SUPPORTING INFORMATION

Fast and Accurate Partial Hydrolysis of Poly(2-ethyl-2-oxazoline) into tailored Linear Polyethylenimine Copolymers

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^{1}H-NMR analysis of PEtOx 3kDa

Poly(2-ethyl-2-oxazoline) (PEtOx) 3kDa**:** ^{1}H NMR (300 MHz, $CDCl_3$, δ): 3.80 – 3.21 (4H, -CH_2-CH_2-N-), 3.1 – 2.8 (3H^{ini}, CH_3-NCOCH$_2$CH$_3$), 2.60 – 2.13 (2H; -NCOCH_2-), 1.23 – 0.95 (3H; -NCOCH$_2$CH_3).

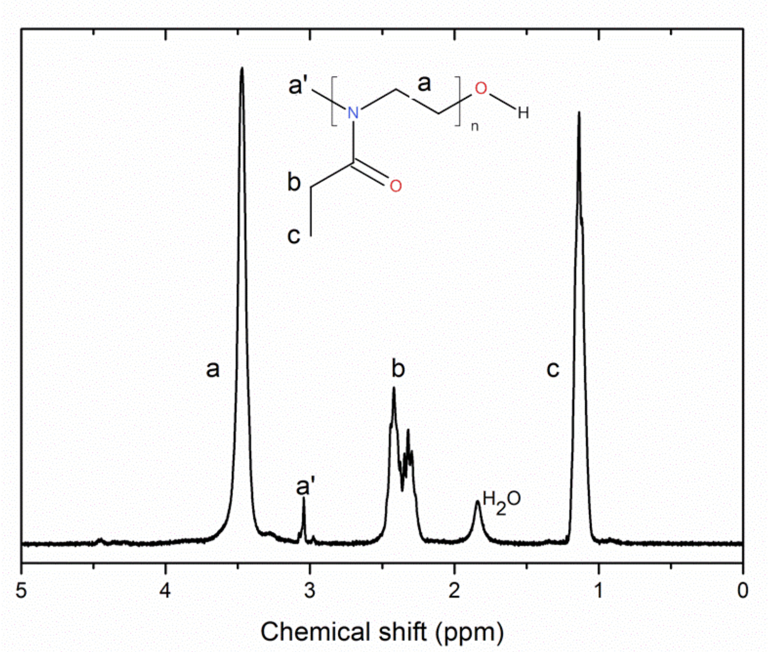

Figure S1. ^{1}H NMR spectrum of poly(2-ethyl-2-oxazoline) 3 kDa in $CDCl_3$.

^{1}H-NMR analysis of PEtOx-*co*-PEI

Poly[(2-ethyl-2-oxazoline)-*co*-ethyleneimine] *(*PEtOx$_{n-x}$-*co*-PEI$_m$*)*: ^{1}H NMR (300 MHz, CD_3OD, δ): PEtOx$_n$, + hydrolysis products: 3.80 – 3.30 (4H, -CH_2-CH_2-N-), 3.00 – 2.65 (4H, -NH-CH_2-CH_2-), 2.65 – 2.25 (2H; -

NCOCH_2-), 2.25 – 2.00 (CH_3CH_2COOH), 1.25 – 0.85 (3H, -$NCOCH_2CH_3$, 3H, CH_3CH_2COOH).

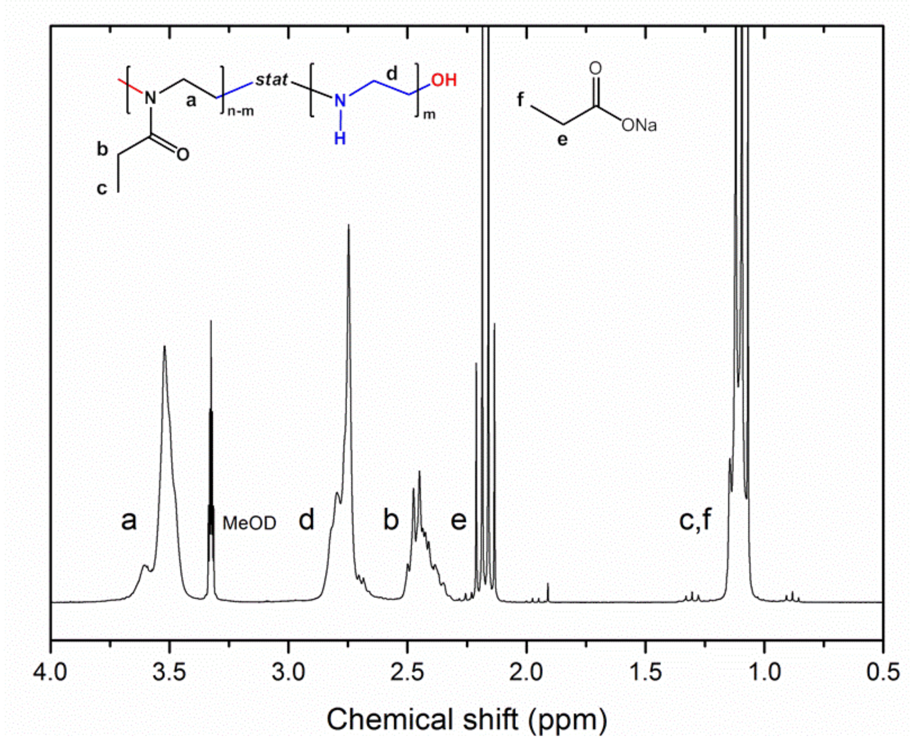

Figure S2. ^{1}H NMR spectrum of partially hydrolysed poly(2-ethyl-2-oxazoline) 3 kDa in CD_3OD. Conditions: 140ºC, 20 min. reaction time (54% hydrolysis conversion).

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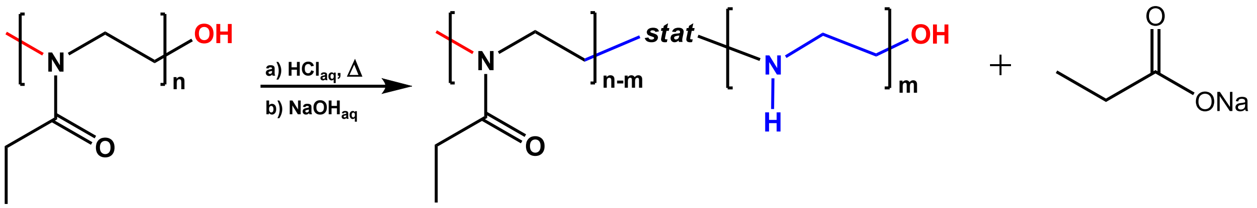
Hydrolysis kinetics of poly(2-ethyl-2-oxazoline) 3kDa under 1M HCl concentration



Scheme S1. Scheme for the hydrolysis of PEtOx.

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The following figures display the evolution of the ^{1}H-NMR spectra with the hydrolysis time. As can be seen, at 140 ºC the hydrolysis occurs progressively while at 220 ºC, most of the PEtOx signals disappear during the first minutes of reaction.

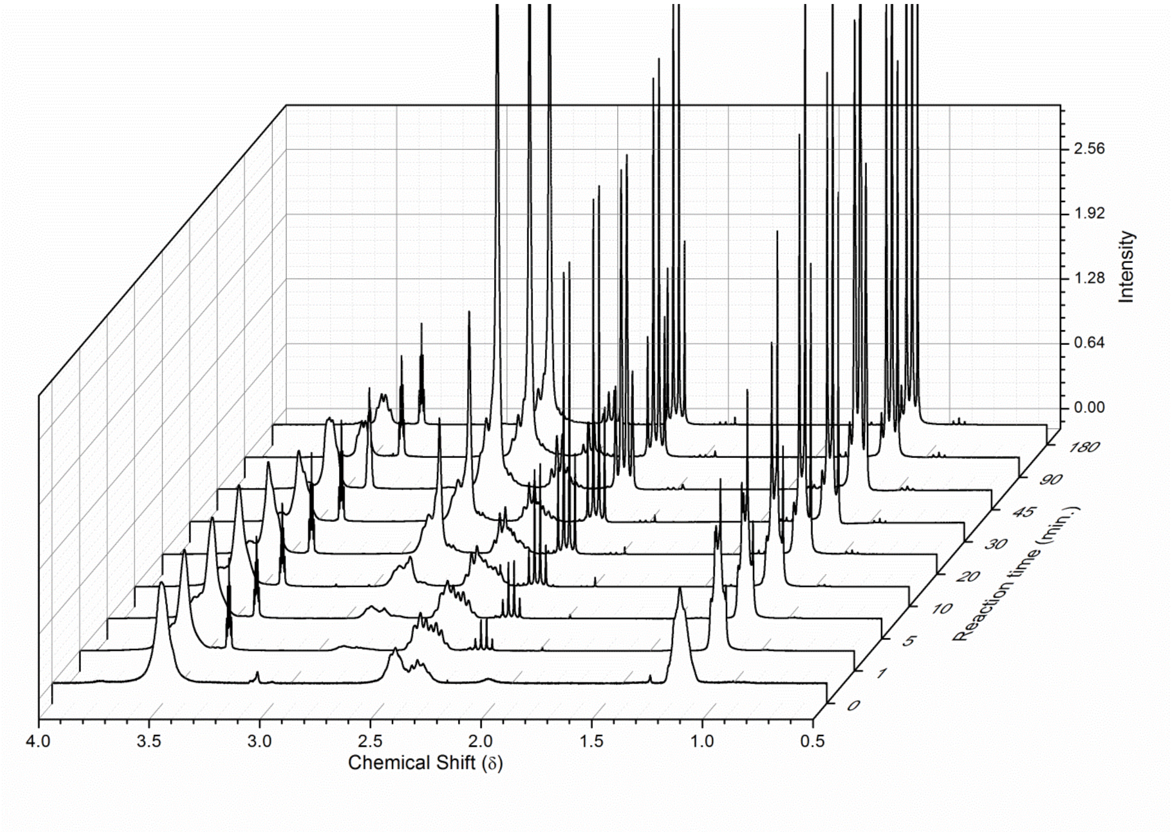

Figure S3. Series of ^{1}H-NMR spectra in CD_3OD corresponding to the hydrolysis of PEtOx 3kDa in 1M $HCl_{(aq)}$ at 140 ºC. [A] = 0.48M. The spectra were normalized with the signal corresponding to deuterated methanol.

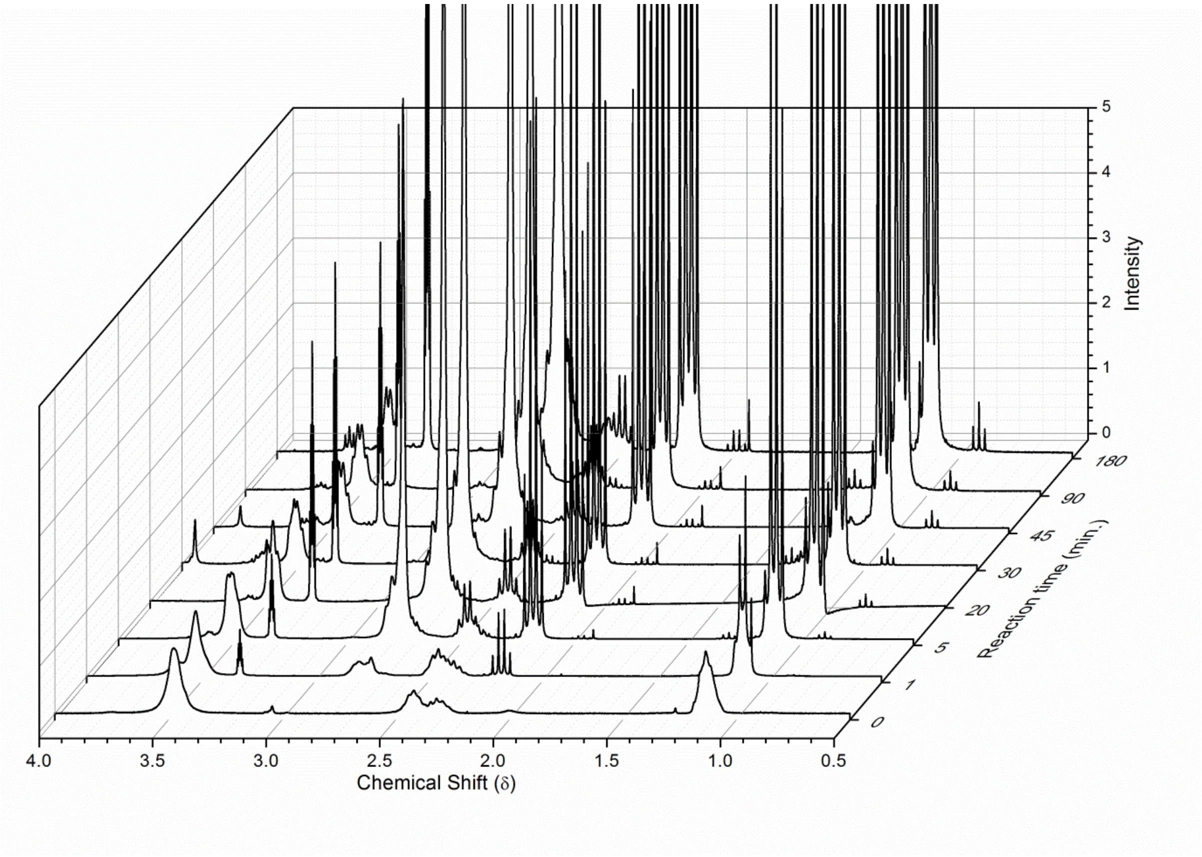

Figure S4. Series of ^{1}H-NMR spectra in CD_3OD corresponding to the hydrolysis of PEtOx 3kDa in 1M $HCl_{(aq)}$ at 180 ºC. [A] = 0.48M. The spectra were normalized with the signal corresponding to the PEtOx backbone. As can be seen, the signals corresponding to PEI and propionic acid already dominate the spectrum after only 5 min. reaction time indicating a large degree of hydrolysis.

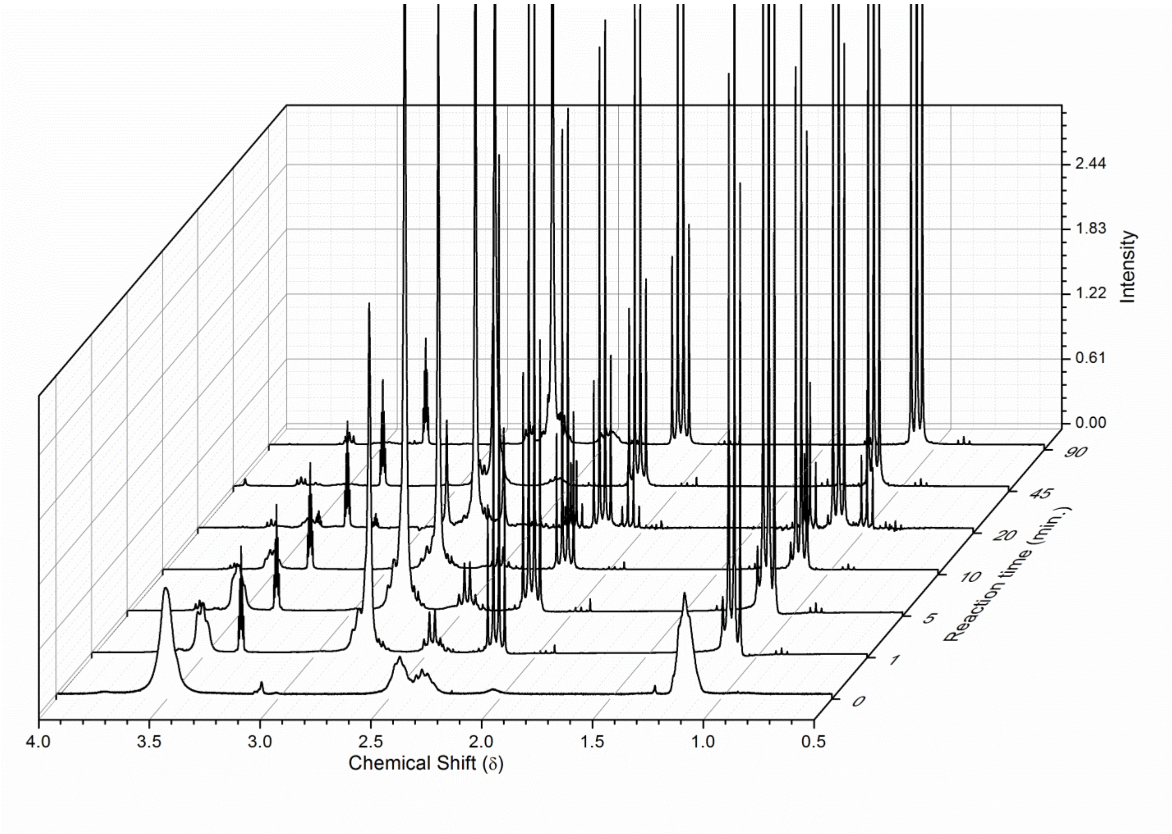

Figure S5. Series of ^{1}H-NMR spectra in CD_3OD corresponding to the hydrolysis of PEtOx 3kDa in 1M $HCl_{aq.}$ at 220 ºC. [A] = 0.48M. The spectra were normalized with the signal corresponding to deuterated methanol.

Size Exclusion Chromatography (SEC) in hexafluoroisopropanol (HFIP) to assess polymer integrity upon hydrolysis (PEtOx 3kDa)

Freeze-dried hydrolysis samples were dissolved in HFIP under sonication, filtered (0.45µm) and injected in the chromatograph.

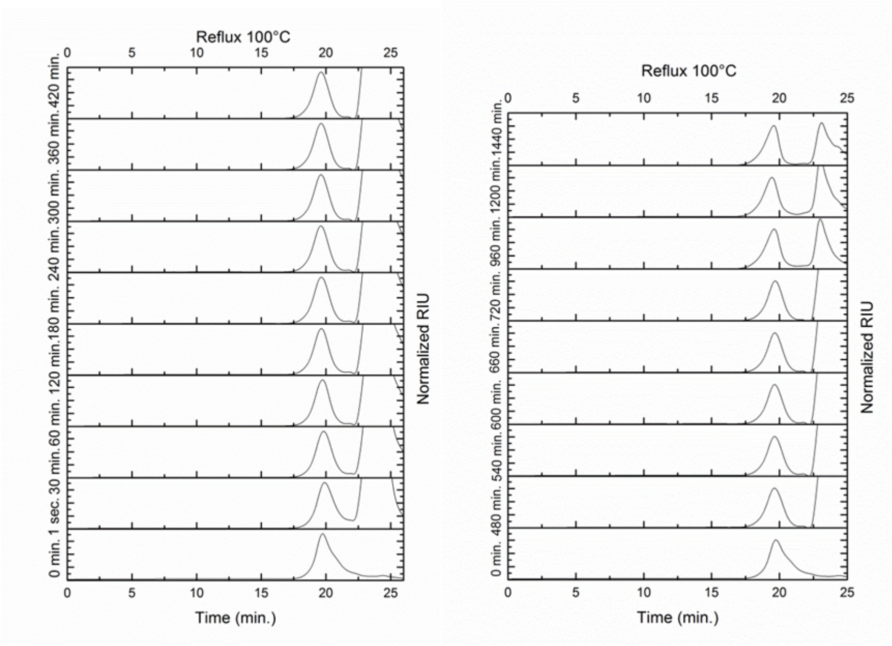

Figure S6. Stack plots containing the SEC traces for the hydrolysis of PEtOx 3kDa after different times under reflux conditions (normalized RI versus time).

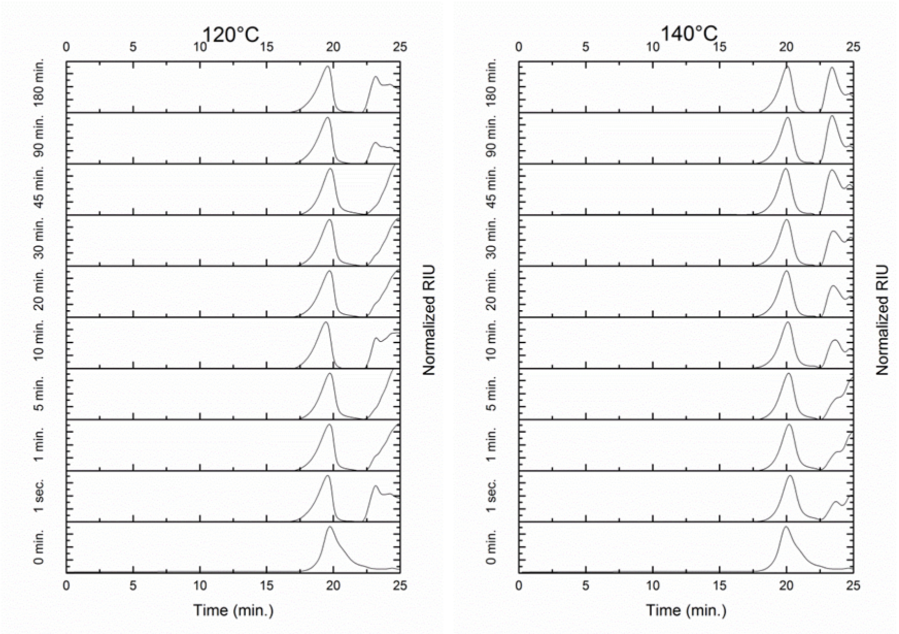

Figure S7. Stack plots containing the SEC traces for the hydrolysis of PEtOx 3kDa after different times at 120ºC and 140 ºC (normalized RI versus time).

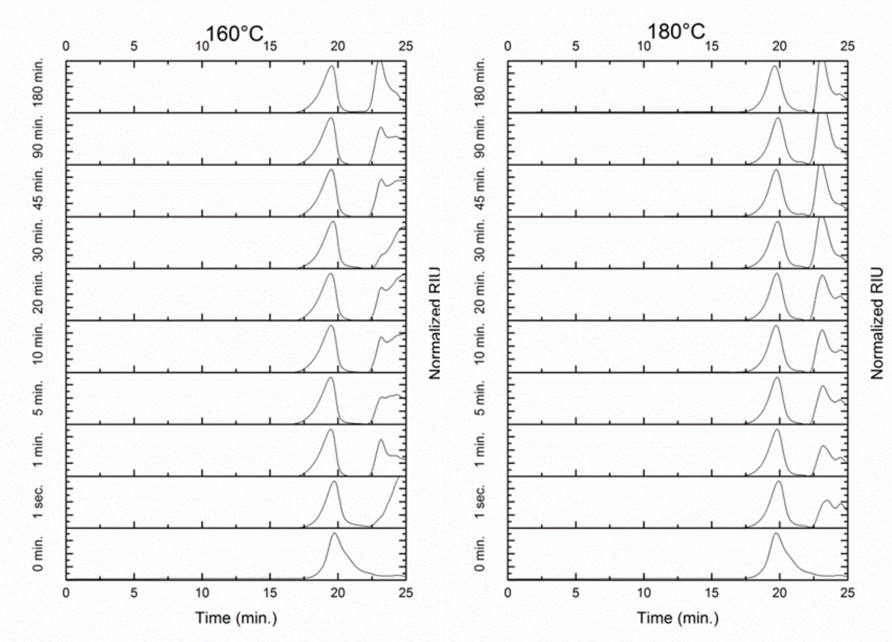

Figure S8. Stack plots containing the SEC traces for the hydrolysis of PEtOx 3kDa after different times at 160ºC and 180 ºC (normalized RI versus time).

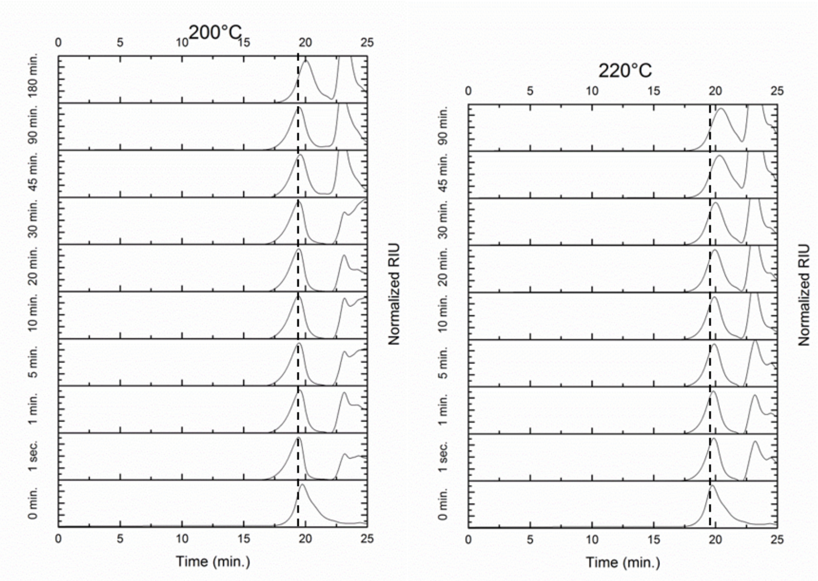

Figure S9. Stack plots containing the SEC traces for the hydrolysis of PEtOx 3kDa after different times at 200ºC and 220 ºC (normalized RI versus time). As can be seen, the elution time decreases beyond 90 min. reaction time at 200 ºC, and after 5 min. at 220 ºC. The strong tailing towards low molecular weight featured by the SEC traces increases over time, and indicates degradation of the polymer into oligomers (dotted line inserted to guide the eye).

Hydrolysis of poly(2-ethyl-2-oxazoline) 3kDa at 180 ºC under various HCl concentrations

The HFIP-SEC traces corresponding to the polymers obtained after 180 minutes of reaction time at different $HCl_{aq.}$ concentrations are depicted in **Figure S10**. As can be seen, the integrity of the obtained poly[(2-ethyl-2-oxazoline)-*co*-(ethylene imine)] copolymers is maintained. Increasing content of PEI leads to an increase in the copolymer hydrodynamic volume, and consequently a reduction of the retention time is observed.

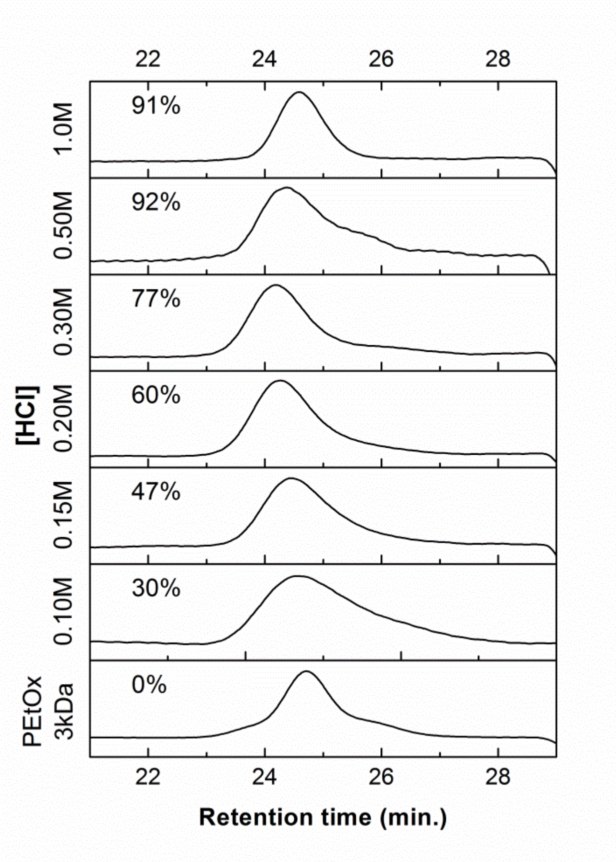

Figure S10. Stack plot containing the SEC traces for the hydrolysis of PEtOx 3kDa at 180ºC after 300 minutes under different $HCl_{(aq)}$ concentrations (normalized RI versus time). The correspondent degree of hydrolysis is shown in each graph. The retention time increases with the degree of hydrolysis, since PEI has a larger hydrodynamic volume than PEtOx. The sample with 1.0M HCl concentration was obtained after only 180 minutes of reaction time.

Kinetics investigations for the Hydrolysis of poly(2-ethyl-2-oxazoline) (PEtOx) 50kDa

The hydrolysis protocol, characterization and data analysis were homologous to the hydrolysis of PEtOx 3kDa. The results are in line with the results obtained for the hydrolysis of PEtOx 3kDa, thus demonstrating that molecular weight has no influence on the hydrolysis kinetics and the found polymer degradation at high temperatures. Therefore, the results reported in this article are applicable to PEtOx regardless of its length.

However, it should be noted that high molecular weight commercial PEtOx comprises two main different distributions, with different sensitivity towards hydrolysis (*vide infra*).

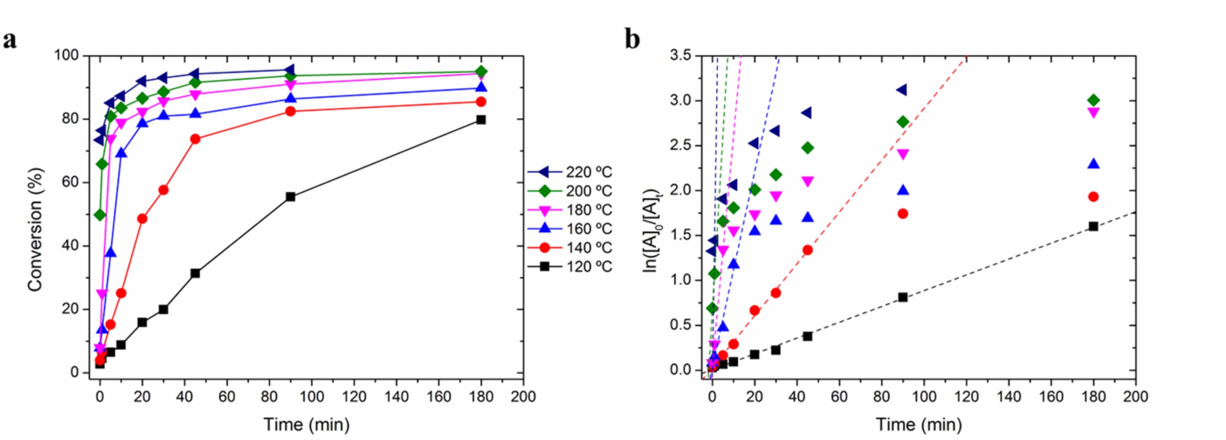

Figure S11. Conversion versus time plot for the hydrolysis of PEtOx 50 kDa at temperatures ranging from 120 ºC to 220 ºC. [HCl] = 1.0M. Increasing temperature greatly accelerates the hydrolysis rate. **b)** Corresponding first order kinetic plot. The deviation from linearity beyond 80% conversion can be ascribed to the protonation of the formed ethylene imine units and the consequent decrease of free protons available to catalyze the hydrolysis.

Size Exclusion Chromatography (SEC) in hexafluoroisopropanol (HFIP) to assess polymer integrity upon hydrolysis (PEtOx 50kDa)

Freeze-dried hydrolysis samples were dissolved in HFIP under sonication, filtered (0.45µm) and injected in the chromatograph.

SEC analyses of commercial Aquazol® 50 evidence the presence of two different molar mass distributions that evolve to a monomodal distribution in the first stages of the hydrolysis reaction. This observation indicates that commercial PEtOx 50 kDa consists of both lower molecular weight linear PEtOx and high molecular weight highly branched PEtOx, featuring hydrolytically unstable branching points. Branching of PEtOx prepared at high M/I and high conversion are a consequence of chain transfer and has been thoroughly studied.[1]

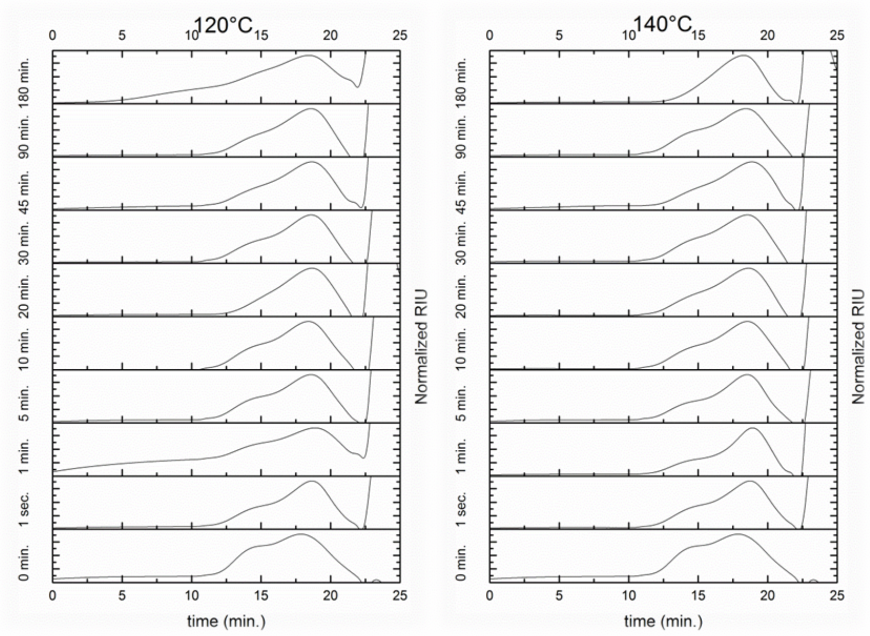

Figure S12. Stack plot containing the SEC traces for the hydrolysis of PEtOx 50kDa at 120ºC and 140 ºC (normalized RI versus time).

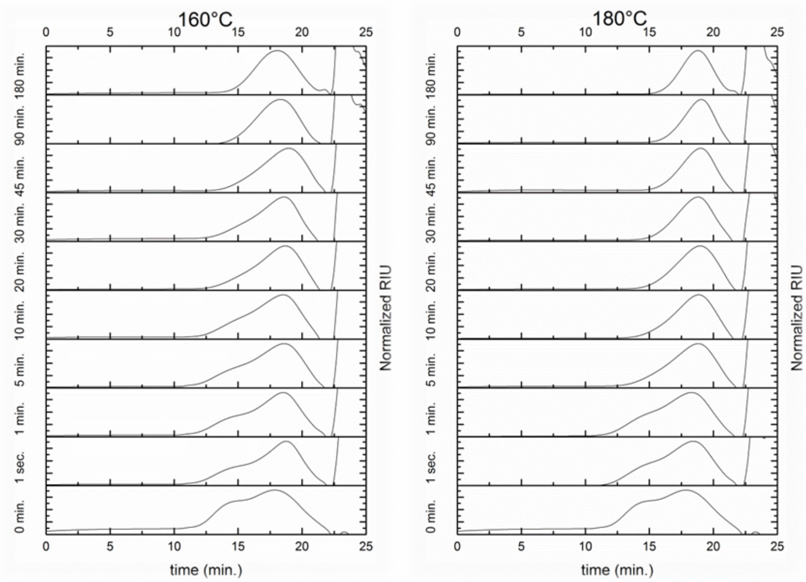

Figure S13. Stack plot containing the SEC traces for the hydrolysis of PEtOx 50kDa at 160ºC and 180 ºC (normalized RI versus time).

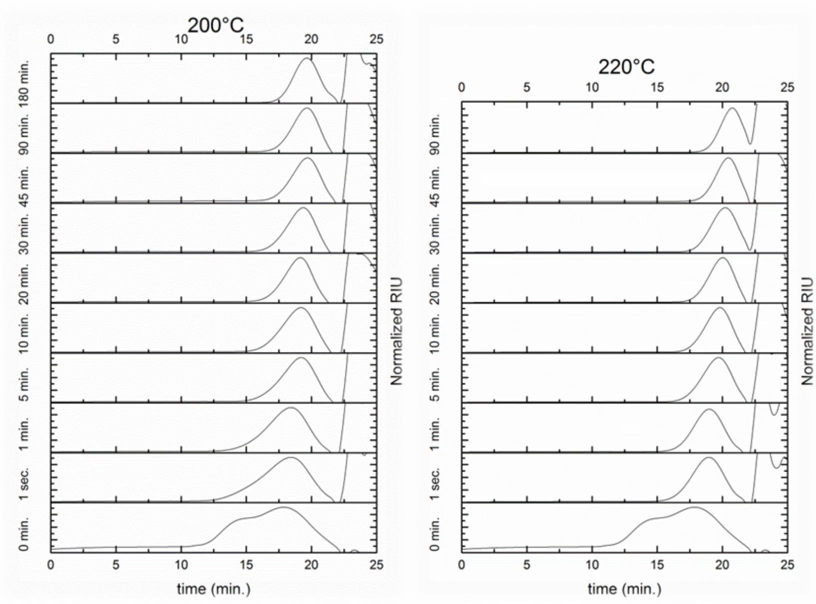

Figure S14. Stack plot containing the SEC traces for the hydrolysis of PEtOx 50kDa at 200ºC and 220 ºC (normalized RI versus time).

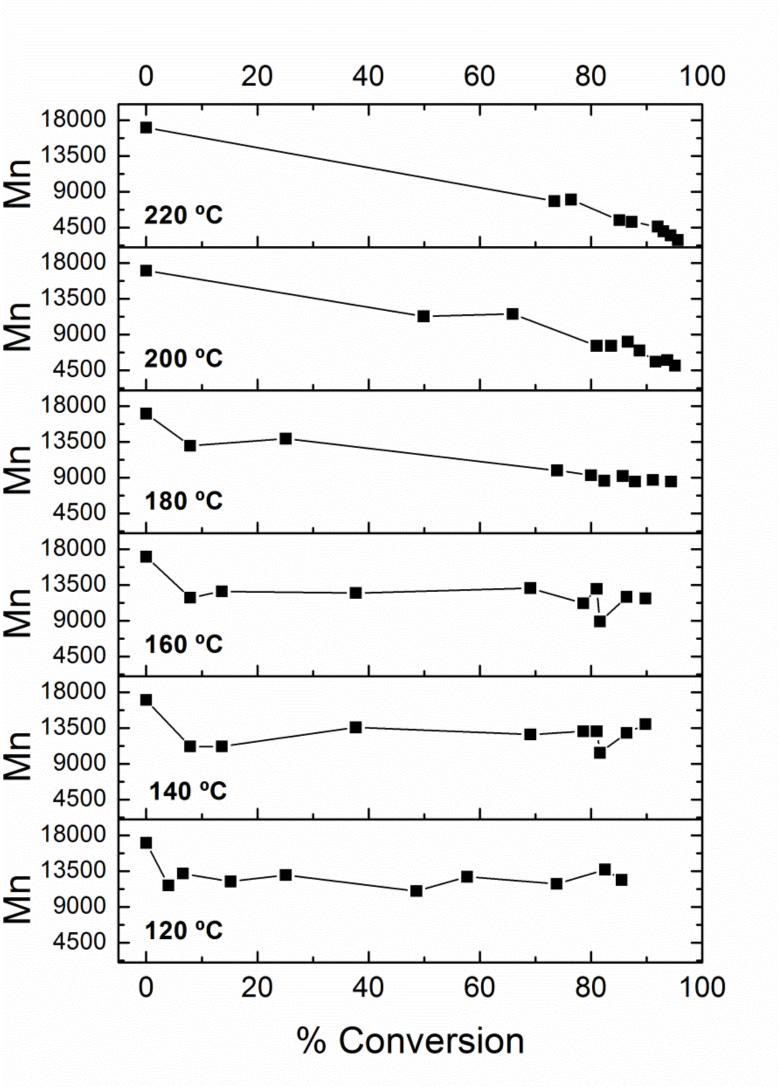

Figure S15. Mn values from the obtained PAOx-*co*-PEI copolymers plotted against the degree of hydrolysis, measured by HFIP-SEC. The molecular weight average increases with the conversion, as PEI units produce an increase in the hydrodynamic volume of the copolymer, but also decreases due to the hydrolysis of cleavable branching points. At 200 ºC and 220 ºC, a sharp decrease in the M_n values is observed, dropping until *ca*. 4000 Da. This sharp drop in molecular weight indicates degradation of the polymer backbone into oligomers.

Investigation of the Hydrolysis of poly(2-ethyl-2-oxazoline) (PEtOx) 200kDa under acid-free near-critical water (NCW) conditions

To explore the possibility of performing the hydrolysis of PEtOx in the absence of any catalyst, a 0.48 M (amide concentration) solution of PEtOx 200kDa was prepared, in the presence of 0.03 M NaCl, following the conditions reported by Kremsner and Kappe.[2] The polymer solutions (15 mL) were placed in heavy-walled quartz reaction vessel of 80 mL nominal volume, and heated for different times at various temperatures. Upon completion of the reaction time set, samples of each reaction solution were basidified with a 4M solution of $NaOH_{(aq)}$., freeze-dried, and analyzed by HFIP-SEC. The most representative results obtained are summarized in the table below.

Temperature (ºC)	Holding time (min.)	Mn	Mm	Đ	% Conversion
NA*	NA	35500	149000	4.20	NA
260	20	4300	2900	1.45	49
260	30	1900	2300	1.18	59
275	60	NA	NA	NA	73

*PEtOx 200kDa, starting material

Table S1. HFIP-SEC data corresponding to the hydrolysis product of PEtOx 200kDa under different heating times and temperatures in near-critical water. The polymer was quickly degraded to small oligomers when heated at 260 ºC, as seen from the drop in molecular weight measured by SEC. The polymer also suffered acute decomposition after 60 min. reaction time at 275 ºC; instead of being a white solid, the sample had a glue-like yellow appearance after freeze-drying and was not measured by SEC.

The results obtained indicate that, at this conditions of high temperatures and pressures (80 bar), PEtOx hydrolyzes but also decomposes into small oligomers and thus this is not a valid method to produce poly(ethylene imine) (co)polymers.

References

1. Warakomski, J. M.; Thill, B. P. Journal of Polymer Science Part A: Polymer Chemistry **1990,** 28, 3551-3563.
2. Kremsner, J. M.; Kappe, C. O. European Journal of Organic Chemistry **2005,** 2005, 3672-3679.