Supporting information for:

Poly[(ethylene oxide)-*co*-(methylene ethylene oxide)]: A hydrolytically-degradable poly(ethylene oxide) platform

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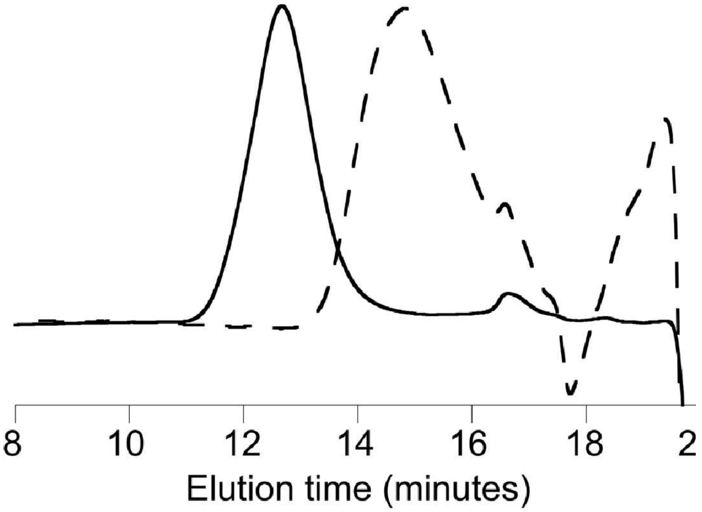

Figure S1. GPC traces of P(EO$_{91\%}$-co-MEO$_{9\%}$) (sample 4, Table 1) before (solid), and after hydrolysis (dashed) by treatment with 1% trifluoroacetic acid (aq.). A large decrease in molecular weight and an increase in polydispersity occurred after TFA treatment.

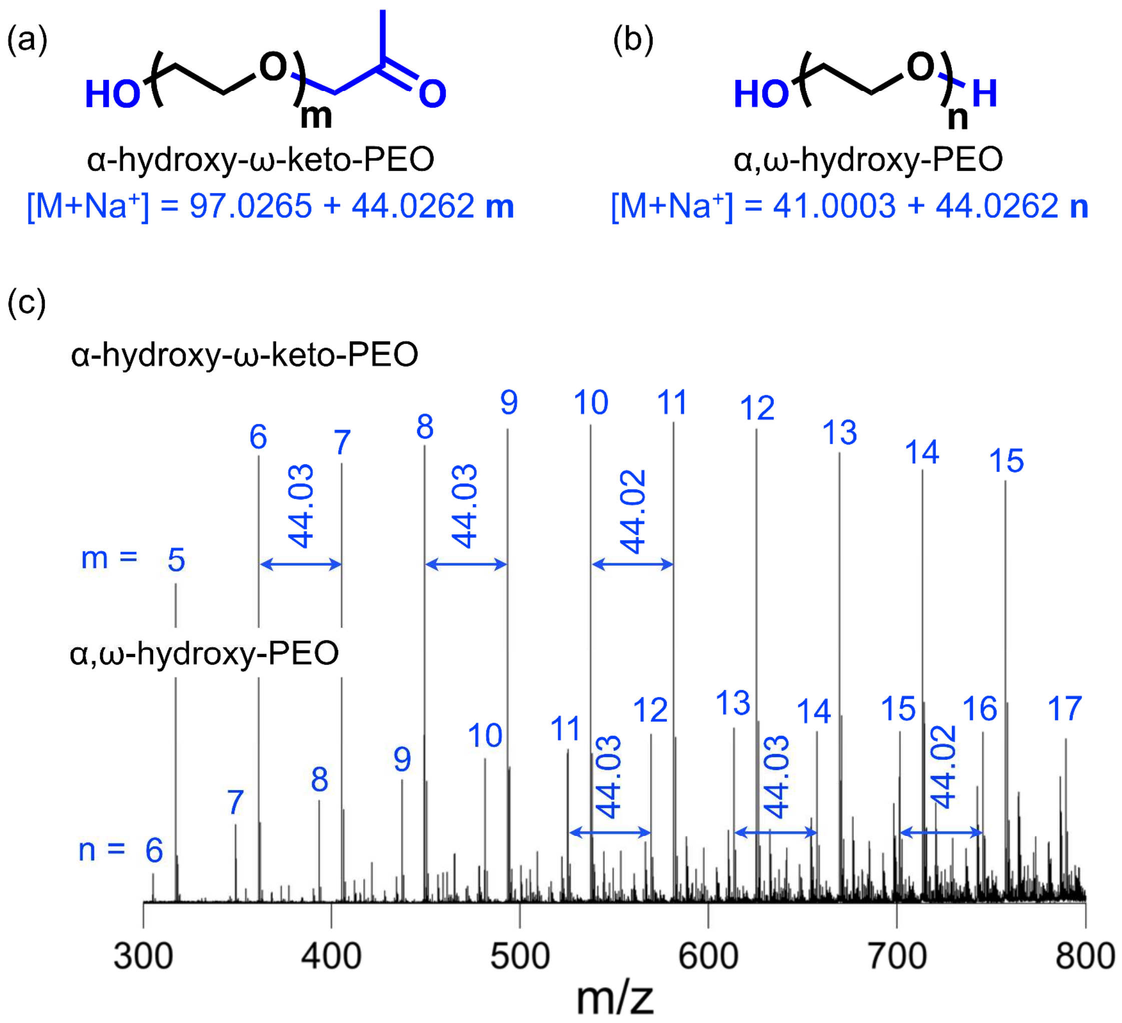

Figure S2. ESI-Mass spectrometry of the product of hydrolytic degradation of P(EO$_{98.9\%}$-co-MEO$_{1.1\%}$) (sample 2, Table 1). Two series of degradation byproducts are present: (a) α-hydroxy-ω-keto-PEO due to vinyl-ether hydrolysis, and (b) α,ω-dihyrdoxy-PEO due to hydrolysis of (a). Both series of products (a & b) are labeled in the mass spectrum (c).

Experimental Section

Characterization: ^{1}H (500 MHz) and ^{13}C (125 MHz) NMR spectroscopy were carried out on a Bruker Avance AC 500 spectrometer in $CDCl_3$. Gel permeation chromatography (GPC) was performed on a Waters Alliance HPLC system with separation provided by two Agilent PLGEL 5µm MIXED-D columns. Detection was provided by a Waters 2414 differential refractometer, and chloroform with 0.25% tetraethlyamine at room temperature was used as the mobile phase. Electrospray ionization mass spectrometry (ESI-MS) was carried out on a Micromass QTOF2 Quadrupole/Time-of-Flight tandem mass spectrometer using electrospray ionization as the source. ESI-MS was carried out at the Mass Spectrometry Facility in the Department of Chemistry and Biochemistry at the University of California-Santa Barbara.

Materials: All chemicals were used as received unless otherwise specified. Methylene Chloride (Sigma-Aldrich) was collected from a dry solvent system and used immediately thereafter. Ethylene oxide (EO) (Sigma-Aldrich) and Epichlorohydrin (ECH) (TCI-America, Inc.) were respectively degassed through several freeze-pump-thaw cycles and distilled to a flame-dried buret immediately before use. Triisobutylaluminium 1.0 mol/L solution in hexane (Sigma-Aldrich) was stored in a glove box with an argon atmosphere.

Synthesis of P(EO-co-ECH): All polymerizations were carried out on a Schlenk line in custom thick-walled glass reactors fitted with threaded ACE-threads under an argon atmosphere. The reactor was fitted with a glass buret containing dry DCM, and a flexible connector attached to a buret containing ethylene oxide at 0 °C. Tetraoctylamonium bromide (Sigma-Aldrich) was added to the reactor and dried under vacuum. The atmosphere in the reactor was cycled between vacuum and argon five times. At the last cycle the reactor was charged with an argon atmosphere above ambient pressure. DCM was added to the reactor to dissolve the tetraoctylammonium bromide initiator and the reactor was then cooled down to –60 °C. ECH was added by gas-tight syringe, and EO was added by opening the valve and tipping the buret allowing the EO to flow into the reactor. The temperature of the reaction mixture was allowed to equilibrate. The addition of triisobutylaluminium *via* gas-tight syringe initiated the polymerization, and the reaction was allowed to run overnight and slowly return to room temperature. The reaction was terminated with isopropanol. The products were washed with water (3x), precipitated out of diethyl ether, and dried *in vacuo*. ^{1}H NMR ($CDCl_3$, rt): δ 3.6–3.8 (broad, multiple overlapping).

Elimination: P(EO-co-ECH) was dissolved in 100 ml of toluene. Potassium *tert*-butoxide was added 1:1wt to the reactor and the reaction mixture was stirred overnight at room temperature. The polymer was then washed with water three times, precipitated in diethyl ether and dried *in vacuo*. ^{1}H NMR (500 MHz, $CDCl_3$, rt): δ 3.6–3.8 (broad, multiple overlapping), δ 4.19 (s, 1H per repeat unit, $–O–CH_2–C(=CH\underline{\mathbf{H}})–O–CH_2–CH_2–$), δ 4.05 (s, 1H per repeat unit, $–O–CH_2–C(=C\underline{\mathbf{H}}H)–O–CH_2–CH_2–$), δ 3.94 (s, 2H per repeat unit, $–O–C\underline{\mathbf{H_2}}–C(=CH_2)–O–CH_2–CH_2–$), δ 3.85 (t, 2H per repeat unit, $–O–CH_2–C(=CH_2)–O–C\underline{\mathbf{H_2}}–CH_2–$), δ 3.74 (t, 2H per repeat unit, $–O–CH_2–C(=CH_2)–O–CH_2–C\underline{\mathbf{H_2}}–$), δ 3.7–3.5 (broad, 2H per repeat unit, $–O–CH_2–C(=CH_2)–O–C\underline{\mathbf{H_2}}–CH_2–$).

Hydrolytic Degradation: 15 mg of P(EO-co-MEO) was dissolved in 15 mL of 100 mM phosphate buffer (pH 7.4 and pH 5.0) and the solutions were incubated at 37 °C. Aliquots were taken at 0, 6, 24, 48, and 72 hours. The aliquots were immediately frozen in N_2(l) and dried under vacuum before analysis by GPC. Molecular weights and polydispersities were recorded relative to PEO standards. For ESI-MS, $P(EO_{98.9\%}$-co-$MEO_{1.1\%})$ was dissolved in 1M HCl and stirred at room temperature for 3h. The solution was neutralized with sodium bicarbonate, and the degradation byproducts were extracted with methylene chloride. The methylene chloride was dried *in vacuo*, and the degraded P(EO-co-MEO) was submitted for analysis by ESI-MS.