Supplementary Material (ESI) for Polymer Chemistry



# Electronic Supplementary Information

# Selective Cleavage of Polymer Grafts from Solid Surfaces: Assessment of Initiator Content and Polymer Characteristics

Susanne Hansson, Per Antoni, Helena Bergenudd and Eva Malmström

*KTH Fibre and Polymer Technology, Royal Institute of Technology, Teknikringen 56-58, SE-100 44 Stockholm, Sweden.*

## Experimental Section

### Materials

4-(Dimethylamino)pyridine (DMAP, 99%), copper(II) bromide (Cu(II)$Br_2$, 99%), *N*,*N*,*N*′,*N*′′,*N*′′-pentamethyldiethylenetriamine (PMDETA, 99%), Whatman No. 1 filter paper, and microcrystalline cellulose (MCC, 20 μm) were purchased from Sigma Aldrich. 1,4-Dithiothreitol (DTT, 99 %) was purchased from Apollo Scientific. Ascorbic acid (AsAc, 99%), sodium bisulfate ($NaHSO_4$), and sodium carbonate ($Na_2CO_3$) were purchased from Fluka. Triethylamine (TEA) was purchased from Merck. Methyl methacrylate (MMA, 99%, Sigma Aldrich) was passed through a column of neutral aluminum oxide ($Al_2O_3$, Sigma Aldrich) prior to use in order to remove the inhibitor.

### Instrumentation

$^1$H NMR spectra were recorded on a Bruker Avance 400 MHz NMR instrument, using $CDCl_3$ as solvent. The solvent residual peak was used as internal standard.

Field-Emission Scanning Electron Microscope (FE-SEM) images were recorded on a Hitachi S-4800 FE-SEM. The samples were mounted on a substrate with carbon tape and coated 3 s of a carbon coater (Cressington 108carbon/A) and subsequently 2 x 4 nm of a gold/palladium sputter coater (Cressington 208HR).

Infrared spectra were recorded on a Perkin-Elmer Spectrum 2000 FT-IR equipped with a MKII Golden Gate$^{TM}$, Single Reflection ATR System (from Specac Ltd, London, UK). The ATR-crystal was a MKII heated Diamond 45º ATR Top Plate.

Size Exclusion Chromatography (SEC) using THF (1.0 mL min$^{-1}$) as the mobile phase was performed at 35 ºC using a Viscotek TDA model 301 equipped with two T5000 columns with porous styrene divinylbenzene copolymer (300 mm L × 7.8 mm ID, exclusion

limit MW polystyrene: 400,000,000 Da) from Malvern (UK), a VE 2500 GPC autosampler, a VE 1121 GPC solvent pump, and a VE 5710 GPC degasser from Viscotek Corp. (the Netherlands). A conventional calibration method was created using narrow linear polystyrene standards. Corrections for the flow rate fluctuations were made by using toluene as an internal standard. Viscotek OmniSEC version 4.0 software was used to process data.

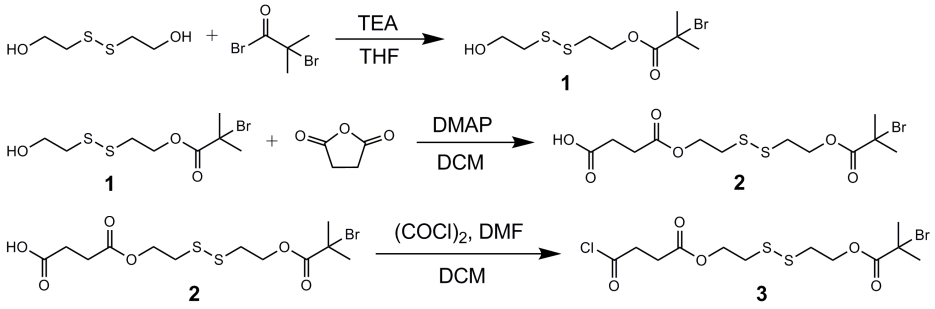
A Cary 100 UV/VIS spectrophotometer (Varian, Palo Alto, CA, USA) was used to record the absorbance increase at 412 nm. The cleaved cellulose substrate was immersed in 20 mL of a 3.0 mM DTNB phosphate buffer solution, pH 7.0, for 30 min to make sure that all thiols on the surface are accessible. An aliquot of the solution (1 mL) was characterized using a 3.0 mM solution of DTNB medium as reference (1 mL). Prior to the DTNB-treatment, each cleaved substrate was weighed (see Sample weight in Table 2), in order to assess the initiator content.

**Synthesis of 2-((2-hydroxyethyl)disulfanyl)ethyl 2-bromo-2-methylpropanoate (1).** See Scheme ESI.1 for the synthetic pathway. 2-Hydroxyethyl disulfide (10.0 g, 64.8 mmol) and TEA (9.8 g, 96.5 mmol) was dissolved in 200 mL of THF and cooled down to 0°C. 2-bromo-2-methylpropanoyl bromide (14.9 g, 64.8 mmol) was added dropwise to the reaction where upon a white salt was formed. The reaction was left to stir and reach room temperature for 3 h. The salt was filtered off and the solution was concentrated and followed by addition of 150 mL DCM. The organic phase was washed using 3 x 20 mL of $NaHSO_4$, 3 x 20 mL of $Na_2CO_3$ and 1 x 20 mL of brine. The organic phase was dried using $MgSO_4$ and then filtered. The solvent was removed and the crude product was purified using flash chromatography by slowly increasing the gradient from 100% heptane to 60/40 heptane/ethyl acetate. Yield: 43.8 % (15.4 g). $^1$H NMR (400 MHz, $CDCl_3$): δ 1.93 (s, 6H, -C*H*$_3$), 2.14 (t, 1H, -O*H*), 2.88 (t, 2H, HOCH$_2$C*H*$_2$S-), 2.96 (t, 2H, -SC*H*$_2$CH$_2$O-), 3.89 (dt, 2H, HOC*H*$_2$CH$_2$S-) and 4.44 (t, 2H, -SCH$_2$C*H*$_2$O-) ppm; $^{13}$C NMR (CDCl3): δ 30.7, 36.5, 41.6, 55.5, 60.2, 63.7, and 171.6 ppm.

**Synthesis of 4-(2-((2-(2-bromo-2-methylpropanoyloxy)ethyl)disulfanyl)ethoxy)-4-oxobutanoic acid (2).** See Scheme ESI.1 for the synthetic pathway. Succinic anhydride (1.89 g, 18.9 mmol) was added to a flask of containing **1** (4.80 g, 15.8 mmol), DMAP (386 mg, 3.16 mmol), and 20 mL DCM. The reaction was left over night at room temperature. The full substitution of the hydroxyl was monitored using $^1$H NMR. The remaining succinic acid anhydride was quenched using 5 mL of $H_2O$ over night. 100 mL of DCM was added to the flask prior to washing of the organic phase using 3x10 mL $NaHSO_4$ and 1x10 mL brine. The organic phase was dried using $MgSO_4$ and filtered. The oily product was obtained after removal of the solvent. Yield: 92% (6.37 g). $^1$H NMR (400 MHz, CDCl3): δ 1.93 (s, 6H, -C*H*$_3$), 2.65 (m, 4H, -OC*H*$_2$C*H*$_2$O-), 2.94 (m, 4H, -C*H*$_2$SSC*H*$_2$-), 4.36 (t, 2H, -OC*H*$_2$CH$_2$S-) and 4.43 (t, 2H, -SC*H*$_2$CH$_2$O-) ppm; $^{13}$C NMR ($CDCl_3$): δ 25.6, 28.8, 28.9, 30.7, 36.7, 55.5, 62.5, 67.9, 171.5, 171.9, and 177.7 ppm.

**Synthesis of 2-((2-(2-bromo-2-methylpropanoyloxy)ethyl)disulfanyl)ethyl 4-chloro-4-oxobutanoate (3).** See Scheme ESI.1 for the synthetic pathway. Oxalyl chloride (1.57 g, 12.3 mmol) and **2** (2.5 g, 6.6 mmol) was dissolved in 5 mL of DCM and cooled down

to 0°C. Three drops of DMF was added to catalyze the reaction. The reaction was left to reach room temperature for three hours. The remaining oxalylchloride was azeotropically removed using 6x20 mL of chloroform. The product was obtained as yellow oil. Yield: 99% (2.78 g). $^{1}$H NMR (400 MHz, $CDCl_3$): δ 1.96 (s, 6H, -C$H_3$), 2.73 (t, 2H, -OCH$_2$C$H_2$O-), 2.94 (m, 4H, -C$H_2$SSC$H_2$-), 3.25 (t, 2H, -OC$H_2$CH$_2$O-), 4.41 (t, 2H, -OC$H_2$CH$_2$S-) and 4.46 (t, 2H, -SC$H_2$CH$_2$O-) ppm. $^{13}$C NMR (CDCl3): δ 29.4, 30.7, 36.7, 41.7, 55.5, 62.8, 63.5, 170.7, 171.5, and 173.0 ppm.




**Scheme ESI.1.** The synthesis of the initiators containing a disulfide linkage.

**Immobilization of initiator 3 on cellulose.** The procedure for immobilization of initiator on the cellulose surface was adopted from Carlmark and Malmström[1]. Prior to the immobilization of the initiator, the filter paper (2 x 3 cm$^2$) was washed with ethanol, acetone, and tetrahydrofuran (THF) and also ultrasonicated for 2 min in each solvent. The available hydroxyl groups on the surface were converted into ATRP initiators by immersing the filter paper in a solution containing **3** (559 mg, 1.33 mmol), TEA (148 mg, 1.46 mmol), and a catalytic amount of DMAP in THF (20 mL). The reaction was allowed to proceed for 0.25, 0.5, 1 or 18 h at room temperature on a shaking device. Thereafter, the filter paper was thoroughly washed in THF and ethanol, in order to remove residual reactants and by-products. The same procedure was used for MCC (0.34 g) with **3** (1.68 g, 3.98 mmol), TEA (0.44 g, 4.38 mmol), and a catalytic amount of DMAP in DCM (50 mL). The reaction time was 3.5 h at room temperature.

**Polymerization of MMA from cellulose and sacrificial initiator 1 via ARGET ATRP.** The initiator-functionalized paper (2 x 3 cm$^2$) was immersed into a 25 mL round-bottomed flask containing anisole (10 g), MMA (10 g, 0.10 mol), sacrificial initiator **1** (39.4 mg, 0.13 mmol), N,N,N′,N′′,N′′-pentamethyldiethylenetriamine (PMDETA) (21.7 mg, 0.13 mmol), Cu(II)$Br_2$ (2.8 mg, 13 μmol), and ascorbic acid (AsAc) (22.0 mg, 0.13 mmol), targeting the final DP of 800. The flask was sealed with a rubber septum and purged with argon for 5 min in an ice-bath, before being placed in a thermostatted oil bath at 40 ˚C. The reaction was monitored with $^{1}$H-NMR and terminated when the desired conversion was reached by exposing the reaction mixture to air and by diluting it with DCM. The free polymer was purified by passing it through a column of activated neutral $Al_3O_2$ and subsequently by precipitation. The filter paper was thoroughly washed in DCM, THF, THF:$H_2O$ (1:1), $H_2O$, methanol, and ethanol.

**Cleavage of PMMA from the grafted cellulose substrate.** The PMMA-grafted filter paper (2 x 3 $cm^2$) was subjected to a mixture containing DTT (160.4 mg, 1.04 mmol) and TEA (210.5 mg, 2.08 mmol) in 20 mL THF. The reaction proceeded for 5 days in room temperature on a shaking device. Thereafter, the paper was carefully rinsed in THF followed by ultrasonication for five repetitive times. The polymer solution was concentrated and analyzed with SEC. The same procedure was employed for the initiator-functionalized filter papers and also for the MCC.

## FT-IR analysis

Fig. ESI.1 demonstrates the spectra of filter papers grafted with different contents of PMMA. The successive increase of the carbonyl peak at 1730 $cm^{-1}$ with DP proposes that it is possible to tailor the amount of polymer on the surface by utilizing a sacrificial initiator. The broad peak at 1640 $cm^{-1}$ corresponds to bound water within the cellulose structure and varies depending on how dry the sample is.

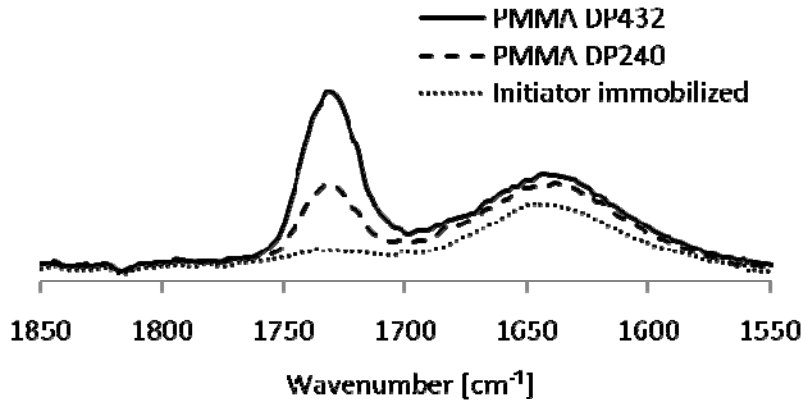



**Fig. ESI.1.** FT-IR spectra of PMMA-grafted filter papers with different DP.

A first trial to cleave off PMMA from a grafted filter paper using DTT (80.2 mg, 0.52 mmol) and TEA (105.2 mg, 1.04 mmol) showed that most polymers were removed after 18 h, see Fig ESI.2. However, to be able to determine the correct initiator content on the surface, all polymers have to be cleaved off. Hence, the filter paper was placed in a new DTT-solution (DTT: 80.2 mg, 0.52 mmol; TEA: 105.2 mg, 1.04 mmol) and left for 41 h and subsequently analyzed with FT-IR, demonstrating that more polymers have been cleaved off, but not all. Therefore, the filter paper was immersed in the same DTT-solution previously used and left for another 48 h. After that, in total 4.5 days, essentially all polymer chains had been cleaved. As a result, 5 days and a doubled amount of DTT

and TEA were employed to ensure complete cleavage, see Fig. ESI.2 and ESI.3 for the successful cleavages of the PMMA-grafted filter papers.

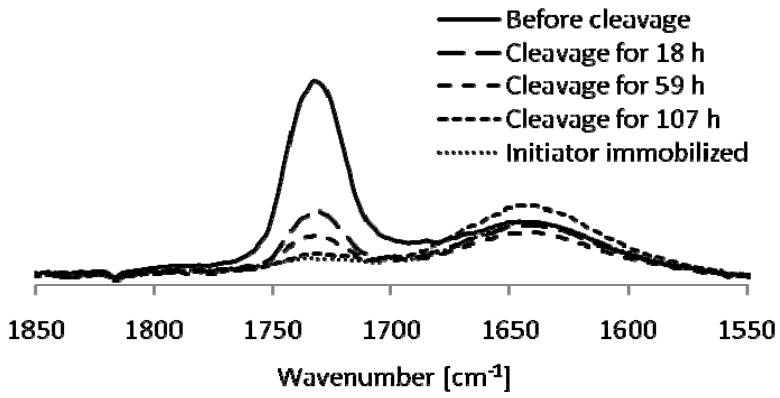



**Fig. ESI.2.**FT-IR spectra of repetitive cleavages of PMMA-grafted filter paper, in total 4.5 days.

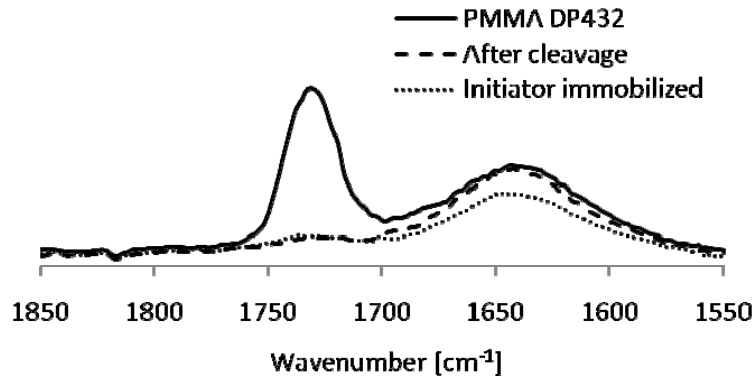



**Fig. ESI.3.** FT-IR spectra of $PMMA_{432}$-grafted filter paper before and after cleavage.

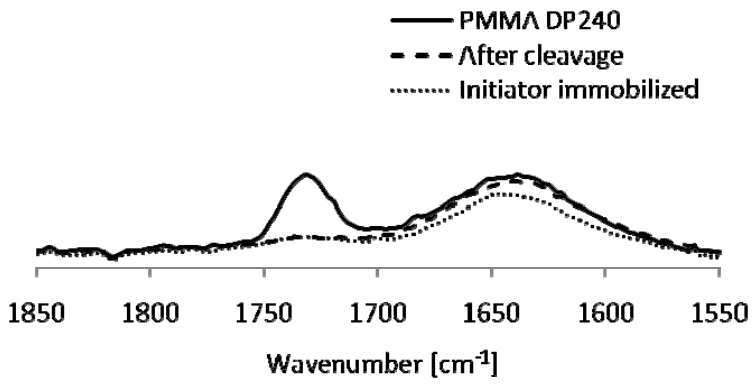



**Fig. ESI.4.** FT-IR spectra of $PMMA_{240}$-grafted filter paper before and after cleavage.

## UV analysis

A linear calibration curve ($R^2 \geq 0.9999$), see Fig. ESI.5, was obtained from measurements on five phosphate buffer solutions, pH 7, containing 3.0 mM DTNB and different concentrations of reduced glutathione[2] (GSH) (3.9, 7.8, 15.6, 31.3, and 62.5 μM). The GSH solutions were prepared directly before the measurements and kept on ice before being transferred to the reagent solution. The absorbance at 412 nm was recorded after 3 min with a 3.0 mM DTNB solution as reference. The extinction coefficient (the slope of the calibration curve) was $0.0130 \cdot 10^{-3}$ $M^{-1}$ $cm^{-1}$.

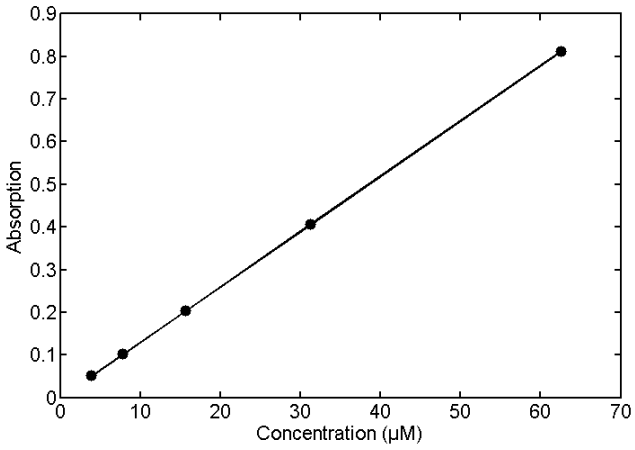



**Fig. ESI.5.** Calibration curve, with linear regression line, for the absorption of GSH in 3.0 mM DTNB solution at 412 nm ($\varepsilon_{GSH,DTNB} = 0.0130 \cdot 10^{-3}$ $M^{-1}$ $cm^{-1}$). The standard deviation is less than 1 %.

Absorption spectra for DTNB in phosphate buffer solution, pH 7.0, were recorded at different concentrations, and from that the extinction coefficient for DTNB at 412 nm was calculated: $0.179 \cdot 10^{-3}$ $M^{-1}$ $cm^{-1}$. Since the DTNB solution has absorption at 412 nm (Fig. ESI.6), which is at a steep part of the absorption curve, the absorption might be sensitive to the wavelength at which it is recorded. This could also be a difficulty when recording the absorption of other species (e.g. GSH) at 412 nm, *vide infra*. The absorption spectrum of TNB in the DTNB solution ($[DTNB]_0$ = 3.0 mM) was also recorded with a 3.0 mM DTNB solution as reference, see Fig. ESI.7, showing a significant increase in absorption at 412 nm.

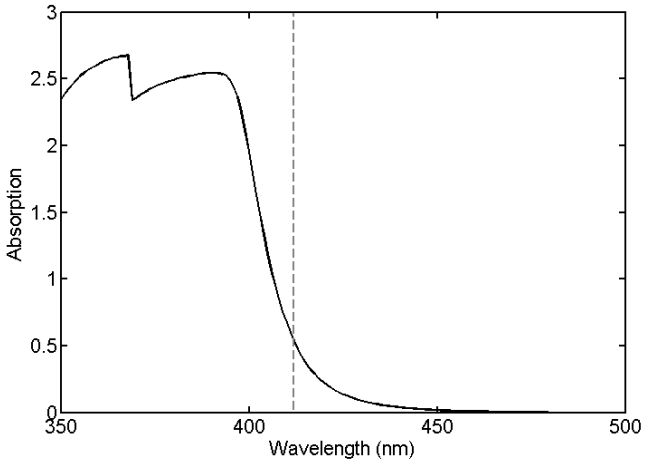



**Fig. ESI.6** Absorption spectrum of 3.0 mM DTNB in phosphate buffer, pH 7.0. The dotted line marks 412 nm.

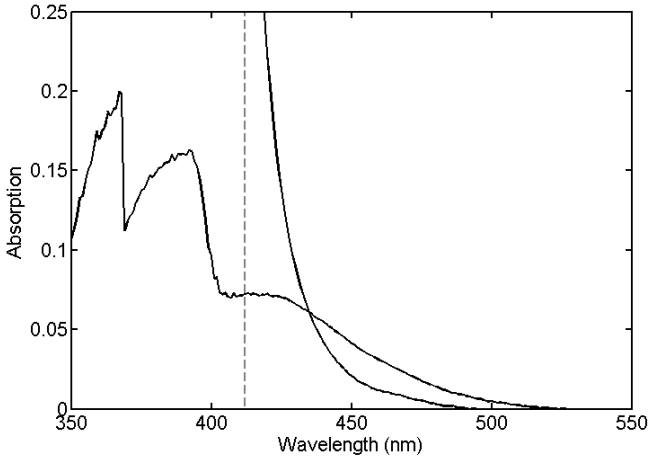



**Fig. ESI.7** Absorption spectrum of TNB in DTNB solution with 3.0 mM DTNB as reference, together with the DTNB spectrum from Fig. ESI.6. The dotted line marks 412 nm.

From the extinction coefficient for the 3.0 mM DTNB solution (i.e. $\varepsilon_{DTNB} = 0.179 \cdot 10^{-3}$ $M^{-1}$ $cm^{-1}$) and for GSH in 3.0 mM DTNB (i.e. $\varepsilon_{GSH,DTNB} = 0.0130 \cdot 10^{-3}$ $M^{-1}$ $cm^{-1}$) the absorptions of DTNB and GSH in the GSH/DTNB solution were calculated and plotted together with the calibration curve from Fig. ESI.5, resulting in Fig. ESI.8. Fig. ESI.8 shows that the DTNB concentration does not change significantly in this system due to its large excess over GSH and, hence, the absorption measurements at the steep part of the absorption spectrum of DTNB should not be a problem as long as the thiol concentration is kept within the linear range of the calibration curve (i.e. [thiol] ≤ 70 μM).

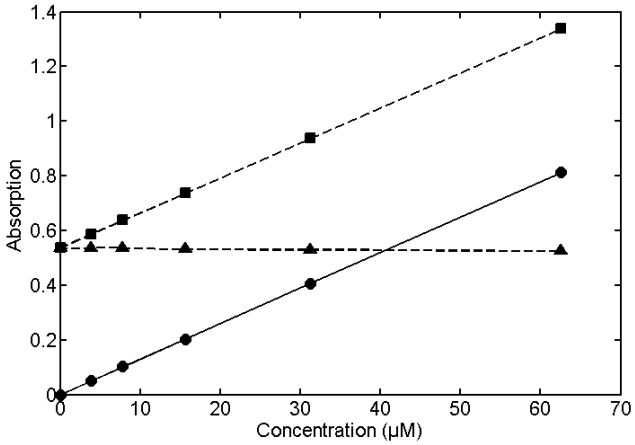



**Fig. ESI.8** Calculated absorption vs. concentration of GSH for a GSH/DTNB solution ($[DTNB]_0 = 3.0$ mM). DTNB (▲) and GSH (■, $\varepsilon_{GSH} = 0.0128 \cdot 10^{-3}$ $M^{-1}$ $cm^{-1}$). The calibration curve from Fig. ESI.5 is also included (●).

## References

1 Carlmark, A.; Malmström, E. *J. Am. Chem. Soc.* **2002**, *124*, 900-1.
2 Eyer, P.; Worek, F.; Kiderlen, D.; Sinko, G.; Stuglin, A.; Simeon-Rudolf, V.; Reiner, E. *Anal. Biochem.* **2003**, *312*, 224-227.