Damages and Repair in Informational Poly(*N*-substituted urethane)s

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Abstract: The degradation and repair of uniform sequence-defined poly(*N*-substituted urethanes) was studied. Polymers containing an ω -OH end-group and only ethyl carbamate main-chain repeat units rapidly degrade in NaOH solution via an $\omega \rightarrow \alpha$ depolymerization mechanism with no apparent sign of random chain cleavage. The degradation mechanism is not notably affected by the nature of the side-chain *N*-substituents and took place for all studied sequences. On the other hand, depolymerization is significantly influenced by the molecular structure of the main-chain repeat units. For instance, hexyl carbamate main-chain motifs block unzipping and can therefore be used to control the degradation of specific sequence sections. Interestingly, the partially-degraded polymers can also be repaired; for example using a combination of *N,N'*-disuccinimidyl carbonate with a secondary amine building-block. Overall, these findings open up interesting new avenues for chain-healing and sequence editing.

Informational polymers are macromolecules that store information in a controlled comonomer sequence.^[1] A typical example of that is DNA, which is a biological storage medium. In recent years, it has also been reported that data (*e.g.* in a binary format) can be stored in synthetic macromolecules, for example in polyamides, polyesters and polyurethanes, just to name a few.^[2] This new class of functional polymers has opened up interesting applications in areas such as data storage, cryptography, anti-counterfeiting, traceability and plastic recycling.^[3] Yet, there are still pronounced differences between natural and non-natural informational polymers. Man-made polymers mainly enable passive information storage, while the information sequences of DNA can be copied, mutated, damaged, modified (*i.e.* through epigenetics) and repaired.^[4] There are currently only a couple of examples of synthetic information sequences that can be degraded or transformed;^[2c, 5] although such behaviors could be useful for the aforementioned applications as well as for more distant goals such as the development of artificial Life.^[6]

Here, we report the controllable degradation and possible repair of informational poly(*N*-substituted urethane)s. Sequence-defined polyurethanes can be synthesized via different solid-phase chemistry approaches.^[2d, 7] Different types of functional sequences can be prepared, including digitally-encoded ones.^[2d, 7e] It is also well-known that some linear or dendritic polyurethanes undergo controllable depolymerization (sometimes referred to as self-immolative behavior).^[8] In these macromolecules, chain-degradation is triggered by a nucleophile (*e.g.* a primary amine) and proceeds via an unzipping mechanism. This interesting mechanism has been explored for biomedical applications, for instance for triggered drug release.^[9] Very recently, Anslyn and coworkers^[10] have reported that the depolymerization of sequence-defined polyurethanes can be kinetically-controlled to enable sequencing.^[11] In this case, chain unzipping was triggered by a terminal OH-group and required basic conditions and elevated temperatures (70°C, microwave) to proceed. In the present work, we investigated the depolymerization in basic medium of sequence-coded poly(*N*-substituted urethane)s,

a promising new family of digital polymers.^[7e] As described in the following paragraphs, depolymerization occurs at room temperature and can be finely tuned by macromolecular design.

The poly(*N*-substituted urethane)s studied in this work were all synthesized using a recently-reported orthogonal solid-phase synthesis protocol.^[7e] Figure 1 shows their general structure. These informational polymers are directional and contains therefore two distinct chain ends denoted as α and ω . The former one is a caproic acid residue, whereas the latter one is either an OH or a methyl group. The coded sequences were constructed using a set of nine different informational monomers **A-I**. Figure S1 shows the molecular structure of the polymers **P1-P13** studied in this work. The molecular uniformity of the polymers was assessed by high-resolution electrospray mass spectrometry (ESI-HRMS) and size exclusion chromatography (SEC), while their coded sequences were characterized by tandem mass spectrometry (MS/MS) (Table S1 and Figures S2-S14).^[12]

Figure 1. General structure of the informational poly(*N*-substituted urethane)s.

Since the depolymerization of sequence-defined poly(*N*-substituted urethane)s was never investigated, the degradation mechanism and kinetics were first analyzed in details. For polymers having an ω -hydroxyl end-group and ethyl carbamate repeat units (x = 1 in Figure 1), complete depolymerization occurs at room temperature in the presence of sodium hydroxide. For example, Figure S2 shows the ESI-HRMS spectrum and SEC chromatogram of **P1** having the sequence α -DCEC-OH after 16 hours in basic medium. Both analytical methods evidence the disappearance of **P1** and the formation of three low molecular weight species of mass 129.1, 142.1 and 177.1 Da, which correspond to the

oxazolidinone rings resulting from the cyclization of repeat units **C**, **D** and **E**, respectively. As proposed in Scheme S1, these compounds are likely formed through a backbiting reaction leading to complete chain depolymerization. To validate this mechanism, **P2** having the same primary structure as **P1** but no terminal OH group (i.e. α -DCEC-CH₃) was studied in the same basic conditions (Figure S3). This experiment indicated no sign of degradation, thus suggesting that depolymerization solely occurs through an $\omega \rightarrow \alpha$ unzipping mechanism, *i.e.* without contribution from other mechanisms such as random chain cleavage.^[13] Furthermore, this behavior is fully orthogonal as shown in Figure 2, which compares the ESI-HRMS spectra of a mixture of **P1** and **P2** before and after basic treatment. The selective depolymerization of **P1** is observed in these conditions.

Figure 2. Positive mode ESI-HRMS spectra of a 1:1 w/w mixture of polymers **P1** and **P2**: (a) before basic treatment and (b) after 16h at RT in NaOH solution in MeOH/H₂O 2:1 v/v. The inset of panel **b** shows a zoom of the 120-180 *m/z* region of the obtained spectrum. As compared to the main spectrum,

the intensity scale of the inset has been increased by a factor of about 18. The asterisks indicate background noise peaks.

Figures 3 and S15 show the kinetics of depolymerization of polymer **P1**, as monitored by SEC. In Figure 3, the evolution of the ratio of the peak areas of the partially-degraded products (α -DCE-OH, α -DC-OH and α -D-OH) over the peak area of the remaining initial polymer **P1** are displayed as a function of time. These results suggest that α -DCE-OH is first predominantly formed, followed by the gradual accumulation of α -DC-OH and α -D-OH. Comparable data were although recorded by ESI-MS (Figure S16), even though peak intensities should be interpreted with caution in mass spectrometry. Altogether, these results suggest a gradual unzipping degradation, as already reported for regular sequence-defined polyurethanes.^[10]

Figure 3. Evolution of SEC peak areas ratios as a function of time for the degradation of **P1** in NaOH solution in MeOH/H₂O 2:1 v/v. Peak areas were estimated by deconvoluting the chromatograms of Figure S15b using the Origin software. For a given time, the ratios α -DCE-OH/**P1**, α -DC-OH/**P1** and α -D-OH/**P1** are calculated from the corresponding chromatogram.

Possible sequence effects were also investigated. Polymers **P3** and **P4** having ω -hydroxyl end-group and ethyl carbamate repeat units but a different sequence and a different terminal monomer unit

from **P1** were examined (Figures S4-S5). **P3** and **P4** have a similar terminal unit but a different penultimate unit. Depolymerization proceeded in all cases and appeared to be sequence-independent and side-group-independent (for both penultimate and terminal positions). Yet, minor deviations in depolymerization kinetics cannot be ruled out but could not be evidenced in the performed experiments.

Furthermore, the influence of the number of the methylene groups in the repeat units was investigated. A series of polymers **P4-P8** having all the same sequence but different terminal monomer units ($R = Bz$, x ranging from 1 to 5, Figure 1) was studied (Figures S5-S9). After 16h of basic treatment in methanol/water, the polymer having an ethyl terminal (**P4**) unit was entirely degraded. The polymer having a propyl-based (**P5**) terminal units was significantly degraded but a residual peak of the initial polymer was still observed. For polymers having butyl- (**P6**) and pentyl-based (**P7**) terminal units, the pristine polymer was still observed as a dominant species, although traces of degradation were detected. The polymer having a hexyl-based terminal unit (**P8**) obviously did not degrade in the studied conditions and only exhibited marginal oxazolidinone peaks. Behaviors comparable to those described for **P5-P8** were obtained with polymers with alternative monomer sequences **P9-P12**. Altogether, these results imply that the depolymerization mechanism proceeds well when 5- and 6-membered rings are formed but is slowed down or hindered by repeat units leading to the formation of larger rings. To confirm this hypothesis, a mixture of polymers **P4-P8** was treated in basic medium for 16h. ESI-HRMS analysis (Figure S17) indicated complete disappearance of **P4**, significant disappearance of **P5**, partial disappearance of **P6** and **P7**, whereas **P8** remained the most abundant species. Although these results should be interpreted with caution due to potential suppression effects during the ionization process, this experiment confirms that main-chain alkyls strongly influence the depolymerization mechanism.

Figure 4. Partial degradation and repair of sequence-coded poly(*N*-substituted urethane) **P13**. Positive mode ESI-HRMS spectra of (a) the original polymer **P13** before basic treatment, (b, c) the degraded polymer **P13'** after NaOH treatment, and (d) the repaired polymer **P13''** after molecular healing. Panel c shows a zoom of the 100-200 *m/z* range for **P13'**. As compared to the spectrum shown in panel b, the intensity scale of the inset in panel c has been increased by a factor of about 11. The asterisks indicate background noise peaks. Experimental conditions: (i) NaOH, MeOH/H₂O, RT (ii) DSC, pyridine, ACN, 60°C, microwave then di-*n*-propyl-amine, pyridine, DMF, RT. (e) SEC chromatograms recorded in THF for **P13**, **P13'** and **P13''**. The high molecular weight shoulders are most likely due to the formation of polyesters, as discussed in previous publications.^[7e, 14]

The fact that chain depolymerization depends on the number of methylene groups in a repeat unit is appealing because it suggests that the content of an informational sequence can be tuned by monomer design. Indeed, in informational polymers, molecular bits are usually set by using side-chain motifs of different molar mass but can also be obtained using main-chain motifs of different length or

composition.^[15] For instance, in the present case, informational units containing hexyl spacers, such as monomer **I**, can be used as a stopper to interrupt depolymerization at a precise chain-location. As a proof-of-concept, polymer **P13** with sequence α -DDBIAACE-OH was investigated (Figure 4a). It contains a single **I** unit placed in between two blocks that are composed of ethyl carbamate repeat units. In NaOH medium, this polymer depolymerizes only until the stopping point, as evidenced by the ESI-MS spectrum (Figure 4b and Figure S18) and SEC chromatogram (Figure 4e) of the resulting polymer **P13'**. In ESI-MS, the transformation **P13**→**P13'** leads to the expected mass decrease of 508 Da, whereas in SEC an apparent diminution of 466 Da is measured between peak maxima M_p . Partial depolymerization is also supported by the appearance of the oxazolidinone rings, expelled from the decomposed AACE sequence, in the ESI-MS spectrum of **P13'** (Figure 4d). These results confirm that preset sequence sections can be selectively degraded using appropriate molecular design. Furthermore, the degraded chain still exhibits reactive chain ends (*i.e.* α -COOH and ω -OH) and can therefore be repaired. Hence, the same sequence (complete or partial) or a different one can be reconstructed on the partially-degraded polymer. Here, **P13'** was partially-repaired by reacting it first with *N,N'*-disuccinimidyl carbonate (DSC) and then with di-*n*-propyl-amine. This modification leads to modification of both chain-ends, as shown in Figure 4c. Yet, it should be noted that the amidification of the α -chain-end can be avoided if needed; for instance by modifying the terminal acid group during or after cleavage. Here, the targeted modification was successfully performed, as evidenced by the ESI-MS spectrum (Figure 4c and Figure S19) and SEC chromatogram (Figure 4e) of the repaired polymer **P13''**. Indeed, the transformation **P13'**→**P13''** led to the expected mass increase of 210 Da in ESI-MS and to an apparent M_p increase of 168 Da in SEC.

In summary, OH-terminated poly(*N*-substituted urethane)s degrade via an ω → α unzipping mechanism in basic conditions at room temperature. If the polymer chain is only composed of ethyl carbamate repeat units, full decomposition can be attained. Yet, if some repeat units of the chain contain longer alkyl spacers, degradation can be slowed down or even suppressed. For instance,

polymers containing a hexyl carbamate terminal unit do not degrade in basic conditions; at least not notably during the investigated periods of times. Furthermore, if the hexyl carbamate unit is placed inside an otherwise ethyl carbamate-based sequence, partial depolymerization proceeds from the ω -terminus to the stopping hexyl carbamate unit. Therefore, specific information sections can be selectively erased from an informational sequence. This property is particularly interesting for anti-counterfeiting applications,^[3b] because molecular barcodes could be purposely altered when exposed to specific conditions. Perhaps even more importantly, the partial degradation mechanism found in this work opens up possibilities of repairing informational polymers. For instance, it was demonstrated herein that intentionally-damaged sequences can be re-engineered using simple modification conditions. This proof-of-concept of molecular healing paves the way for the development of more complex deconstruction/reconstruction mechanisms, including chain rewriting and editing.

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Supporting Information for

Damages and Repair in Informational Poly(*N*-substituted urethane)s

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A. Experimental procedures

A.1. Materials. The Wang resin (0.94 mmol/g, IRIS Biotech) utilized for the synthesis of *N*-substituted polyurethanes was modified with a cleavable linker as previously reported.^[1] All the following reagents were purchased and used as received: 2-(methylamino)ethanol (TCI; $\geq 98\%$), 2-(ethylamino)ethanol (TCI; $\geq 98\%$), 2-(propylamino)ethanol (Sigma-Aldrich; $\geq 98\%$), 2-(butylamino)ethanol (TCI; $\geq 98\%$), di-*n*-propylamine (Alfa-aesar; 99%), 2-benzyl amino ethanol (TCI; $\geq 95\%$), 3-benzyl amino 1-propanol (TCI; $\geq 98\%$), 4-benzyl amino 1-butanol (TCI; $\geq 96\%$), 5-benzyl amino 1-pentanol (TCI; $\geq 98\%$), 6-benzyl amino 1-hexanol (TCI; $\geq 97\%$), trifluoroacetic acid (TFA ; Alfa-aesar, 99%), anhydrous pyridine (Sigma-Aldrich, 99.8%), *N,N*-disuccinimidyl carbonate (DSC; TCI, $>98.0\%$), anhydrous acetonitrile (dry ACN; Sigma-Aldrich, 99.8%), dichloromethane (DCM, Sigma-Aldrich, 99.9%), diethyl ether (Carlo Erba), anhydrous *N,N*-dimethylformamide (dry DMF; Sigma-Aldrich, 99.8%), DMF (Sigma-Aldrich, R99.0%).

A.2. General procedure for the synthesis of poly(*N*-substituted urethanes) P1-P13. All the polymers **P1-P13** were synthesized using a previously-reported stepwise solid phase protocol.^[2] In brief, the synthesis is performed on an OH-functionalized modified Wang resin and involves two successive coupling steps. In the first step, the OH-groups of the resin are reacted with *N,N*-disuccinimidyl carbonate in a microwave reactor (Monowave 300, Anton Paar). This step is performed in anhydrous acetonitrile and anhydrous pyridine at 60°C under microwave irradiation. In the second step, the formed activated carbonate is reacted with the secondary amine function of an amino alcohol building block in a solid-phase extraction tube. This step is performed at RT in anhydrous DMF. Both steps were repeated a certain number of times until a desired chain-length and sequence were achieved. The cleavage of the polymers from the resin was achieved using a TFA/CH₂Cl₂ mixture. After filtering-off the resin, the organic layer with TFA was evaporated under reduced pressure to achieve the desired oligo/polyurethanes as pale yellow sticky solids.

A.3. Example of basic degradation of a poly(*N*-substituted urethane). The poly(*N*-substituted urethane) **P1** (25 mg, 0.035 mmol) was introduced in a small vial. Then 1.5 equivalent of NaOH (2 mg) in 2 mL of methanol and 1 mL of water (methanol/water 2/1 v:v) was added to the vial and the reaction mixture was stirred for 16 h at room temperature. After the alkaline treatment the reaction was stopped and methanol was evaporated out followed by the addition of an equivalent amount of aqueous HCl solution with respect to NaOH. Then the aqueous phase was extracted with dichloromethane and the organic layer was collected, concentrated and dried under vacuum. A similar procedure was applied for all polymers **P1-P13**.

A.4. General procedure for repair of partially-degraded poly(*N*-substituted urethanes). The poly(*N*-substituted urethane) **P13** (1 Eq., 50 mg, 0.039 mmol) was introduced in a small vial and reacted with NaOH following the procedure described in section A.3, thus affording the partially-degraded polymer **P13'** as well as oxazolidinone rings resulting from the degradation. The cyclic residues were washed out by dissolving them in diethyl ether. Afterwards, **P13'** was treated with DSC (6 Eq, 60 mg, 0.234 mmol) in presence of anhydrous pyridine (10 Eq, 31 mg, 0.39 mmol) in 2 mL of anhydrous acetonitrile solution (60°C, microwave, 1h, 600 rpm). Afterwards, an excess of di-*n*-propyl amine (20 Eq, 78 mg, 0.78 mmol) and 10 equivalent anhydrous pyridine (10 Eq, 31 mg, 0.39 mmol) along with 1 mL anhydrous DMF were added in the same reaction vial and stirred for 30 min. After the reaction, the solvents were evaporated under vacuum. Then, 2 mL acidic aqueous solution (1 M HCl solution) was added to the reaction mixture and extracted with dichloromethane. The organic layer was separated and concentrated. Finally, the oily organic compound was washed with *n*-hexane to afford the sticky yellowish final product **P13''** with a yield of about 95%.

B. Characterization.

B.1. ¹H Nuclear Magnetic Resonance (NMR). The polymers were analyzed by ¹H NMR spectrometry on a Bruker Avance 400 MHz spectrometer equipped with Ultrashield magnet. The spectra were recorded in deuterated chloroform (CDCl₃) (Sigma-Aldrich; 99,8%).

B.2. Size Exclusion Chromatography (SEC). The molecular weight and the distribution of the polymers were determined by size exclusion chromatography in THF solvent. The SEC instrument was equipped with four PLGel Mixed C columns (5 mm, 30 cm, diameter: 7.5 mm), a Wyatt Viscostar-II viscometer, a Wyatt TREOS light-scattering detector, a Shimadzu SPD-M20A diode array UV detector and a Wyatt Optilab T-rEX refractometer. All the chromatograms displayed in this article are refractometer signals. This set-up was used for polystyrene characterization (1,000-3,000,000 g·mol⁻¹). The mobile phase was THF with a flow rate of 1 mL/min. Toluene was used as the internal reference. The calibration was established on linear PS standards from Polymer Laboratories.

B.3. Electrospray Mass Spectrometry.

High resolution MS and MS/MS experiments were performed using a QStar Elite mass spectrometer (Applied Biosystems SCIEX, Concord, ON, Canada) equipped with an electrospray ionization (ESI) source operated in the positive ion mode (capillary voltage: +5500 V; cone

voltage: +75 V). Air was used as the nebulizing gas (10 psi) and nitrogen as the curtain gas (20 psi). Sample solutions were introduced in the ESI source with a syringe pump at a 10 $\mu\text{L min}^{-1}$ flow rate. Ions were accurately mass measured after internal calibration of the orthogonal acceleration time-of-flight (oa-TOF) mass analyzer, using two cationic adducts of PMMA to bracket the targeted analyte m/z value in the MS mode^[3] or the precursor ion signal in the MS/MS mode. In CID experiments, precursor ions were selected in a quadrupole mass analyzer, injected into the collision cell filled with nitrogen, and product ions were measured in the oa-TOF. Instrument control, data acquisition and data processing of all experiments were achieved using Analyst software (QS 2.0) provided by Applied Biosystems SCIEX.

MS/MS sequencing of poly(N-substituted urethane)s has recently be described in details.^[4] Briefly, collisional activation of ammonium adducts, $[\text{Px}+\text{NH}_4]^+$, first leads to elimination of ammonia to produce protonated molecules, $[\text{Px}+\text{H}]^+$, which further experience cleavage of the $\text{CH}_2\text{--O}$ bond between two repeating units, yielding α_i^+ fragments. A specific feature in these MS/MS spectra is an abundant internal fragment corresponding to the first repeating unit holding one proton. However, the abundance of α_i^+ fragments rapidly decreases as the size of the dissociating chain increases, so such a dissociation pathway allows sequencing of very short oligomers only ($\text{DP} < 6$). Alternatively, MS/MS sequencing can be efficiently performed from CID data recorded for sodiated oligomers, $[\text{Px}+\text{Na}]^+$, using three fragment series, α_i^+ ions containing the α termination and w_i^+ and y_i^+ ions containing the ω termination. A fourth series of ions containing ω and named $w_i'^+$ are formed when activating doubly charged precursors, $[\text{Px}+2\text{Na}]^{2+}$.

C. Additional data and figures

Table S1. Characterization of the poly(*N*-substituted urethane)s studied in this work.

	Sequence ^a	<i>m/z</i> _{exp}	<i>m/z</i> _{th}	Yield [%]
P1	α-DCEC-OH	728.4470 ^b	728.4440	96
P2	α-DCEC-CH ₃	726.4654 ^b	726.4648	98
P3	α-CAAE-OH	658.3663 ^b	658.3658	99
P4	α-BCDE-OH	714.4277 ^b	714.4284	90
P5	α-BCDF-OH	728.4447 ^b	728.4440	88
P6	α-BCDG-OH	742.4594 ^b	742.4597	91
P7	α-BCDH-OH	756.4765 ^b	756.4753	89
P8	α-BCDI-OH	770.4908 ^b	770.4910	88
P9	α-DDBF-OH	742.4591 ^b	742.4597	95
P10	α-CCDG-OH	756.4756 ^b	756.4753	92
P11	α-DCAH-OH	742.4598 ^b	742.4597	97
P12	α-CACI-OH	742.4592 ^b	742.4597	98
P13	α-DDBIAACE-OH	646.8839 ^c	646.8836	84

^a Sequence of the polymers written following the nomenclature rules established in Figure 1 of the main text. ^b Detected as [M+NH₄]⁺ in positive mode ESI-HRMS. ^c Detected as [M+H+NH₄]²⁺ in positive mode ESI-HRMS. ^d Measured by SEC in THF using a polystyrene calibration.

Figure S1. Molecular structure of the polymers **P1-P13** studied in this work.

Figure S1 (cont'd). Molecular structure of the polymers **P1-P13** studied in this work.

Scheme S1. Proposed mechanism for the degradation of poly(N-substituted urethane)s.

Figure S2. Characterization of **P1** (α -DCEC-OH). Positive mode ESI-HRMS recorded (**a**) before and (**b**) after treatment in basic medium, with degradation products at m/z 130.1 (from C), m/z 144.1 (from D) and m/z 178.1 (from E) shown in inset. As compared to the inset, the intensity scale of the main spectrum shown in (**b**) was increased by a factor of about 500.

Figure S2 (cont'd). Characterization of **P1** (α -DCEC-OH). (c) MS/MS of $[\mathbf{P1}+\text{NH}_4]^+$ at m/z 728.4 recorded before treatment in basic medium (inset: dissociation scheme for fragment assignment). (d) SEC chromatograms recorded in THF before (black trace) and after (blue trace) treatment in basic medium. The high molecular weight shoulder observed in the initial chromatogram might be due to polyester formation, as discussed in previous publications.^[2, 5]

Figure S3. Characterization of **P2** (α -DCEC-CH₃). Positive mode ESI-HRMS recorded (**a**) before and (**b**) after treatment in basic medium (no degradation product is observed the 120-180 *m/z* range enlarged in inset). As compared to the main spectrum shown in (**b**), the intensity scale in the inset was increased by a factor of about 85.

Figure S3 (cont'd). Characterization of **P2** (α -DCEC-CH₃). (c) MS/MS of $[P2+NH_4]^+$ at m/z 726.4 recorded before treatment in basic medium (inset: dissociation scheme for fragment assignment). (d) SEC chromatograms recorded in THF before (black trace) and after (blue trace) treatment in basic medium.

Figure S4. Characterization of **P3** (α -CAAE-OH). Positive mode ESI-HRMS recorded (**a**) before and (**b**) after treatment in basic medium, with degradation products at *m/z* 102.1 (from A), *m/z* 130.1 (from C) and *m/z* 178.1 (from E) shown in inset. Peaks designated by an asterisk in (**a**) correspond to impurities. As compared to the inset, the intensity scale of the main spectrum shown in (**b**) was increased by a factor of about 40.

Figure S4 (cont'd). Characterization of **P3** (α -CAAE-OH). **(c)** MS/MS of $[\mathbf{P3}+\text{NH}_4]^+$ at m/z 658.4 recorded before treatment in basic medium (inset: dissociation scheme for fragment assignment). **(d)** SEC chromatograms recorded in THF before (black trace) and after (blue trace) treatment in basic medium. The high molecular weight shoulder observed in the initial chromatogram might be due to polyester formation, as discussed in previous publications.^[2, 5]

Figure S5. Characterization of **P4** (α -BCDE-OH). Positive mode ESI-HRMS recorded **(a)** before and **(b)** after treatment in basic medium, with degradation products at m/z 116.1 (from B), m/z 130.1 (from C), m/z 144.1 (from D) and m/z 178.1 (from E) shown in inset. Peaks designated by an asterisk in **(a)** correspond to impurities. As compared to the inset, the intensity scale of the main spectrum shown in **(b)** was increased by a factor of about 7.

Figure S5 (cont'd). Characterization of **P4** (α -BCDE-OH). **(c)** MS/MS of $[\mathbf{P4}+\text{NH}_4]^+$ at m/z 714.4 recorded before treatment in basic medium (inset: dissociation scheme for fragment assignment). **(d)** SEC chromatograms recorded in THF before (black trace) and after (blue trace) treatment in basic medium. The high molecular weight shoulder observed in the initial chromatogram might be due to polyester formation, as discussed in previous publications.^[2, 5]

Figure S6 (cont'd). Characterization of **P5** (α -BCDF-OH). **(c)** MS/MS of $[\mathbf{P5}+\text{NH}_4]^+$ at m/z 728.4 recorded before treatment in basic medium (inset: dissociation scheme for fragment assignment). **(d)** SEC chromatograms recorded in THF before (black trace) and after (blue trace) treatment in basic medium. The high molecular weight shoulder observed in the initial chromatogram might be due to polyester formation, as discussed in previous publications.^[2, 5]

Figure S7 (cont'd). Characterization of **P6** (α -BCDG-OH). **(c)** MS/MS of $[\mathbf{P6}+\text{NH}_4]^+$ at m/z 742.5 recorded before treatment in basic medium (inset: dissociation scheme for fragment assignment). **(d)** SEC chromatograms recorded in THF before (black trace) and after (blue trace) treatment in basic medium. The high molecular weight shoulder observed in the initial chromatogram might be due to polyester formation, as discussed in previous publications.^[2, 5]

Figure S8 (cont'd). Characterization of **P7** (α -BCDH-OH). **(c)** MS/MS of $[\mathbf{P7}+\text{NH}_4]^+$ at m/z 756.5 recorded before treatment in basic medium (inset: dissociation scheme for fragment assignment). **(d)** SEC chromatograms recorded in THF before (black trace) and after (blue trace) treatment in basic medium. The high molecular weight shoulder observed in the initial chromatogram might be due to polyester formation, as discussed in previous publications.^[2, 5]

Figure S9. Characterization of **P8** (α -BCDI-OH). Positive mode ESI-HRMS recorded **(a)** before and **(b)** after treatment in basic medium, with degradation products at m/z 116.1 (from B), m/z 130.1 (from C) and m/z 144.1 (from D) shown in inset. As compared to the main spectrum shown in **(b)**, the intensity scale in the inset was increased by a factor of about 12.

Figure S9 (cont'd). Characterization of **P8** (α -BCDI-OH). **(c)** MS/MS of $[\mathbf{P8}+\text{NH}_4]^+$ at m/z 770.5 recorded before treatment in basic medium (inset: dissociation scheme for fragment assignment). **(d)** SEC chromatograms recorded in THF before (black trace) and after (blue trace) treatment in basic medium. The high molecular weight shoulder observed in the initial chromatogram might be due to polyester formation, as discussed in previous publications.^[2, 5]

Figure S10 (cont'd). Characterization of **P9** (α -DDBF-OH). (c) MS/MS of $[\mathbf{P9}+\text{NH}_4]^+$ at m/z 742.4 recorded before treatment in basic medium (inset: dissociation scheme for fragment assignment). (d) SEC chromatograms recorded in THF before (black trace) and after (blue trace) treatment in basic medium. The high molecular weight shoulder observed in the initial chromatogram might be due to polyester formation, as discussed in previous publications.^[2, 5]

Figure S11. Characterization of **P10** (α -CCDG-OH). Positive mode ESI-HRMS recorded **(a)** before and **(b)** after treatment in basic medium, with degradation products at m/z 130.1 (from C), and m/z 144.1 (from D) shown in inset. Peaks designated by an asterisk in **(a)** correspond to impurities. As compared to the main spectrum shown in **(b)**, the intensity scale in the inset was increased by a factor of about 65.

Figure S11 (cont'd). Characterization of **P10** (α -CCDG-OH). **(c)** MS/MS of $[\mathbf{P10}+\text{NH}_4]^+$ at m/z 756.5 recorded before treatment in basic medium (inset: dissociation scheme for fragment assignment). **(d)** SEC chromatograms recorded in THF before (black trace) and after (blue trace) treatment in basic medium. The high molecular weight shoulder observed in the initial chromatogram might be due to polyester formation, as discussed in previous publications.^[2, 5]

Figure S12. Characterization of **P11** (α -DCAH-OH). Positive mode ESI-HRMS recorded **(a)** before and **(b)** after treatment in basic medium, with degradation products at m/z 102.1 (from A), m/z 130.1 (from C), and m/z 144.1 (from D) shown in inset. Peaks designated by an asterisk in **(a)** correspond to impurities. As compared to the main spectrum shown in **(b)**, the intensity scale in the inset was increased by a factor of about 5.

Figure S12 (cont'd). Characterization of **P11** (α -DCAH-OH). (**c**) MS/MS of $[P11+NH_4]^+$ at m/z 742.5 recorded before treatment in basic medium (inset: dissociation scheme for fragment assignment). (**d**) SEC chromatograms recorded in THF before (black trace) and after (blue trace) treatment in basic medium. The high molecular weight shoulder observed in the initial chromatogram might be due to polyester formation, as discussed in previous publications.^[2, 5]

Figure S13. Characterization of **P12** (α -CACL-OH). Positive mode ESI-HRMS recorded (a) before and (b) after treatment in basic medium, with degradation products at m/z 102.1 (from A), and m/z 130.1 (from C) shown in inset. Peaks designated by an asterisk in (a) correspond to impurities. As compared to the main spectrum shown in (b), the intensity scale in the inset was increased by a factor of about 4.

Figure S13 (cont'd). Characterization of **P12** (α -CACI-OH). **(c)** MS/MS of $[\text{P12}+\text{NH}_4]^+$ at m/z 742.5 recorded before treatment in basic medium (inset: dissociation scheme for fragment assignment). **(d)** SEC chromatograms recorded in THF before (black trace) and after (blue trace) treatment in basic medium. The high molecular weight shoulder observed in the initial chromatogram might be due to polyester formation, as discussed in previous publications.^[2, 5]

Figure S14. MS/MS recorded for **P13** before treatment in basic medium, activated as $[P13+2Na]^{2+}$ at m/z 660.4. Top: dissociation scheme for fragment assignment. Peaks annotated by grey symbols are secondary fragments, including sodiated repeating units designated by stars: $[A+Na]^+$ at m/z 124.0, $[B+Na]^+$ at m/z 138.1, $[C+Na]^+$ at m/z 152.1, $[D+Na]^+$ at m/z 166.1, and $[I+Na]^+$ at m/z 256.1.

Figure S15. SEC chromatograms recorded in THF as a function of time for the degradation of **P1** in NaOH solution in MeOH/H₂O 2:1 v/v. **(a)** Non-normalized raw chromatograms. **(b)** Mass-rescaled chromatograms. To draw these chromatograms: (1) refractometer intensities were first divided by corresponding mass values; (2) the resulting mass-corrected chromatograms were normalized on the highest peak of the displayed area for clarity. (3) each chromatogram was deconvoluted (data not shown) using the Origin software to calculate the peak areas ratios displayed in Figure 3.

Figure S16. MS monitoring of the degradation of **P1** in basic medium after (a) 5 minutes, (b) 15 minutes, (b) 30 minutes, (d) 1 hour, (e) 2 hours, (f) 3 hours, (g) 3 hours, (h) 8 hours, (i) 24 hours, and (j) 48 hours. # impurities. α -DCE-OH at m/z 582.4 with H^+ and m/z 599.4 with NH_4^+ ; α -DC-OH at m/z 405.3 with H^+ ; α -D-OH at m/z 276.2 with H^+ .

Figure S16 (cont'd). MS monitoring of the degradation of **P1** in basic medium after (a) 5 minutes, (b) 15 minutes, (h) 30 minutes, (d) 1 hour, (e) 2 hours, (f) 3 hours, (g) 3 hours, (h) 8 hours, (i) 24 hours, and (j) 48 hours. # impurities. α -DCE-OH at m/z 582.4 with H^+ and m/z 599.4 with NH_4^+ ; α -DC-OH at m/z 405.3 with H^+ ; α -D-OH at m/z 276.2 with H^+ .

a.

b.

Figure S17. Positive mode ESI-HRMS recorded for a mixture of polymers **P4-P8** (a) before and (b) after treatment in basic medium.

Figure S18. MS/MS recorded for **P13'** before treatment in basic medium, activated as $[P13'+Na]^+$ at m/z 789.4. Top: dissociation scheme for fragment assignment. Grey symbols designate secondary fragments, including sodiated repeating units designated by stars: $[B+Na]^+$ at m/z 138.1 and $[D+Na]^+$ at m/z 166.1.

Figure S19. MS/MS recorded for **P13''** before treatment in basic medium, activated as $[P13''+Na]^+$ at m/z 999.7. Top: dissociation scheme for fragment assignment. Grey symbols designate secondary fragments, with @ for those arising from dissociation of the α end-group.

D. References

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