Electronic Supplementary Information

Environmental Control of Nucleophilic Catalysis in Water

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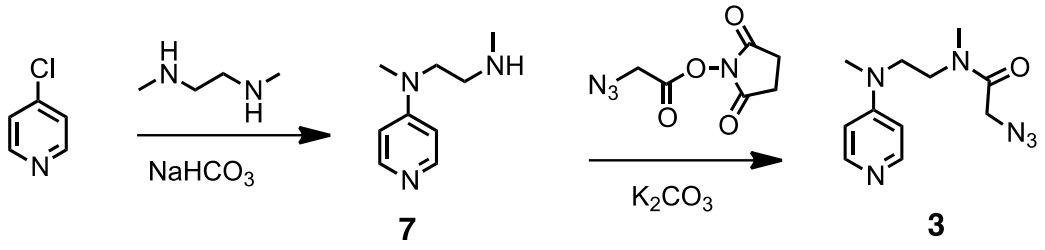
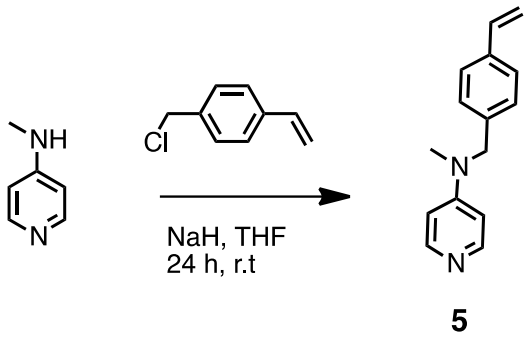
General Experimental Methods.

All reagents and solvents were of ACS-certified grade or higher and used as received from commercial suppliers. Millipore water was used to prepare buffers and nanoparticles. ^{1}H and ^{13}C NMR spectra were recorded on a VARIAN MR-400 or on a VARIAN VXR-400 spectrometer. Dynamic light scattering (DLS) was performed on a PD2000DLSPLUS dynamic light scattering detector. Mass spectrometry was performed on AGILENT 6540 QTOF mass spectrometer. UV-vis spectra were recorded on a Cary 100 Bio UV-visible spectrophotometer.



Scheme 1S. Synthesis of compound **3**



Scheme 2S. Synthesis of compound **5**

Syntheses

Syntheses of compounds **1**,[1] **2**,[1] **4**,[2] and **6**[2] were previously reported.

Compound 7.[3] A mixture of 4-chloropyridine hydrochloride (0.25 g, 1.70 mmol), N, N-dimethyl-1,2-ethanediamine (0.46 mL, 4.25 mmol), and sodium bicarbonate (0.43 mg, 5.10 mmol) in isoamyl

[1] Zhang, S. Y.; Zhao, Y. *Macromolecules*, **2010**, *43*, 4020-4022.
[2] Awino, J. K.; Zhao, Y. *J. Am. Chem. Soc*., **2013**, *135*, 12552-12555.
[3] Cho, H. K.; Zhong, Z. Q.; Zhao, Y. *Tetrahedron*, **2009**, *65*, 7311-7316.

alcohol (50 mL) was heated to reflux for 48 h. The mixture was concentrated by rotary evaporation and the residue was purified by column chromatography over silica gel using CH_2Cl_2/CH_3OH (5: 1) and CH_3OH /TEA (4: 0.5) as the eluents to give a yellowish oil (0.20 g, 71%). ^1H NMR (400 MHz, $CDCl_3$, ´) 8.18 (dd, 2H), 6.51 (dd, 2H), 3.44 (t, 2H), 2.98 (s, 3H), 2.77 (t, 2H), 2.44 (s, 3H).

Compound 3. A solution of compound **7** (0.08 g, 0.48 mmol), azidoacetic acid N-hydroxysccinimide ester[4] (0.192 g, 0.96 mmol), and K_2CO_3 (0.40 g, 2.88 mmol) in acetonitrile (5 mL) was stirred for 2 d under nitrogen. The solid was removed by filtration. The filtrate was concentrated in vacuo to give a yellow oil, which was purified by preparative TLC using 3:1 CH_2Cl_2/CH_3OH as the developing solvent to afford a white powder (90 mg, 75%). ^1H NMR (400 MHz, $CDCl_3$, ´) 8.31 (d, 2H), 6.79 (d, 2H), 3.86 (s, 2H), 3.70 (t, 2H), 3.60 (t, 2H), 3.17 (s, 3H), 2.99 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$, ´): 167.8, 153.4, 149.9, 106.4, 50.5, 48.1, 46.1, 37.4, 35.9. [M + H]+ calcd for $C_{11}H_{16}N_6O$, 249.1458 found, 249.1460.

Compound 5.[5] NaH (0.05 g, 60 % in mineral oil, 1.38 mmol) was added to a solution of 4-(methylamino)pyridine (0.10 g, 0.92 mmol) in dry THF (5 mL) at 0 ºC under nitrogen. The mixture was stirred at room temperature for 2 h and cooled to 0 ºC again, followed by slow addition of 4-vinyl benzyl chloride (0.09 mL, 0.64 mmol) in dry THF (2 mL). The reaction mixture was allowed to warm to room temperature and was stirred for 24 h. The insoluble solid was removed by filtration and the filtrate was concentrated in vacuo. The residue was dissolved in CH_2Cl_2 (50 mL). The organic solution was washed with water (2 × 30 mL), dried with anhydrous Na_2SO_4, filtered, and concentrated in vacuo. The residue was purified by column chromatography over silica gel with CH_2Cl_2/MeOH = 10/1 to 5/1 as the eluents to give a light brown powder. (0.18 g, 89%) ^1H NMR (400 MHz, CDCl3, ´): 8.20 (d, 2H), 7.36 (d, 2H), 7.11 (d, 2H), 6.71 (dd, 1H), 6.54 (dd, 2H), 5.73 (d, 1H), 5.23 (d, 1H), 4.50 (s, 2H),

[4] Ghosh, P. S.; Hamilton, A. D. *Chem. Eur. J*., **2012**, *18*, 2361-2365.
[5] Kwong, C. K. W.; Huang, R.; Zhang, M.; Shi, M.; Toy, P. H. *Chem. Eur. J.*, **2007**, *13*, 2369-2376.

3.07 (s, 3H). ^{13}C NMR (100 MHz, CDCl3, ´): 154.0, 149.4, 136.8, 136.5, 136.2, 126.6, 126.6, 113.9, 106.7, 54.8, 37.8.

Preparation of DMAP-SCM. Compound **3** (1.7 mg, 0.0068 mmol), 1,4-diazidobutane-2,3-diol (compound **2**, 4.6 mg, 0.026 mmol), $CuCl_2$ (10 μL of a 9 mg/mL aqueous solution, 0.5 μmol), and sodium ascorbate (100 μL of a 13 mg/mL aqueous solution, 5 μmol) were added to a micellar solution of compound **1** (10 mg, 0.02 mmol) in Millipore water (2.5 mL). The reaction mixture was stirred slowly at room temperature for 24 h after which the mixture was dialyzed for 3 d against deionized water using 500 Da molecular weight cut-off tubing. The detailed preparation, cross-linking chemistry, and characterization of the SCMs were reported previously.[1,2,6,7]

Preparation of SCM(DMAP). To a micellar solution of compound **4** (20 mg, 0.047 mmol) in D_2O (2.0 mL), cetyltrimethylammonium bromide (CTAB, 8.6 mg, 0.024 mmol), xylene (12 μL, 0.094 mmol), compound **5** in DMF (35 μL of a solution of 60 mg/mL, 0.0096 mmol), and 2,2-dimethoxy-2-phenylacetophenone (DMPA, 6 μL of a 55 mg/mL solution in DMSO, 0.0012 mmol) were added. The mixture was subjected to ultrasonication for 10 min before compound **2** (8.89 mg, 0.052 mmol), $CuCl_2$ (10 μL of a 16 mg/mL solution in D_2O, 0.0012 mmol), and sodium ascorbate (100 μL of a 23 mg/mL solution in D_2O, 0.012 mmol) were added. After the reaction mixture was stirred slowly at room temperature for 12 h, compound **6** (26 mg, 0.094 mmol), $CuCl_2$ (10 μL of a 16 mg/mL solution in D_2O, 0.0012 mmol), and sodium ascorbate (100 μL of a 23 mg/mL solution in D_2O, 0.012 mmol) were added. After being stirred for another 6 h at room temperature, the reaction mixture was transferred to a glass vial, purged with nitrogen for 15 min, sealed with a rubber stopper, and irradiated in a Rayonet reactor for 12 h. The reaction mixture was poured into acetone (8 mL). The precipitate

[6] Peng, H.-Q.; Chen, Y.-Z.; Zhao, Y.; Yang, Q.-Z.; Wu, L.-Z.; Tung, C.-H.; Zhang, L.-P.; Tong, Q.-X. *Angew. Chem. Int. Ed.* **2012**, *51*, 2088-2092.
[7] Chen, Y.-Z.; Chen, P.-Z.; Peng, H.-Q.; Zhao, Y.; Ding, H.-Y.; Wu, L.-Z.; Tung, C.-H.; Yang, Q.-Z. *Chem. Commun.* **2013**, *49*, 5877-5879.

was collected by centrifugation and washed with a mixture of acetone/water (5 mL/1 mL) five times. The off-white powder was redissolved in 2.4 mL of Millipore water to give a 20 mM stock solution of SCM(DMAP).

Kinetic measurement

p-Nitrophenyl acetate (PNPA, 50 mg) was dissolved in 10 mL of methanol. The methanol stock solution (10 mM) was stored in a refrigerator and used within a week. p-Nitrophenyl hexanoate stock solution (PNPH, 12 mg/5mL in acetonitrile, 10 mM) was prepared freshly each day. HPNPP was prepared according to a literature procedure.[8] A stock solution (10 mM) of HPNPP in Millipore water was prepared. For the kinetic experiments, a typical procedure is as follows: Aliquots of the SCM(DMAP) solution were added to a series of cuvettes containing 800 μL of HEPES buffer (25 mM, pH = 4, 5, 6, 7, 8). The concentration of the catalytic pyridyl group was 0.10 mM in all cases. The cuvettes were placed in the UV-vis spectrometer and equilibrated to 35.0 °C. After 5 min, aliquots (40 μL) of the PNPA aqueous solution, prepared freshly each day by mixing 3.7 mL of the methanol PNPA stock solution with 6.3 mL of deionized water, were added to the cuvettes. The hydrolysis was monitored by the absorbance of p-nitrophenol at 400 nm over a period of 6 min for PNPA, 1–4 min for PNPH, and 3 h for HPNPP. The experiments were generally performed in duplicates.

[8] Tsang, J. S. W.; Neverov, A. A.; Brown, R. S, *J. Am. Chem. Soc.*, **2003**, *125*, 1559-1566.

Table 1S. Rate constants for the hydrolysis of HPNPP in aqueous buffer catalyzed by the SCMs at 35 °C.[a]

Entry	Micelle	Solution pH	$k \times 10^5$ (min^{-1})
1	DMAP-SCM	8	50
2	SCM(DMAP)	8	110
3	DMAP	8	2.4
4	DMAP-SCM	7	20
5	SCM(DMAP)	7	40
6	DMAP	7	0[b]
7	DMAP-SCM	6	3.3
8	SCM(DMAP)	6	7.5
9	DMAP	6	0[b]
10	DMAP-SCM	5	0[b]
11	SCM(DMAP)	5	0[b]
12	DMAP	5	0[b]

[a] The concentration of the catalytic pyridyl group was 0.10 mM for all the SCMs. [HPNPP] = 0.20 mM. The reactions were performed in HEPES buffer. The rate constants were measured in duplicates and the error between the two sets of data was generally within 15%. [b] The reaction rate was too slow to be measured accurately.

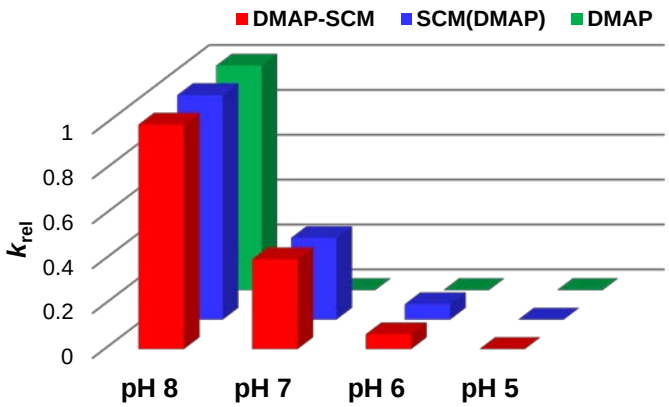


Figure 1S. Relative rate constants of hydrolysis of HPNPP catalyzed by the three different DMAP catalysts.

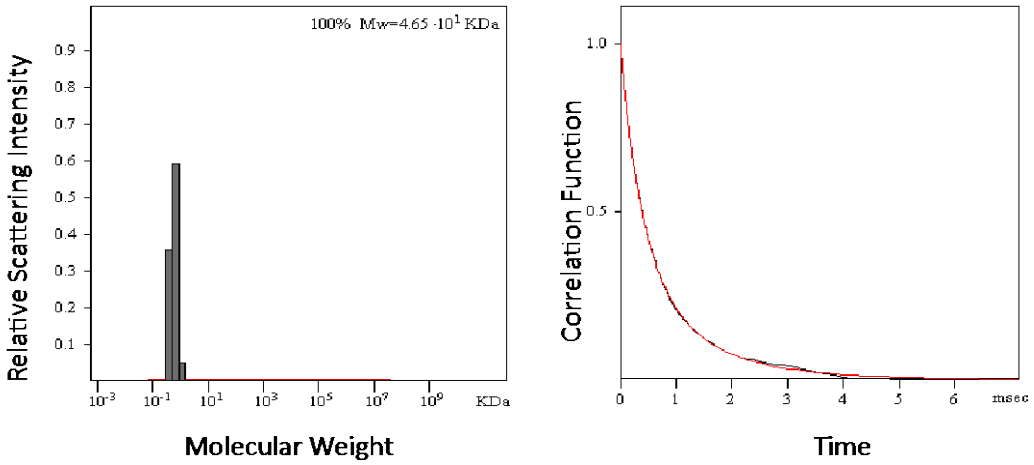


Figure 2S. Distribution of the molecular weights of the SCM(DMAP) and the correlation curve for DLS. The molecular weight distribution was calculated by the PRECISION DECONVOLVE program assuming the intensity of scattering is proportional to the mass of the particle squared.

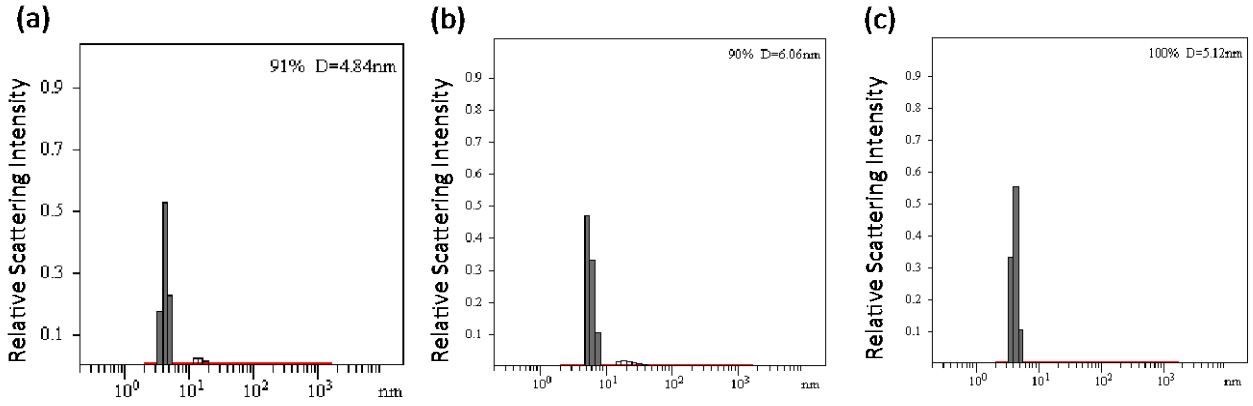


Figure 3S. Distribution of the hydrodynamic diameters of the nanoparticles in water as determined by DLS for (a) alkynyl-SCM (b) surface-functionalized SCM, and (c) SCM(DMAP) after purification.

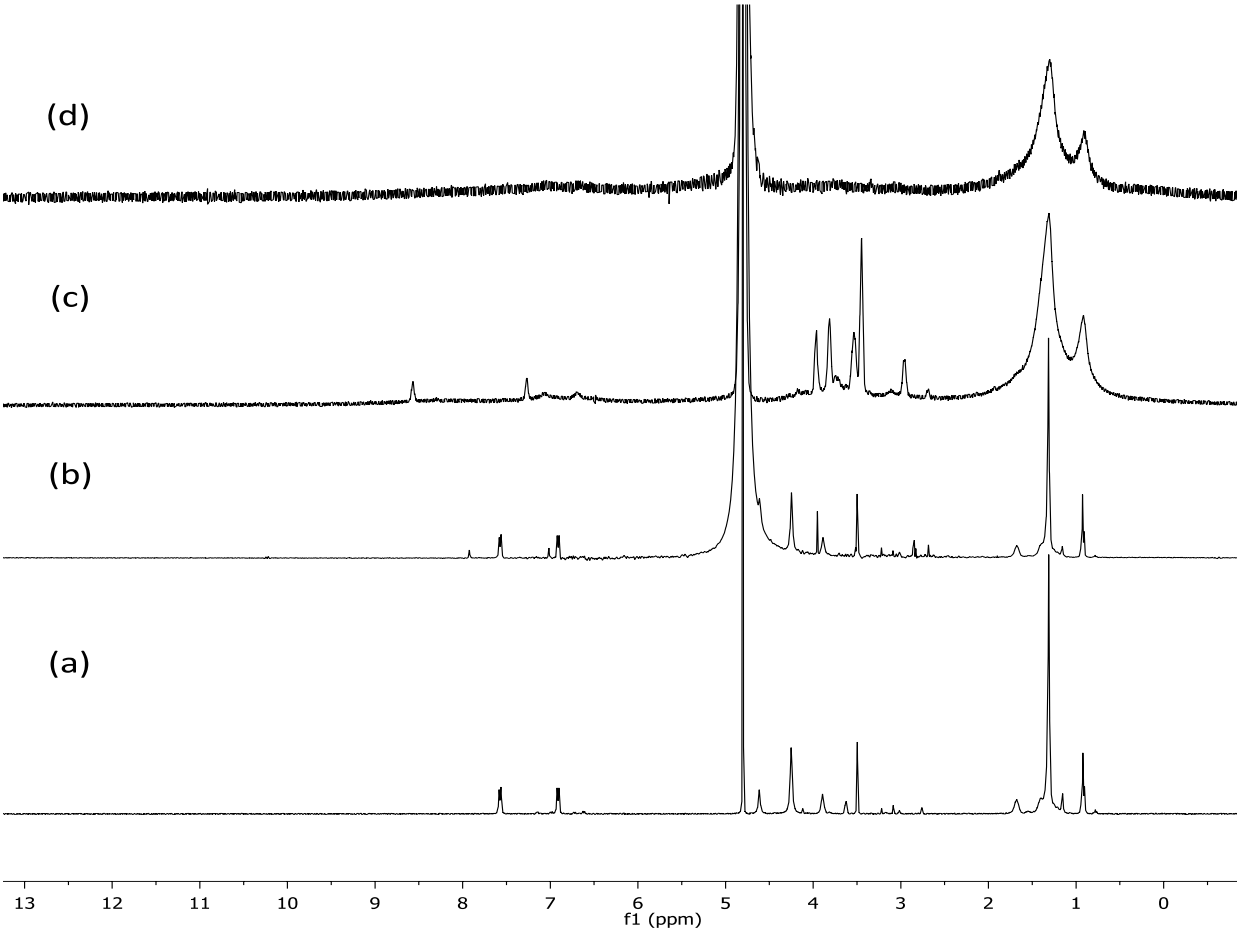


Figure 4S. ^{1}H NMR spectra of (a) 10 mM micellar solution of **1** in D_2O, (b) after the addition of 0.2 equiv of compound **3**, (c) after surface-crosslinking, and (d) purified DMAP-SCM in D_2O.

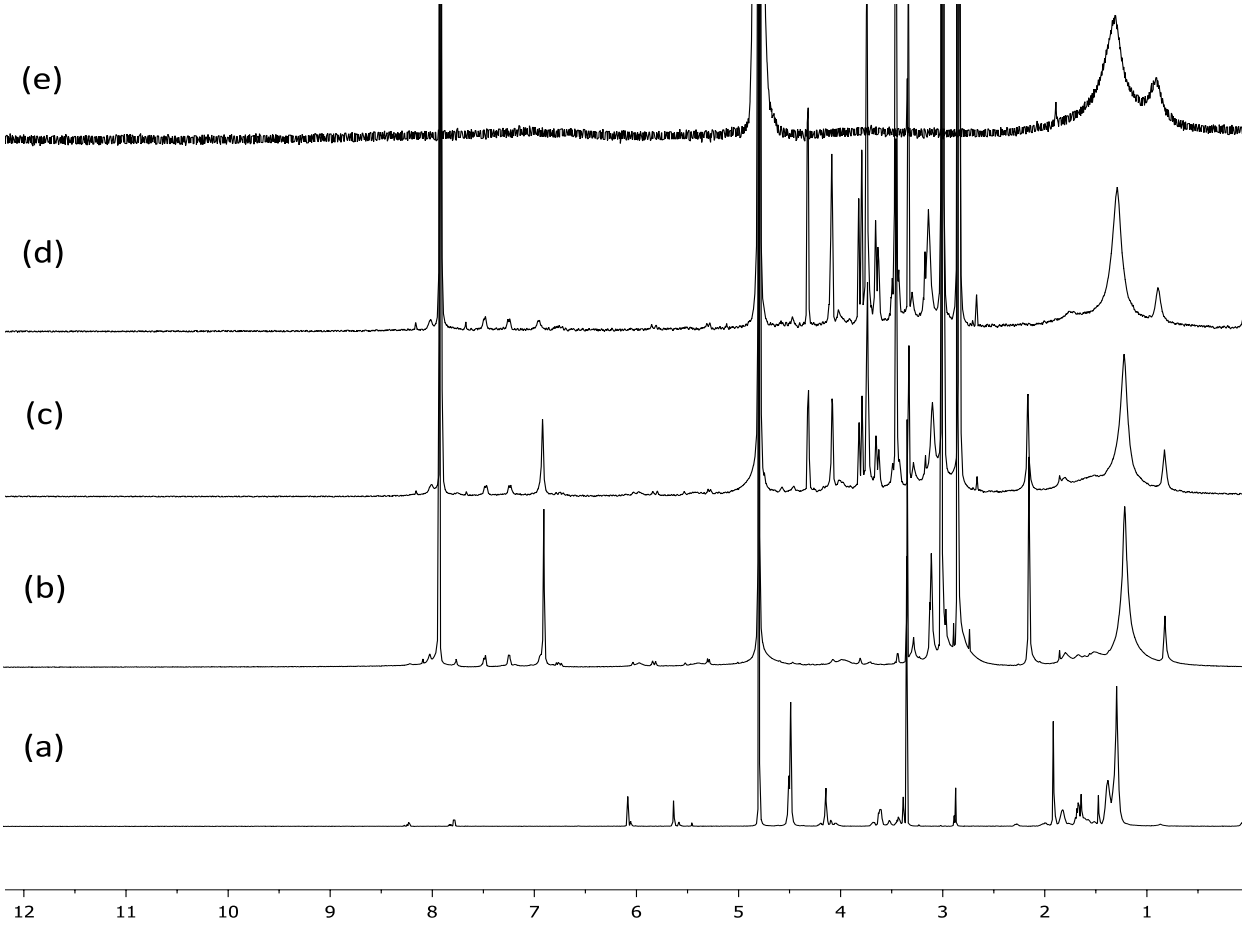
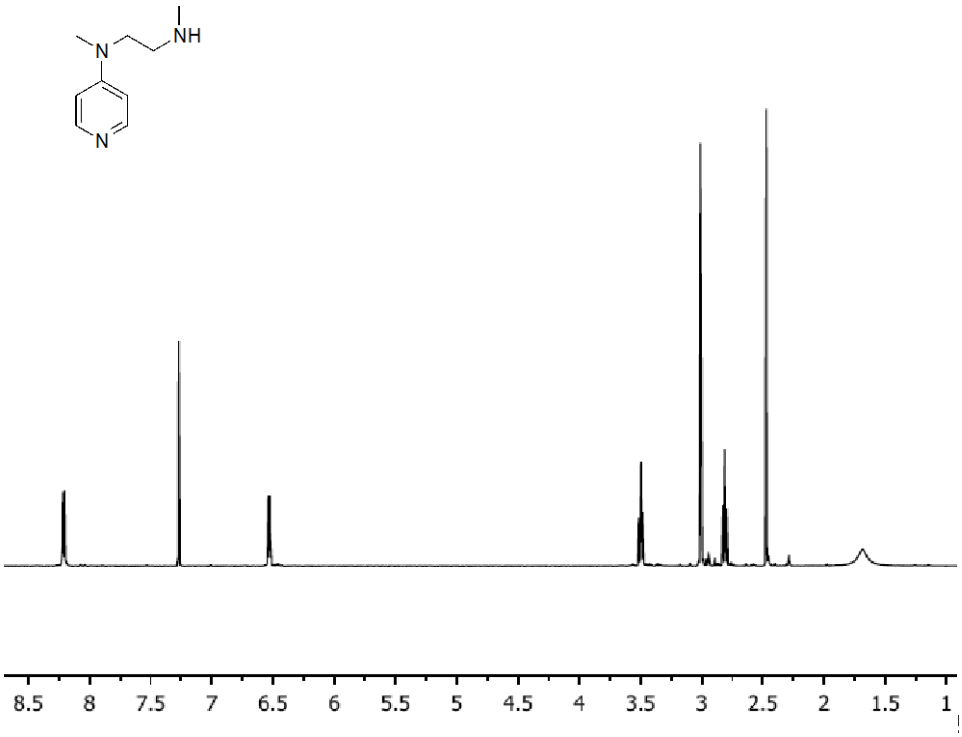
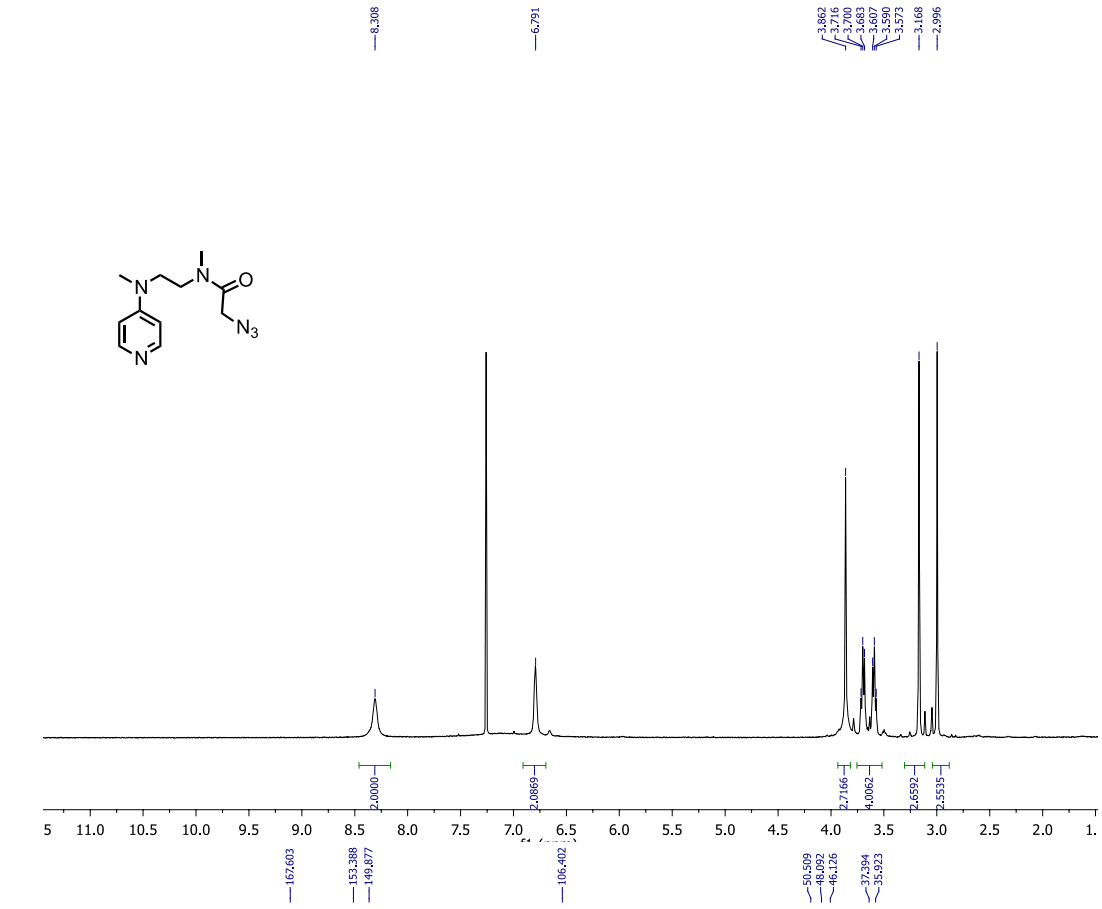


Figure 5S. ^{1}H NMR spectra of (a) 10 mM micellar solution of **4** in D_2O, (b) after surface-crosslinking (12 h after the addition of compound **5**, compound **2**, xylene, CTAB, DMPA, and Cu^{1} catalysts), (c) after surface-functionalization with compound **6**, (d) after core-cross-linking (after 12 h under UV irradiation), and (e) purified SCM(DMAP) in D_2O.

^{1}H and ^{13}C NMR spectra of key compounds

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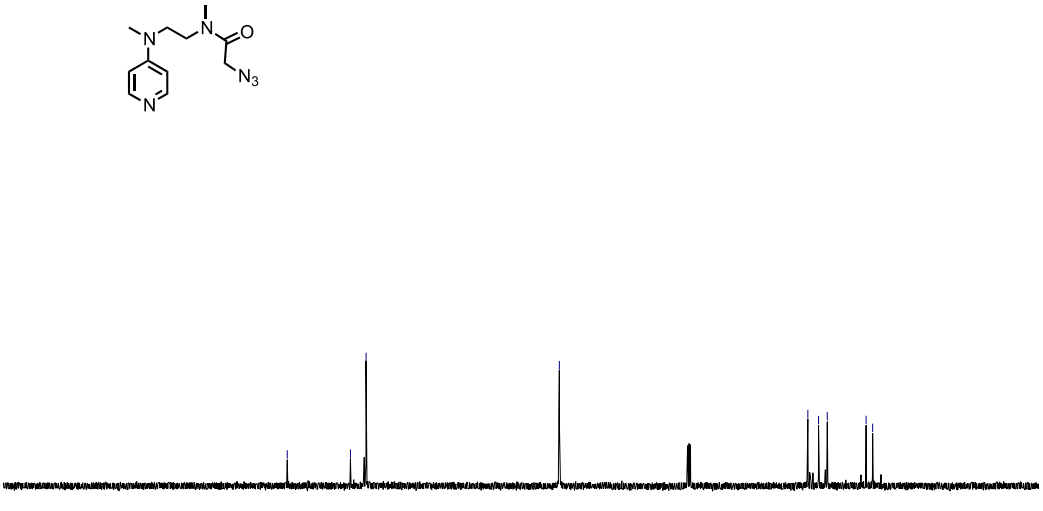

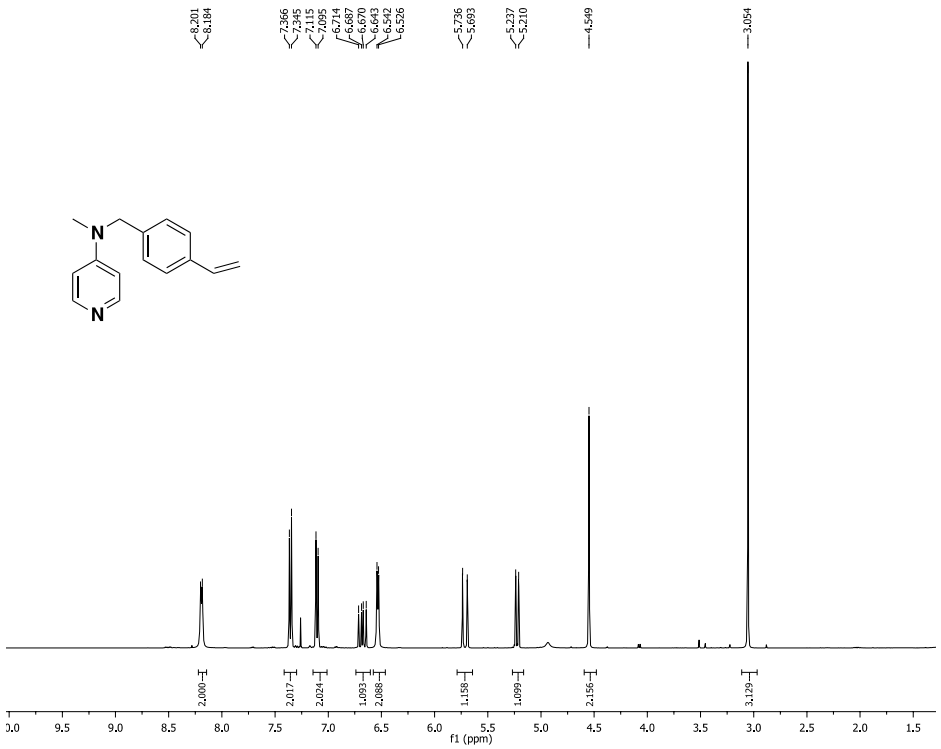
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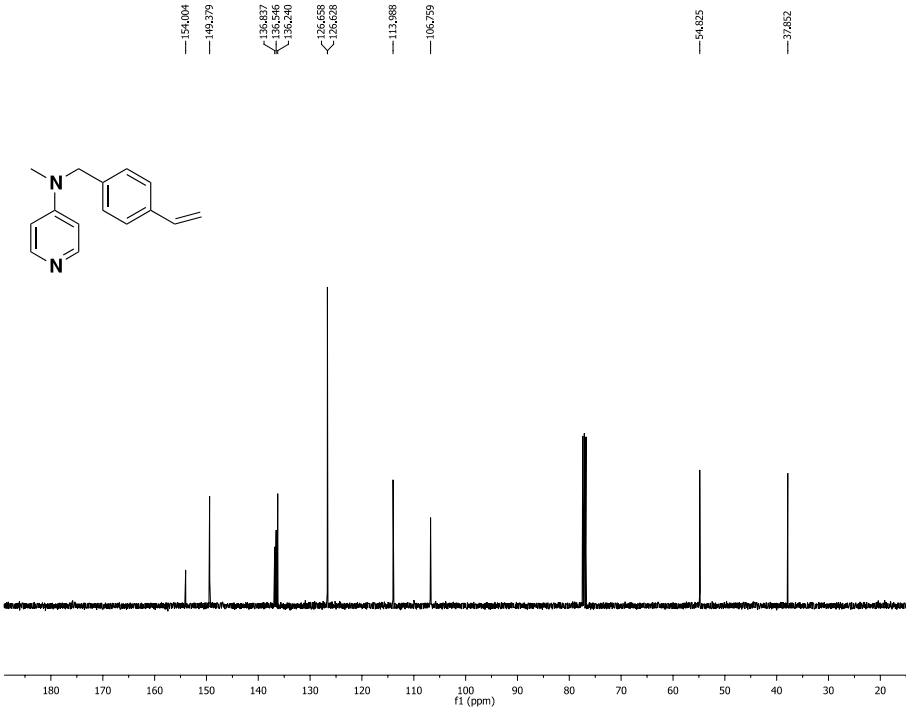
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