

# Supporting information for Specific molecular recognition driven catalysis using polymeric nanoreactors

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## Contents

Materials:.....	1
Instrumentation: .....	1
Chain extension of DMAP-co-styrene with NIPAM: .....	2
Formation of micelles.....	3
General protocol for the selective acylation reaction of 1-phenylpropanol (Table 1): .....	4
One pot selective acylation of different alcohols with butyric anhydride (Table 2 & Table 3): .....	6
Additional competitive reactions between 2 alcohols: .....	7

## Materials:

NIPAM (*N*-isopropylacrylamide) and AIBN (2,2'-azo-bis(isobutyronitrile)) were recrystallized from a 9:1 mixture of hexane/acetone and methanol respectively, and stored at 4°C. All other materials were used as received from Sigma-Aldrich, Fluka, and Acros.

## Instrumentation:

<sup>1</sup>H NMR spectra were recorded on a Bruker DPX-300 spectrometer in CDCl<sub>3</sub> at 25 °C (128 scans). Chemical shifts are given in ppm downfield from an internal reference of TMS. Size exclusion chromatography (SEC) measurements were performed with HPLC grade solvents (Fisher), tetrahydrofuran (THF) with 2 % of TEA, at 30 °C or dimethylformamide (DMF) with 1.06 g LiCl per liter at 40 °C as an eluent at a flow rate of 1 mL/min. The molecular weights of the synthesized polymers were calculated relative to polystyrene (PSt) or polymethylmethacrylate (PMMA) standards. For the

characterization of the particles, the micelle solutions were diluted with nanopure water to obtain a final concentration of ca. 0.1 mg/mL. TEM images were obtained using a JEOL electron microscope operating at 200 kV equipped with a LaB6 gun and a Gatan digital camera. To prepare TEM samples, carbon grids were prepared by air plasma treatment to increase the surface hydrophilicity and then 5  $\mu$ L of an aqueous solution of micelle was placed on a carbon-coated copper grid for 60s, and the water droplet was removed by a vacuum absorption. Aqueous UA solution (1%) was used to stain the particles using the blotting away method. DLS studies were conducted at 25 °C using a Zetasizer Nano series instrument (Malvern Instruments), at a fixed scattering angle of 173°. The data were processed by cumulants analysis of the experimental correlation function and particle diameters were calculated from the computed diffusion coefficients using the Stokes-Einstein equation. Each reported measurement was the average of three runs. For the HPLC measurements, the aliquots taken were analyzed on a reversed-phase Discovery C18 HPLC column, using a gradient method going from 95:5 water:methanol to 5:95 water:methanol over a 12 minute time period, at 2.0 mL/min using a PDA detector. Mesitylene was used as a standard ( $t_R$  = 10.31 min). For the GC measurements, the aliquots taken were analyzed on chiral capillary column (Varian CP-Chirasil-DEX fused WCOT, 25m x 0.25mm, with hydrogen, 1 kPa), using a gradient of temperature from 40 to 200 °C over a 9 minutes period, 2 mL/min, in combination with an FID detector. Mesitylene was used as a standard ( $t_R$  = 4.50 min).

### **Chain extension of DMAP-co-styrene with NIPAM:**

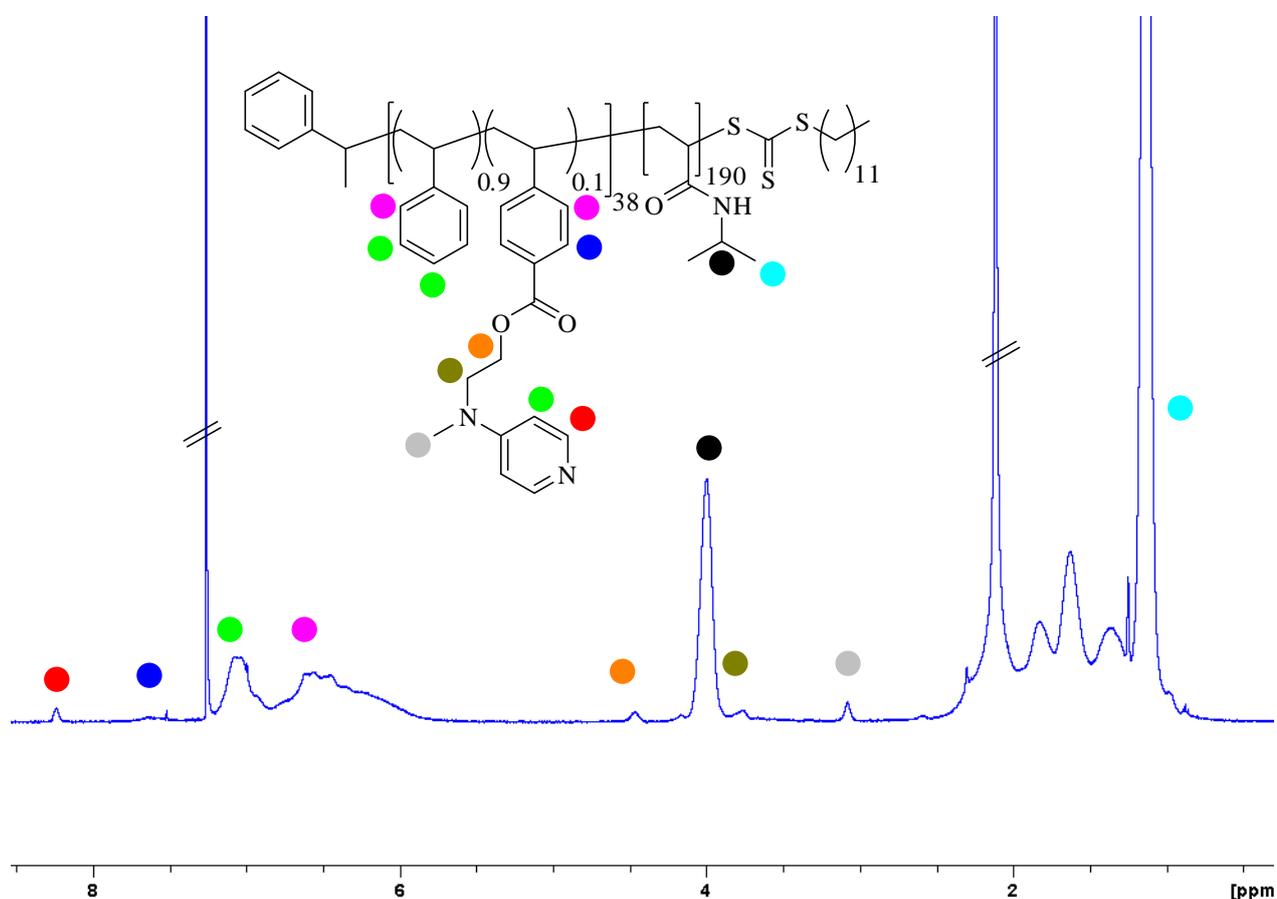
The synthesis of the DMAP containing monomer and its copolymerization with styrene has been previously reported.<sup>[1]</sup>

$$M_n(\text{NMR}) = 5.1 \text{ kDa}, n = 38, x = 0.9, M_n(\text{SEC THF, PS}) = 4.0 \text{ kDa}, M_w/M_n = 1.11.$$

The previously synthesized DMAP containing polymer (1 eq, 0.02 mmol), NIPAM (200 eq, 4 mmol) and AIBN (0.2 eq, 0.004 mmol) were dissolved in 2.2 mL of THF in a glass ampoule. The oxygen was removed by three freeze-pump-thaw evacuation cycles. For the last cycle, nitrogen was flushed into the

ampoule before thawing. The solution was heated at 65 °C in an oil bath with stirring. Following polymerization the polymer was precipitated twice into a stirred solution of cold diethyl ether, filtered and placed in the vacuum oven overnight at 40 °C.

$^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ ):  $\delta$  (ppm) 8.19 (br d, 2H, CH), 7.77-5.61 (br m, Ar-H), 4.40 (br t, 2H,  $\text{CH}_2$ ), 3.94 (br s, 1H, CH), 3.68 (br t, 2H,  $\text{CH}_2$ ), 3.00 (br s, 3H,  $\text{CH}_3$ ), 2.45-0.65 (br m, backbone).  $M_n(\text{NMR}) = 26.4$  kDa,  $n = 38$ ,  $m = 190$ ,  $M_n(\text{SEC DMF, PMMA}) = 8.7$  kDa,  $M_w/M_n = 1.63$ .

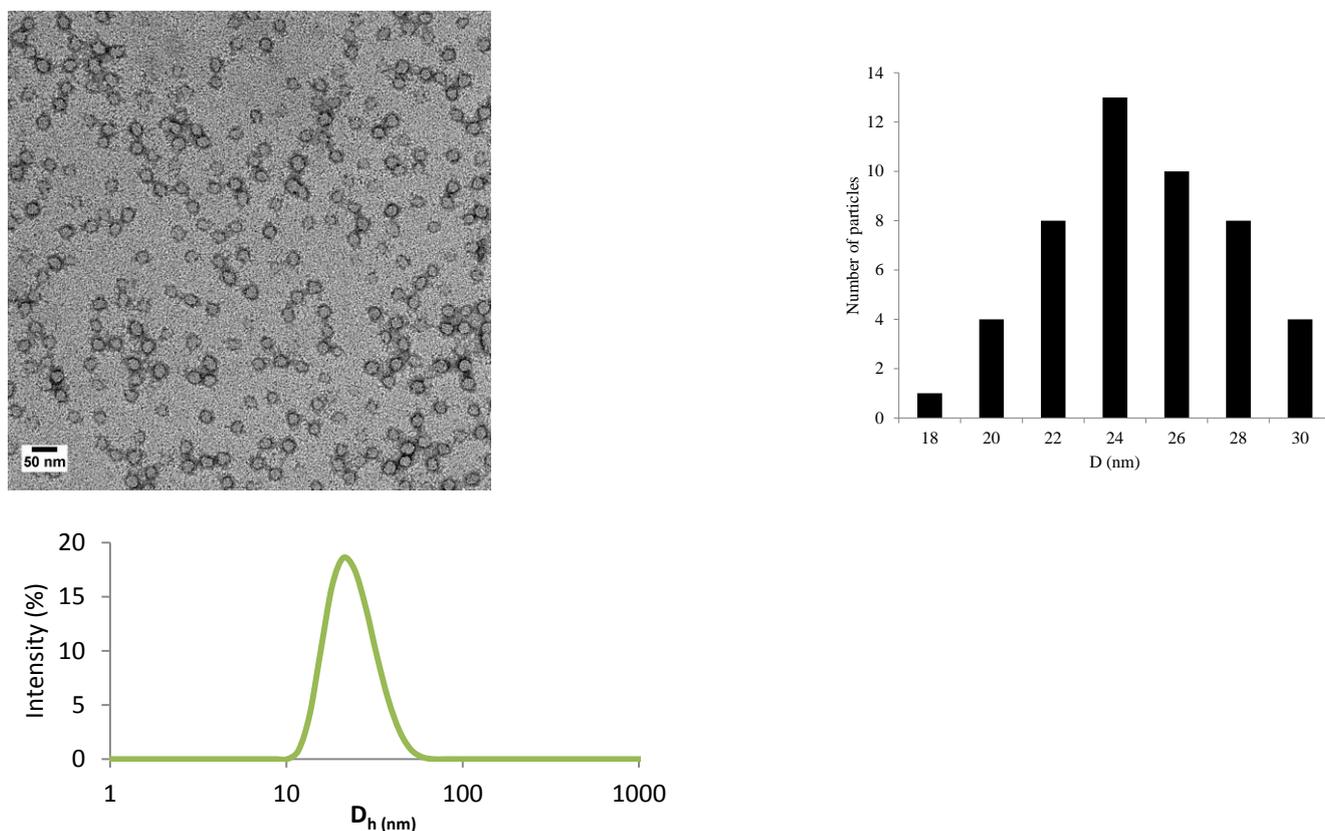


**Figure S1:**  $^1\text{H}$  NMR spectrum of DMAP containing amphiphilic block copolymer in  $\text{CDCl}_3$ .

### Formation of micelles M-DMAP

500 mg of polymer was dissolved in the minimum amount of acetone (at ca. 100 mg/mL) in a round bottom flask. The solution was placed in a cold room at 5 °C and 100 mL of water were added dropwise

with continuous stirring using a peristaltic pump (drop rate = 15 mL/h). When the addition of water was completed, the acetone was removed under vacuum keeping the flask in an ice bath. These micelles solutions (5 mg/mL) were stored at 5 °C. For each of the esterification reactions, 2 mL of this solution was used (1.3 mg of DMAP).



**Figure S2:** Representative TEM micrograph and histogram of micelles **M-DMAP** ( $D_{av} = 24.1$  nm) stained with uranyl acetate (1% solution). Scale bar = 50 nm. DLS showing a  $D_{h,number} = 21$  nm.

### **General protocol for the selective acylation reaction of 1-phenylpropanol (Table 1):**

#### *In the micelle (M-DMAP):*

Under continuous stirring, 1 equivalent (0.115 mmol) of alcohol (0.06 M), 1.5 equivalents of the auxiliary base, 1.5 equivalents of butyric anhydride and 1.5 equivalents of acetic anhydride were added together to 2 mL of **M-DMAP** solution (10 mg of polymer = 0.14 mg of DMAP). A sample of 0.1 mL

was taken after 1 hour, dissolved in 1 mL of THF with a known amount of mesitylene as the internal standard and filtered through a plug of silica prior to HPLC analysis;

$t_R(\mathbf{1a}) = 7.71$  min,  $t_R(\mathbf{1b}) = 9.64$  min.

*In the bulk (DMAP):*

1 equivalent (1.15 mmol) of alcohol, 1.5 equivalents of the auxiliary base, 1.5 equivalents of butyric anhydride and 1.5 equivalents of acetic anhydride were mixed together to 0.14 mg of unsupported DMAP (1 mol %). Samples of 0.005 mL were taken after 1 hour of stirring at RT, dissolved in 1 mL of THF with a known amount of mesitylene as the internal standard and analyzed by HPLC;

$t_R(\mathbf{1a}) = 7.71$  min,  $t_R(\mathbf{1b}) = 9.64$  min.

*In the SDS micellar system:*

Under continuous stirring, 0.001 mmol of **sDMAP** (1% mol catalyst) was dissolved in 0.03 mL of DIPEA (1.5 equivalents) and added to a 2 mL of a stock solution of SDS in nanopure water (5 mg/mL). After 2 hours stirring, 1 equivalent (0.115 mmol) of alcohol (0.06 M), 1.5 equivalents of the auxiliary base, 1.5 equivalents of butyric anhydride and 1.5 equivalents of acetic anhydride were added to the micellar solution. A sample of 0.1 mL was taken after 1 hour, dissolved in 1 mL of THF with a known amount of mesitylene as the internal standard and analyzed by HPLC;

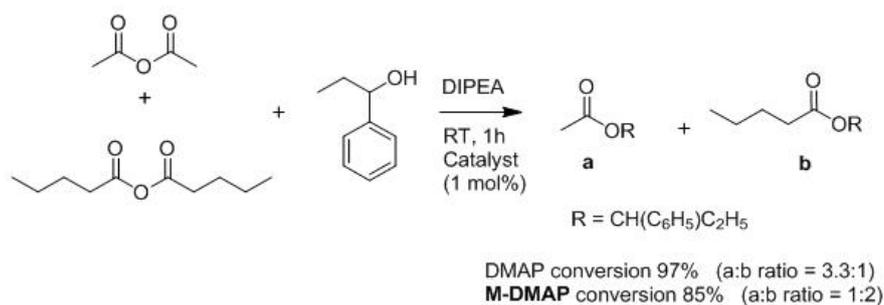
$t_R(\mathbf{1a}) = 7.71$  min,  $t_R(\mathbf{1b}) = 9.64$  min.

*Competitive reactions between acetic anhydride and valeric anhydride:*

1 mol % of catalyst (DMAP or **M-DMAP**), 1.5 equivalent of each anhydride, 1.5 equivalents of auxiliary base (DIPEA) and 1 equivalents of 1-phenylpropanol we stirred together at room temperature. Aliquots were taken after 1 hour and the conversions determined by HPLC analysis with mesitylene as the internal standard;

$t_R(\mathbf{a}) = 7.71$  min,  $t_R(\mathbf{b}) = 11.13$  min.

**Scheme S1:** Competitive acylation reaction between acetic and valeric anhydride.



### One pot selective acylation of different alcohols with butyric anhydride (Table 2 & Table 3):

*In the micelle (M-DMAP):*

1 equivalent (0.115 mmol) of each alcohol (0.06 M), 1.5 equivalents of DIPEA, and 3 or 4 equivalents of butyric anhydride were added together to 2 mL of **M-DMAP** solution (10 mg of polymer = 0.14 mg of DMAP). Samples of 0.1 mL were taken after 1 hour, dissolved in 1 mL of dioxane with a known amount of mesitylene as the internal standard and analyzed by GC. Samples were also taken at  $t = 0$  (before addition of anhydride) to calculate the conversions by the disappearance of the alcohol peak compared to the reference.

*In the bulk (DMAP):*

1 equivalent (1.15 mmol) of alcohol, 1.5 equivalents of the auxiliary base and 3 or 4 equivalents of butyric anhydride were mixed together to 0.14 mg of unsupported DMAP (1 mol %). Samples of 0.005 mL were taken after 1 hour, dissolved in 1 mL of dioxane with a known amount of mesitylene as the internal standard and analyzed by GC. Samples were also taken at  $t = 0$  (before addition of anhydride) to calculate the conversions by the disappearance of the alcohol peak compared to the reference.

$t_R(\text{mesitylene}) = 4.50 \text{ min}$ ,  $t_R(\text{methanol}) = 1.27 \text{ min}$ ,  $t_R(\text{allyl alcohol}) = 2.39 \text{ min}$ ,  $t_R(1,4\text{-butandiol}) = 5.9 \text{ min}$ ,  $t_R(1\text{-decanol}) = 6.50 \text{ min}$ ,  $t_R(\text{linalool}) = 5.81 \text{ min}$ .

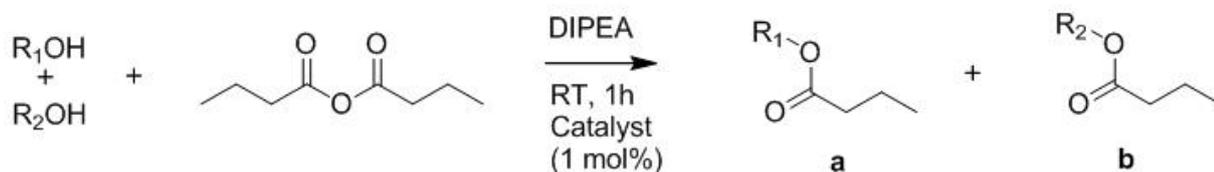
In the SDS micellar system (Table 2):

0.001 mmol of **sDMAP** (1% mol catalyst) was dissolved in 0.03 mL of DIPEA (1.5 equivalents) and added to a 2 mL of a stock solution of SDS in nanopure water (5 mg/mL). After 2 hours stirring, 1 equivalent (1.15 mmol) of each alcohol and 3 equivalents of butyric anhydride were added to the mixture with continuous stirring. Samples of 0.005 mL were taken after 1 hour, dissolved in 1 mL of dioxane with a known amount of mesitylene as the internal standard and analyzed by GC. Samples were also taken at  $t = 0$  (before addition of anhydride) to calculate the conversions by the disappearance of the alcohol peak compared to the reference.

$t_R(\text{mesitylene}) = 4.50 \text{ min}$ ,  $t_R(\text{methanol}) = 1.27 \text{ min}$ ,  $t_R(\text{linalool}) = 5.81 \text{ min}$ .

### Additional competitive reactions between 2 alcohols:

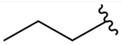
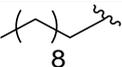
**Scheme S1:** Competitive acylation reaction with a range of alcohols.



**Table S1:** Competitive acylation reaction with a range of alcohols.

Catalyst	R <sub>1</sub>	R <sub>2</sub>	a:b
DMAP			1:1
<b>M-DMAP</b>			0.5:1
DMAP			1:1
<b>M-DMAP</b>			0.8:1

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DMAP			1:1
<b>M-DMAP</b>			0.6:1

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Reactions contained 1 mol % (DMAP or **M-DMAP**) of catalyst, 1 equivalent of each alcohol, 1.5 equivalents of auxiliary base (DIPEA) and 3 equivalents of anhydride. Conversions determined by GC analysis with mesitylene as the internal standard.

## References

[1]P. Cotanda, A. Lu, J. P. Patterson, N. Petzetakis, R. K. O'Reilly, *Macromolecules* **2012**, *45*, 2377-2384.