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Supporting Information

Dual-Responsive Material Based on Catechol-Modified Self-Immolative Poly(Disulfide) Backbones

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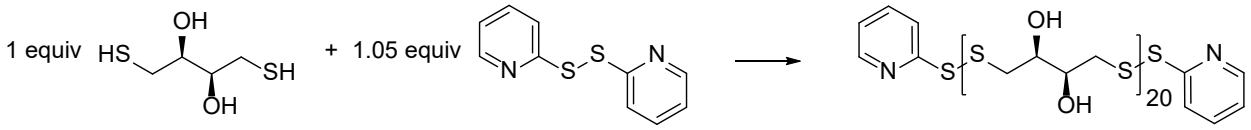
Experimental procedures

General procedures

All synthetic procedures were carried out under ambient conditions unless otherwise stated. Most solvents and chemicals were purchased from Sigma Aldrich except dithiothreitol (DTT) which was purchased from Fischer Scientific. All chemicals were used without further purification. ^{1}H NMR spectra were recorded using a Bruker 400 MHz spectrometer with $CDCl_3$ or DMSO-d_6 as internal reference. For kinetic studies of depolymerization, ^{1}H NMR spectra were recorded using a Varian 400 MHz spectrometer with DMSO-d_6 as internal reference. Size exclusion chromatography was performed using a system comprising a LC-20AD Shimadzu HPLC pump, a Shimadzu RID-10A refractive index detector, and a DAWN HELEOS 8 light scattering detector from Wyatt. The detector was SPD-M20A PDA, equipped with an Mz-Gel SDplus Linear column (8 × 300 mm) using 5 µm particles from MZ-Analysentechnik to provide an effective molecular weight range of 1 kDa to 1 MDa. *N*,*N*-Dimethylformamide (DMF) containing 10 mM LiBr was employed as solvent. For molar weight calculations, the average d*n*/d*c* value was calculated to be 0.1146 determined on the assumption of full mass recovery. The mechanical mixer used for the synthesis of pDTT was a DAC 150.1 FVZ-K SpeedMixer from Hauchchild. UV-Vis spectra were recorded using a Genesys 10S (G10S UV-Vis) spectrophotometer.

Synthesis of compounds

Poly(dithiotreitol)



Poly(dithiothreitol) (pDTT) was synthesized according to a previously reported method.[S1] To target a degree of polymerization (DP) of 20, 3.00 g dithiotreitol (1 equiv.) and 4.50 g 2,2'-dithiodipyridine (1.05 equiv.) were added to a 125 mL polypropylene container, and immediately mixed using a speedmixer (Hauschild) in cycles of 1 min at 3000 RPM, for three consecutive cycles in total. The crude, a light yellow solid, was dissolved in DMF and precipitated into a 1:1 (v/v) mixture of chloroform and pentane. The precipitation procedure was repeated at least three times, or until no impurity from the activating agent (2-thiopyridine) was detectable by ^{1}H NMR, and the product was obtained as a pale yellow solid (2.91 g, 73%). ^{1}H NMR (400 MHz, DMSO-d_6) δ = 8.46 (d, J = 4.6 Hz, 2H), 7.82 (m, 4H), 7.24 (t, *J* = 5.7 Hz, 2H), 5.15 (d, *J* = 6.1 Hz, 2H), 4.99 (d, *J* = 6.2 Hz, 2H), 4.91 (d, *J* = 6.2 Hz, 28H), 3.72 (bs, 32H), 2.96–2.71 (m, overlapping DMF residuals).

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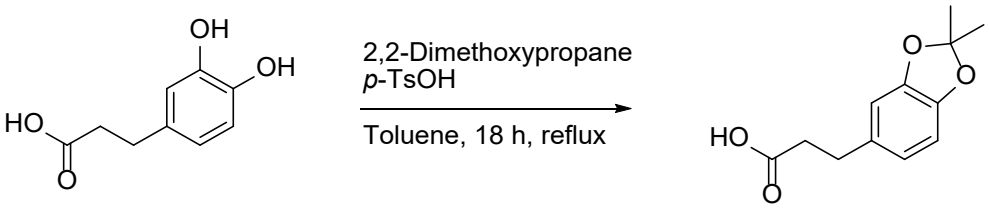
3-(2,2-Dimethylbenzo[d][1,3]dioxol-5-yl)propanoic acid (Ace-DHCA) (1)



Dihydroxydihydrocinnamic acid (5 g, 27 mmol, 1 equiv.), dimethoxypropane (5.5 g, 54 mmol, 2 equiv.), and p-toluenesulfonic acid (180 mg, 1 mmol, 0.04 equiv.) were added to a three-necked flask equipped with a soxleth extractor with $CaCl_2$ in the thimble, and a reflux condenser. 200 mL dry toluene was added to the flask, and the reaction refluxed overnight. After cooling, most of the toluene was removed under reduced pressure. Cold pentane (~100 mL) was added to the remaining solution (~15 mL) upon which the product precipitated as a light tan powder, resulting in **1** (4.36 g, 75 %). ^{1}H NMR (400 MHz, $CDCl_3$) δ = 6.68–6.54 (m, 3H), 2.86 (t, *J* = 7.7 Hz, 2H), 2.63 (t, *J* = 7.7 Hz, 2H), 1.66 (s, 6H).

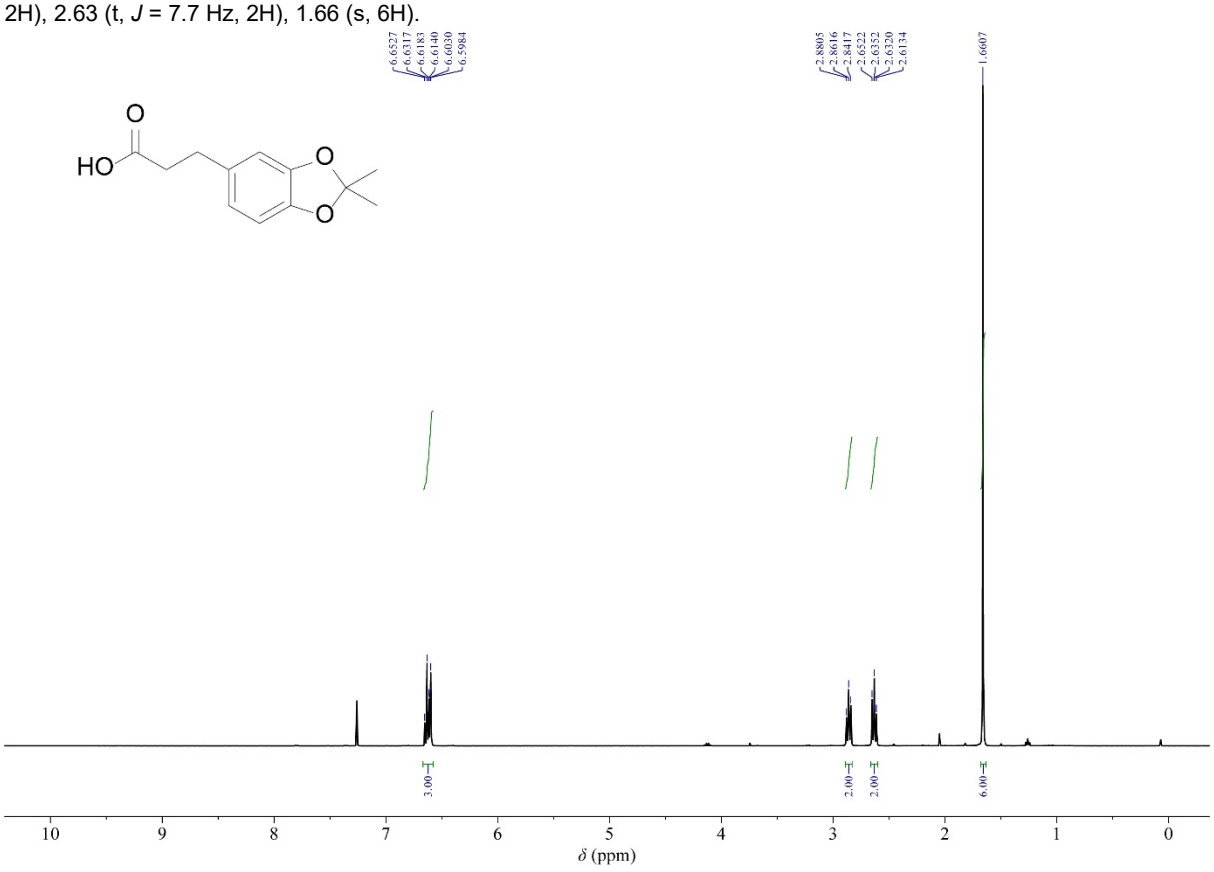
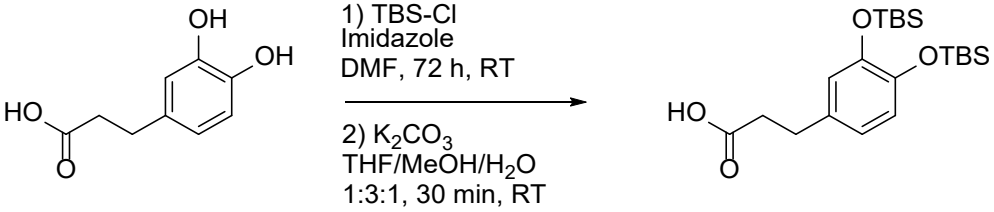


Figure S1. ^{1}H NMR spectrum of synthesized Ace-DHCA (**1**) in $CDCl_3$.

3-(3,4-Bis((tert-butyldimethylsilyl)oxy)phenyl)propanoic acid (TBS-DHCA) (2)



Dihydrocaffeic acid (1 g, 5.5 mmol, 1 equiv.) was dissolved in DMF (10 mL) in a round bottomed flask and the vessel purged with Ar. Imidazole (3.72 g, 55 mmol, 10 equiv.) and TBS-Cl (3.73 g, 24.8 mmol, 4.5 equiv.) were added and the reaction stirred for 48 h. The reaction was worked up according to a previously reported procedure, resulting in **2** (1.12 g, 50%).[S2] ^{1}H NMR (400 MHz, chloroform-d) δ = 6.74 (d, J = 8.1 Hz, 1H), 6.67 (d, J = 2.2 Hz, 1H), 6.63 (dd, J = 8.1, 2.2 Hz, 1H), 2.83 (t, J = 7.7 Hz, 2H), 2.62 (t, J = 7.7 Hz, 2H), 0.98 (s, 18H), 0.18 (s, 12H).

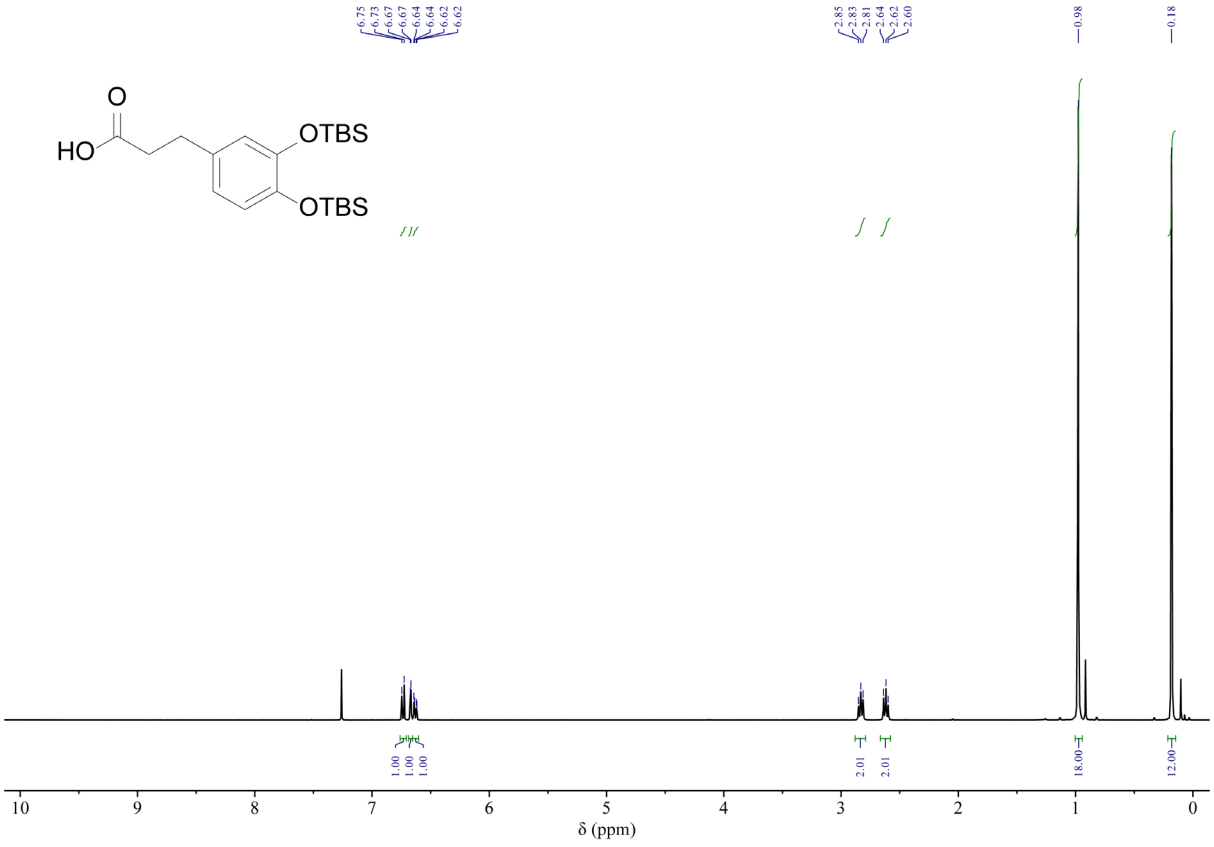


Figure S2. ^{1}H NMR of synthesized TBS-DHCA (**2**) in $CDCl_3$.

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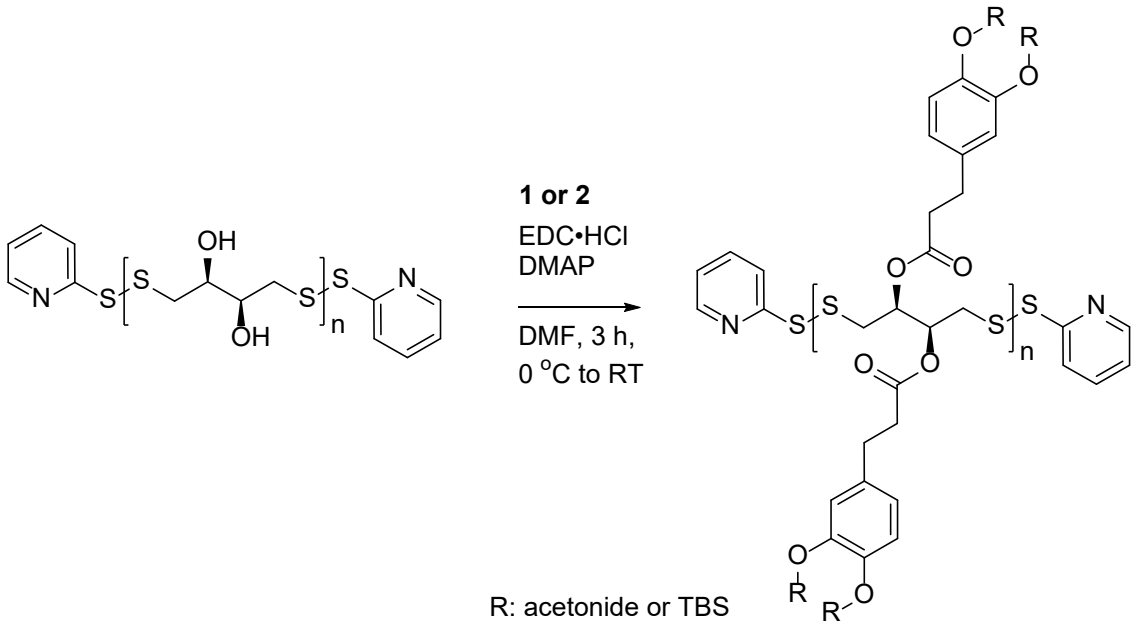
Esterification of pDTT



pDTT (n = 16, *M* = 2652 g/mol, 700 mg, 0.26 mmol, 1 equiv.) and the desired amount of carboxylic acid (**1** or **2**) were added to a round bottom flask and dissolved in as little DMF as possible. EDC•HCl (1.1 equiv. with respect to the carboxylic acid) and *N*,*N*-dimethylaminopyridine (0.08 equiv. with respect to carboxylic acid) were added. After 3 h at RT, the reaction was poured into EtOAc. The organic phase was washed with water (3 × 40 mL) and brine (40 mL), and dried over Na_2SO_4. The solvent was removed under reduced pressure, yielding the product as a light beige powder. For 20% conversion of backbone alcohols, the yield was 77% when using **1** and 76% with **2**. When targeting a 100% conversion of backbone hydroxyl groups, (i.e. pDTT-Ace-$DHCA_{100}$) the yield was 97%. See **Figure S4** for ^{1}H NMR and assignments of pDTT-Ace-$DHCA_{100}$ and **Figure S6** for ^{1}H NMR and assignments of pDTT-Ace-$DHCA_{20}$ and **Figure S7** for ^{1}H NMR and assignments of pDTT-TBS-$DHCA_{20}$.

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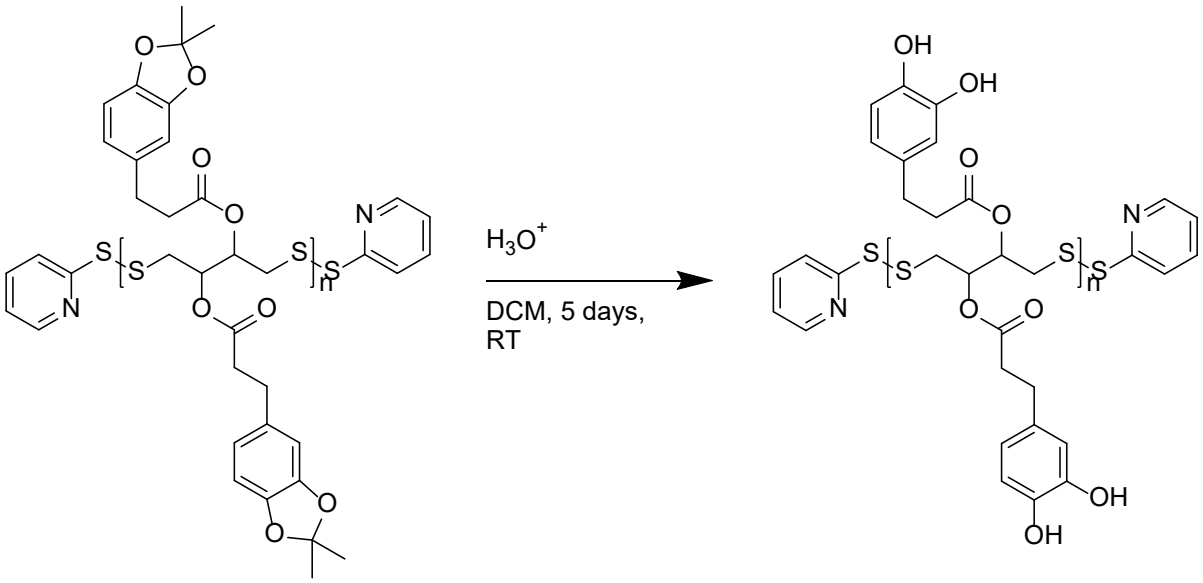
Acetonide hydrolysis



pDTT-Ace-DHCA$_{100}$ (n = 16, *M* = 9191 g/mol, 400 mg, 0.044 mmol, 1 equiv.) was dissolved in DCM (5 mL). The flask was purged with Ar for 10 min and trifluoroacetic acid (298 mg, 2.6 mmol) in 1 mL DCM and water (40 mg, 2.2 mmol) were added. After 5 days at RT, the solvent was removed under reduced pressure at RT until a viscous crude (~1 mL) was obtained. This concentrated crude was precipitated in ether at 0 °C. The ether solution was centrifuged for 10 min at 3000 RPM and the precipitate collected and dried under reduced pressure, to obtain the product as a slightly purple powder (30 mg, 9%). See **Figure S5** for ^{1}H NMR and assignments of pDTT-Cat$_{100}$.

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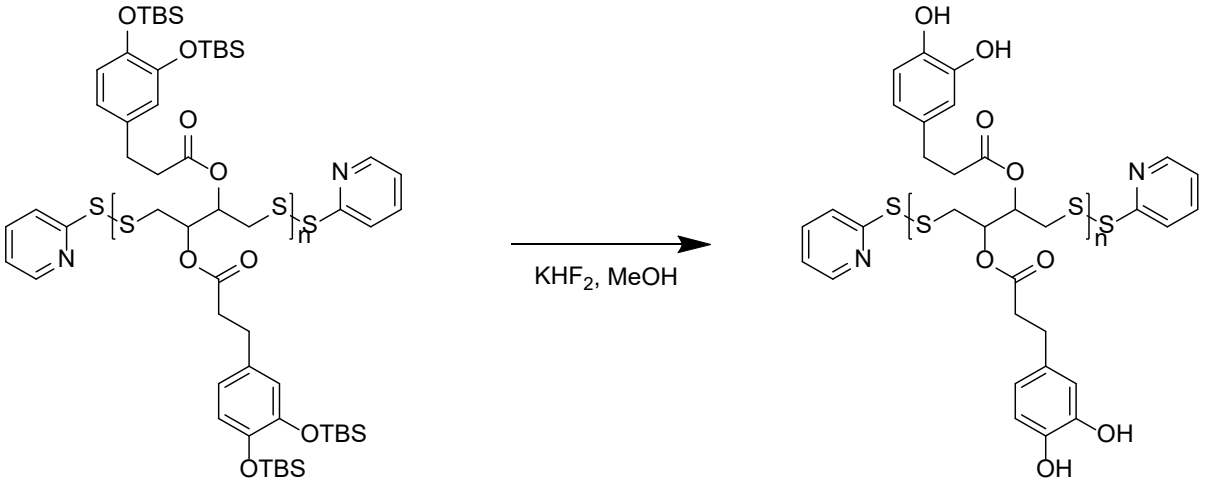
Silyl ether cleavage



Inspired by a previously reported procedure, KHF_2 was utilized for removal of the TBS protection group.[S3] pDTT modified with TBS-DHCA (n = 16, *M* = 15203 g/mol, 1.06 g, 0.07 mmol) was placed in a round bottom flask and dissolved in 5 mL dry MeOH. To this, KHF_2 (436 mg, 5.6 mmol, 1.25 equiv. with respect to silyl ether) was added and left to react for 8 h at RT. The reaction was filtered, and $CaCl_2$ (1 g, 9 mmol) dissolved in MeOH (25 mL) was added dropwise to precipitate any remaining fluoride, until no precipitate formed. The solution was filtrated and reduced in vacuo to a viscous liquid (~1 mL), followed by final precipitation by dropwise addition into cold (0 °C) diethyl ether (~100 mL). The precipitate was collected using centrifugation at 3000 RPM for 10 min, followed by decantation of the supernatant. The product was dried under reduced pressure (<2 mbar) to obtain the desired product, pDTT-Cat_{20}, as a white powder (300 mg, 49% yield). See **Figure S8** for ^{1}H NMR and assignments of pDTT-Cat_{20}.

Polymer analysis

For this section, several pDTT samples were synthesized with DP ranging from 16–18. Thus, some of the modified polymers have DP values slightly different from the one obtained from the spectrum in **Figure S3** with DP = 16. In general, yields of acetonide hydrolysis were poor (10–15%), independent of the degree of backbone modification. Nevertheless, the acetonide route enabled synthesis of pDTT-Cat$_{100}$. In contrast, removal of the silyl ether resulted in moderate yields of 40–50% for pDTT-Cat$_{20}$. Unfortunately, solubility issues with pDTT-TBS-DHCA$_{100}$ meant that the silyl ether could not be removed to generate pDTT-Cat$_{100}$ by this route. Thus, pDTT-Cat$_{100}$ was obtained via the acetonide route in low yields, while pDTT-Cat$_{20}$ could be synthesized in moderate yield using the silyl ether route.

Polymer composition of pDTT

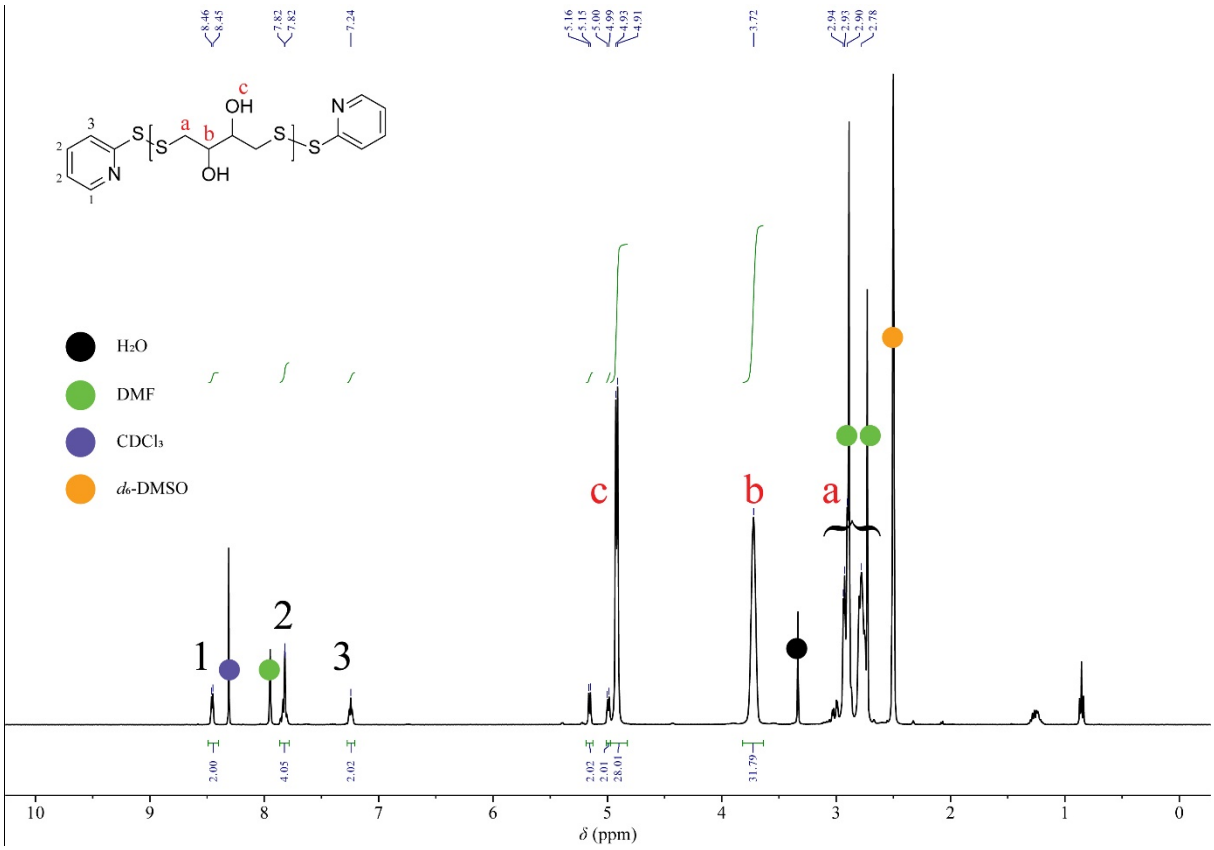


Figure S3. ^{1}H NMR of pDTT in DMSO-d_6. Marked peaks assigned according to structure shown in inset; trace impurities from solvent residual peak and water marked in black and orange, respectively. All integrals are relative to peak 1 assigned to the pyridinic end-caps.

Integrals in **Figure S3** were measured relative to the end-cap associated pyridinic peak at 8.44 ppm (marked 1) assuming two end-caps per polymer. DP was calculated from the area of peak c, including the two smaller peaks, shifted slightly due to end-cap hydrogen bonding,[S1] using equation S1.

$$\mathrm{DP} = \frac{\#\ \mathrm{CHO}\mathbf{H_c}}{2} = \frac{32.04}{2} = 16 \qquad \text{(S1)}$$

Since each monomer contains 2 O**H** protons, the area is divided by 2.

Polymer composition of pDTT-Ace-DHCA$_{100}$

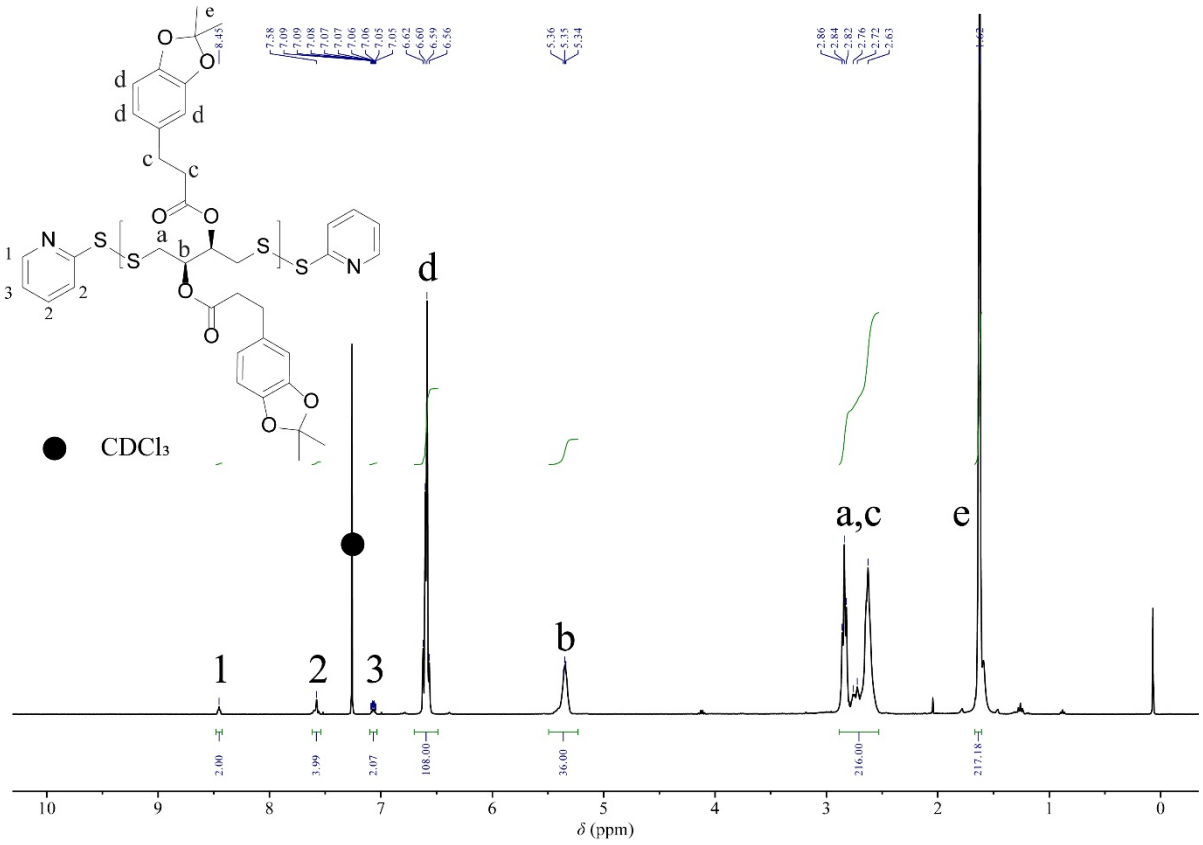


Figure S4. ^{1}H NMR spectrum of pDTT-Ace-DHCA$_{100}$ in $CDCl_3$. Marked peaks assigned according to structure shown in inset; trace impurities from solvent residual peak marked in black. All integrals are relative to end-cap associated peak 1.

Integrals in **Figure S4** were measured relative to the end-cap associated pyridinic peak at 8.44 ppm (marked 1) assuming two end-caps per polymer. DP of pDTT-Ace-DHCA$_{100}$ was estimated by end-group analysis based on the ^{1}H NMR spectrum above (**Figure S4**) according to equation S2.

$$\begin{aligned} \mathrm{DP} &= \frac{\#\ \mathrm{C}\mathbf{H_b}\mathrm{OH}}{2} \\ &= \frac{36.00}{2} \\ &= 18 \end{aligned} \tag{S2}$$

M_n was calculated using the composition determined above and equation S3, using only the peak for the doubly modified repeating unit and its corresponding molecular weight M_2 (since there is no presence of singly- and un-modified repeating units, they are not included) together with the contribution from end-caps, M_{EC}.

$$\begin{aligned} M_{\mathrm{n_{NMR}}} &= \frac{\#\ \mathrm{C}\mathbf{H_b}\mathrm{OH}}{2} M_2 + 2M_{\mathrm{EC}} \\ &= \frac{36.00}{2} \times 560.68 \frac{\mathrm{g}}{\mathrm{mol}} + 2 \times 110.15 \frac{\mathrm{g}}{\mathrm{mol}} \\ &= 10313 \frac{\mathrm{g}}{\mathrm{mol}} \end{aligned} \tag{S3}$$

The **H** in bold refers to the proton next to the ester group (b**, Figure S4**).

Fraction of converted backbone hydroxyl groups, $OH_{conversion}$, was calculated according to equation S4.

$$\mathrm{OH}_{\mathrm{conversion}} = \frac{\frac{36}{2}}{18} \times 100\% = 100\% \quad \text{(S4)}$$

Polymer composition of pDTT-Cat$_{100}$

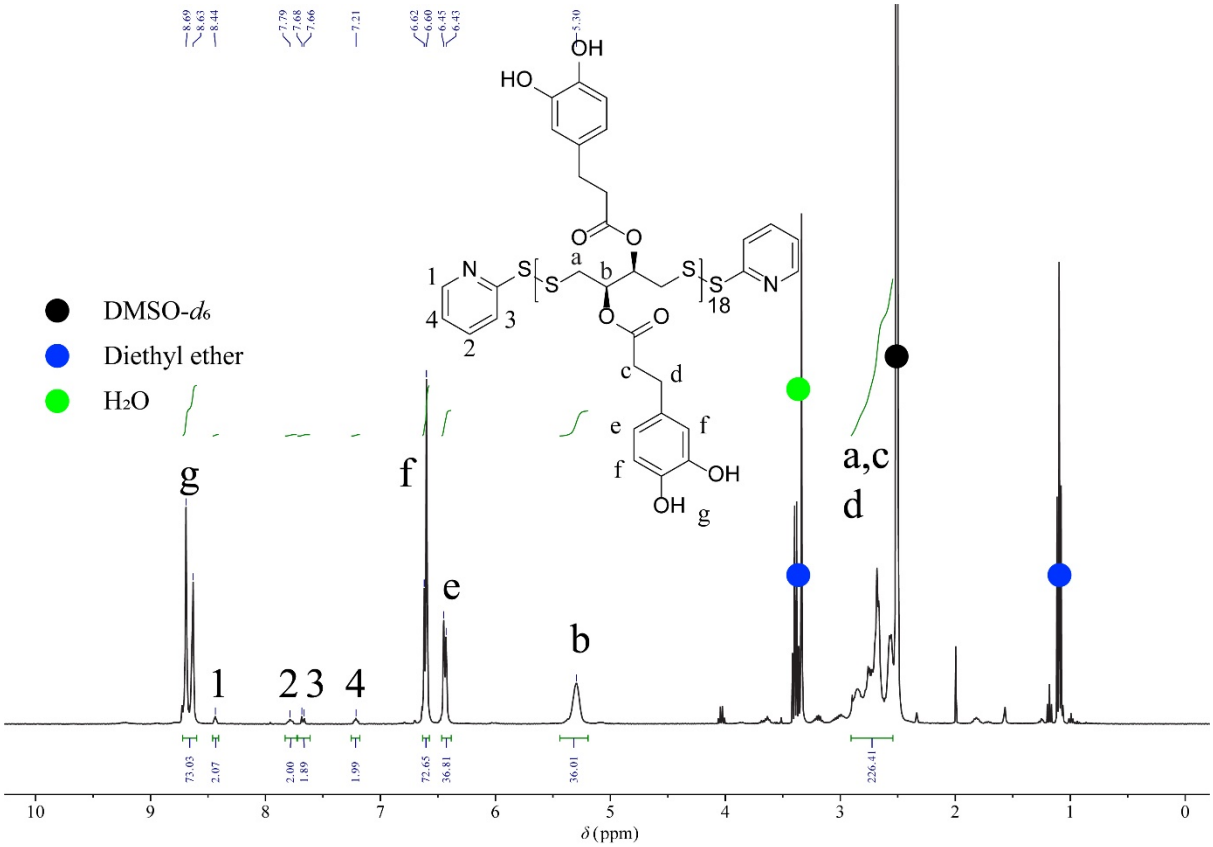


Figure S5. ^{1}H NMR spectrum of pDTT-Cat$_{100}$ in DMSO-d_6. Marked peaks assigned according to structure shown in inset; trace impurities from solvent residual peak marked in black, green, and blue. All integrals are relative to the end-cap.

Integrals in **Figure S5** were measured relative to the end-cap associated pyridinic peak at 7.78 ppm (marked **2**) assuming two end-caps per polymer. DP of pDTT-Cat$_{100}$ was estimated by end-group analysis based on the ^{1}H NMR spectrum above (**Figure S5**) according to equation S5.

$$\begin{aligned} \mathrm{DP} &= \frac{\#\ \mathrm{C}\mathbf{H_b}\mathrm{OH}}{2} \\ &= \frac{36.01}{2} \\ &= 18 \end{aligned} \qquad \text{(S5)}$$

The **H** in bold refers to the proton next to the ester group (b**, Figure S5**).

M_n was calculated using the composition determined above and equation S6, using only the peak for the doubly modified repeating unit and its corresponding molecular weight M_2 (since there is no presence of singly- and un-modified repeating units, they are not included) together with the contribution from end-caps, M_{EC}.

$$M_{\mathrm{n_{NMR}}} = \frac{\#\ \mathrm{C}\mathbf{H_b}\mathrm{OH}}{2} M_2 + 2M_{\mathrm{EC}} \quad \text{(S6)}$$
$$= \frac{36.00}{2} \times 480.55 \frac{\mathrm{g}}{\mathrm{mol}} + 2 \times 110.15 \frac{\mathrm{g}}{\mathrm{mol}}$$
$$= 8870 \frac{\mathrm{g}}{\mathrm{mol}}$$

Fraction of converted backbone hydroxyl groups was determined according to equation S7.

$$\mathrm{OH_{conversion}} = \frac{\frac{36}{2}}{18} \times 100\% \quad \text{(S7)}$$
$$= 100\%$$

Polymer composition of pDTT-Ace-DHCA$_{20}$

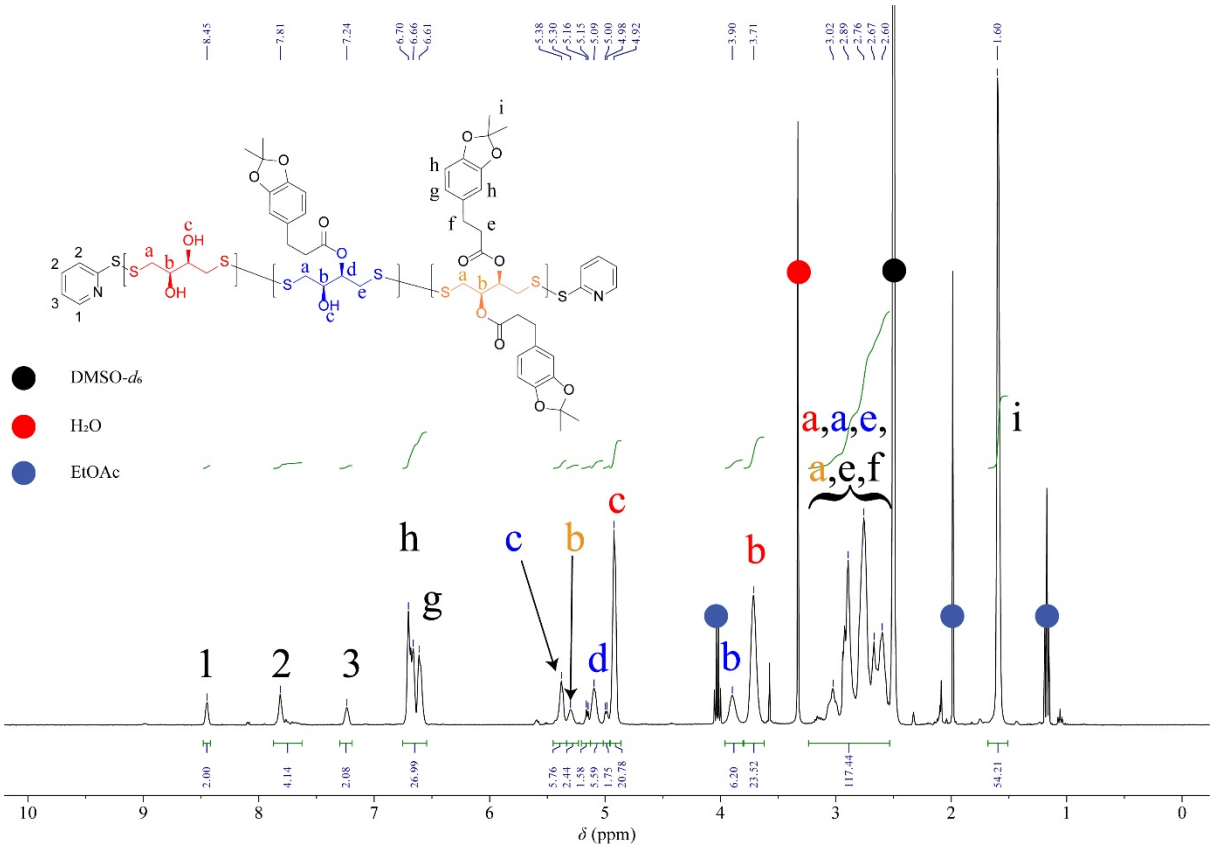


Figure S6. ^{1}H NMR spectrum of pDTT-Ace-DHCA$_{20}$ in DMSO-d_6. Marked peaks assigned according to structure shown in inset; trace impurities from EtOAc, solvent residual peak, and water marked in blue, black, and red, respectively. All integrals are relative to end-cap associated peak 1.

Integrals in **Figure S6** were measured relative to the end-cap associated pyridinic peak at 8.45 ppm (marked 1) assuming two end-caps per polymer. DP of pDTT-Ace-DHCA$_{20}$ was estimated using end-group analysis based on the ^{1}H NMR spectrum above (**Figure S6**), according to equation S8.

$$\begin{aligned} \mathrm{DP} &= \frac{\#\,\mathrm{CH_bOH}}{2} + \#\,\mathrm{CH_bO} + \frac{\#\,\mathrm{CH_bO}}{2} \\ &= \frac{23.52}{2} + 6.20 + \frac{2.44}{2} \\ &= 19.18 \end{aligned} \tag{S8}$$

Molecular weight was determined using the composition found above, and the molar mass of each type of repeat unit and the two pyridinic end-caps, according to equation S9.

$$\begin{aligned} M_{\mathrm{n_{NMR}}} &= \frac{\#\,\mathrm{CH_bOH}}{2} M_0 + \#\,\mathrm{CH_bO} \times M_1 + \frac{\#\,\mathrm{CH_bO}}{2} M_2 + 2M_{\mathrm{EC}} \\ &= \frac{23.52}{2} \times 152.21 \frac{\mathrm{g}}{\mathrm{mol}} + 6.20 \times 356.45 \frac{\mathrm{g}}{\mathrm{mol}} + \frac{2.44}{2} \times 560.68 \frac{\mathrm{g}}{\mathrm{mol}} + 2 \times 110.15 \frac{\mathrm{g}}{\mathrm{mol}} \\ &= 4904 \frac{\mathrm{g}}{\mathrm{mol}} \end{aligned} \tag{S9}$$

Fraction of converted backbone hydroxyl groups was then determined from the DP, the number of singly modified repeat units, doubly modified repeat units and unmodified repeat units, according to equation S10.

$$\mathrm{OH_{conversion}} = \frac{\#\,\mathrm{CH_bO} + \#\,\mathrm{CH_bO}}{2\mathrm{DP}} \times 100\% \qquad (S10)$$

$$= \frac{6.20 + 2.44}{2 \times 19.18} \times 100\%$$

$$= 22.5\%$$

Polymer composition of pDTT-TBS-DHCA$_{20}$

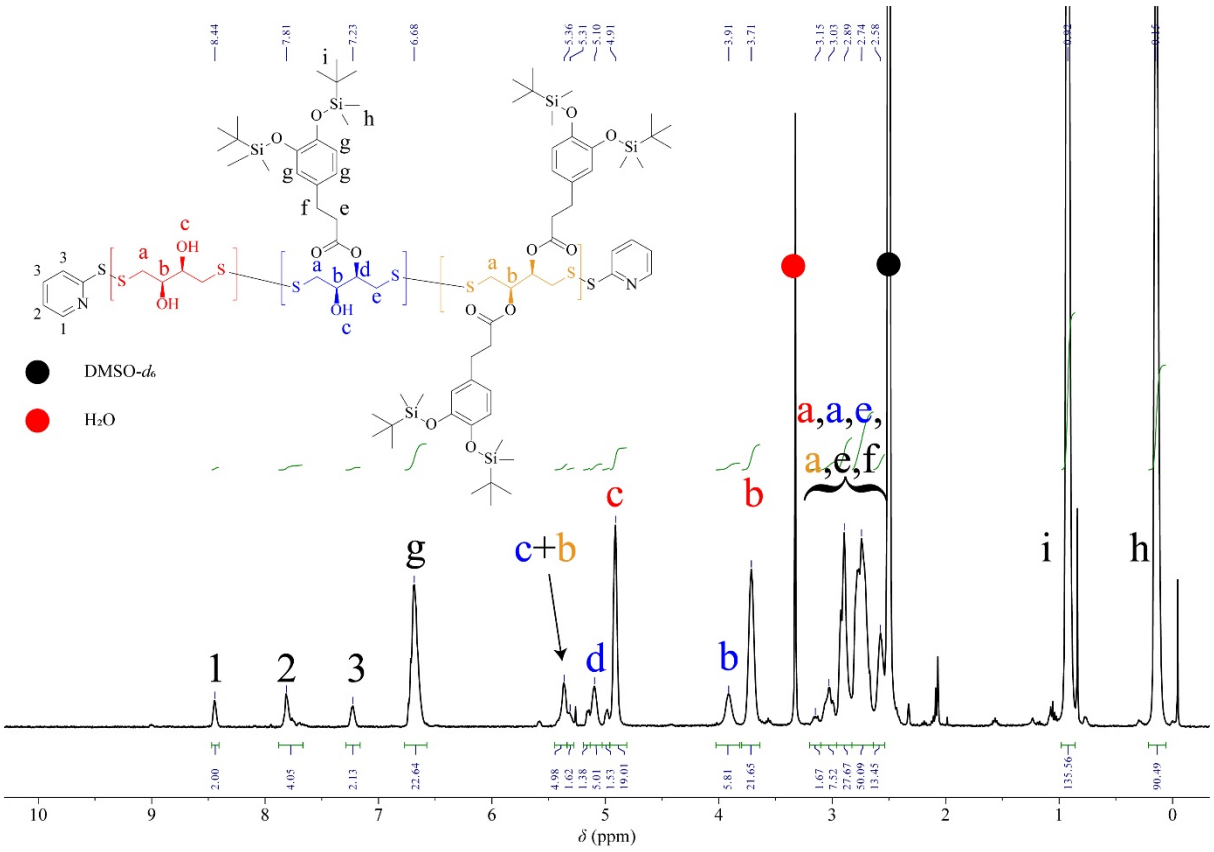


Figure S7. ^{1}H NMR spectrum of pDTT-TBS-DHCA$_{20}$ in DMSO-d_6. Marked peaks assigned according to structure in inset; trace impurities from solvent residual peak and water marked in black and red, respectively. All integrals are relative to end-cap associated peak 1.

Integrals in **Figure S7** were measured relative to the end-cap associated pyridinic peak at 8.44 ppm (marked 1) assuming two end-caps per polymer. DP of pDTT-TBS-DHCA$_{20}$ was calculated by end-group analysis based on the ^{1}H NMR spectrum above (**Figure S7**) according to equation S11.

$$\mathrm{DP} = \frac{\#\,\mathrm{CH_bOH}}{2} + \#\,\mathrm{CH_bO} + \frac{\#\,\mathrm{CH_bO}}{2} \qquad \text{(S11)}$$

$$= \frac{21.65}{2} + 5.81 + \frac{1.62}{2}$$

$$= 17.45$$

In this expression, **H** in bold refers to the proton next to the hydroxyl (b or b, **Figure S7**) or ester groups (b, **Figure S7**) on the backbone. Since singly modified repeat units (blue in **Figure S7**) have two unique protons (one next to ester and one next to hydroxyl moiety), and unmodified (red) and doubly modified (orange) repeat units have two identical protons next to oxygen, the areas of the peaks pertaining to the latter are divided by 2.

Molecular weight was determined using the same peaks and the molar mass of each repeating unit where M_0, M_1, M_2, and M_{EC} represents the molar mass of unmodified, singly modified, doubly modified repeating units and the end-cap, respectively (equation S12).

$$M_{n_{NMR}} = \frac{\#\,CH_bOH}{2} M_0 + \#\,CH_bO \times M_1 + \frac{\#\,CH_bO}{2} M_2 + 2M_{EC} \quad (S12)$$
$$= \frac{21.65}{2} \times 152.21 \frac{g}{mol} + 5.81 \times 544.91 \frac{g}{mol} + \frac{1.62}{2} \times 937.61 \frac{g}{mol} + 2 \times 110.15 \frac{g}{mol}$$
$$= 5793 \frac{g}{mol}$$

Fraction of converted backbone hydroxyl groups, $OH_{conversion}$ (referred to as 'x' in the main article text), was determined from DP, number of singly modified repeat units, and doubly modified repeat units according to equation S13.

$$OH_{conversion} = \frac{\#\,CH_bO + \#\,CH_bO}{2DP} \quad (S13)$$
$$= \frac{5.81 + 1.62}{2 \times 17.45} \times 100\%$$
$$= 21.3\%$$

Polymer composition of pDTT-Cat$_{20}$

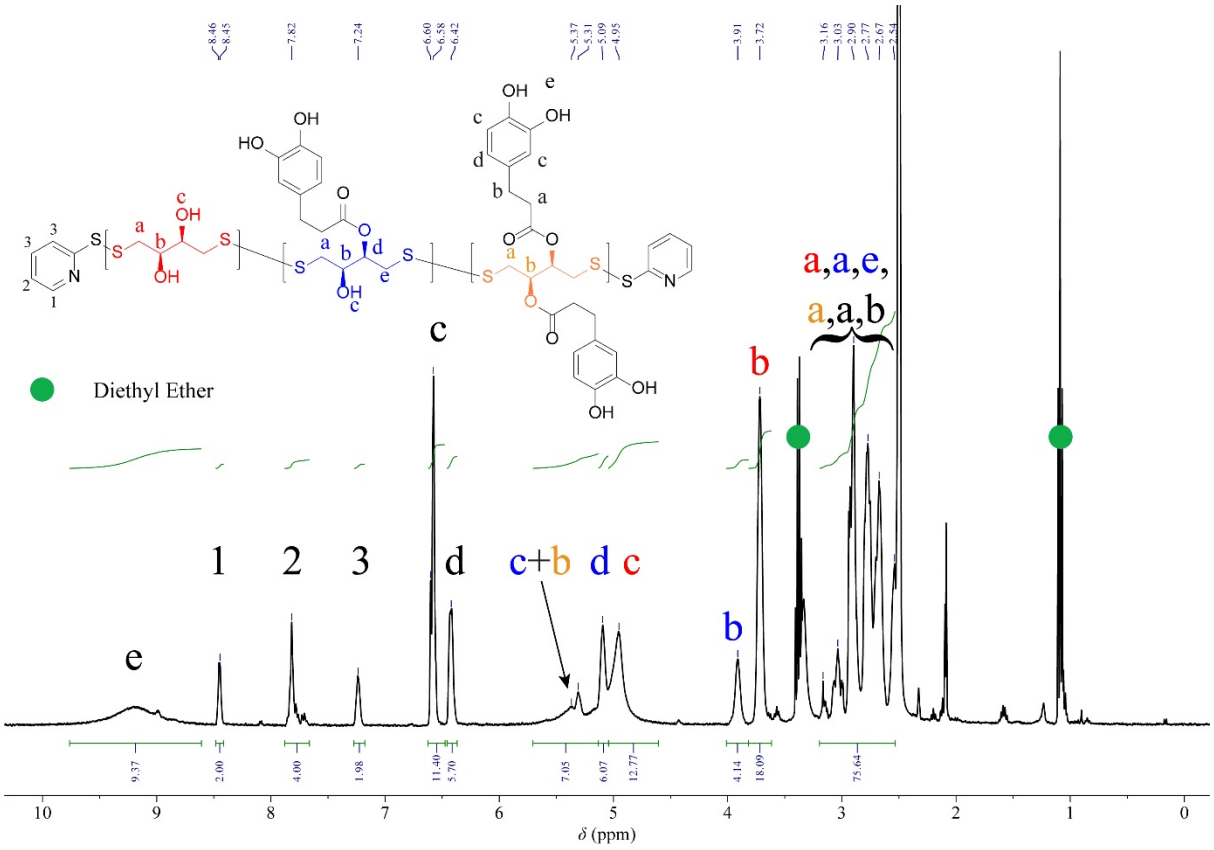


Figure S8. ^{1}H NMR spectrum of pDTT-Cat$_{20}$ in DMSO-d_6. Marked peaks assigned according to structure shown in inset; trace impurities from residual diethyl ether marked in green. All integrals are relative to end-cap associated peak 1.

Integrals in **Figure S8** were measured relative to the end-cap associated pyridinic peak at 8.45 ppm (marked 1) assuming two end-caps per polymer. DP pDTT-Cat$_{20}$ was determined by end-group analysis based on the ^{1}H NMR spectrum above (**Figure S8**), according to equation S14. It should be noted that it is difficult to determine the degree of double modification (# $\mathrm{CH_bO}$) directly, due to peak overlap between c and b. One way to estimate this is by considering the number of aryl units compared to singly modified repeat units (d–b): 5.70 – 4-14 = 1.66. The remainder protons must be from doubly modified repeat units, i.e. 1.66/2 = 0.83, meaning that we have, on average, 0.83 doubly modified units.

.

$$\begin{aligned} \mathrm{DP} &= \frac{\#\,\mathrm{CH_bOH}}{2} + \#\,\mathrm{CH_bO} + \frac{\#\,\mathrm{CH_bO}}{2} \\ &= \frac{18.09}{2} + 4.14 + 0.83 \\ &= 13.97 \end{aligned} \tag{S14}$$

Molecular weight was determined using the composition found above, and the molar mass of each type of repeat unit and the two pyridinic end-caps, according to equation S15.

$$M_{\mathrm{n_{NMR}}} = \frac{\#\,\mathrm{CH_bOH}}{2} M_0 + \#\,\mathrm{CH_bO} \times M_1 + \frac{\#\,\mathrm{CH_bO}}{2} M_2 + 2M_{\mathrm{EC}} \tag{S15}$$

$$= \frac{18.0}{2} \times 152.21 \frac{\text{g}}{\text{mol}} + 4.14 \times 316.39 \frac{\text{g}}{\text{mol}} + 0.97 \times 480.55 \frac{\text{g}}{\text{mol}} + 2 \times 110.15 \frac{\text{g}}{\text{mol}}$$

$$= 3366 \frac{\text{g}}{\text{mol}}$$

Fraction of converted backbone hydroxyl groups, $OH_{conversion}$, was determined according to equation S16.

$$OH_{conversion} = \frac{\#\,C\mathbf{H_b}O + \#\,C\mathbf{H_b}O}{2DP} \quad \text{(S16)}$$

$$= \frac{5.7}{2 \times 13.97} \times 100\%$$

$$= 20.4\%$$

SUPPORTING INFORMATION

Molecular weight determination using size exclusion chromatography

Table S1 compiles molecular weight estimates and dispersities of pDTT, pDTT-TBS-DHCA$_{20}$, pDTT-Ace-DHCA$_{20}$, pDTT-Ace-DHCA$_{100}$, pDTT-Cat$_{100}$, and pDTT-Cat$_{20}$ determined by ^{1}H NMR, SEC, or SEC-MALS in 10 mM LiBr/DMF. For ^{1}H NMR size analysis, see Polymer Analysis section above. M_w was estimated from SEC, and the results were divided into three categories:

a: Sample solution of 4 mg mL^{-1} polymer concentration, analyzed using SEC-MALS. M_w was estimated using ASTRA 6.1 Software from Wyatt Technology to determine d*n*/d*c* assuming full mass recovery. Reported standard uncertainties are based solely on the fitting of the data carried out by the ASTRA software.

b: Four samples of increasing polymer concentration (2, 4, 6, and 8 mg mL^{-1}) were analyzed using SEC-MALS. M_w was estimated using ASTRA 6.1 Software from Wyatt Technology to determine d*n*/d*c* assuming full mass recovery.

c: Samples pDTT-Cat$_{100}$, and pDTT-Cat$_{20}$ were found to absorb laser light at 661.3 nm (applied laser for SEC-MALS equipment) and as result exhibited negative light scattering measurements inapplicable for further size calculations (see **Figures S12** and **S13**). M_w and M_n for said samples were estimated by referring to a pMMA standard series (100, 50, 20, 8, 4 kDa, unidisperse), and calculated as a weighted average based entirely on their relative refractive index chromatograms (Relative refractive index vs. Elution time).

Table S1. M_n from ^{1}H NMR, M_w and PDI from SEC for All Studied Polymers.

Name	M_n (Da) (^{1}H NMR)	M_w (Da) (SEC)	PDI (SEC)
pDTT (DP = 18)	2657	4073 ± 215[a]	1.36 ± 0.15[a]
pDTT-TBS-DHCA$_{20}$	5793	2 mg mL^{-1}: 8630 (±1387)[b] 4 mg mL^{-1}: 6788 (±430)[b] 6 mg mL^{-1}: 6302 (±183)[b] 8 mg mL^{-1}: 6984 (±205)[b]	2 mg mL^{-1}: 1.19 (±0.27)[b] 4 mg mL^{-1}: 1.26 (±0.14)[b] 6 mg mL^{-1}: 1.36 (±0.08)[b] 8 mg mL^{-1}: 1.27 (±0.08)[b]
pDTT-Ace-DHCA$_{20}$	4904	5874 ± 226[a]	1.234 ± 0.09[a]
pDTT-Ace-DHCA$_{100}$	10313	13860 ± 480[a]	1.25 ± 0.72[a]
pDTT-Cat$_{100}$	8870	18250[c]	1.50[c]
pDTT-Cat$_{20}$	3366	2 mg mL^{-1}: 6703[c] 4 mg mL^{-1}: 6789[c] 6 mg mL^{-1}: 6733[c] 8 mg mL^{-1}: 6783[c]	2 mg mL^{-1}: 1.85[c] 4 mg mL^{-1}: 1.80[c] 6 mg mL^{-1}: 1.78[c] 8 mg mL^{-1}: 1.81[c]

[a] Estimated by SEC-MALS from a single sample using d*n*/d*c* calculated assuming 100% mass recovery, with uncertainty reported from ASTRA software. [b] Estimated by SEC-MALS from four individual solutions of increasing polymer concentration (2, 4, 6, and 8 mg mL^{-1}) using d*n*/d*c* calculated assuming 100% mass recovery. [c] Measured relative to pMMA standards entirely from RI vs. Elution time chromatograms.

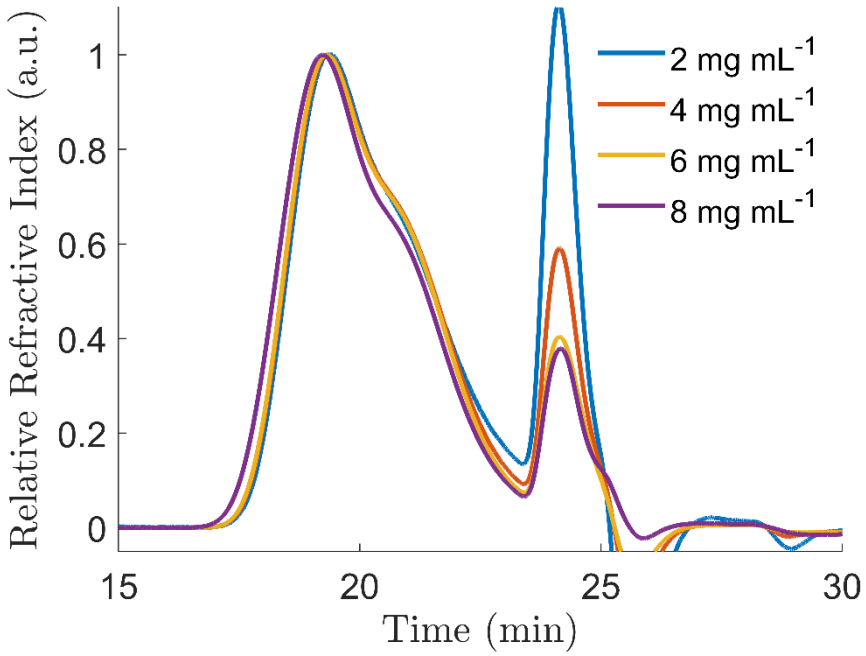


Figure S9. SEC traces of pDTT-Cat_{20} at varying polymer concentration showing a small effect on elution time, due to interactions between catechol groups.

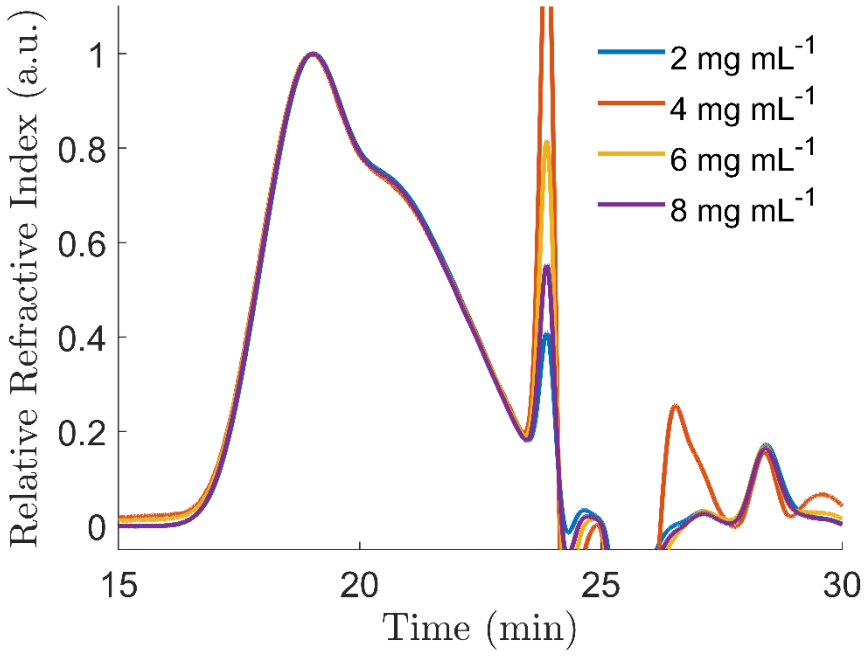


Figure S10. SEC traces of pDTT-TBS-$DHCA_{20}$ at varying polymer concentration showing no effect on elution time.

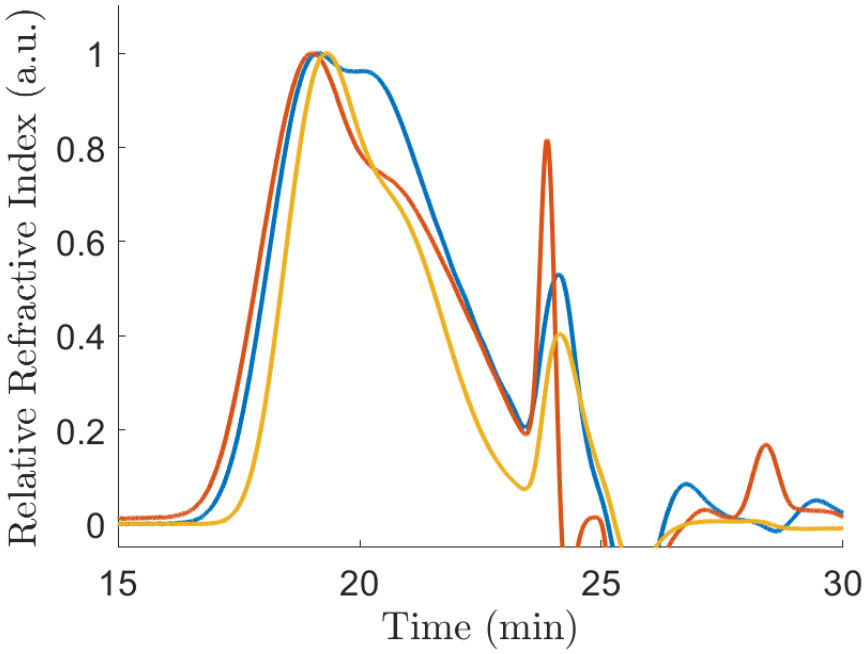


Figure S11. SEC traces of pDTT (blue), pDTT-TBS-DHCA$_{20}$ (orange), and pDTT-Cat$_{20}$ (yellow). All sample concentrations were 4 mg mL^{-1}.

Plots of Rayleigh ratio vs. elution time showing negative light scattering

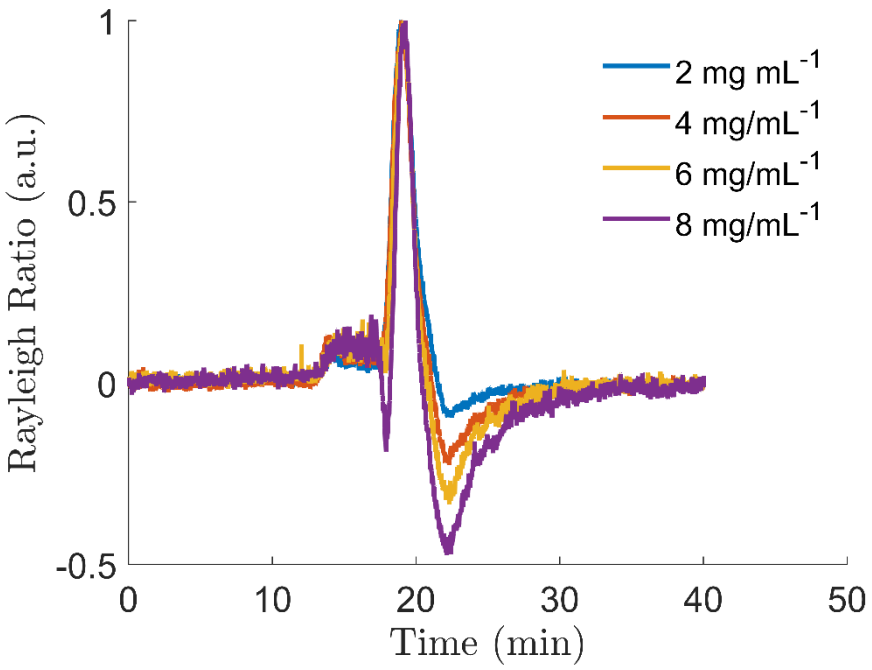


Figure S12. SEC traces of pDTT-Cat_{20} at varying polymer concentration where the partially negative Rayleigh Ratio makes interpretation through light scattering theory unreliable.

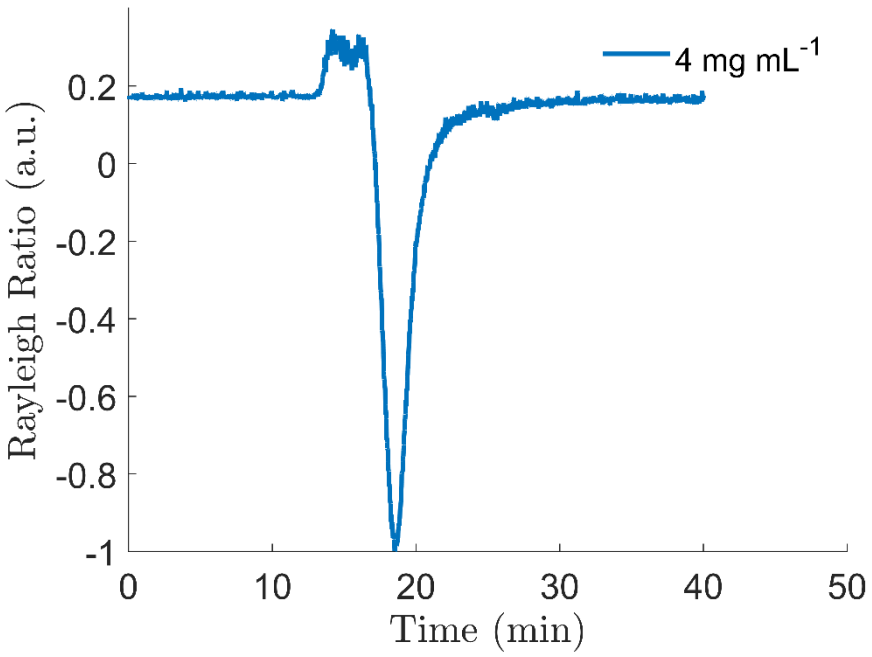


Figure S13. SEC trace of pDTT-Cat_{100} where the negative Rayleigh ratio makes interpretation through light scattering theory unreliable.

Degradation studies

Degradation of pDTT-Cat_{20} and pDTT-Cat_{100} was studied using ^{1}H NMR and SEC. For ^{1}H NMR experiments, 1.1 µmol polymer (10 mg pDTT-Cat_{100}, M_n = 8870 g mol^{-1}, and 3.8 mg pDTT-Cat_{20}, M_n = 3366 g mol^{-1}) was dissolved in 0.6 mL DMSO-d_6 in an NMR tube. DTT (3.5 mg, 22 µmol) and Et_3N (1.1 mg, 11 µmol) was dissolved in 1 mL DMSO-d_6, and 0.1 mL of this solution, corresponding to 1 equiv. DTT (0.34 mg, 2.2 µmol) and 0.5 equiv. Et_3N (0.11 mg, 1.1 µmol) with respect to polymer end-caps, was added to the NMR tube immediately prior to recording the first spectrum. The polymer concentration was 1.6 mM in all experiments. In a control experiment, only Et_3N was added to DMSO-d_6 and to the NMR tube.

^{1}H NMR analysis of depolymerization of pDTT-Cat_{100}

Figure S14 shows ^{1}H NMR spectrum of completely depolymerized pDTT-Cat_{100}. Besides cyclic monomer, cDTT-$(Cat)_2$, the spectrum shows a signal from unmodified cDTT (C**H**-OH, 5.23 ppm, red star). For reference, **Figure S15** shows a ^{1}H NMR spectrum of cDTT in DMSO-d_6. The peak from cDTT seen in **Figure S14** owes to the unmodified, linear DTT added to the sample to initiate the cyclization cascade through the polymer backbone.

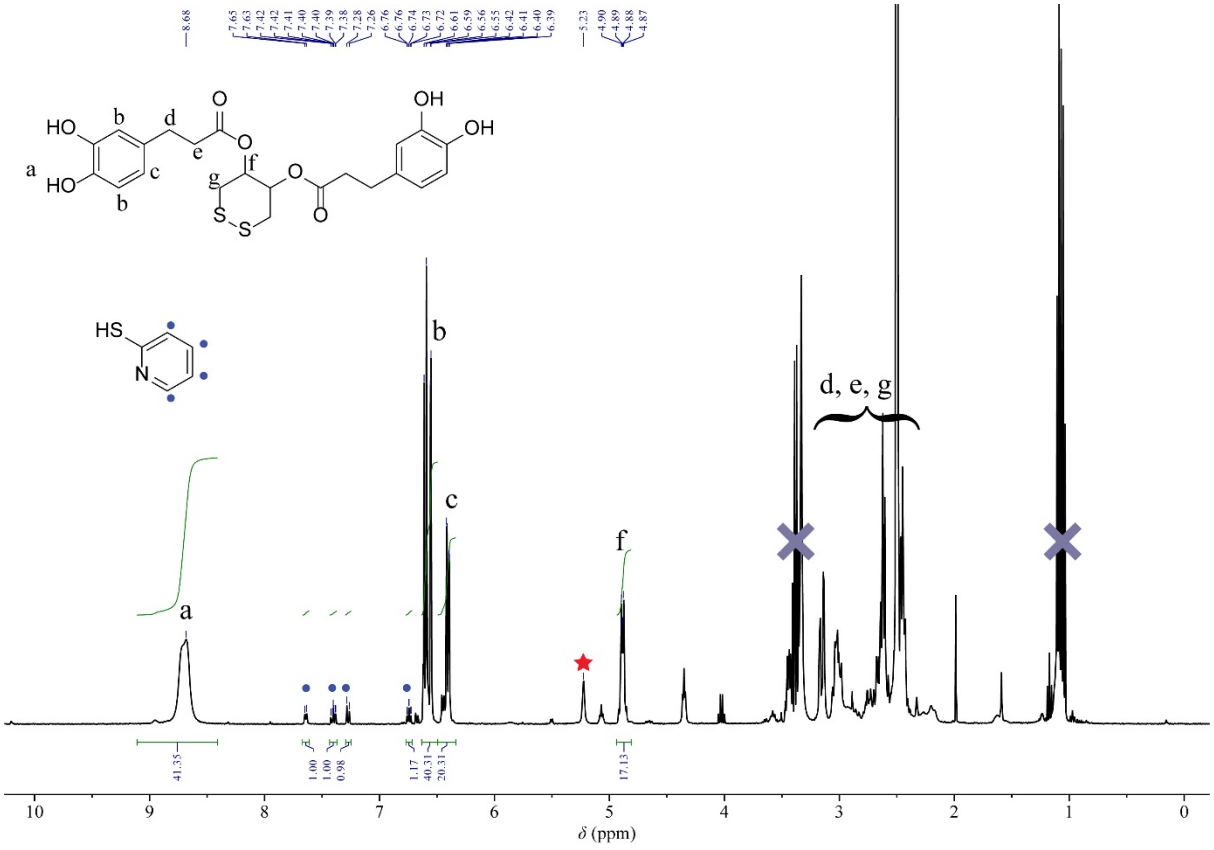


Figure S14. ^{1}H NMR of pDTT-Cat_{100} in DMSO-d_6, after completion of depolymerization upon addition of DTT/Et_3N. Signals are assigned according to the structure shown, and integrals are relative to end-cap proton (7.64 ppm). Solvent impurities (diethyl ether and water) are marked with grey crosses while the red star (5.23 ppm) indicates signal from cDTT (C**H**-OH), originating from the DTT added to initiate the cyclization cascade reaction.

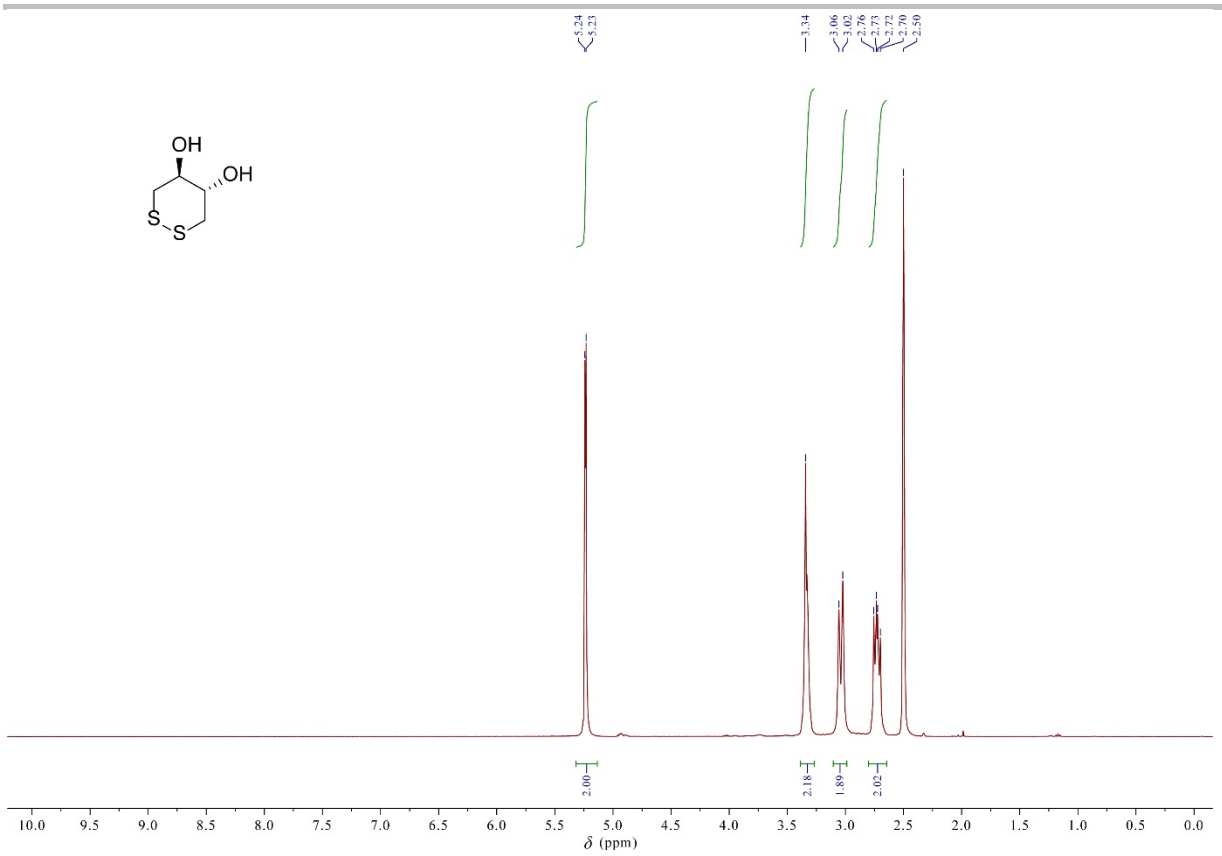


Figure S15. Reference ^{1}H NMR spectrum of cyclic DTT in DMSO-d_6.

Figure S16 shows an array of ^{1}H NMR spectra of pDTT-Cat$_{100}$, recorded in succession after adding DTT and Et_3N. Each spectrum was recorded for 20 s. Bottom spectrum is recorded prior to initiating depolymerization while top spectrum is the final spectrum recorded after 15 min. %Depolymerization was taken as the fraction of proton f in polymeric form at 5.28 ppm and in the monomeric, cyclic form at 4.89 ppm. Thus, %Depolymerization was determined according to equation S17.

$$\%\text{Depolymerization} = \frac{\text{Area}_{4.89\ \text{ppm}}}{\text{Area}_{4.89\ \text{ppm}} + \text{Area}_{5.28\ \text{ppm}}} \times 100\% \qquad \text{(S17)}$$

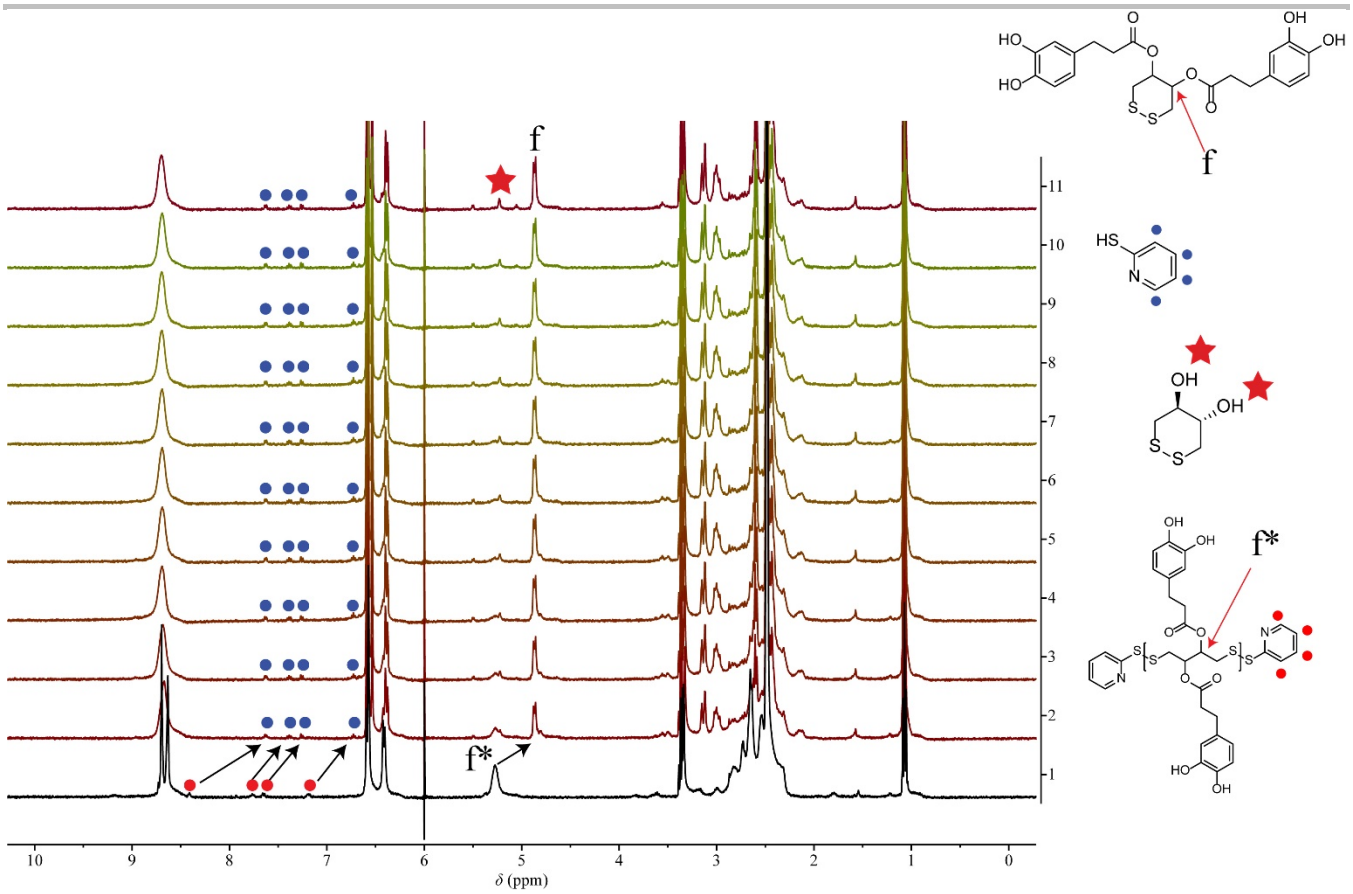


Figure S16. Successive ^{1}H NMR spectra recorded during depolymerization of pDTT-Cat$_{100}$, initiated through decapping by base-catalyzed thiol/disulfide exchange through reaction with DTT and Et_3N. Relevant peaks are labelled using symbols according to chemical structures shown on the right.

^{1}H NMR analysis of depolymerization of pDTT-Cat$_{20}$

Figure S17 shows ^{1}H NMR spectra for pDTT-Cat$_{20}$ and the products of complete depolymerization. Since most peaks before and after depolymerization overlap, depolymerization was described by the ratio of the peak at 3.72 ppm, ascribed to the proton C**H**-OH on unmodified repeat units, before and after initiating depolymerization. Furthermore, this is the peak that is most representative of the polymer, as it constitutes ~80% of the polymer. Thus, %Depolymerization was taken as equation S18.

$$\%\text{Depolymerization} = \frac{\text{Area}_{3.72\ \text{ppm}-\text{depolymerizing}}}{\text{Area}_{3.72\ \text{ppm}-\text{intact polymer}}} \times 100\% \quad \text{(S18)}$$

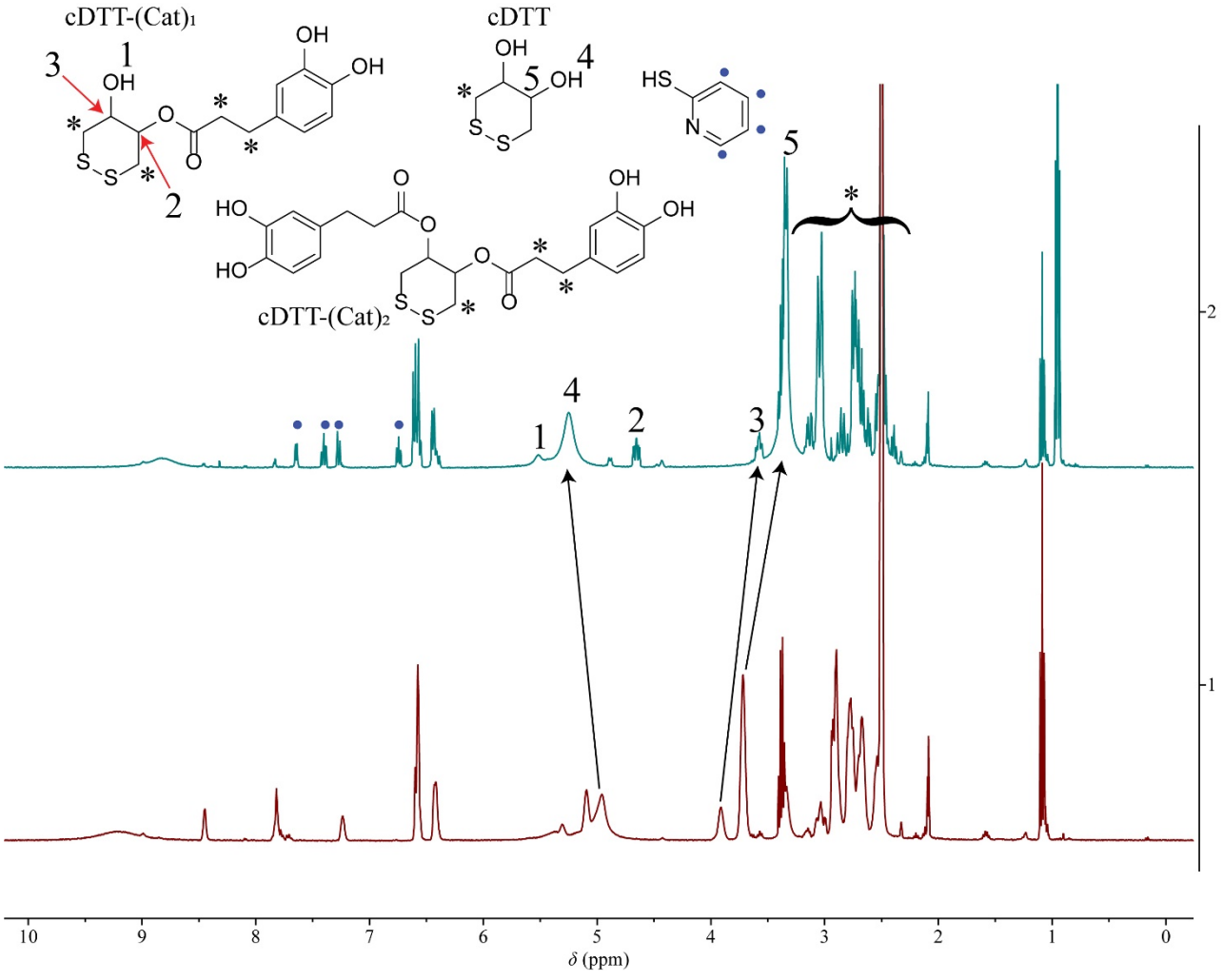


Figure S17. ^{1}H NMR Spectra of pDTT-Cat$_{20}$ (bottom) and products of depolymerizing pDTT-Cat$_{20}$ (cDTT-(Cat)$_2$, cDTT-(Cat)$_1$, cDTT, and end-caps) (top).

Response of adding only Et_3N to pDTT-Cat_{20}

To test if background reaction between the catalytic base (Et_3N) and the polymers should take place, a kinetic degradation experiment was carried out by adding only Et_3N to a solution of pDTT-Cat_{20}. Briefly, two separate solutions was prepared, the first consisting of pDTT-Cat_{20} (n = 16, M_n = 3366 g mol^{-1}, 3.8 mg, 1.1 µmol, 1 equiv.) dissolved in 0.6 mL DMSO-d_6. The second solution was Et_3N (1.1 mg, 11 µmol) in 1 mL DMSO-d_6. 0.1 mL of the second solution, corresponding to 0.11 mg Et_3N (1.1 µmol, 0.5 equiv. with respect to end-caps), was added to the solution containing pDTT-Cat_{20}. **Figure S18** shows the NMR spectrum of pDTT-Cat_{20} obtained prior to adding Et_3N as well as the final spectrum of the array of spectra obtained every 15 s over a 10 min period. After 10 min, no discernible difference is observed and end-caps are still installed on the polymers. This shows that Et_3N alone does not trigger depolymerization nor end-cap removal on the timescale on which depolymerization with DTT and Et_3N takes place.

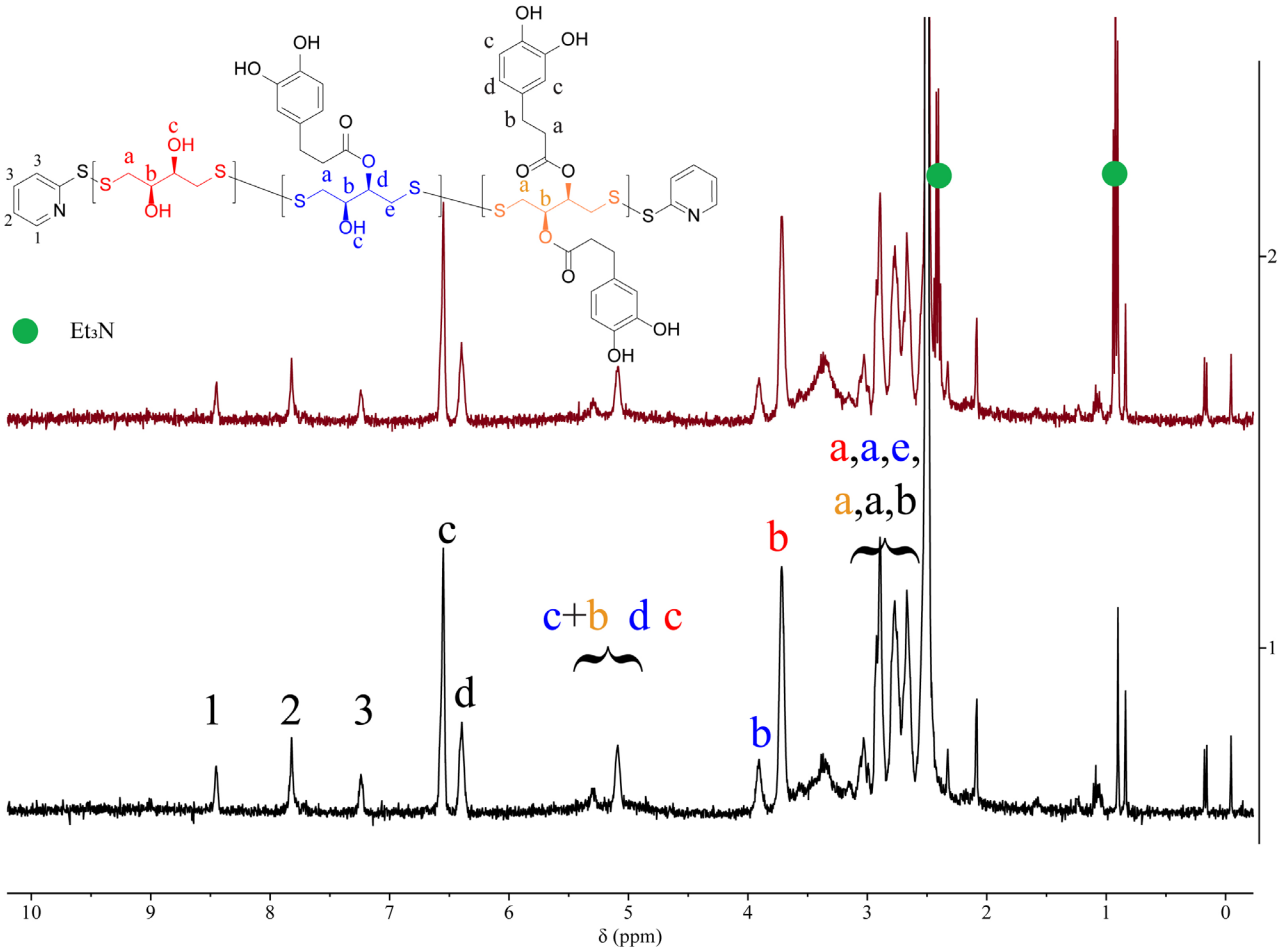


Figure S18. NMR spectrum of pDTT-Cat_{20} in DMSO-d_6 before (bottom) and 10 min after (top) addition of 0.5 equiv. Et_3N (top).

Size exclusion chromatography

For SEC studies of polymer degradation, 5 mg polymer was dissolved in 1.0 mL DMF with 10 mM LiBr. To this solution, 1 equiv. DTT and 0.5 equiv. Et_3N w.r.t. end-caps were added, as in the ^1H NMR experiment. The reaction was left overnight to ensure complete degradation. **Figure S19** shows traces of depolymerization products from pDTT-Cat_{100} (orange), pDTT-Cat_{20} (blue) and cDTT reference (yellow). Depolymerization products originating from pDTT-Cat_{100} shows a single peak at 23 min, indicating presence of just one monomer type, i.e. cDTT-$(Cat)_2$. In contrast, degradation products of pDTT-Cat_{20} show three distinct peaks. The peak at 27 min is ascribed to cDTT, as it matches the cDTT SEC trace in **Figure S19** well, while the one found at 25 min is assigned to cDTT-Cat. The peak at 24 min is most likely a solvent peak, as it is also observed in the SEC trace of initial polymer sample (see **Figure S9**).

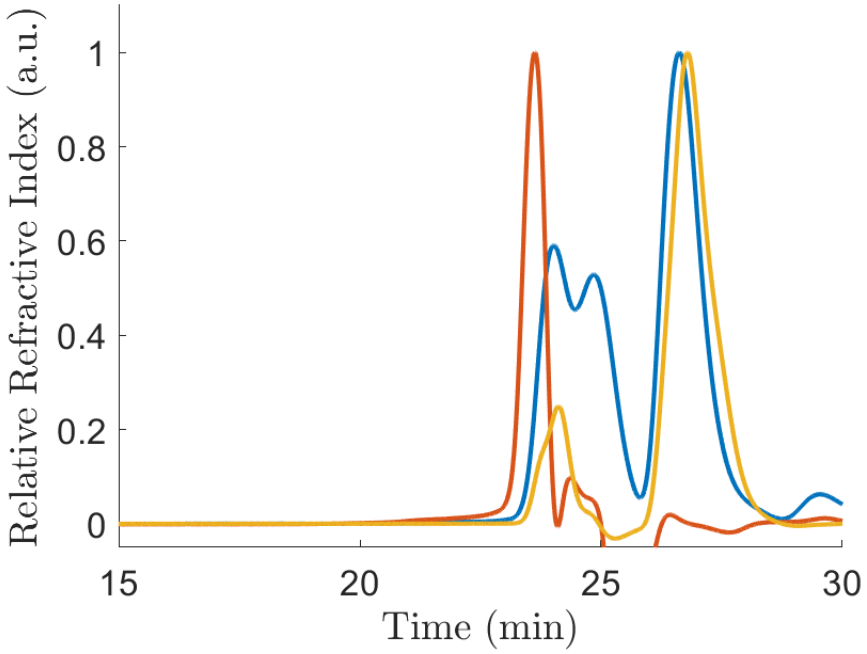


Figure S19. SEC traces of degradation products of pDTT-Cat_{100} (orange), pDTT-Cat_{20} (blue), and cDTT reference (yellow).

Figure S20 shows SEC-MALS traces obtained from concentrated solutions of pDTT (n = 16, M_n = 2652 g/mol) after various degradation conditions, described below. The concentration was 100 mg mL^{-1}; 40 mM, and was diluted to 4 mg mL^{-1} prior to GPC measurements. To 1 mL of concentrated pDTT solution (corresponding to 100 mg polymer, 37 µmol, 1 equiv.), either DTT (1.4 mg, 9.3 µmol, 0.25 equiv. with respect to end-caps) or DTT (1.4 mg, 9.3 µmol, 0.25 equiv. with respect to end-caps) and Et_3N (1.9 mg, 18.6 µmol, 0.5 equiv. with respect to end-caps) were added to investigate if larger, cyclic molecules resulting from inter-chain reactions could be detected. However, as **Figure S20** shows, only one peak is observed, ascribed to cyclic monomer, cDTT. Chromatograms can be compared with that of unmodified pDTT (see **Figure S11**) to demonstrate the difference.

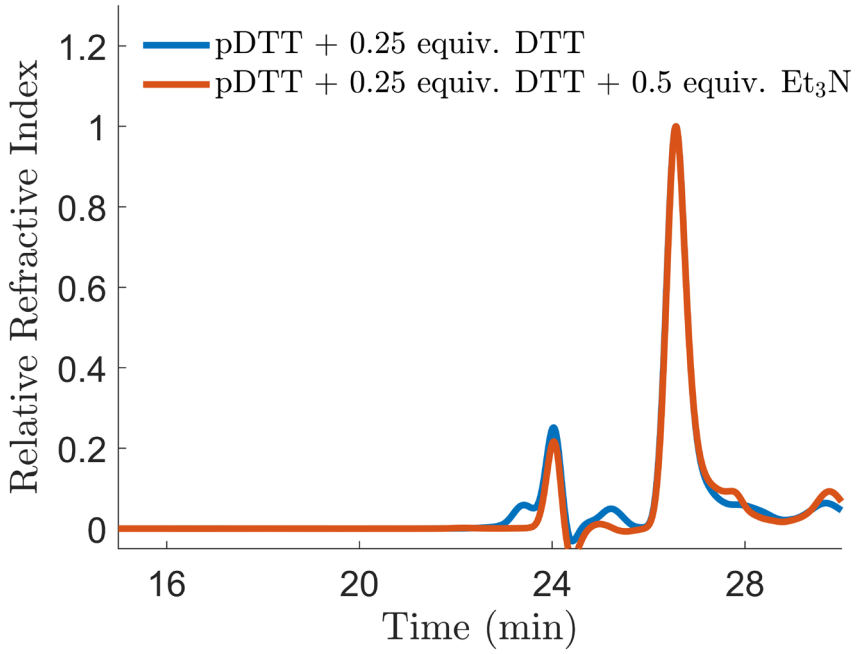


Figure S20. SEC traces obtained from concentrated solutions of pDTT (40 mM, 100 mg mL^{-1}) with either 0.25 equiv. DTT or 0.25 equiv. DTT and 0.5 equiv. Et_3N w.r.t. end-caps.

SUPPORTING INFORMATION

Gel formation

In a 2 mL screw cap vial, pDTT-Cat_{20} (n = 16, M_n = 3366 g mol^{-1}, 20 mg, 5.9 µmol) was dissolved in 155 µL of a 5 mg mL^{-1} solution of Rhodamine 6G in MeOH. To this, 26 µL of aqueous 0.6 M $AlCl_3 \bullet 6H_2O$ was added. Finally, 250 µL 0.5 M NaOH (aq) was added to adjust pH and induce formation of tris-catecholato-Al^{3+} complexes, resulting in formation of a gel. **Figure S21a,b** shows formation of gels.

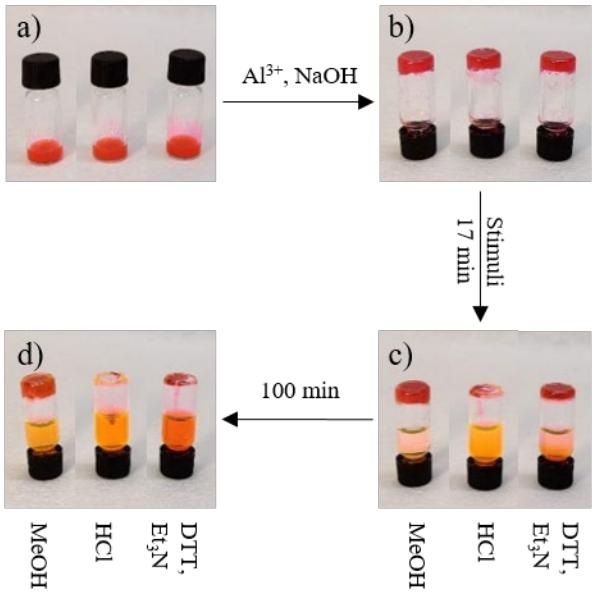


Figure S21. a) Three identical vials containing pDTT-Cat_{20}, Rhodamine 6 G, and Al^{3+} in MeOH until b) adding NaOH to raise pH and induce hydrogel formation. c) Pictures taken 17 min and d) 100 min after adding (from left to right) pure MeOH, 1 M HCl in MeOH, or DTT/ET_3N in MeOH.

Gel degradation

To induce gel degradation, either of the following solutions was added to the gel: pure MeOH (0.7 mL), 1M HCl in MeOH (0.7 mL), or a solution of DTT (18.2 mg, 118 µmol, 10 equiv. with respect to end-caps) and Et_3N (6 mg, 59 µmol, 5 equiv. with respect to end caps) in MeOH (0.7 mL). Structural integrity of gels was assessed using the inverted vial test i.e. inversion of vials with cast gels in the bottom, to assess whether the gel remain intact and stick to the vial. Under acidic conditions, the catecholato-metal crosslinks quickly dissolve and the gel vanishes within 17 min (**Figure S21c**). Addition of DTT/Et_3N also induces gel degradation, although minor amounts of gel now remain after 100 min, because of relatively slower depolymerization kinetics (**Figure S21d**). In contrast, the reference sample with the gel submerged in pure MeOH retained structural integrity with only little dye leaching from the material over time.

UV -study of dye release from gels

Gels were cast as described above. Either of the following solutions was added to the vial containing the gel: pure MeOH, 1 M HCl in MeOH, or DTT/Et_3N in MeOH. At specific times, the vial with the gel was carefully inverted to homogenize the dye into the solution, immediately prior to withdrawing a small aliquot of the solution (10 µL). The aliquot was diluted into 2 mL MeOH, and the absorbance at 529 nm was measured. Figures below show the original UV vis spectra for dye release from gels in MeOH (**Figure S22**), 1 M HCl in MeOH (**Figure S23**) and DTT (18.2 mg, 118 µmol, 10 equiv. with respect to end-caps) and Et_3N (6 mg, 59 µmol, 5 equiv. with respect to end caps) end-caps in MeOH (**Figure S24**).

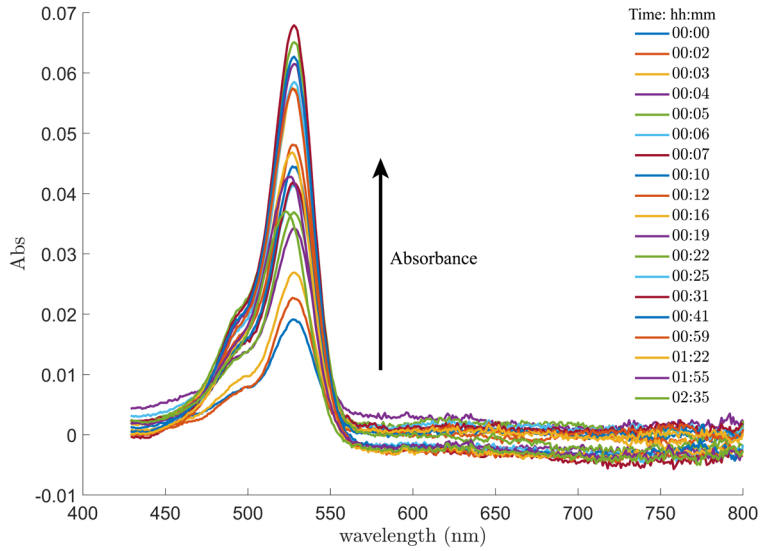


Figure S22. UV-vis spectra measured (as function of time) on the solution above a pDTT-Cat_{20} gel immersed in pure MeOH.

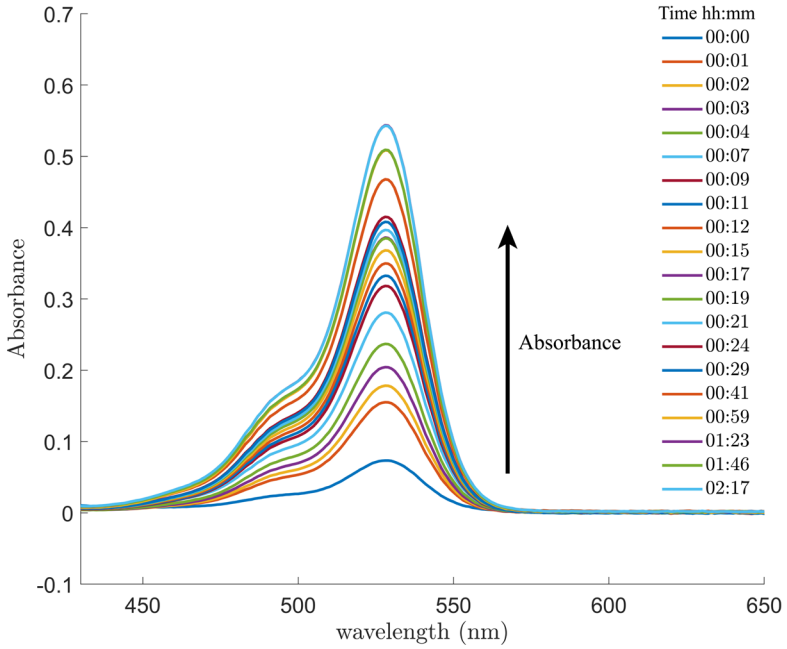


Figure S23. UV-vis spectra measured (as function of time) on the solution above a pDTT-Cat_{20} gel immersed in 1 M HCl in MeOH.

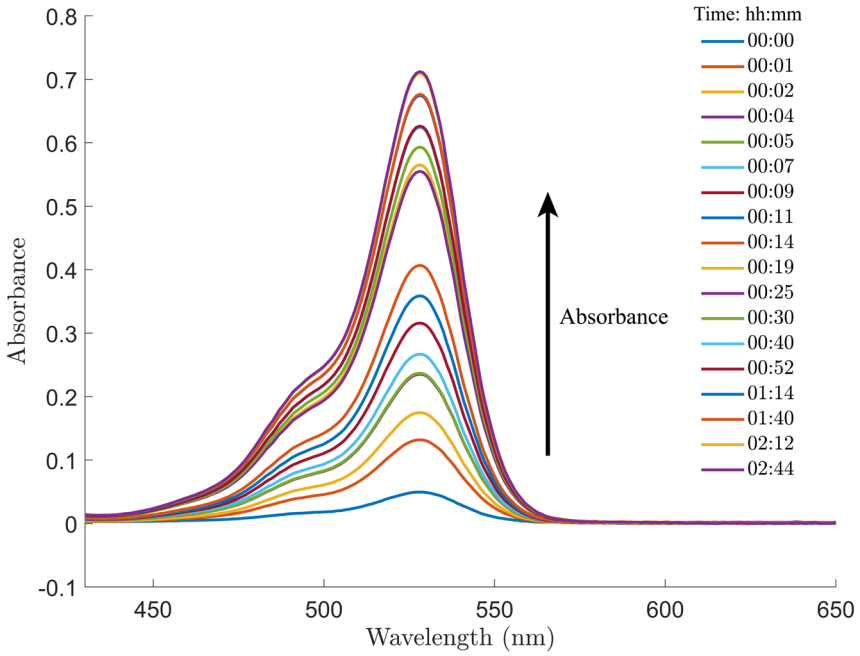


Figure S24. UV Vis spectra measured (as function of time) on the solution above a pDTT-Cat_{20} gel immersed in MeOH with 10 equiv. DTT and 5 equiv. Et_3N with respect to end-caps.

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[S2] G. Allegretta, E. Weidel, M. Empting, R. W. Hartmann, *Eur. J. Med. Chem.,* **2015**, *90*, 351–9.
[S3] M. K. Lakshman, F. A. Tine, T. A. Khandaker, V. Basava, N. B. Agyemang, M. S. A. Benavidez, et al., *Synlett,* **2017**, *28*, 381–5.

Author Contributions

A.H.A., H.B., and K.D. conceived the idea; A.H.A. and A.S. synthesized and characterized all compounds; all authors discussed results, analyzed and interpreted data, and commented on the manuscript.