Supporting Information

Functionally Diverse Nylon-3 Copolymers from Readily Accessible β-Lactams

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Figure S1. Transmittance of visible light (500 nm) as a function of pH for aqueous solutions of polymer P8-b-6 (1 mg/mL).

Figure S2. Proposed structure adopted by P8-b-6 in pH = 12 buffer. The green and red bands, respectively, indicate the regions in which CF and NR are hypothetically concentrated.
Experimental section

General experimental details

All chemicals were purchased from Sigma-Aldrich (Milwaukee, WI) and used as received unless stated otherwise. 1-Ethyl-3-(3-dimethylaminopropyl) carbodiimide hydrochloride (EDCI) was purchased from Chem-Impex International (Wood Dale, IL). (±)-trans-3-Phthalimidylmethyl-4-methyl azetidin-2-one (1), (±)-3-phthalimidylmethyl-4,4-dimethyl azetidin-2-one (2), (±)-cis-7-azabicyclo[4.2.0]octan-8-one (13) and (±)-trans-tert-butyl ((2-methyl-4-oxoazetidin-3-yl)methyl)carbamate (5) were synthesized according to the previously reported method.1 2-(Tritylthio)acetic acid was synthesized based on a literature procedure.2 Toluene and CH₂Cl₂ were distilled over sodium prior to use. THF used for polymerization was purchased from Sigma-Aldrich (anhydrous, inhibitor-free). 1H and 13C NMR spectra were recorded on Bruker AC-300 spectrometers at 300 and 75 MHz, respectively. Molecular weight information for polymers was obtained using a gel permeation chromatography (GPC) instrument equipped with a Shimadzu LC-10AD pump and a Wyatt Technology miniDAWN multi-angle light scattering (MALSS) detector in series with a Wyatt Technology Optilab-rEX refractive index detector (dn/dc = 0.1). All measurements were performed using two GPC columns in series (Waters Styragel HR4E) with THF as mobile phase at a flow rate of 1.0 mL/min at 40 °C.

4-tert-Butoxy-4-oxobutanoic acid. A procedure modified from the literature method3 was used. To a mixture of succinic anhydride (10 g, 0.1 mol, 1 eq.), N-hydroxysuccinimide (NHS) (3.56 g, 0.03 mol, 0.3 eq.) and 4-dimethylaminopyridine (DMAP) (1.22 g, 0.01 mol, 0.1 eq.) in 50 mL dry toluene was added tert-butanol (25 mL, 0.27 mol, 2.7 eq.) and then triethylamine (4.1 mL, 0.03 mol, 0.3 eq.). The suspension was refluxed for 24 h. Ethyl acetate (100 mL) was added to dilute the reaction mixture. The mixture was washed by 10% aqueous (w/v) citric acid (3×50 mL) and brine. The organic phase was collected and dried over MgSO₄. After the drying agent was filtered off, the solvent was removed under reduced pressure to give the crude product as a dark brown solid. The crude product was recrystallized from CH₂Cl₂/hexane to give the product as white crystals (7.1 g, 41%): mp = 51-

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52 °C. $^1$H NMR (CDCl$_3$): $\delta$ 1.45 (s, 9 H, tBu), 2.52-2.65 (m, 4 H, CH$_2$CH$_2$). MS-ESI/EMM: $m/z$ = Calc.: 173.1[M-H]$^-$, Obs.: 173.0 [M-H]$^-$.

$^{13}$C NMR (CDCl$_3$): $\delta$ 28.18, 29.39, 30.28, 81.19, 171.62, 178.88, 178.90.

2,2,5-Trimethyl-1,3-dioxane-5-carboxylic acid. 3-Hydroxy-2-(hydroxymethyl)-2-methyl propanoic acid (Bis-MPA, 20 g, 0.146 mol, 1 eq.), 2,2-dimethoxypropane (27 mL, 0.219 mol, 1.5 eq.), p-toluenesulfonic acid (0.98 g, 52 mmol, 3.5 mol%) were suspended in 100 mL acetone. The mixture turned clear in 30 min, and it was stirred at room temperature for another 4.5 h. The reaction was quenched by addition of 8 mL NH$_4$OH/ethanol (1:1 v/v). The resulting precipitate was filtered off, and the filtrate was concentrated under reduced pressure to give a viscous liquid. The liquid was dissolved in 80 mL CH$_2$Cl$_2$ and washed with 20 mL water. The organic phase was collected and dried over MgSO$_4$. After the drying agent was filtered off, the solvent was removed under reduced pressure to give the product as a white solid (17.1 g, 67%): mp = 118-120 °C. $^1$H NMR (CDCl$_3$): $\delta$ 1.21(s, 3 H, CCH$_3$), 1.43 (d, 6 H, J = 9.9 Hz, C(CH$_3$)$_2$), 3.68 (d, 2 H, J = 12 Hz, CH$_2$), 4.20 (d, 2 H, J = 12 Hz, CH$_2$), 10.11 (br, 1 H, OH). $^{13}$C NMR (CDCl$_3$): $\delta$ 18.68, 22.37, 25.18, 41.95, 66.05, 98.53, 180.35. MS-ESI/EMM: $m/z$ = Calc.: 173.1[M-H]$^-$, Obs.: 173.0 [M-H]$^-$.

**General procedure for $\beta$-lactam side-chain functionalization**

To a suspension of 1 or 2 (1 eq.) in methanol (0.5 – 0.75 M) was injected anhydrous hydrazine (3 eq.) through a syringe. The mixture was stirred under N$_2$ at room temperature for 2 h or until TLC showed complete disappearance of the starting material. The resulting precipitate was removed by filtration and washed with CHCl$_3$. The solvent and excess hydrazine were removed from the filtrate by rotary evaporation. Dry CH$_2$Cl$_2$ was added to the residue (3 or 4, colorless or light yellow oil, assumed as 100% conversion), and the insoluble material was removed by filtration. The filtrate was transferred to a round-bottom flask, to which were added acylating agent and other reagents, as described below. The reaction mixture was stirred at room temperature overnight or until TLC showed the completion of the reaction. The reaction solution was washed with 1 N HCl or saturated aqueous solution of NH$_4$Cl, 1 N NaOH or saturated aqueous NHCO$_3$ and brine before being dried over MgSO$_4$. After the drying agent was filtered off and the solvent was removed under reduced pressure, the crude product was purified by column chromatography using ethyl acetate or ethyl acetate-methanol mixtures.
(±) *trans*-tert-Butyl 4-(2-methyl-4-oxoazetidin-3-yl)methylamino)-4-oxobutanoate (7). To a solution of crude 3 (10 mmol, 1 eq.) in 50 mL dry CH₂Cl₂ was added a solution of 4-tert-butoxy-4-oxobutanoic acid (2.61 g, 15 mmol, 1.5 eq.) , EDCI (3.07 g, 16 mmol, 1.6 eq.) , HOBt (2.16 g, 16 mmol, 1.6 eq.) and DIEA (2.79 mL, 16 mmol, 1.6 eq.) in 50 mL dry CH₂Cl₂. β-Lactam 7 was obtained as a colorless gel/oil (0.36 g, 10%): ¹H NMR (CDCl₃): δ 1.35 (d, 3 H, J = 6 Hz, Me), 1.44 (s, 9 H, tBu), 2.37-2.62 (m, 4 H, CH₂CH₂), 3.90 (tdd, 1 H, J = 6.3, 2.1, 0.6 Hz, CHC=O), 3.60-3.66 (m, 3 H, CΗ₂NHC=O and CHNH), 6.22 (br, 1 H, CH₂NHC=O), 6.46 (br, 1 H, lactam NH). ¹³C NMR (CDCl₃): δ 20.42, 28.26, 28.73, 30.84, 31.14, 36.91, 48.73, 58.07, 80.95, 169.36, 172.52, 172.67. MS-ESI/EMM: m/z = Calc.: 293.1[M+Na]⁺ Obs.: 292.8 [M+Na]⁺.

(±) tert-Butyl 4-(2,2-dimethyl-4-oxoazetidin-3-yl)methylamino)-4-oxobutanoate (8). To a solution of crude 4 (10 mmol, 1 eq.) in 50 mL dry CH₂Cl₂ was added a solution of 4-tert-butoxy-4-oxobutanoic acid (2.61 g, 15 mmol, 1.5 eq.) , EDCI (3.07 g, 16 mmol, 1.6 eq.) , HOBt (2.16 g, 16 mmol, 1.6 eq.) and DIEA (2.79 mL, 16 mmol, 1.6 eq.) in 50 mL dry CH₂Cl₂. β-Lactam 8 was obtained as a colorless gel/oil (1.53 g, 54%): ¹H NMR (CDCl₃): δ 1.37 (s, 3 H, Me), 1.44 (s, 9 H, tBu), 1.45 (s, 3 H, Me), 2.40 (t, 2 H, J = 6.0 Hz, CH₂CH₂), 2.57 (t, 2 H, J = 6.0 Hz, CH₂CH₂), 2.96 (qd, 1 H, J = 6.6, 1.2 Hz, CH), 3.27 (ddd, 1 H, J = 19.5, 9.3, 3.6 Hz, CH₂), 3.86 (dd, 1 H, J = 13.8, 6.2 Hz, CH₂), 6.13 (br, 1 H, CH₂NHC=O), 6.29 (br, 1 H, lactam NH). ¹³C NMR (CDCl₃): δ 23.12, 28.29, 28.73, 30.92, 31.38, 36.08, 50.09, 58.00, 80.93, 169.19, 172.02, 172.38. MS-ESI/EMM: m/z = Calc.: 307.2 [M+Na]⁺ Obs.: 307.2 [M+Na]⁺.
(±) \textit{N-}((2,2-dimethyl-4-oxoazetidin-3-yl)methyl)-2,2,5-trimethyl-1,3-dioxane-5-carboxamide (9). To a solution of crude 4 (10 mmol, 1 eq.) in 50 mL dry CH$_2$Cl$_2$ was added a solution of 2,2,5-trimethyl-1,3-dioxane-5-carboxylic acid (2.26 g, 13 mmol, 1.3 eq.), EDCI (2.69 g, 14 mmol, 1.4 eq.), HOBt (1.89 g, 14 mmol, 1.4 eq.) and DIEMA (2.44 mL, 14 mmol, 1.4 eq.) in 50 mL dry CH$_2$Cl$_2$. β-Lactam 9 was obtained as a white solid (1.60 g, 56%): mp = 114-116 °C. $^1$H NMR (CDCl$_3$): δ 1.02 (s, 3 H, CCH$_3$), 1.41 (s, 3 H, Me), 1.47 (m, 9 H, Me and C(CH$_3$)$_2$), 3.03 (t, 1 H, J = 7.5 Hz, CH), 3.42 (m, 1 H, CH$_2$NHC=O), 3.75-3.96 (m, 5 H, CH$_2$NHC=O and CCH$_2$O), 5.98 (br, 1 H, lactam NH), 7.37 (br, 1 H, CH$_2$NHC=O). $^{13}$C NMR (CDCl$_3$): δ 18.06, 18.79, 23.17, 28.74, 28.84, 35.93, 40.43, 55.09, 58.53, 67.19, 67.31, 98.80, 168.54, 175.12. MS-ESI: m/z = Calc.: 307.2 [M+Na]$^+$ Obs.: 307.0 [M+Na]$^+$.

(±) \textit{trans-N-}((2-Methyl-4-oxoazetidin-3-yl)methyl)-2-(tritylthio)acetamide (10). To a solution of crude 3 (3 mmol, 1 eq.) in 15 mL dry CH$_2$Cl$_2$ was added a solution of 2-(tritylthio)acetic acid (1.0 g, 3 mmol, 1 eq.), EDCI (0.58 g, 3 mmol, 1 eq.) and DIEMA (1.04 mL, 6 mmol, 2 eq.) in 15 mL dry CH$_2$Cl$_2$. β-Lactam 10 was obtained as a white solid (0.61 g, 46%): mp = 67-69 °C. $^1$H NMR (CDCl$_3$): δ 1.30 (d, 3 H, J = 6 Hz, Me), 2.72 (tdd, 1 H, J = 6.3, 2.1, 0.6 Hz, CH), 3.10 (d, 2 H, J = 3.3, CH$_2$S), 3.22-3.41 (m, 2 H, CH$_2$NHC=O), 3.46-3.53 (qd, 1H, J = 6, 2.1 Hz, CHNHN), 5.79 (br, 1 H, CH$_2$NHC=O), 6.25 (br, 1 H, lactam NH), 7.22-7.34 (m, 9 H, Ph), 7.41-7.45 (m, 6 H, Ph). $^{13}$C NMR (CDCl$_3$): δ 20.56, 36.17, 37.54, 49.09, 57.84, 127.29, 128.42, 129.71, 144.16, 168.40, 168.88. MS-ESI: m/z = Calc.: 453.2 [M+Na]$^+$ Obs.: 453.2 [M+Na]$^+$. 
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(±) 11

(±) N-((2,2-Dimethyl-4-oxazetidin-3-yl)methyl)-2-(tritylthio)acetamide (11). To a solution of crude 4 (3 mmol, 1 eq.) in 15 mL dry CH₂Cl₂ was added a solution of 2-(tritylthio)acetic acid (1.0 g, 3 mmol, 1 eq.), EDCI (0.58 g, 3 mmol, 1 eq.) and DIEA (1.04 mL, 6 mmol, 2 eq.) in 15 mL dry CH₂Cl₂. β-Lactam 11 was obtained as a white solid (0.61 g, 46%): mp = 168-169 °C. ¹H NMR (CDCl₃): δ 1.29 (s, 3 H, Me), 1.39 (s, 3 H, Me), 2.75 (t, 1 H, J = 7.8 Hz, CH), 3.00 (m, 1 H, CH₂NHC=O), 3.09 (s, 2 H, CH₂S), 3.53 (m, 1 H, CH₂NHC=O), 5.89 (br, 1 H, CH₂NHC=O), 6.36 (br, 1 H, lactam NH), 7.20-7.32 (m, 9 H, Ph). ¹³C NMR (CDCl₃): δ 23.19, 28.78, 28.73, 36.22, 54.93, 57.78, 127.24, 1 28.38, 129.75, 144.19, 168.41, 168.51. MS-ESI: m/z = Calc.: 466.6 [M+Na]⁺ Obs.: 466.9 [M+Na]⁺.

(±) tert-Butyl 2-((2,2-dimethyl-4-oxazetidin-3-yl)methylamino)-2-oxoethyl(methyl)carbamate (12). To a solution of crude 4 (10 mmol, 1 eq.) in 50 mL dry CH₂Cl₂ was added a solution of 2-(tert-butoxycarbonyl(methyl)amino)acetic acid (2.50 g, 13 mmol, 1.3 eq.), EDCI (2.69 g, 14 mmol, 1.4 eq.), HOBt (1.89 g, 14 mmol, 1.4 eq.) and DIEA (2.44 mL, 14 mmol, 1.4 eq.) in 50 mL dry CH₂Cl₂. β-Lactam 12 was obtained as a white solid (1.30 g, 43%): mp = 71-73 °C. ¹H NMR (CDCl₃): δ 1.38 (s, 3 H, Me), 1.45 (s, 3 H, Me), 1.47 (S, 9 H, tBu), 2.94 (m, 5 H, MeN and CH₂NHC=O), 3.33 (m, 1 H, CH), 3.88 (m, 3 H, CH₂N(Me)C=O, CH₂NHC=O), 6.10 (br, 1 H, CH₂NHC=O), 6.58 (br, 1 H, lactam NH). ¹³C NMR (CDCl₃): δ 23.17, 28.51, 28.77, 35.92, 53.23, 55.03, 57.91, 80.91, 168.72, 169.66, 169.68. MS-ESI: m/z = Calc.: 322.2 [M+Na]⁺ Obs.: 322.0 [M+Na]⁺.
Synthesis of (±) tert-butyl methyl((2-methyl-4-oxoazetidin-3-yl)methyl)carbamate (14)

Boc-protected β-lactam 5 (2.14 g, 10 mmol, 1 eq.) was dissolved in 20 mL DMF. The solution was cooled to 0 °C, and tert-butyldimethylsilyl chloride (TBS-Cl) (1.87 g, 12 mmol, 1.2 eq.) and triethylamine (1.7 mL, 12 mmol, 1 eq.) were added. The reaction mixture was allowed to warm to room temperature and stirred overnight. The reaction mixture was quenched by saturated aqueous NH₄Cl, and then extracted with ethyl acetate (2 × 80 mL). The combined organic phase was washed with brine and dried over MgSO₄. After the drying agent was filtered off, the solvent was removed under reduced pressure to give the TBS-protected 3 as a colorless oil in quantitative yield. This product was used in the next step without purification.

The TBS-protected 3 was dissolved in 15 mL DMF, and the solution was cooled to 0 °C. To this solution was added dropwise a solution of NaH (0.38 g, 15 mmol, 1.5 eq.) in 10 mL DMF. The reaction flask was intermittently opened to air to release H₂ generated from the reaction. After 30 min, methyl iodide (1.25 mL, 20 mmol, 2 eq.) was added to the mixture at 0 °C. The resulting solution was stirred at room temperature for 2 h. The reaction solution was quenched with saturated aqueous NH₄Cl, and then extracted with ethyl acetate (2 × 80 mL). The combined organic phase was washed with brine and dried over MgSO₄. After the drying agent was filtered off, the solvent was removed under reduced pressure to give the TBS-protected N-methylated 3 as a colorless oil, which was used in the next step without purification.

To a solution of the TBS-protected N-methylated 3 in 60 mL methanol was added solid KF (1.74 g, 30 mmol, 3 eq.) at room temperature. The mixture was stirred at room temperature for 1 h. The reaction solution was quenched with saturated aqueous NH₄Cl, and then extracted with ethyl acetate (2 × 100 mL). The combined organic phase was washed with brine twice and dried over MgSO₄. After the drying agent was filtered off, the solvent was removed under reduced pressure to give the crude product, which was purified by column chromatography using CH₂Cl₂ and then ethyl acetate as eluent. β-Lactam 14 was obtained as a colorless oil (1.30 g, 57%): ¹H NMR (CDCl₃): δ 1.36 (d, 3 H, J = 5.7 Hz, Me), 1.46 (s, 9 H, Boc), 2.90-2.96 (m, 4 H, MeN and CHC=O), 3.44-3.71 (m
and br, 3 H, CH₂NHC=O and CHNH), 6.00 (br, 1 H, lactam NH). $^{13}$C NMR (CDCl₃): δ 20.60, 28.59, 35.12, 47.00, 49.47, 57.65, 79.90, 156.11, 169.25. MS-ESI/EMM: m/z = Calc.: 251.1 [M+Na]$^+$ Obs.: 250.9 [M+Na]$^+$.

**Synthesis of tert-butyl 1-oxo-2,5-diazaspiro[3.4]octane-5-carboxylate (15)**

(±) tert-butyl 2-(4-methoxyphenyl)-1-oxo-2,5-diazaspiro[3.4]octane-5-carboxylate. The precursor 16 was synthesized based on literature procedures. To a solution of 16 (0.39 g, 1.7 mmol, 1 eq.) in 10 mL dry CH₂Cl₂ was added triethylamine (0.26 mL, 1.87 mmol, 1.1 eq.) and then a solution of Boc₂O (0.41 g, 1.87 mmol, 1.1 eq.) in 5 mL dry CH₂Cl₂. The mixture was stirred at room temperature overnight. The reaction solution was quenched by additions of saturated aqueous NH₄Cl. The organic phase was washed with saturated aqueous NaHCO₃ and brine and then dried over MgSO₄. After the drying agent was filtered off, the solvent was removed under reduced pressure to give the product as a white solid (0.51 g, 91%): mp = 118-120 °C. $^1$H NMR (CDCl₃): δ 1.29 (s, 9 H, $t$Bu), 1.81-2.05 (m, 2 H, CCH₂CH₂CH₂), 2.17-2.25 (m, 1 H, CCH₂CH₂CH₂N), 2.36-2.47 (m, 1 H, CCH₂CH₂CH₂N), 3.46-3.90 (m, 4 H, CCH₂CH₂CH₂N and NCH₂), 3.79 (s, 3 H, OCH₃), 6.84-6.90 (m, 2 H, Ph), 7.28-7.34 (m, 2 H, Ph). $^{13}$C NMR (CDCl₃): δ 23.11, 28.47, 35.23, 47.94, 54.14, 55.69, 58.10, 72.03, 81.04, 114.60, 117.73, 132.32, 156.22, 166.84. MS-ESI/EMM: m/z = Calc.: 355.2 [M+Na]$^+$ Obs.: 354.9 [M+Na]$^+$.

(±) tert-Butyl 1-oxo-2,5-diazaspiro[3.4]octane-5-carboxylate (15). The entire yield of the above product (0.51 g, 1.5 mmol, 1 eq.) was dissolved in 15 mL acetonitrile. The solution was cooled to 0 °C, and a solution of cerium ammonium nitrate (CAN) (2.46, 4.5 mmol, 3 eq.) in 15 mL water was added dropwise. The orange mixture was stirred at 0 °C for 1 h or until TLC showed complete consumption of the starting material. The reaction solution was quenched with 20 mL 10% (w/v) Na₂SO₄ and the mixture was extracted with ethyl acetate three times. The combined organic phase was washed with water, and then brine, and dried over MgSO₄. After the drying agent was filtered off, the solvent was removed under reduced pressure to give the crude product as an orange oil. The crude

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product was purified by column chromatography using ethyl acetate as eluent. The solid obtained was recrystallized from ethyl acetate/hexane to give β-lactam 15 as a white solid (120 mg, 35%): mp = 107-109°C. 1H NMR (CDCl₃): δ 1.47 (s, 9 H, tBu), 1.72-2.01 (m, 2 H, CCH₂CH₂CH₂N), 2.09-2.20 (m, 1 H, CCH₂CH₂CH₂N), 2.30-2.44 (m, 1 H, CCH₂CH₂CH₂N), 3.19-3.89 (m, 4 H, CCH₂CH₂CH₂N and NCH₂C), 5.91-5.96 (br, 2 H, CH₂NHC=O and lactam NH). 13C NMR (CDCl₃): δ 22.96, 23.54, 28.34, 28.62, 34.33, 35.48, 47.95, 48.13, 49.71, 51.13, 57.96, 74.41, 81.28, 153.65, 154.34, 171.84. MS-ESI: m/z = Calc.: 249.1 [M+Na]⁺ Obs.: 249.0 [M+Na]⁺.

**General polymerization procedure**

All polymerizations were carried out in a nitrogen-purged dry box at room temperature. In a typical polymerization, the β-lactam monomer or a mixture of monomers was weighed and placed in a reaction vial with a magnetic stirring bar. Then the appropriate amounts of co-initiator and anhydrous THF were added to achieve the desired monomer to co-initiator ratio ([M]₀/[I]₀) and monomer concentration. The mixture was allowed to stir until all solid material was dissolved. The polymerization was started by addition of a LiN(SiMe₃)₂ solution in THF. The polymerization was stopped by adding a small amount of methanol. The resultant polymer was precipitated by pouring the reaction solution into pentane. The precipitate was collected by filtration or centrifugation. The precipitate was then re-dissolved in CHCl₃ and re-precipitated by pouring this solution into pentane. The resulting polymer was dried under a gentle N₂ stream.

**Synthesis of di-block copolymer poly(8)-b-poly(6)**

In a nitrogen-purged dry box at room temperature, β-lactam 8 (0.2 mmol) and co-initiator p-(tert-butyl)benzoyl chloride (0.01 mmol) were dissolved in THF. An aliquot of LiN(SiMe₃)₂ solution in THF (0.02 mmol) was injected to start the polymerization. After 4 h, β-lactam 6 (0.2 mmol) as a solution in THF was added. The reaction was allowed to proceed for 2 h before being quenched by addition of a small amount of methanol. The resulting side-chain protected block copolymer was precipitated by pouring the reaction solution into pentane. The precipitate was collected by centrifugation, and dried under a nitrogen stream.
General polymer deprotection procedures

The deprotection reactions were accomplished in neat TFA with essentially quantitative conversion. In a typical reaction, 100 mg protected polymer was dissolved in 2 mL of TFA, and the reaction solution was shaken on at room temperature for 2-4 h. The reaction mixture was then poured into ca. 14 mL cold diethyl ether to induce precipitation of the deprotected polymer. After being dried under gentle \( \text{N}_2 \) stream, the precipitate was dissolved in DI water. The solution was lyophilized to give the deprotected polymer as a white solid. For (co)polymers containing residues generated from 5, 12, 14 or 15, only TFA was used. For (co)polymers containing residues generated from 8 or 10 and poly(8)-b-poly(6) 50-100 µL triethylsilane was used with TFA to aid the removal of tert-butyl group or trityl group.

For the copolymer generated from 9 and 13, 45 mg of the protected copolymer was dissolved in 0.5 mL 1,4-dioxane. To the solution was added 0.5 mL 12 \( N \) HCl. A precipitate formed and disappeared quickly upon stirring. The reaction stayed clear and homogeneous. The reaction solution was stirred for 2 h before being diluted with 4 mL DI water. The diluted solution was dialyzed against DI water for 24 h using a MWCO = 1000 membrane. The deprotected copolymer was obtained as a white solid (20 mg, 52%) after the dialyzed solution was lyophilized.

Turbidity test of polymer P8-b-6

Sample of P8-b-6 was weighed and mixed with various buffer solutions (pH = 2 – 13) in vials (1 mg/mL). The mixtures were vortexed for one minute and transferred to plastic 1 cm UV cells. The transmission of visible light at 500 nm was determined for each cell on a UV-Vis spectrometer.

Fluorescence microscopy of P8-b-6

An Olympus IX81 epifluorescence microscope equipped with 4x, 10x, 40x, 60x and 100x objectives was used. Nile red-labeled P8-b-6 were prepared by mixing 10 µL sample solution in pH = 12 aqueous buffer (\( \text{Na}_2\text{HPO}_4 \)-\( \text{NaOH} \)) with 10 µL 0.5 mg/L Nile red solution in 80:20 (v/v) methanol/ water in a vial. The mixture is vortexed and allowed to stand for at least 24 h. Then 10 µL of the solution was deposited onto a glass slide. The solution was dried under \( \text{N}_2 \) prior to the observation. Samples were excited at 543 nm and observed at 637 nm.
Images (gray scale) were processed by the software ImageJ. No modification other than background subtraction was used. The images were rendered red in order to reflect what was actually seen under the microscope.

**Antibacterial and hemolytic assays**

Antibacterial assays were performed as previously reported. The bacterial strains used in these assays were *Escherichia coli* JM109, *Bacillus subtilis* BR151, *Staphylococcus aureus* 1206 (methicillin-resistant), and *Enterococcus faecium* A634 (vancomycin-resistant). The antibacterial activity for the polymers was determined in sterile 96-well plates (BD Falcon 353072 tissue culture plates). Bacterial cells were grown overnight at 37 °C in agar, after which a bacterial suspension of approximately $2 \times 10^6$ CFU/mL in Brain-Heart Infusion (BHI) growth medium was prepared. Samples (50 µL) were added to 50 µL of medium containing the polymer in 2-fold serial dilutions for a total volume of 100 µL in each well. The plates were then incubated at 37 °C for 6 h. Bacterial growth was determined by measuring the optical density (OD) at a wavelength of 650 nm using a Molecular Devices Emax precision microplate reader.

Hemolytic assays were performed according to the reported procedure. Freshly drawn human red blood cells (hRBC, blood type O) were washed three times with Tris-buffered saline (pH 7.2, 0.01 M Tris-HCl, 0.155 M NaCl) and centrifuged at 3500 rpm for 5 min. Two-fold serial dilutions of polymer in Tris-buffered saline were added to each well in a sterile 96-well plate (BD Falcon 353072 tissue culture plates), for a total volume of 50 µL in each well. A 2% (v/v) hRBC suspension (50 µL in Tris buffer) was added to each well. The plate was incubated at 37 °C for 1 h, and then the cells were pelleted by centrifugation at 3500 rpm for 5 min. The supernatant (80 µL) was transferred to a fresh plate, and hemoglobin was detected by measuring the OD at 405 nm. The average OD of cells incubated with TX-100 at 200, 400, 800 and 1600 µg/mL defines 100%; the OD of cells incubated in Tris-buffered saline defines 0%.


$^1$H and $^{13}$C NMR spectra of $\beta$-lactams

$^1$H NMR of $\beta$-lactam 7 in CDCl$_3$.

$^{13}$C NMR of $\beta$-lactam 7 in CDCl$_3$. 
\(^1\)H NMR of \(\beta\)-lactam 8 in CDCl\(_3\).

\(^{13}\)C NMR of \(\beta\)-lactam 8 in CDCl\(_3\).
$^1$H NMR of β-lactam 9 in CDCl$_3$.

$^{13}$C NMR of β-lactam 9 in CDCl$_3$. 
$^1$H NMR of $\beta$-lactam 10 in CDCl$_3$.

$^{13}$C NMR of $\beta$-lactam 10 in CDCl$_3$. 
$^1$H NMR of β-lactam 11 in CDCl$_3$.

$^{13}$C NMR of β-lactam 11 in CDCl$_3$. 
\(^1\)H NMR of \(\beta\)-lactam 12 in CDCl\(_3\).

\(^1\)C NMR of \(\beta\)-lactam 12 in CDCl\(_3\).
$^{1}H$ NMR of β-lactam 14 in CDCl$_3$.

$^{13}C$ NMR of β-lactam 14 in CDCl$_3$. 
$^1$H NMR of $\beta$-lactam 14 in CDCl$_3$.

$^{13}$C NMR of $\beta$-lactam 15 in CDCl$_3$. 
Characterization data for polymers

GPC of protected poly(8). $M_n = 5740$, PDI = 1.22, $dn/dc = 0.1$. Solid curve: RI; dotted curve: LS.
GPC of poly(8-r-13) (8:13 = 50:50). $M_n = 8580$, PDI = 1.07, $dn/dc = 0.1$. Solid curve: RI; dotted curve: LS.

$^1$H NMR of deprotected poly(8-r-13) (8:13 = 50:50) in D$_2$O (containing ~0.5 M NaOD)
GPC of protected poly(6-r-8) (6:8 = 50:50). $M_n = 5330$, PDI = 1.12, $dn/dc = 0.1$. Solid curve: RI; dotted curve: LS.

GPC of poly(8) (solid curve) and poly(8)-b-poly(6) (dotted curve). Poly(8): $M_n$(theo) = 5849, $M_n$ (obs) = 5740, PDI = 1.22, $dn/dc = 0.1$. Poly(8)-b-Poly(6): $M_n$(theo) = 10413, $M_n$ (obs) = 11500, PDI = 1.14, $dn/dc = 0.1$

$^1$H NMR of polymer P8-b-6 in 10:1 (v/v) DMSO-d$_6$:TFA-d.
GPC of poly(9-r-13) (9:13 = 75:25). $M_n = 5827$, PDI = 1.07, $dn/dc = 0.1$ (the major peak only). Some unreacted monomers are present. Solid curve: RI; dotted curve: LS.

GPC of poly(5-\(r\)-11-\(r\)-13) (5:11:13 = 60:30:10). M\(_n\) = 17760, PDI = 1.07, dn/dc = 0.1. Solid curve: RI; dotted curve: LS.

^1^H NMR of deprotected poly(5-\(r\)-11-\(r\)-13) (5:11:13 = 60:30:10) in D\(_2\)O.
GPC of poly(15). $M_n = 3250$, PDI = 1.09, $dn/dc = 0.1$. Solid curve: RI; dotted curve: LS.

MALDI-TOF spectrum of deprotected poly(15).
$^1$H NMR of poly(15). Top: protected polymer in CDCl$_3$. Bottom: deprotected polymer in D$_2$O. Degree of polymerization (determined by the NMR in D$_2$O) = 22.
GPC of the Boc-protected form of copolymer P13-r-14. $M_n = 3730$, PDI = 1.06, $dn/dc = 0.1$. Solid curve: RI; dotted curve: LS

$^1$H NMR of copolymer P13-r-14 in D$_2$O. DP $\approx 20$. 

\[ \text{N} \quad \text{O} \]
\[ \text{NH}_2 \quad \text{NH} \]
\[ \text{R'} \quad \text{Boc} \]
GPC of the Boc-protected form of copolymer P13-r-12. $M_n = 5400$, PDI = 1.06, $dn/dc = 0.1$ (the major peak only).

Solid curve: RI; dotted curve: LS

$^1$H NMR of copolymer P13-r-12 in D$_2$O. DP $\approx 25$. 
GPC of the Boc-protected form of copolymer **P13-r-15**. $M_n = 3490$, PDI = 1.14, $dn/dc = 0.1$. Solid curve: RI; dotted curve: LS.

$^1$H NMR of copolymer **P13-r-15** in D$_2$O. DP ≈ 19.
Antibacterial and hemolytic assays

Antibacterial assay of copolymer P13-r-14.

Antibacterial assay of copolymer P13-r-12.
Antibacterial assay of copolymer P13-r-15.

Hemolytic assay of copolymers P13-r-14, P13-r-12 and P13-r-15.