Supporting Information

Alendronate-Functionalized Poly(2-oxazoline)s with Tunable Affinity for Calcium Cations

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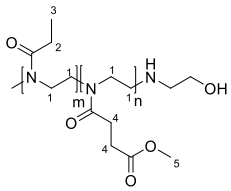
S1. Procedures for the Synthesis of Alendronate-Functionalized Poly(2-oxazoline)s.

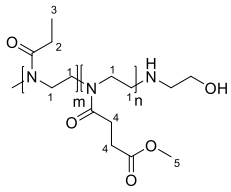
Polymerization: Synthesis of Methyl Ester-Functionalized Polymers P1a–P5a

P(EtOx$_{90}$-MestOx$_{10}$) P1a



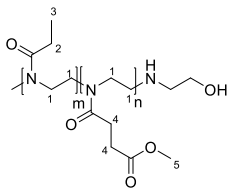
According to the general procedure described in the experimental section, polymerization was conducted using methyl tosylate (0.68 mL, 4.52 mmol), 2-ethyl-2-oxazoline (41.04 mL, 406.59 mmol) and 2-methoxycarbonylethyl-2-oxazoline (6.23 mL, 45.18 mmol) in dry MeCN (68 mL, 4 M). The polymerization was terminated by the addition of 2-ethanolamine (2.72 mL, 45.18 mmol) affording the desired polymer **P1a** (52.12 g, 4.39 mmol). **^{1}H NMR** [400 MHz, δ (ppm), $CDCl_3$]: 3.63 (br, 3 H, 5-CH_3), 3.65–3.35 (br, 8 H, 1-CH_2), 2.70–2.50 (br, 4 H, 4-CH_2), 2.50–2.20 (br, 2 H, 2-CH_2), 0.95–1.15 (br, 3 H, 3-CH_3). Experimentally determined comonomer ratio: *m*/*n* 90:10. **SEC**: M_n 10.6 kDa, $Đ$ 1.11. **MALDI-TOF MS**: M_n 9.7 kDa. **Yield**: 97%.

P(EtOx$_{80}$-MestOx$_{20}$) P2a



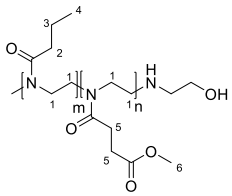
According to the general procedure described in the experimental section, the reaction of a solution of methyl tosylate (0.46 mL, 3.01 mmol), 2-ethyl-2-oxazoline (24.32 mL, 240.94 mmol) and 2-methoxycarbonylethyl-2-oxazoline (8.31 mL, 60.24 mmol) in dry MeCN (43 mL, 4 M), terminated by the addition of 2-ethanolamine (1.82 mL, 30.12 mmol) afforded the desired polymer **P2a** (36.22 g, 2.93 mmol). **^{1}H NMR** [400 MHz, δ (ppm), $CDCl_3$]: 3.65 (br, 3 H, 5-CH_3), 3.65–3.35 (br, 8 H, 1-CH_2), 2.75–2.50 (br, 4 H, 4-CH_2), 2.50–2.20 (br, 2 H, 2-CH_2), 0.95–1.15 (br, 3 H, 3-CH_3). Experimentally determined comonomer ratio: *m*/*n* 80:20. **SEC**: M_n 9.6 kDa, $Đ$ 1.17. **MALDI-TOF MS**: M_n 9.8 kDa. **Yield**: 97%.

P(EtOx$_{70}$-MestOx$_{30}$) P3a



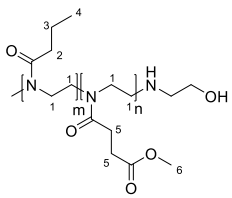
According to the general procedure described in the experimental section, the reaction of a solution of methyl tosylate (0.68 mL, 4.52 mmol), 2-ethyl-2-oxazoline (31.92 mL, 316.23 mmol) and 2-methoxycarbonylethyl-2-oxazoline (18.68 mL, 135.53 mmol) in dry MeCN (63 mL, 4 M), terminated by the addition of 2-ethanolamine (2.72 mL, 45.18 mmol) afforded the desired polymer **P3a** (55.78 g, 4.40 mmol). **^{1}H NMR** [400 MHz, δ (ppm), $CDCl_3$]: 3.65 (br, 3 H, 5-CH_3), 3.70–3.35 (br, 8 H, 1-CH_2), 2.70–2.50 (br, 4 H, 4-CH_2), 2.50–2.20 (br, 2 H, 2-CH_2), 0.95–1.15 (br, 3 H, 3-CH_3). Experimentally determined comonomer ratio: *m*/*n* 70:30. **SEC**: M_n 10.6 kDa, *Đ* 1.11. **MALDI-TOF MS**: M_n 10.6 kDa. **Yield**: 98%.

P(PropOx$_{90}$-MestOx$_{10}$) P4a



According to the general procedure described in the experimental section, the reaction of a solution of methyl tosylate (0.57 mL, 3.76 mmol), *n*-propyl-2-oxazoline (37.59 mL, 338.82 mmol) and 2-methoxycarbonylethyl-2-oxazoline (5.19 mL, 37.65 mmol) in dry MeCN (52 mL, 4 M), terminated by the addition of 2-ethanolamine (2.72 mL, 37.65 mmol) afforded the desired polymer **P4a** (42.08 g, 3.55 mmol). **^{1}H NMR** [400 MHz, δ (ppm), $CDCl_3$]: 3.65 (br, 3 H, 6-CH_3), 3.65–3.35 (br, 8 H, 1-CH_2), 2.70–2.50 (br, 4 H, 5-CH_2), 2.40–2.10 (br, 2 H, 2-CH_2), 1.70–1.50 (br, 2 H, 3-CH_2), 1.00–0.80 (br, 3 H, 4-CH_3). Experimentally determined comonomer ratio: *m*/*n* 90:10. **SEC**: M_n 10.2 kDa, *Đ* 1.08. **MALDI-TOF MS**: M_n 10.4 kDa. **Yield**: 94%.

P(PropOx$_{70}$-MestOx$_{30}$) P5a

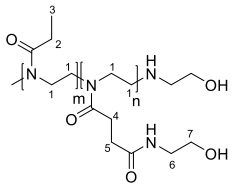


According to the general procedure described in the experimental section, the reaction of a solution of methyl tosylate (0.57 mL, 3.76 mmol), *n*-propyl-2-oxazoline (29.24 mL, 263.53 mmol) and 2-methoxycarbonylethyl-2-oxazoline (15.57 mL, 112.94 mmol) in dry MeCN (50 mL, 4 M),

terminated by the addition of 2-ethanolamine (2.72 mL, 37.65 mmol) afforded the desired polymer **P5a** (46.44 g, 3.62 mmol). **^{1}H NMR** [400 MHz, δ (ppm), $CDCl_3$]: 3.65 (br, 3 H, 6-CH_3), 3.65–3.30 (br, 8 H, 1-CH_2), 2.65–2.45 (br, 4 H, 5-CH_2), 2.40–2.10 (br, 2 H, 2-CH_2), 1.70–1.50 (br, 2 H, 3-CH_2), 1.00–0.80 (br, 3 H, 4-CH_3). Experimentally determined comonomer ratio: *m*/*n* 70:30. **SEC**: M_n 10.1 kDa, $Đ$ 1.12. **MALDI-TOF MS**: M_n 10.9 kDa. **Yield**: 96%.

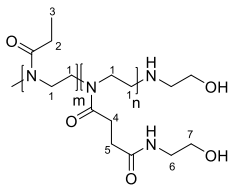
Amidation reaction: Synthesis of Hydroxyl-Functionalized Polymers P1b–P5b

P(EtOx$_{90}$-OH$_{10}$) P1b



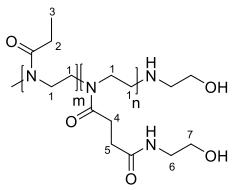
According to the general procedure described in the experimental section, the reaction of **P1a** (43 g, 4.07 mmol) with 2-aminoethanol (8.60 mL, 142.40 mmol) afforded the desired polymer **P1b** (38.05 g, 3.50 mmol). **^{1}H NMR** [400 MHz, δ (ppm), D_2O]: 3.65 (br, 2 H, 7-CH_2), 3.75–3.45 (br, 8 H, 1-CH_2), 3.35–3.25 (br, 2 H, 6-CH_2), 2.75–2.60 (br, 2 H, 5-CH_2), 2.60–2.40 (br, 2 H, 4-CH_2), 2.45–2.25 (br, 2 H, 2-CH_2), 1.00–0.80 (br, 3 H, 3-CH_3). Experimentally determined comonomer ratio: *m*/*n* 90:10. **MALDI-TOF MS**: M_n 10.2 kDa. **Yield**: 86%.

P(EtOx$_{80}$-OH$_{20}$) P2b



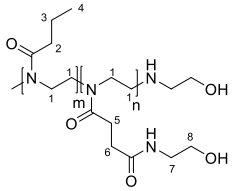
According to the general procedure described in the experimental section, the reaction of **P2a** (34 g, 3.05 mmol) with 2-aminoethanol (12.88 mL, 213.47 mmol) afforded the desired polymer **P2b** (31.46 g, 2.64 mmol). **^{1}H NMR** [400 MHz, δ (ppm), D_2O]: 3.65 (br, 2 H, 7-CH_2), 3.75–3.45 (br, 8 H, 1-CH_2), 3.35–3.25 (br, 2 H, 6-CH_2), 2.80–2.60 (br, 2 H, 5-CH_2), 2.60–2.50 (br, 2 H, 4-CH_2), 2.50–2.25 (br, 2 H, 2-CH_2), 1.00–0.80 (br, 3 H, 3-CH_3). Experimentally determined comonomer ratio: *m*/*n* 80:20. **MALDI-TOF MS**: M_n 9.9 kDa. **Yield**: 87%.

P(EtOx$_{70}$-OH$_{30}$) P3b



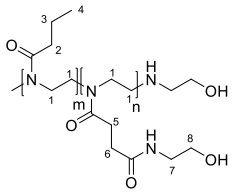
According to the general procedure described in the experimental section, the reaction of **P3a** (51 g, 4.35 mmol) with 2-aminoethanol (27.55 mL, 456.55 mmol) afforded the desired polymer **P3b** (43.98 g, 3.49 mmol). **^{1}H NMR** [400 MHz, δ (ppm), D_2O]: 3.66 (br, 2 H, 7-CH_2), 3.75–3.45 (br, 8 H, 1-CH_2), 3.35–3.25 (br, 2 H, 6-CH_2), 2.75–2.60 (br, 2 H, 5-CH_2), 2.60–2.50 (br, 2 H, 4-CH_2), 2.45–2.25 (br, 2 H, 2-CH_2), 1.00–0.80 (br, 3 H, 3-CH_3). Experimentally determined comonomer ratio: *m*/*n* 70:30. **MALDI-TOF MS**: M_n 11.1 kDa. **Yield**: 80%.

P(PropOx$_{90}$-OH$_{10}$) P4b



According to the general procedure described in the experimental section, the reaction of **P4a** (42 g, 3.55 mmol) with 2-aminoethanol (21.43 mL, 354.99 mmol) afforded the desired polymer **P4b** (34.49 g, 2.80 mmol). **^{1}H NMR** [400 MHz, δ (ppm), D_2O]: 3.65 (br, 2 H, 8-CH_2), 3.75–3.45 (br, 8 H, 1-CH_2), 3.35–3.30 (br, 2 H, 7-CH_2), 2.75–2.60 (br, 2 H, 6-CH_2), 2.60–2.50 (br, 2 H, 5-CH_2), 2.45–2.25 (br, 2 H, 2-CH_2), 1.65–1.50 (br, 2 H, 3-CH_2), 1.00–0.80 (br, 3 H, 4-CH_3). Experimentally determined comonomer ratio: *m*/*n* 90:10. **MALDI-TOF MS**: M_n 10.7 kDa. **Yield**: 79%.

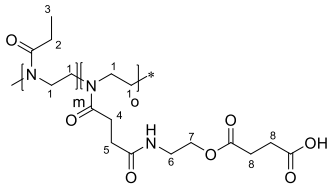
P(PropOx$_{70}$-OH$_{30}$) P5b



According to the general procedure described in the experimental section, the reaction of **P5a** (46 g, 3.62 mmol) with 2-aminoethanol (22.93 mL, 379.97 mmol) afforded the desired polymer **P5b** (37.13 g, 2.72 mmol). **^{1}H NMR** [400 MHz, δ (ppm), D_2O]: 3.65 (br, 2 H, 8-CH_2), 3.75–3.45 (br, 8 H, 1-CH_2), 3.35–3.20 (br, 2 H, 7-CH_2), 2.70–2.60 (br, 2 H, 6-CH_2), 2.60–2.50 (br, 2 H, 5-CH_2), 2.40–2.15 (br, 2 H, 2-CH_2), 1.65–1.45 (br, 2 H, 3-CH_2), 0.9–0.70 (br, 3 H, 4-CH_3). Experimentally determined comonomer ratio: *m*/*n* 70:30. **MALDI-TOF MS**: M_n 11.6 kDa. **Yield**: 75%.

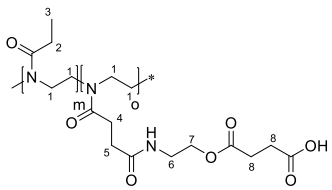
Succinic Anhydride Coupling: Synthesis of Carboxylic Acid-Functionalized Polymers P1c–P9c

P(EtOx$_{90}$-COOH$_{10}$) P1c



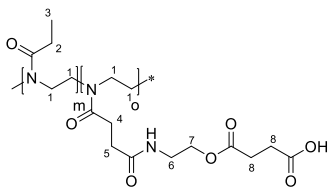
According to the general procedure described in the experimental section, the reaction of a solution of **P1b** (38 g, 3.50 mmol), 4-dimethylamino pyridine (0.86 g, 7.00 mmol) and succinic anhydride (4.20 g, 41.98 mmol) in CH_2Cl_2/MeCN 9:1 (27 mL, 2 M) afforded the desired polymer **P1c** (36.01 g, 3.03 mmol). **^{1}H NMR** [400 MHz, δ (ppm), D_2O]: 4.25–4.15 (br, 2 H, 7-C*H*$_2$), 3.70–3.40 (br, 10 H, 1-C*H*$_2$ + 6-C*H*$_2$), 2.75–2.60 (br, 6 H, 5-C*H*$_2$ + 8-C*H*$_2$), 2.60–2.45 (br, 2 H, 4-C*H*$_2$), 2.40–2.25 (br, 2 H, 2-C*H*$_2$), 1.10–0.95 (br, 3 H, 3-C*H*$_3$). Experimentally determined comonomer ratio: *m*/*o* 90:10. **MALDI-TOF MS**: M_n 11.1 kDa. **Yield**: 87%.

P(EtOx$_{80}$-COOH$_{20}$) P2c



According to the general procedure described in the experimental section, the reaction of a solution of **P2b** (31 g, 2.64 mmol), 4-dimethylamino pyridine (1.29 g, 10.56 mmol) and succinic anhydride (6.34 g, 63.38 mmol) in CH_2Cl_2/MeCN 9:1 (38 mL, 2 M) afforded the desired polymer **P2c** (29.74 g, 2.18 mmol). **^{1}H NMR** [400 MHz, δ (ppm), D_2O]: 4.25–4.15 (br, 2 H, 7-C*H*$_2$), 3.70–3.40 (br, 10 H, 1-C*H*$_2$ + 6-C*H*$_2$), 2.75–2.55 (br, 6 H, 5-C*H*$_2$ + 8-C*H*$_2$), 2.50–2.45 (br, 2 H, 4-C*H*$_2$), 2.40–2.25 (br, 2 H, 2-C*H*$_2$), 1.10–0.95 (br, 3 H, 3-C*H*$_3$). Experimentally determined comonomer ratio: *m*/*o* 80:20. **MALDI-TOF MS**: M_n 11.2 kDa. **Yield**: 83%.

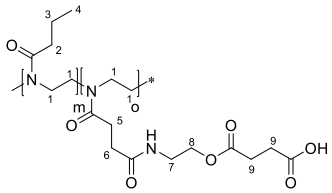
P(EtOx$_{70}$-COOH$_{30}$) P3c



According to the general procedure described in the experimental section, the reaction of a solution of **P3b** (10 g, 0.79 mmol), 4-dimethylamino pyridine (0.58 g, 4.76 mmol) and succinic

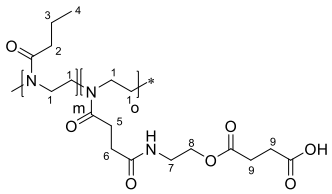
anhydride (2.86 g, 28.54 mmol) in CH_2Cl_2/MeCN 9:1 (17 mL, 2 M) afforded the desired polymer **P3c** (9.85 g, 0.64 mmol). **^{1}H NMR** [400 MHz, δ (ppm), D_2O]: 4.25–4.15 (br, 2 H, 7-CH_2), 3.80–3.45 (br, 10 H, 1-CH_2 + 6-CH_2), 2.75–2.60 (br, 6 H, 5-CH_2 + 8-CH_2), 2.60–2.45 (br, 2 H, 4-CH_2), 2.40–2.25 (br, 2 H, 2-CH_2), 1.15–1.00 (br, 3 H, 3-CH_3). Experimentally determined comonomer ratio: *m*/*o* 70:30. **MALDI-TOF MS**: M_n 13.5 kDa. **Yield**: 81%.

P(PropOx$_{90}$-COOH$_{10}$) P4c



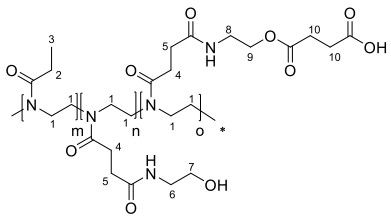
According to the general procedure described in the experimental section, the reaction of a solution of **P4b** (28 g, 2.31 mmol), 4-dimethylamino pyridine (0.56 g, 4.62 mmol) and succinic anhydride (2.67 g, 26.7 mmol) in CH_2Cl_2/MeCN 9:1 (17 mL, 2 M) afforded the desired polymer **P4c** (21.20 g, 1.61 mmol). **^{1}H NMR** [400 MHz, δ (ppm), D_2O]: 4.10–4.00 (br, 2 H, 8-CH_2), 3.60–3.20 (br, 10 H, 1-CH_2 + 7-CH_2), 2.65–2.50 (br, 6 H, 6-CH_2 + 9-CH_2), 2.50–2.30 (br, 2 H, 5-CH_2), 2.30–2.10 (br, 2 H, 2-CH_2), 1.55–1.40 (br, 2 H, 3-CH_2), 1.00–0.80 (br, 3 H, 4-CH_3). Experimentally determined comonomer ratio: *m*/*o* 90:10. **MALDI-TOF MS**: M_n 11.5 kDa. **Yield**: 70%.

P(PropOx$_{70}$-COOH$_{30}$) P5c



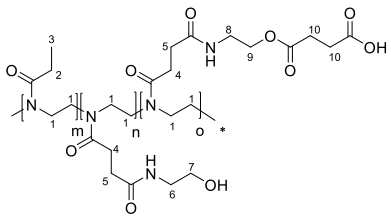
According to the general procedure described in the experimental section, the reaction of a solution of **P5b** (34 g, 2.50 mmol), 4-dimethylamino pyridine (1.83 g, 15.01 mmol) and succinic anhydride (9.01 g, 90.03 mmol) in CH_2Cl_2/MeCN 9:1 (54 mL, 2 M) afforded the desired polymer **P5c** (39.91 g, 2.41 mmol). **^{1}H NMR** [400 MHz, δ (ppm), D_2O]: 4.05–3.85 (br, 2 H, 8-CH_2), 3.55–3.10 (br, 10 H, 1-CH_2 + 7-CH_2), 2.65–2.50 (br, 6 H, 6-CH_2 + 9-CH_2), 2.50–2.10 (br, 4 H, 2-CH_2 + 5-CH_2), 1.55–1.35 (br, 2 H, 3-CH_2), 0.90–0.75 (br, 3 H, 4-CH_3). Experimentally determined comonomer ratio: *m*/*o* 70:30. **MALDI-TOF MS**: M_n 12.1 kDa. **Yield**: 96%.

P(EtOx$_{70}$-OH$_{20}$-COOH$_{10}$) P6c



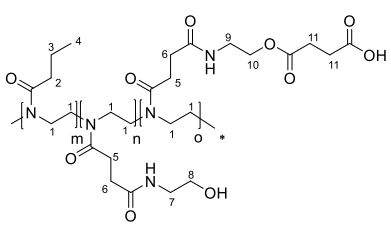
According to the general procedure described in the experimental section, the reaction of a solution of **P3b** (15 g, 1.19 mmol), 4-dimethylamino pyridine (0.29 g, 2.38 mmol) and succinic anhydride (1.43 g, 14.27 mmol) in CH_2Cl_2/MeCN 9:1 (9 mL, 2 M) afforded the desired polymer **P6c** (12.28 g, 0.90 mmol). **^{1}H NMR** [400 MHz, δ (ppm), D_2O]: 4.25–4.15 (br, 2 H, 9-C*H*$_2$), 3.80–3.45 (br, 16 H, 1-C*H*$_2$ + 7-C*H*$_2$ + 8-C*H*$_2$), 3.35–3.25 (br, 2 H, 6-C*H*$_2$), 2.75–2.60 (br, 8 H, 5-C*H*$_2$ + 10-C*H*$_2$), 2.60–2.45 (br, 4 H, 4-C*H*$_2$), 2.45–2.25 (br, 2 H, 2-C*H*$_2$), 1.15–1.00 (br, 3 H, 3-C*H*$_3$). Experimentally determined comonomer ratio: *m*/*n*/*o* 70:21:9. **MALDI-TOF MS**: M_n 12.2 kDa. **Yield**: 76%.

P(EtOx$_{70}$-OH$_{10}$-COOH$_{20}$) P7c



According to the general procedure described in the experimental section, the reaction of a solution of **P3b** (15 g, 1.19 mmol), 4-dimethylamino pyridine (0.58 g, 4.76 mmol) and succinic anhydride (2.86 g, 28.54 mmol) in CH_2Cl_2/MeCN 9:1 (17 mL, 2 M) afforded the desired polymer **P7c** (17.33 g, 1.19 mmol). **^{1}H NMR** [400 MHz, δ (ppm), D_2O]: 4.25–4.15 (br, 2 H, 9-C*H*$_2$), 3.80–3.45 (br, 16 H, 1-C*H*$_2$ + 7-C*H*$_2$ + 8-C*H*$_2$), 3.35–3.25 (br, 2 H, 6-C*H*$_2$), 2.75–2.60 (br, 8 H, 5-C*H*$_2$ + 10-C*H*$_2$), 2.60–2.45 (br, 4 H, 4-C*H*$_2$), 2.40–2.25 (br, 2 H, 2-C*H*$_2$), 1.15–1.00 (br, 3 H, 3-C*H*$_3$). Experimentally determined comonomer ratio: *m*/*n*/*o* 70:12:18. **MALDI-TOF MS**: M_n 12.5 kDa. **Yield**: 94%.

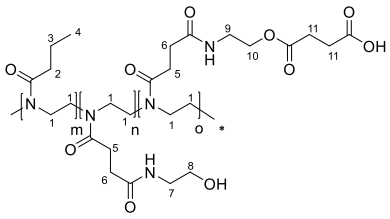
P(PropOx$_{70}$-OH$_{20}$-COOH$_{10}$) P8c



According to the general procedure described in the experimental section, the reaction of a solution of **P5b** (13 g, 0.96 mmol), 4-dimethylamino pyridine (0.23 g, 1.91 mmol) and succinic anhydride (1.15 g, 11.47 mmol) in

CH_2Cl_2/MeCN 9:1 (7 mL, 2 M) afforded the desired polymer **P8c** (11.62 g, 0.80 mmol). **^{1}H NMR** [400 MHz, δ (ppm), D_2O]: 4.10–3.90 (br, 2 H, 10-C*H*$_2$), 3.70–3.20 (br, 16 H, 1-C*H*$_2$ + 8-C*H*$_2$ + 9-C*H*$_2$), 3.15–3.00 (br, 2 H, 7-C*H*$_2$), 2.75–2.60 (br, 8 H, 6-C*H*$_2$ + 11-C*H*$_2$), 2.65–2.40 (br, 4 H, 5-C*H*$_2$), 2.40–2.10 (br, 2 H, 2-C*H*$_2$), 1.60–1.35 (br, 2 H, 3-C*H*$_2$), 1.00–0.70 (br, 3 H, 4-C*H*$_3$). Experimentally determined comonomer ratio: *m*/*n*/*o* 70:20:10. **MALDI-TOF MS**: M_n 11.5 kDa. **Yield**: 79%.

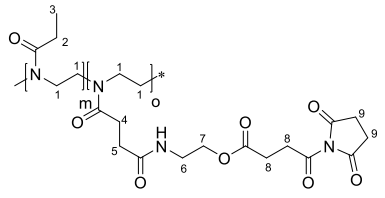
P(PropOx$_{70}$-OH$_{10}$-COOH$_{20}$) P9c



According to the general procedure described in the experimental section, the reaction of a solution of **P5b** (38 g, 2.80 mmol), 4-dimethylamino pyridine (1.37 g, 11.18 mmol) and succinic anhydride (6.71 g, 67.08 mmol) in CH_2Cl_2/MeCN 9:1 (41 mL, 2 M) afforded the desired polymer **P9c** (41.10 g, 2.64 mmol). **^{1}H NMR** [400 MHz, δ (ppm), D_2O]: 4.10–3.90 (br, 2 H, 10-C*H*$_2$), 3.70–3.20 (br, 16 H, 1-C*H*$_2$ + 8-C*H*$_2$ + 9-C*H*$_2$), 3.15–3.00 (br, 2 H, 7-C*H*$_2$), 2.65–2.60 (br, 8 H, 6-C*H*$_2$ + 11-C*H*$_2$), 2.65–2.40 (br, 4 H, 5-C*H*$_2$), 2.40–2.10 (br, 2 H, 2-C*H*$_2$), 1.60–1.35 (br, 2 H, 3-C*H*$_2$), 1.00–0.70 (br, 3 H, 4-C*H*$_3$). Experimentally determined comonomer ratio: *m*/*n*/*o* 70:10:20. **MALDI-TOF MS**: M_n 12.8 kDa. **Yield**: 94%.

Carbodiimide Reaction: Synthesis of *N*-Hydroxysuccinimide-Functionalized Polymers P1d–P9d

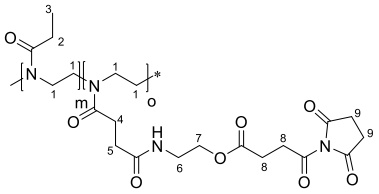
P(EtOx$_{90}$-NHS$_{10}$) P1d



According to the general procedure described in the experimental section, the reaction of a solution of **P1c** (6 g, 0.51 mmol), *N*-hydroxysuccinimide (0.64 g, 5.57 mmol) and *N,N'*-diisopropylcarbodiimide (0.94 mL, 6.07 mmol) in CH_2Cl_2/MeCN 9:1 (60 mL, 0.2 M)

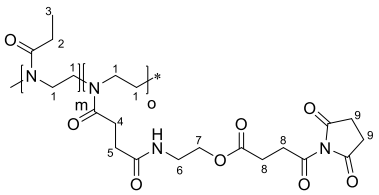
afforded the desired polymer **P1d** (5.65 g, 0.44 mmol). **^{1}H NMR** [400 MHz, δ (ppm), DMSO-d_6]: 4.00–3.90 (br, 2 H, 7-CH_2), 3.50–3.10 (br, 10 H, 1-CH_2 + 6-CH_2), 2.90–2.85 (br, 2 H, 8-CH_2), 2.75–2.70 (br, 4 H, 9-CH_2), 2.65–2.60 (br, 2 H, 8-CH_2), 2.60–2.40 (br, 2 H, 5-CH_2), 2.30–2.10 (br, 4 H, 2-CH_2 + 4-CH_2), 0.85–0.70 (br, 3 H, 3-CH_3). Experimentally determined comonomer ratio: *m*/*o* 90:10. **SEC**: M_n 11.7 kDa, $Đ$ 1.25. **MALDI-TOF MS**: M_n 11.5 kDa. **Yield**: 87%.

P(EtOx$_{80}$-NHS$_{20}$) P2d



According to the general procedure described in the experimental section, the reaction of a solution of **P2c** (33 g, 2.40 mmol), *N*-hydroxysuccinimide (6.08 g, 52.87 mmol) and *N,N'*-diisopropylcarbodiimide (8.93 mL, 57.67 mmol) in CH_2Cl_2/MeCN 9:1 (556 mL, 0.2 M) afforded the desired polymer **P2d** (35.63 g, 2.27 mmol). **^{1}H NMR** [400 MHz, δ (ppm), DMSO-d_6]: 4.00–3.90 (br, 2 H, 7-CH_2), 3.50–3.10 (br, 10 H, 1-CH_2 + 6-CH_2), 2.90–2.85 (br, 2 H, 8-CH_2), 2.75–2.70 (br, 4 H, 9-CH_2), 2.65–2.60 (br, 2 H, 8-CH_2), 2.60–2.40 (br, 2 H, 5-CH_2), 2.30–2.10 (br, 4 H, 2-CH_2 + 4-CH_2), 0.85–0.70 (br, 3 H, 3-CH_3). Experimentally determined comonomer ratio: *m*/*o* 80:20. **SEC**: M_n 12.6 kDa, $Đ$ 1.21. **MALDI-TOF MS**: M_n 13.0 kDa. **Yield**: 95%.

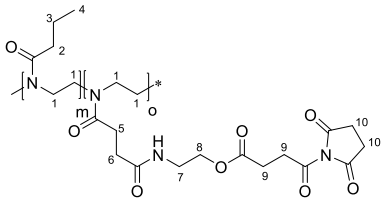
P(EtOx$_{70}$-NHS$_{30}$) P3d



According to the general procedure described in the experimental section, the reaction of a solution of **P3c** (61 g, 3.91 mmol), *N*-hydroxysuccinimide (14.85 g, 129.00 mmol) and *N,N'*-diisopropylcarbodiimide (21.79 mL, 140.72 mmol) in CH_2Cl_2/MeCN 9:1 (1346 mL, 0.2 M) afforded the desired polymer **P3d** (57.06 g, mmol). **^{1}H NMR** [400 MHz, δ (ppm), DMSO-d_6]: 4.00–3.90 (br, 2 H, 7-CH_2), 3.50–3.10 (br, 10 H, 1-CH_2 + 6-CH_2), 2.90–2.85 (br, 2 H, 8-CH_2), 2.75–2.70 (br, 4 H, 9-CH_2), 2.65–2.60 (br, 2 H, 8-CH_2), 2.60–2.40 (br, 2 H, 5-

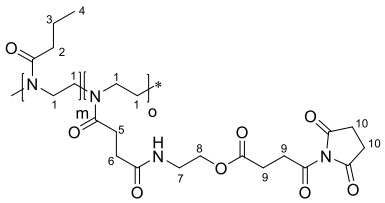
CH_2), 2.30–2.10 (br, 4 H, 2-CH_2 + 4-CH_2), 0.85–0.70 (br, 3 H, 3-CH_3). Experimentally determined comonomer ratio: *m*/*o* 70:30. **SEC**: M_n 15.6 kDa, $Đ$ 1.25. **MALDI-TOF MS**: M_n 16.9 kDa. **Yield**: 79%.

P(PropOx$_{90}$-NHS$_{10}$) P4d



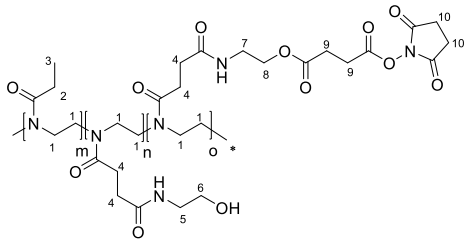
According to the general procedure described in the experimental section, the reaction of a solution of **P4c** (20 g, 1.52 mmol), *N*-hydroxysuccinimide (1.93 g, 16.76 mmol) and *N,N'*-diisopropylcarbodiimide (2.83 mL, 18.29 mmol) in CH_2Cl_2/MeCN 9:1 (180 mL, 0.2 M) afforded the desired polymer **P4d** (19.88 g, 1.41 mmol). **^{1}H NMR** [400 MHz, δ (ppm), DMSO-d_6]: 4.10–4.00 (br, 2 H, 8-CH_2), 3.50–3.30 (br, 10 H, 1-CH_2 + 7-CH_2), 2.95–2.90 (br, 2 H, 9-CH_2), 2.75–2.70 (br, 4 H, 10-CH_2), 2.70–2.65 (br, 2 H, 9-CH_2), 2.65–2.40 (br, 2 H, 6-CH_2), 2.35–2.10 (br, 4 H, 2-CH_2 + 5-CH_2), 1.60–1.40 (br, 2 H, 3-CH_2), 0.90–0.80 (br, 3 H, 4-CH_3). Experimentally determined comonomer ratio: *m*/*o* 90:10. **SEC**: M_n 12.2 kDa, $Đ$ 1.21. **MALDI-TOF MS**: M_n 12.1 kDa. **Yield**: 93%.

P(PropOx$_{70}$-NHS$_{30}$) P5d



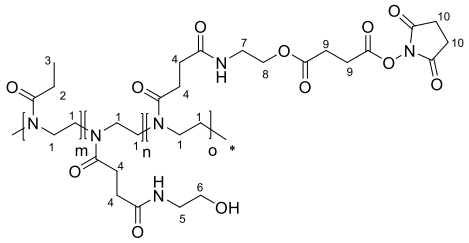
According to the general procedure described in the experimental section, the reaction of a solution of **P5c** (28 g, 1.69 mmol), *N*-hydroxysuccinimide (6.41 g, 55.71 mmol) and *N,N'*-diisopropylcarbodiimide (9.41 mL, 60.77 mmol) in CH_2Cl_2/MeCN 9:1 (581 mL, 0.2 M) afforded the desired polymer **P5d** (26.28 g, 1.35 mmol). **^{1}H NMR** [400 MHz, δ (ppm), DMSO-d_6]: 4.00–3.90 (br, 2 H, 8-CH_2), 3.50–3.10 (br, 10 H, 1-CH_2 + 7-CH_2), 2.90–2.85 (br, 2 H, 9-CH_2), 2.75–2.70 (br, 4 H, 10-CH_2), 2.65–2.60 (br, 2 H, 9-CH_2), 2.60–2.40 (br, 2 H, 6-CH_2), 2.35–2.10 (br, 4 H, 2-CH_2 + 5-CH_2), 1.65–1.40 (br, 2 H, 3-CH_2), 0.85–0.70 (br, 3 H, 4-CH_3). Experimentally determined comonomer ratio: *m*/*o* 90:10. **SEC**: M_n 15.7 kDa, $Đ$ 1.20. **MALDI-TOF MS**: M_n 13.7 kDa. **Yield**: 80%.

P(EtOx$_{70}$-OH$_{20}$-NHS$_{10}$) P6d



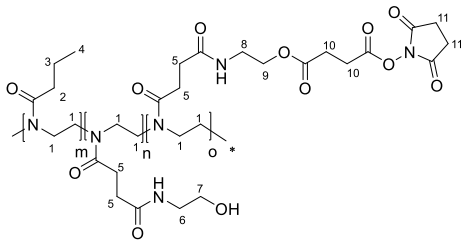
According to the general procedure described in the experimental section, the reaction of a solution of **P6c** (12 g, 0.88 mmol), *N*-hydroxysuccinimide (1.12 g, 9.70 mmol) and *N,N'*-diisopropylcarbodiimide (1.64 mL, 10.58 mmol) in CH_2Cl_2/MeCN 9:1 (104 mL, 0.2 M) afforded the desired polymer **P6d** (11.48 g, 0.79 mmol). **^{1}H NMR** [400 MHz, δ (ppm), DMSO-d_6]: 4.25–4.15 (br, 2 H, 8-CH_2), 3.75–3.40 (br, 16 H, 1-CH_2 + 6-CH_2 + 7-CH_2), 3.35–3.25 (br, 2 H, 5-CH_2), 3.10–3.00 (br, 2 H, 9-CH_2), 3.00–2.90 (br, 4 H, 10-CH_2), 2.90–2.80 (br, 2 H, 9-CH_2), 2.65–2.45 (br, 8 H, 4-CH_2), 2.45–2.25 (br, 2 H, 2-CH_2), 1.10–1.00 (br, 3 H, 3-CH_3). Experimentally determined comonomer ratio: *m*/*n*/*o* 70:21:9. **SEC**: M_n 12.7 kDa, *Đ* 1.25. **MALDI-TOF MS**: M_n 12.6 kDa. **Yield**: 89%.

P(EtOx$_{70}$-OH$_{10}$-NHS$_{20}$) P7d



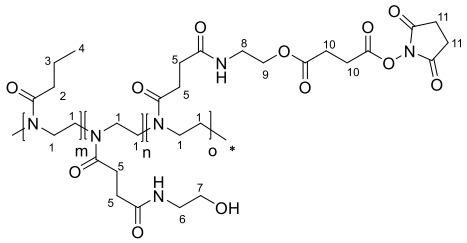
According to the general procedure described in the experimental section, the reaction of a solution of **P7c** (12 g, 0.82 mmol), *N*-hydroxysuccinimide (2.08 g, 18.07 mmol) and *N,N'*-diisopropylcarbodiimide (3.05 mL, 19.72 mmol) in CH_2Cl_2/MeCN 9:1 (190 mL, 0.2 M) afforded the desired polymer **P7d** (11.95 g, 0.72 mmol). **^{1}H NMR** [400 MHz, δ (ppm), DMSO-d_6]: 4.15–4.00 (br, 2 H, 8-CH_2), 3.75–3.40 (br, 16 H, 1-CH_2 + 6-CH_2 + 7-CH_2), 3.35–3.25 (br, 2 H, 5-CH_2), 3.05–2.95 (br, 2 H, 9-CH_2), 2.95–2.85 (br, 4 H, 10-CH_2), 2.85–2.70 (br, 2 H, 9-CH_2), 2.75–2.65 (br, 8 H, 4-CH_2), 2.40–2.10 (br, 2 H, 2-CH_2), 1.05–0.95 (br, 3 H, 3-CH_3). Experimentally determined comonomer ratio: *m*/*n*/*o* 70:12:18. **SEC**: M_n 14.7 kDa, *Đ* 1.25. **MALDI-TOF MS**: M_n 14.4 kDa. **Yield**: 88%.

P(PropOx$_{70}$-OH$_{20}$-NHS$_{10}$) P8d



According to the general procedure described in the experimental section, the reaction of a solution of **P8c** (20 g, 1.37 mmol), *N*-hydroxysuccinimide (1.74 g, 15.08 mmol) and *N,N'*-diisopropylcarbodiimide (2.55 mL, 16.45 mmol) in CH_2Cl_2/MeCN 9:1 (162 mL, 0.2 M) afforded the desired polymer **P8d** (17.41 g, 1.12 mmol). **^{1}H NMR** [400 MHz, δ (ppm), DMSO-d_6]: 4.15–4.00 (br, 2 H, 9-CH_2), 3.55–3.30 (br, 16 H, 1-CH_2 + 7-CH_2 + 8-CH_2), 3.30–3.20 (br, 2 H, 6-CH_2), 3.00–2.90 (br, 2 H, 10-CH_2), 2.85–2.75 (br, 4 H, 11-CH_2), 2.75–2.65 (br, 2 H, 10-CH_2), 2.65–2.45 (br, 8 H, 5-CH_2), 2.35–2.05 (br, 2 H, 2-CH_2), 1.55–1.30 (br, 2 H, 3-CH_2), 0.90–0.70 (br, 3 H, 4-CH_3). Experimentally determined comonomer ratio: *m*/*n*/*o* 70:20:10. **SEC**: M_n 12.2 kDa, $Đ$ 1.25. **MALDI-TOF MS**: M_n 12.1 kDa. **Yield**: 70%.

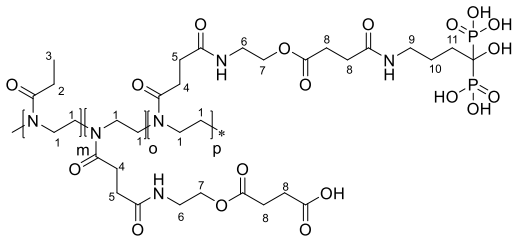
P(PropOx$_{70}$-OH$_{10}$-NHS$_{20}$) P9d



According to the general procedure described in the experimental section, the reaction of a solution of **P9c** (41 g, 2.63 mmol), *N*-hydroxysuccinimide (6.66 g, 57.86 mmol) and *N,N'*-diisopropylcarbodiimide (9.77 mL, 63.12 mmol) in CH_2Cl_2/MeCN 9:1 (608 mL, 0.2 M) afforded the desired polymer **P9d** (38.62 g, 2.20 mmol). **^{1}H NMR** [400 MHz, δ (ppm), DMSO-d_6]: 4.05–3.90 (br, 2 H, 9-CH_2), 3.55–3.30 (br, 16 H, 1-CH_2 + 7-CH_2 + 8-CH_2), 3.30–3.20 (br, 2 H, 6-CH_2), 3.05–2.95 (br, 2 H, 10-CH_2), 2.95–2.85 (br, 4 H, 11-CH_2), 2.85–2.70 (br, 2 H, 10-CH_2), 2.70–2.55 (br, 8 H, 5-CH_2), 2.35–2.05 (br, 2 H, 2-CH_2), 1.55–1.30 (br, 2 H, 3-CH_2), 0.90–0.70 (br, 3 H, 4-CH_3). Experimentally determined comonomer ratio: *m*/*n*/*o* 70:10:20. **SEC**: M_n 14.9 kDa, $Đ$ 1.21. **MALDI-TOF MS**: M_n 14.4 kDa. **Yield**: 84%.

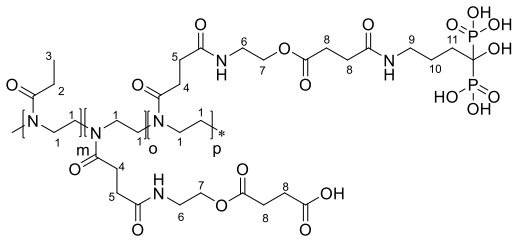
Amidation Reaction: Synthesis of Alendronate-Functionalized Polymers P1e–P13e

P(EtOx$_{90}$-Ale$_{10}$) P1e



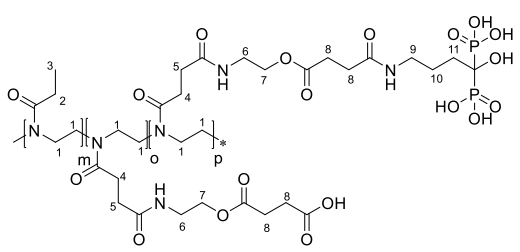
According to the general procedure described in the experimental section, the reaction of a solution of **P1d** (5.0 g, 0.39 mmol), sodium alendronate trihydrate (2.53 g, 7.79 mmol), *N*-hydroxysuccinimide (0.45 g, 3.90 mmol) and *N*-(3-dimethylaminopropyl)-*N'*-ethylcarbodiimide hydrochloride (0.75 g, 3.90 mmol) in PBS (32 mL, 0.5 M) afforded the desired polymer **P1e** (1.29 g, 0.09 mmol). **^{1}H NMR** [400 MHz, δ (ppm), D_2O]: 4.30–4.10 (br, 4 H, 7-CH_2), 3.75–3.40 (br, 16 H, 1-CH_2 + 6-CH_2), 3.30–3.20 (br, 2 H, 9-CH_2), 2.75–2.45 (br, 16 H, 4-CH_2 + 5-CH_2 + 8-CH_2), 2.45–2.20 (br, 2 H, 2-CH_2), 2.05–1.75 (br, 4 H, 10-CH_2 + 11-CH_2), 1.15–0.95 (br, 3 H, 3-CH_3). **^{31}P NMR** [400 MHz, δ (ppm), D_2O]: 18.19. Experimentally determined comonomer ratio: *m*/*o*/*p* 90:1:9. **MALDI-TOF MS**: M_n 12.0 kDa. **Yield**: 24%.

P(EtOx$_{80}$-Ale$_{20}$) P2e



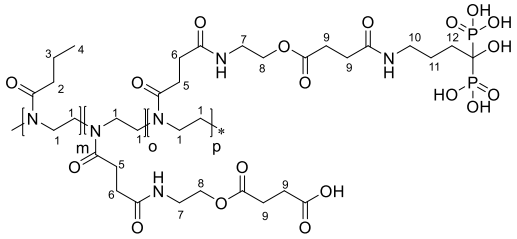
According to the general procedure described in the experimental section, the reaction of a solution of **P2d** (15 g, 0.96 mmol), sodium alendronate trihydrate (12.45 g, 38.28 mmol), *N*-hydroxysuccinimide (2.20 g, 19.14 mmol) and *N*-(3-dimethylaminopropyl)-*N'*-ethylcarbodiimide hydrochloride (3.67 g, 19.14 mmol) in PBS (155 mL, 0.5 M) afforded the desired polymer **P2e** (5.47 g, 0.30 mmol). **^{1}H NMR** [400 MHz, δ (ppm), D_2O]: 4.25–4.10 (br, 4 H, 7-CH_2), 3.80–3.35 (br, 16 H, 1-CH_2 + 6-CH_2), 3.30–3.20 (br, 2 H, 9-CH_2), 2.75–2.45 (br, 16 H, 4-CH_2 + 5-CH_2 + 8-CH_2), 2.45–2.25 (br, 2 H, 2-CH_2), 2.05–1.75 (br, 4 H, 10-CH_2 + 11-CH_2), 1.15–0.95 (br, 3 H, 3-CH_3). Experimentally determined comonomer ratio: *m*/*o*/*p* 80:1:19. **^{31}P NMR** [400 MHz, δ (ppm), D_2O]: 18.15. **MALDI-TOF MS**: M_n 15.0 kDa. **Yield**: 31%.

P(EtOx$_{70}$-Ale$_{30}$) P3e



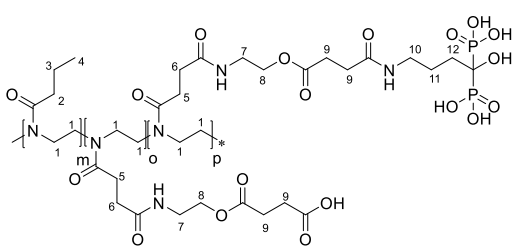
According to the general procedure described in the experimental section, the reaction of a solution of **P3d** (15 g, 0.81 mmol), sodium alendronate trihydrate (15.80 g, 48.61 mmol), *N*-hydroxysuccinimide (2.80 g, 24.31 mmol) and *N*-(3-dimethylaminopropyl)-*N'*-ethylcarbodiimide hydrochloride (4.66 g, 24.31 mmol) in PBS (66 mL, 0.5 M) afforded the desired polymer **P3e** (5.81 g, 0.26 mmol). **^{1}H NMR** [400 MHz, δ (ppm), D_2O]: 4.25–4.10 (br, 4 H, 7-CH_2), 3.80–3.30 (br, 16 H, 1-CH_2 + 6-CH_2), 3.25–3.15 (br, 2 H, 9-CH_2), 2.75–2.45 (br, 16 H, 4-CH_2 + 5-CH_2 + 8-CH_2), 2.45–2.15 (br, 2 H, 2-CH_2), 2.15–1.70 (br, 4 H, 10-CH_2 + 11-CH_2), 1.15–0.95 (br, 3 H, 3-CH_3). **^{31}P NMR** [400 MHz, δ (ppm), D_2O]: 18.25. Experimentally determined comonomer ratio: *m*/*o*/*p* 70:2:28. **MALDI-TOF MS**: M_n 19.5 kDa. **Yield**: 32%.

P(PropOx$_{90}$-Ale$_{10}$) P4e



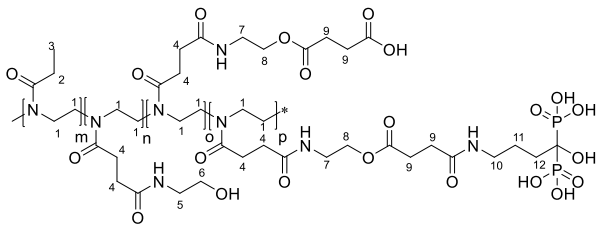
According to the general procedure described in the experimental section, the reaction of a solution of **P4d** (15 g, 1.06 mmol), sodium alendronate trihydrate (6.92 g, 21.29 mmol), *N*-hydroxysuccinimide (1.23 g, 10.64 mmol) and *N*-(3-dimethylaminopropyl)-*N'*-ethylcarbodiimide hydrochloride (2.04 g, 10.64 mmol) in PBS (87 mL, 0.5 M) afforded the desired polymer **P4e** (6.57 g, 0.43 mmol). **^{1}H NMR** [400 MHz, δ (ppm), D_2O]: 4.30–4.15 (br, 4 H, 8-CH_2), 3.80–3.30 (br, 16 H, 1-CH_2 + 7-CH_2), 3.30–3.20 (br, 2 H, 10-CH_2), 2.75–2.45 (br, 16 H, 5-CH_2 + 6-CH_2 + 9-CH_2), 2.45–2.15 (br, 2 H, 2-CH_2), 2.05–1.75 (br, 4 H, 11-CH_2 + 12-CH_2), 1.65–1.45 (br, 2 H, 3-CH_2), 1.15–0.95 (br, 3 H, 4-CH_3). **^{31}P NMR** [400 MHz, δ (ppm), D_2O]: 18.17. Experimentally determined comonomer ratio: *m*/*o*/*p* 90:1:9. **MALDI-TOF MS**: M_n 12.2 kDa. **Yield**: 40%.

P(PropOx$_{70}$-Ale$_{30}$) P5e



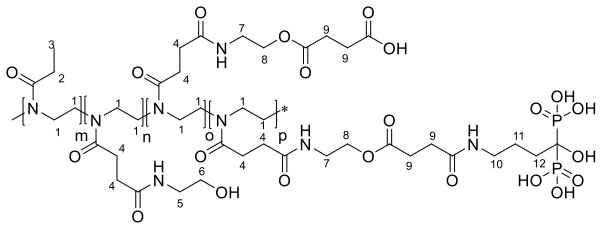
According to the general procedure described in the experimental section, the reaction of a solution of **P5d** (8.0 g, 0.41mmol), sodium alendronate trihydrate (8.00 g, 24.62 mmol), *N*-hydroxysuccinimide (1.42 g, 12.31 mmol) and *N*-(3-dimethylaminopropyl)-*N'*-ethylcarbodiimide hydrochloride (2.36 g, 12.31 mmol) in PBS (99 mL, 0.5 M) afforded the desired polymer **P5e** (2.93 g, 0.13 mmol). **^{1}H NMR** [400 MHz, δ (ppm), D_2O]: 4.30–4.15 (br, 4 H, 8-CH_2), 3.80–3.30 (br, 16 H, 1-CH_2 + 7-CH_2), 3.20–3.10 (br, 2 H, 10-CH_2), 2.75–2.45 (br, 16 H, 5-CH_2 + 6-CH_2 + 9-CH_2), 2.45–2.15 (br, 2 H, 2-CH_2), 2.05–1.75 (br, 4 H, 11-CH_2 + 12-CH_2), 1.65–1.45 (br, 2 H, 3-CH_2), 1.00–0.85 (br, 3 H, 4-CH_3). **^{31}P NMR** [400 MHz, δ (ppm), D_2O]: 18.15. Experimentally determined comonomer ratio: *m*/*o*/*p* 70:3:27. **MALDI-TOF MS**: M_n 17.5 kDa. **Yield**: 31%.

P(EtOx$_{70}$-OH$_{20}$-Ale$_{10}$) P6e



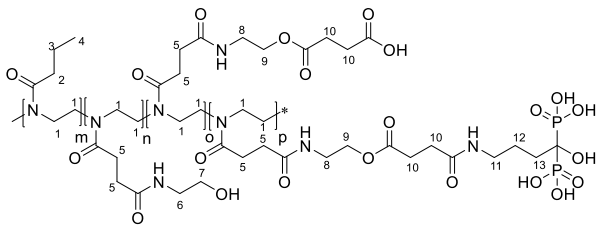
According to the general procedure described in the experimental section, the reaction of a solution of **P6d** (12 g, 0.83 mmol), sodium alendronate trihydrate (4.88 g, 15.02 mmol), *N*-hydroxysuccinimide (0.86 g, 7.51 mmol) and *N*-(3-dimethylaminopropyl)-*N'*-ethylcarbodiimide hydrochloride (1.44 g, 7.51 mmol) in PBS (62 mL, 0.5 M) afforded the desired polymer **P6e** (3.41 g, 0.22 mmol). **^{1}H NMR** [400 MHz, δ (ppm), D_2O]: 4.30–4.10 (br, 4 H, 8-CH_2), 3.80–3.40 (br, 22 H, 1-CH_2 + 6-CH_2 + 7-CH_2), 3.40–3.30 (br, 2 H, 5-CH_2), 3.30–3.20 (br, 2 H, 10-CH_2), 2.75–2.15 (br, 22 H, 2-CH_2 + 4-CH_2 + 9-CH_2), 2.05–1.75 (br, 4 H, 11-CH_2 + 12-CH_2), 1.15–0.95 (br, 3 H, 3-CH_3). **^{31}P NMR** [400 MHz, δ (ppm), D_2O]: 18.15. Experimentally determined comonomer ratio: *m*/*n*/*o*/*p* 70:21:1:8. **MALDI-TOF MS**: M_n 12.6 kDa. **Yield**: 26%.

P(EtOx$_{70}$-OH$_{10}$-Ale$_{20}$) P7e



According to the general procedure described in the experimental section, the reaction of a solution of **P7d** (12 g, 0.74 mmol), sodium alendronate trihydrate (8.69 g, 6.74 mmol), *N*-hydroxysuccinimide (1.54 g, 13.37 mmol) and *N*-(3-dimethylaminopropyl)-*N'*-ethylcarbodiimide hydrochloride (2.56 g, 13.37 mmol) in PBS (108 mL, 0.5 M) afforded the desired polymer **P7e** (4.15 g, 0.23 mmol). **^{1}H NMR** [400 MHz, δ (ppm), D_2O]: 4.30–4.10 (br, 4 H, 8-CH_2), 3.80–3.40 (br, 22 H, 1-CH_2 + 6-CH_2 + 7-CH_2), 3.40–3.30 (br, 2 H, 5-CH_2), 3.30–3.20 (br, 2 H, 10-CH_2), 2.75–2.15 (br, 22 H, 2-CH_2 + 4-CH_2 + 9-CH_2), 2.05–1.75 (br, 4 H, 11-CH_2 + 12-CH_2), 1.15–0.95 (br, 3 H, 3-CH_3). **^{31}P NMR** [400 MHz, δ (ppm), D_2O]: 18.25. Experimentally determined comonomer ratio: *m*/*n*/*o*/*p* 70:12:2:16. **MALDI-TOF MS**: M_n 14.6 kDa. **Yield**: 30%.

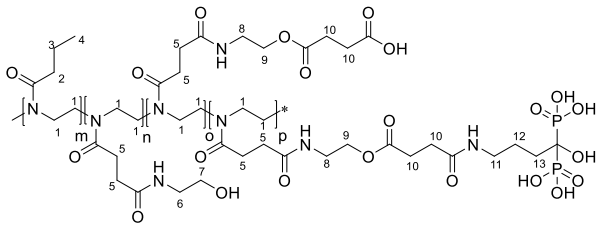
P(PropOx$_{70}$-OH$_{20}$-Ale$_{10}$) P8e



According to the general procedure described in the experimental section, the reaction of a solution of **P8d** (7.0 g, 0.45 mmol), sodium alendronate trihydrate (2.93 g, 9.00 mmol), *N*-hydroxysuccinimide (0.52 g, 4.50 mmol) and *N*-(3-dimethylaminopropyl)-*N'*-ethylcarbodiimide hydrochloride (0.86 g, 4.50 mmol) in PBS (37 mL, 0.5 M) afforded the desired polymer **P8e** (2.71 g, 0.16 mmol). **^{1}H NMR** [400 MHz, δ (ppm), D_2O]: 4.30–4.10 (br, 4 H, 9-CH_2), 3.80–3.40 (br, 22 H, 1-CH_2 + 7-CH_2 + 8-CH_2), 3.40–3.30 (br, 2 H, 6-CH_2), 3.30–3.20 (br, 2 H, 11-CH_2), 2.75–2.15 (br, 22 H, 2-CH_2 + 5-CH_2 + 10-CH_2), 2.05–1.75 (br, 4 H, 12-CH_2 + 13-CH_2), 1.65–1.45 (br, 2 H, 3-CH_2), 1.15–0.85 (br, 3 H, 4-CH_3). **^{31}P NMR** [400

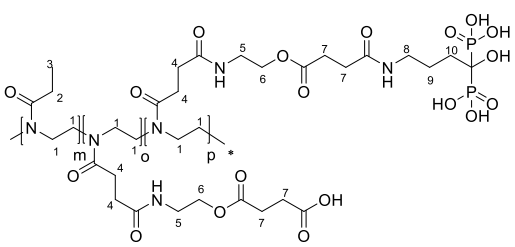
MHz, δ (ppm), D_2O]: 18.20. Experimentally determined comonomer ratio: *m*/*n*/*o*/*p* 70:20:1:9. **MALDI-TOF MS**: M_n 12.5 kDa. **Yield**: 36%.

P(PropOx$_{70}$-OH$_{10}$-Ale$_{20}$) P9e



According to the general procedure described in the experimental section, the reaction of a solution of **P9d** (12.5 g, 0.62 mmol), sodium alendronate trihydrate (12.05 g, 37.07 mmol), *N*-hydroxysuccinimide (2.13 g, 18.54 mmol) and *N*-(3-dimethylaminopropyl)-*N'*-ethylcarbodiimide hydrochloride (3.55 g, 18.54 mmol) in PBS (150 mL, 0.5 M) afforded the desired polymer **P9e** (4.82 g, 0.22 mmol). **^{1}H NMR** [400 MHz, δ (ppm), D_2O]: 4.25–4.10 (br, 4 H, 9-CH_2), 3.80–3.40 (br, 22 H, 1-CH_2 + 7-CH_2 + 8-CH_2), 3.35–3.30 (br, 2 H, 6-CH_2), 3.25–3.15 (br, 2 H, 11-CH_2), 2.75–2.20 (br, 22 H, 2-CH_2 + 5-CH_2 + 10-CH_2), 2.05–1.75 (br, 4 H, 12-CH_2 + 13-CH_2), 1.65–1.45 (br, 2 H, 3-CH_2), 1.00–0.85 (br, 3 H, 4-CH_3). **^{31}P NMR** [400 MHz, δ (ppm), D_2O]: 18.12. Experimentally determined comonomer ratio: *m*/*n*/*o*/*p* 70:10:3:17. **MALDI-TOF MS**: M_n 17.9 kDa. **Yield**: 35%.

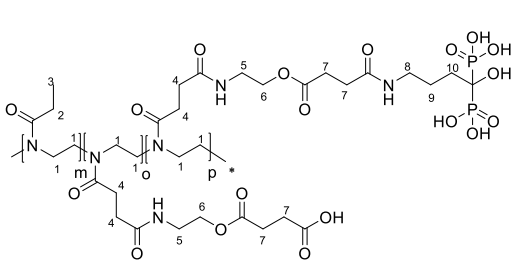
P(EtOx$_{70}$-COOH$_{20}$-Ale$_{10}$) P10e



According to the general procedure described in the experimental section, the reaction of a solution of **P3d** (15 g, 0.81 mmol), sodium alendronate trihydrate (10.54 g, 32.41 mmol), *N*-hydroxysuccinimide (1.86 g, 16.20 mmol) and *N*-(3-dimethylaminopropyl)-*N'*-ethylcarbodiimide hydrochloride (1.86 g, 16.20 mmol) in PBS (131 mL, 0.5 M) afforded the desired polymer **P10e** (5.22 g, 0.28 mmol). **^{1}H NMR** [400 MHz, δ (ppm), D_2O]: 4.30–4.10 (br, 4 H, 6-CH_2), 3.80–3.40 (br, 16 H, 1-CH_2 + 5-CH_2), 3.30–3.20 (br, 2 H, 8-CH_2), 2.75–2.15 (br, 18 H, 2-CH_2 + 4-CH_2 + 7-CH_2), 2.05–1.75 (br, 4 H, 9-CH_2 + 10-CH_2), 1.15–0.95 (br, 3 H, 3-

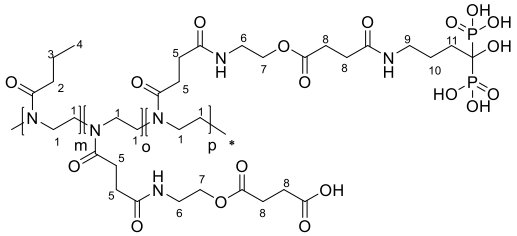
CH_3). **^{31}P NMR** [400 MHz, δ (ppm), D_2O]: 18.18. Experimentally determined comonomer ratio: *m*/*o*/*p* 70:17:13. **MALDI-TOF MS**: M_n 16.3 kDa. **Yield**: 34%.

P(EtOx$_{70}$-COOH$_{10}$-Ale$_{20}$) P11e



According to the general procedure described in the experimental section, the reaction of a solution of **P3d** (15 g, 0.81 mmol), sodium alendronate trihydrate (10.54 g, 32.41 mmol), *N*-hydroxysuccinimide (1.86 g, 16.2 mmol) and *N*-(3-dimethylaminopropyl)-*N'*-ethylcarbodiimide hydrochloride (3.11 g, 16.20 mmol) in PBS (131 mL, 0.5 M) afforded the desired polymer **P11e** (4.99 g, 0.24 mmol). **^{1}H NMR** [400 MHz, δ (ppm), D_2O]: 4.25–4.10 (br, 4 H, 6-CH_2), 3.80–3.40 (br, 16 H, 1-CH_2 + 5-CH_2), 3.25–3.15 (br, 2 H, 8-CH_2), 2.75–2.15 (br, 18 H, 2-CH_2 + 4-CH_2 + 7-CH_2), 2.05–1.70 (br, 4 H, 9-CH_2 + 10-CH_2), 1.15–0.95 (br, 3 H, 3-CH_3). **^{31}P NMR** [400 MHz, δ (ppm), D_2O]: 18.25. Experimentally determined comonomer ratio: *m*/*o*/*p* 70:10:20. **MALDI-TOF MS**: M_n 16.3 kDa. **Yield**: 30%.

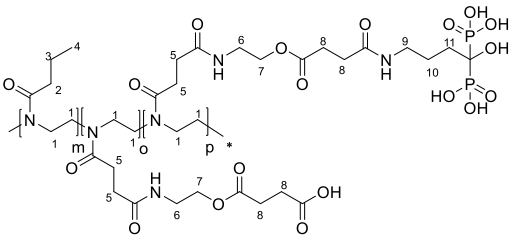
P(PropOx$_{70}$-COOH$_{20}$-Ale$_{10}$) P12e



According to the general procedure described in the experimental section, the reaction of a solution of **P5d** (5.0 g, 0.26 mmol), sodium alendronate trihydrate (1.67 g, 5.13 mmol), *N*-hydroxysuccinimide (0.30 g, 2.56 mmol) and *N*-(3-dimethylaminopropyl)-*N'*-ethylcarbodiimide hydrochloride (0.49 g, 2.56 mmol) in PBS (21 mL, 0.5 M) afforded the desired polymer **P12e** (2.17 g, 0.12 mmol). **^{1}H NMR** [400 MHz, δ (ppm), D_2O]: 4.30–4.15 (br, 4 H, 7-CH_2), 3.80–3.30 (br, 16 H, 1-CH_2 + 6-CH_2), 3.30–3.20 (br, 2 H, 9-CH_2), 2.75–2.15 (br, 18 H, 2-CH_2 + 5-CH_2 + 8-CH_2), 2.05–1.75 (br, 4 H, 10-CH_2 + 11-CH_2), 1.65–1.45 (br, 2 H, 3-

CH_3), 1.15–0.95 (br, 3 H, 4-CH_3). **^{31}P NMR** [400 MHz, δ (ppm), D_2O]: 18.00. Experimentally determined comonomer ratio: *m*/*o*/*p* 70:22:8. **MALDI-TOF MS**: M_n 14.8 kDa. **Yield**: 46%.

P(PropOx$_{70}$-COOH$_{10}$-Ale$_{20}$) P13e



According to the general procedure described in the experimental section, the reaction of a solution of **P5d** (15 g, 0.77 mmol), sodium alendronate trihydrate (30.77 g, 10.01 mmol), *N*-hydroxysuccinimide (1.77 g, 15.39 mmol) and *N*-(3-dimethylaminopropyl)-*N'*-ethylcarbodiimide hydrochloride (2.95 g, 15.39 mmol) in PBS (125 mL, 0.5 M) afforded the desired polymer **P13e** (4.33 g, 0.20 mmol). **^{1}H NMR** [400 MHz, δ (ppm), D_2O]: 44.30–4.15 (br, 4 H, 7-CH_2), 3.80–3.30 (br, 16 H, 1-CH_2 + 6-CH_2), 3.30–3.20 (br, 2 H, 9-CH_2), 2.75–2.15 (br, 18 H, 2-CH_2 + 5-CH_2 + 8-CH_2), 2.05–1.75 (br, 4 H, 10-CH_2 + 11-CH_2), 1.65–1.45 (br, 2 H, 3-CH_3), 1.05–0.80 (br, 3 H, 4-CH_3). **^{31}P NMR** [400 MHz, δ (ppm), D_2O]: 18.21. Experimentally determined comonomer ratio: *m*/*o*/*p* 70:10:20. **MALDI-TOF MS**: M_n 17.0 kDa. **Yield**: 26%.

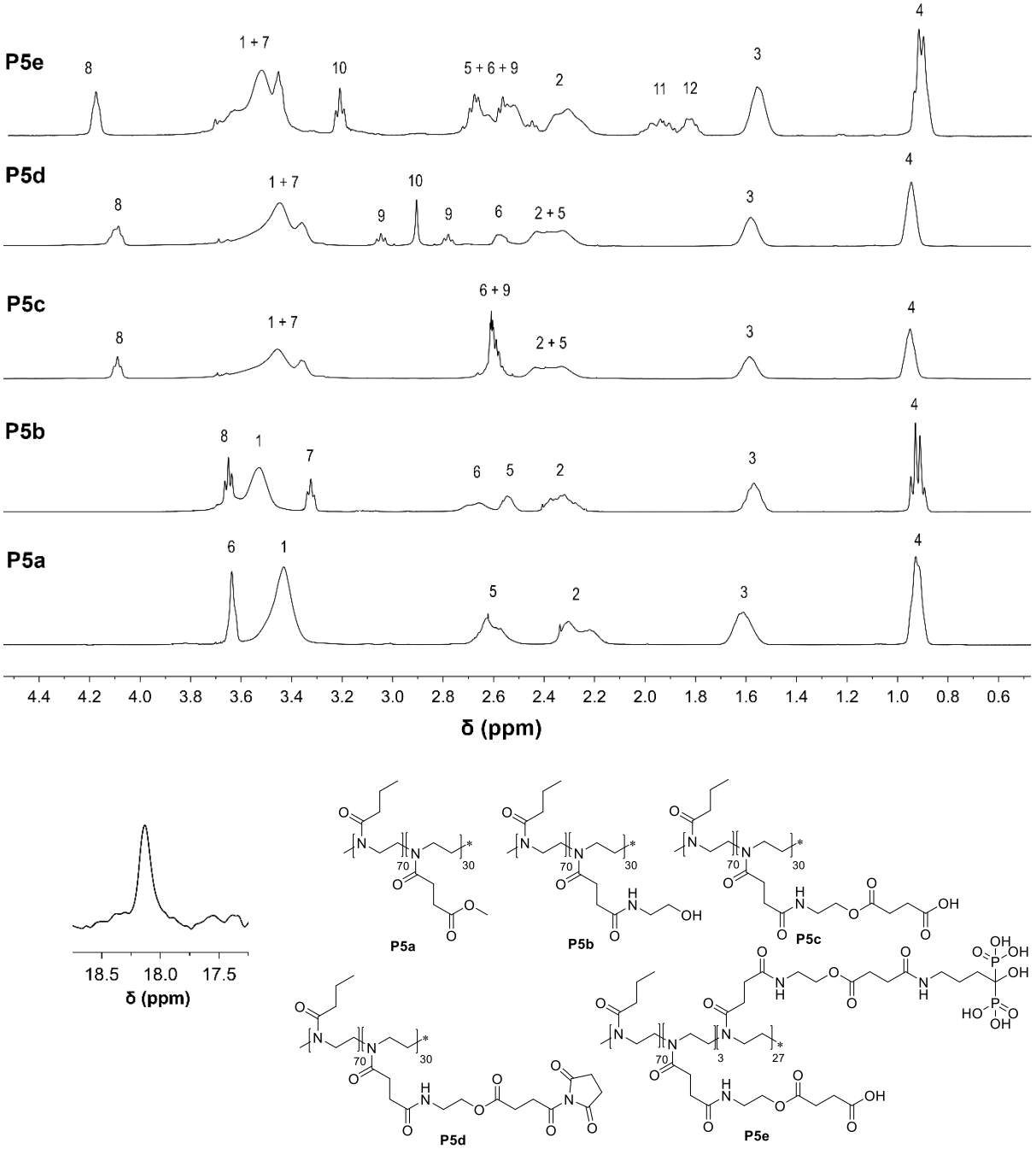


Figure S1. ^{1}H NMR spectra of P(PropOx$_{70}$-MestOx$_{30}$) **P5a**, P(PropOx$_{70}$-OH$_{30}$) **P5b**, (PropOx$_{70}$-COOH$_{30}$) **P5c**, P(PropOx$_{70}$-NHS$_{30}$) **P5d,** and P(PropOx$_{70}$-Ale$_{30}$) **P5e** and ^{31}P NMR spectrum of P(PropOx$_{70}$-Ale$_{30}$) (bottom).

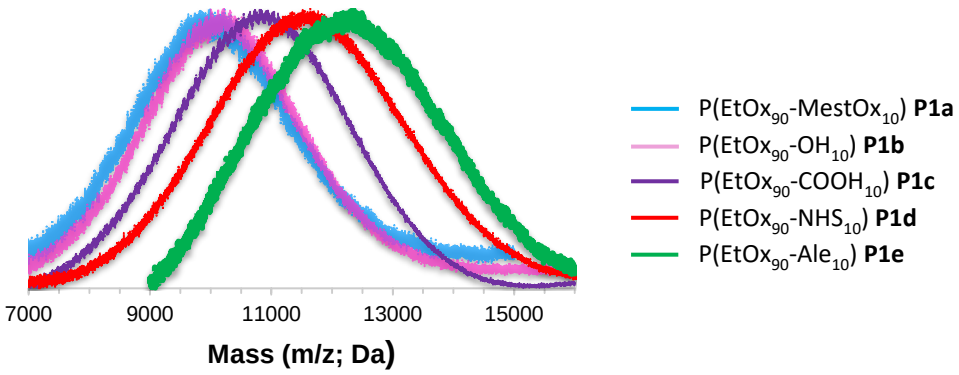


Figure S2. Overlay of normalized MALDI-TOF MS M_n spectra.

Table S1. Thermodynamic Parameters, i.e., Binding Constant K_{Ca}^{2+}, Stoichiometry N between Ca^{2+} and Polymer, Enthalpy ΔH and Entropy ΔS of the Interaction between POx-Ale and Ca^{2+} as Quantified Using ITC (n = 3).

	Polymer	Stoichiometry, N	K_{Ca}^{2+} (M^{-1})	ΔH (cal mol^{-1})	ΔS (cal deg^{-1} mol^{-1})
	Alendronate	0.5 ± 0.0	$7.8 \times 10^3 \pm 1.8 \times 10^3$	$1.3 \times 10^3 \pm 8.5 \times 10^2$	22.4 ± 2.3
P1e	P($EtOx_{90}$-Ale_{10})	6.3 ± 0.1	$1.2 \times 10^4 \pm 1.8 \times 10^3$	$2.5 \times 10^3 \pm 1.5 \times 10^2$	27.1 ± 0.3
P2e	P($EtOx_{80}$-Ale_{20})	14.3 ± 1.4	$9.1 \times 10^4 \pm 3.9 \times 10^3$	$1.2 \times 10^3 \pm 1.3 \times 10^2$	26.9 ± 0.4
P3e	P($EtOx_{70}$-Ale_{30})	25.6 ± 2.4	$2.4 \times 10^5 \pm 4.0 \times 10^3$	$1.5 \times 10^3 \pm 2.4 \times 10^2$	29.6 ± 0.8
P6e	P($EtOx_{70}$-OH_{20}-Ale_{10})	6.1 ± 0.4	$1.8 \times 10^4 \pm 6.7 \times 10^2$	$1.9 \times 10^3 \pm 1.0 \times 10^2$	25.9 ± 0.3
P7e	P($EtOx_{70}$-OH_{10}-Ale_{20})	15.1 ± 0.2	$1.2 \times 10^5 \pm 3.6 \times 10^3$	$1.1 \times 10^3 \pm 2.7 \times 10^2$	27.1 ± 0.9
P10e	P($EtOx_{70}$-$COOH_{20}$-Ale_{10})	12.3 ± 0.9	$6.7 \times 10^4 \pm 2.7 \times 10^3$	$1.8 \times 10^3 \pm 2.3 \times 10^2$	28.0 ± 0.7
P11e	P($EtOx_{70}$-$COOH_{10}$-Ale_{20})	18.7 ± 1.1	$1.6 \times 10^5 \pm 5.7 \times 10^3$	$1.8 \times 10^3 \pm 8.6 \times 10^1$	29.5 ± 0.3
P4e	P($PropOx_{90}$-Ale_{10})	7.9 ± 0.4	$3.5 \times 10^4 \pm 2.3 \times 10^3$	$2.2 \times 10^3 \pm 3.2 \times 10^2$	28.0 ± 0.9
P5e	P($PropOx_{70}$-Ale_{30})	24.2 ± 1.0	$1.6 \times 10^5 \pm 1.0 \times 10^4$	$2.0 \times 10^3 \pm 9.3 \times 10^1$	30.6 ± 0.2
P8e	P($PropOx_{70}$-OH_{20}-Ale_{10})	8.2 ± 0.5	$4.2 \times 10^4 \pm 8.7 \times 10^3$	$2.1 \times 10^3 \pm 1.1 \times 10^2$	27.0 ± 0.4
P9e	P($PropOx_{70}$-OH_{10}-Ale_{20})	13.8 ± 1.6	$1.1 \times 10^5 \pm 1.8 \times 10^4$	$2.2 \times 10^3 \pm 2.9 \times 10^2$	29.9 ± 0.9
P12e	P($PropOx_{70}$-$COOH_{20}$-Ale_{10})	9.9 ± 0.7	$2.2 \times 10^4 \pm 1.7 \times 10^3$	$2.1 \times 10^3 \pm 3.3 \times 10^2$	27.8 ± 1.0
P13e	P($PropOx_{70}$-$COOH_{10}$-Ale_{20})	17.6 ± 0.1	$10.0 \times 10^5 \pm 3.3 \times 10^3$	$2.2 \times 10^3 \pm 1.9 \times 10^2$	30.4 ± 0.4

Table S2. Visual Screening of Gelation at Different Polymer and Calcium Concentrations.

				[Ca^{2+}] (mM)		
	Polymer	**[POx] (wt %)**	**[Ale] (mM)**	**90**	**1800**	**3600**
P1e	$P(EtOx_{90}\text{-}Ale_{10})$	10	73	X	X	X
		20	146	X	X	X
		30	219	●	●	●
P2e	$P(EtOx_{80}\text{-}Ale_{20})$	10	134	X	X	X
		20	268	X	X	X
		30	402	X	●	●
P3e	$P(EtOx_{70}\text{-}Ale_{30})$	10	154	X	Δ	Δ
		20	308	X	Δ	Δ
		30	462	X	●	●
P6e	$P(EtOx_{70}\text{-}OH_{20}\text{-}Ale_{10})$	10	63	X	X	X
		20	126	X	X	X
		30	189	X	●	●
P7e	$P(EtOx_{70}\text{-}OH_{10}\text{-}Ale_{20})$	10	127	Δ	Δ	Δ
		20	254	●	●	✓
		30	381	✓	✓	✓
P10e	$P(EtOx_{70}\text{-}COOH_{20}\text{-}Ale_{10})$	10	80	X	X	X
		20	160	X	X	X
		30	240	●	●	●
P11e	$P(EtOx_{70}\text{-}COOH_{10}\text{-}Ale_{20})$	10	127	X	Δ	Δ
		20	254	X	Δ	Δ
		30	381	X	●	●

Legend: X solution; ● viscous solution; ✓ transparent gel; Δ white gel. The physical appearance of transparent ($P(EtOx_{70}\text{-}OH_{10}\text{-}Ale_{20})$) and white gels ($P(EtOx_{70}\text{-}Ale_{30})$ and $P(EtOx_{70}\text{-}COOH_{10}\text{-}Ale_{20})$) is shown in Figure S4.

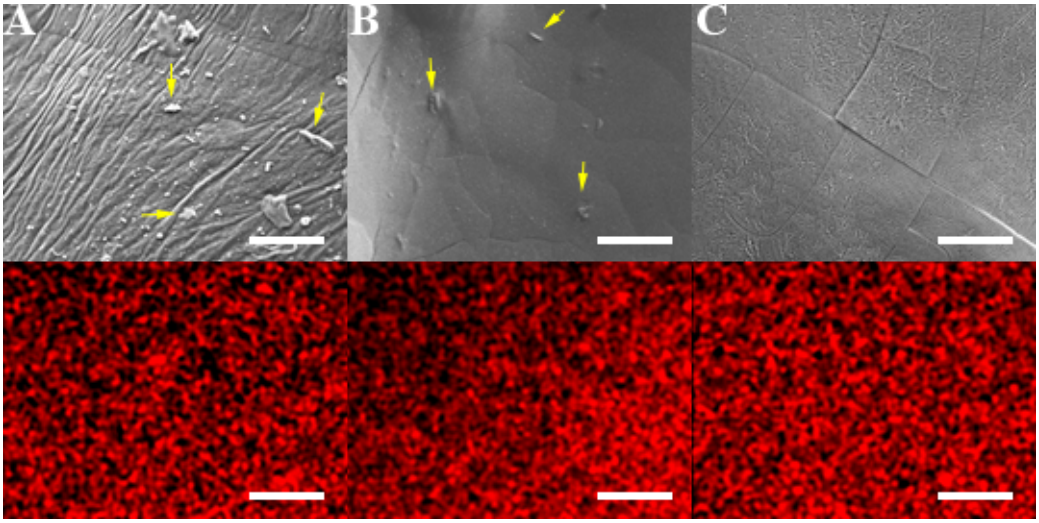


Figure S3. Scanning electron micrographs with elemental mapping for calcium of lyophilized gels containing 30 wt % of: (A) P($EtOx_{70}$-Ale_{30}), (B) P($EtOx_{70}$-$COOH_{10}$-Ale_{20}), and (C) P($EtOx_{70}$-OH_{10}-Ale_{20}) and 20 wt % of $CaCl_2$. Scale bars correspond to 50 µm. In (A) and (B), yellow arrows indicate localization of precipitates.

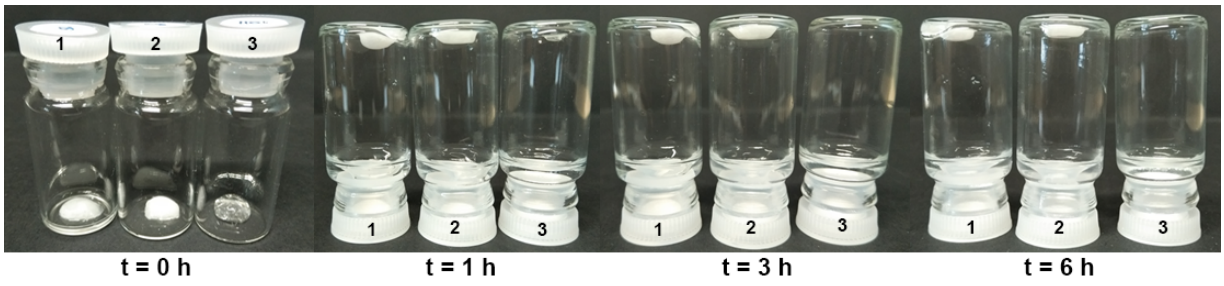


Figure S4. In vitro stability of hydrogels: **1** P($EtOx_{70}$-Ale_{30}), **2** P($EtOx_{70}$-$COOH_{10}$-Ale_{20}) and **3** P($EtOx_{70}$-OH_{10}-Ale_{20}) in 100 mM EDTA. Stable hydrogels were stuck to the bottom of the glass vials for all polymers except for polymer **3** P($EtOx_{70}$-OH_{10}-Ale_{20}) which disintegrated completely after 3 h of immersion in 100 mM EDTA.