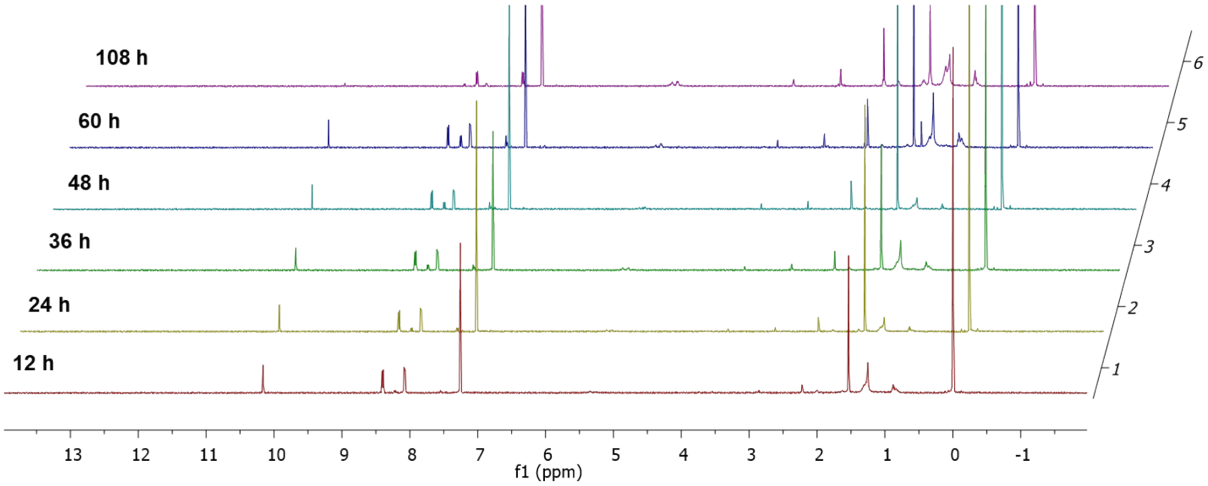


Fig. S14 ^{1}H-NMR result by time for the percentage conversion of the asymmetric aldol reaction by homogeneous proline.

Chiral stationary phase HPLC methods condition.

Reagents: Hexane (gradient HPLC grade from Honeywell (Art. No.65801)), IrOH (gradient grade from J.T. Baker (Art. No.65702)). Sample solvent: MeOH, 2.0 mg mL^{-1}, injection volume: 5 µL, column: Chiralpak IA, 250 x 4.6 mm, 5 µm (Daicel), flow rate: 1 mL/min, run time: 30.0 min, column temperature: 30 °C, detection (DAD) at 254 nm (BW16nm), mobile phase: hexane/IrOH (9:1). Retention time of the minor/major products are 13.95 min/14.17 min and *%* ee of products are 44%.

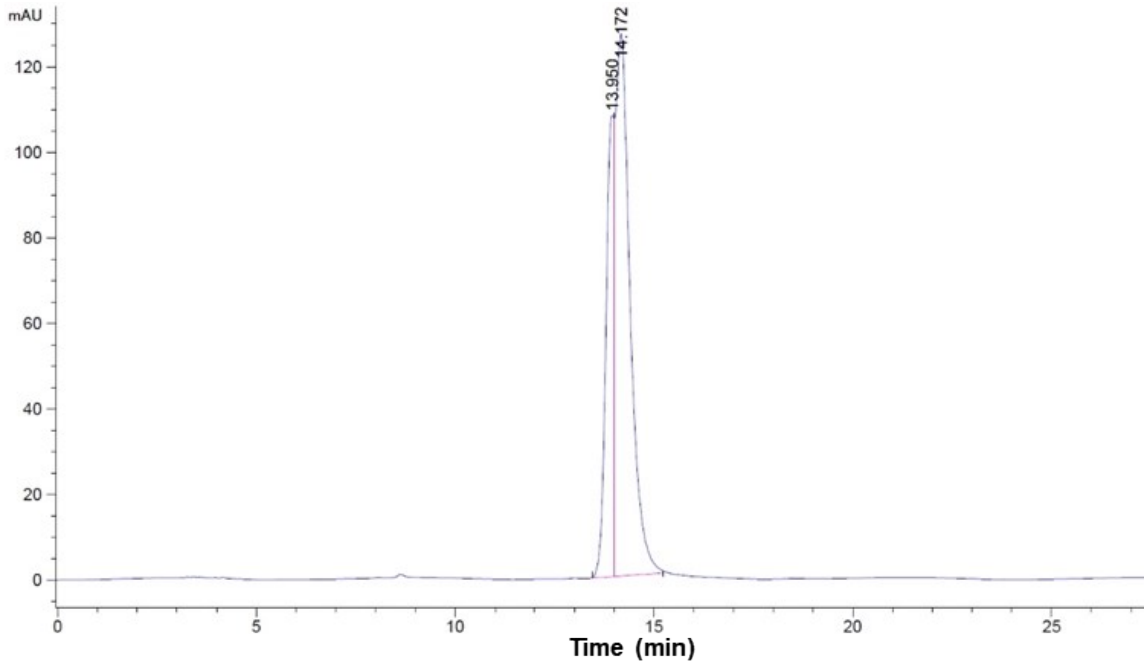


Fig. S15 Chiral HPLC result of product (R)-4-hydroxy-4-(4-nitrophenyl) butan-2-one.

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