

## Fine-tuning the Degree of Organic Functionalization of Mesoporous Silica Nanosphere Materials via an Interfacially Designed Co-condensation Method

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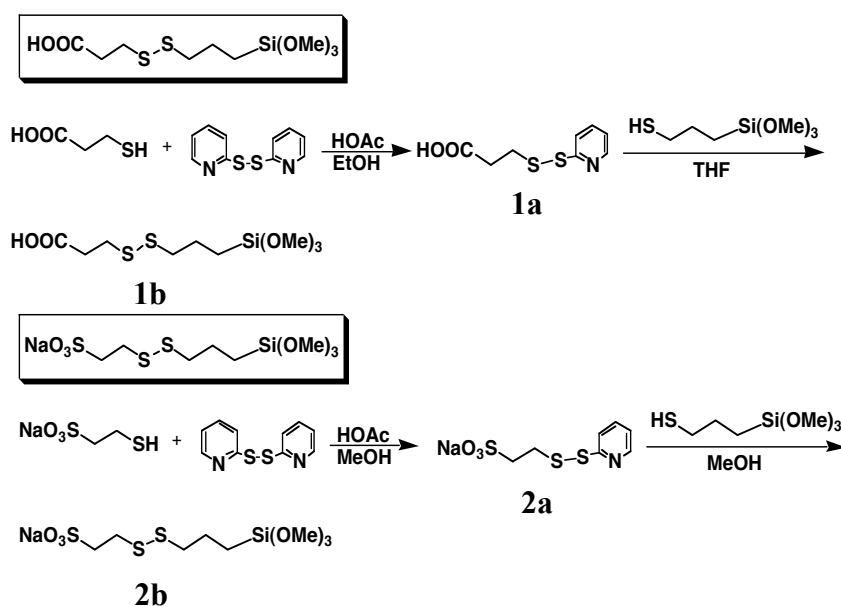
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### Experimental Section

**A. Materials.** 3-Mercaptopropionic acid (99+%), 2,2'-dipyridyl disulfide (98%), (3-mercaptopropyl)trimethoxysilane (MPTES) (95%), 2-mercaptoethanesulfonic acid sodium salt (98%), cetyltrimethylammonium bromide (CTAB), tetraethyl orthosilicate (TEOS, 96%) and dithiothreitol (DTT) were purchased from Aldrich Chemical Co. (Milwaukee, WI). Acetic acid (Glacial), hydrochloric acid (37.4%), sodium hydroxide, ethanol (anhydrous), methanol (HPLC grade), tetrahydrofuran (HPLC grade), hexanes (pesticide grade) and ethyl ether (anhydrous) were obtained from Fisher Scientific Co. (Pittsburgh, PA). Nanopure water was deionized to 18.0 MΩ-cm in a Barnstead E-pure water purification system and used for the synthesis of MSN materials.

### B. Synthesis of organoalkoxysilane precursors:



**Fig. S1.** Schematic representation of the synthesis of organoalkoxysilane precursors

*2-[3-(trimethoxysilyl)-propyl]disulfanyl-propionic acid (1b):*

As depicted in Fig. S1, 2-Carboxyethyl-2-pyridyl-disulfide, compound (**1a**), was prepared according to a procedure published by Carlsson *et al.*<sup>1</sup> In a typical synthesis, 3.75 g (17 mmol) of 2,2'-dipyridyl disulfide (Aldrithiol-2) was dissolved in 30 mL of ethanol and a solution of 0.87 mL of mercaptopropionic acid in 5 mL ethanol was injected dropwise. After 20 h of stirring at room temperature, the crude yellow oil product was isolated by rotary evaporation. The purified product (1.45 g, yield = 40%) was obtained from an alumina column chromatography (eluent = CH<sub>2</sub>Cl<sub>2</sub>/EtOH 3:2 v/v). The product 1.45 g (6.8 mmol) is corresponding to 40% yield. The characterization of compound **1a** is consistent with the literature reported data.

2-[3-(trimethoxysilyl)-propyl]disulfanyl-propionic acid, compound (**1b**), was prepared by dissolving compound **1a** (1.51 g, 7 mmol) in 30 mL of THF, followed by a dropwise addition of MPTMS (1.1 g, 5.6 mmol). The resulting yellow solution was stirred under N<sub>2</sub> atmosphere for 12 h. After flash evaporation of the solvent, the yellow product was purified by silicagel column chromatography using EA/ hexane in 1:2 ratio as eluent. The purified product (1 g) was isolated with a 60% yield. <sup>1</sup>H-NMR (CDCl<sub>3</sub>), δ 0.76 (*t*, 2H, CH<sub>2</sub>(1)), 1.81 (*q*, 2H, CH<sub>2</sub>(2)), 2.71 (*t*, 2H, CH<sub>2</sub>(5)), 2.81 (*t*, 2H, CH<sub>2</sub>(3)), 2.91 (*t*, 2H, CH<sub>2</sub>(4)), 3.60 (*s*, 1H, OCH<sub>3</sub>); <sup>13</sup>C-NMR (D<sub>2</sub>O), δ 10.25, 13.69, 23.75, 34.83, 36.98, 42.26, 180.99.

*2-[3-(trimethoxysilyl)-propyl]disulfanyl-ethanesulfonic acid, (2b)*

As depicted in Fig. S1, 2,2'-Dipyridyl disulfide (8.82 g, 40.0 mmol) was dissolved in 50.0 mL of methanol, followed by an addition of 1.6 mL of glacial acetic acid as catalyst. To this mixture, 2-mercaptoethanesulfonic acid sodium salt (3.82 g, 20.0 mmol) in 30.0 mL of methanol was added dropwise in 30 min with stirring. The reaction mixture was protected from light and stirred at room temperature overnight, followed by solvent evaporation under vacuum. The crude product was purified by dissolving in a small amount of methanol, followed by recrystallization in ethyl ether and dried under vacuum to yield compound **2a** (5.14 g, yield = 94.0%). <sup>1</sup>H-NMR (300 MHz; DMSO-d<sub>6</sub>), δ 2.73 (*m*, 2H, CH<sub>2</sub>), 3.02 (*m*, 2H, CH<sub>2</sub>), 7.24 (*d*, 1H, ArH), 7.81 (*m*, 2H, ArH), 8.45 (*d*, 1H, ArH).

To synthesize 2-[3-(trimethoxysilyl)-propyl]disulfanyl-ethanesulfonic acid sodium salt (**2b**), compound **2a** (1.36 g, 5.0 mmol) was dissolved in 20.0 mL of methanol with 1.0 mL of glacial acetic acid. To this mixture, (3-mercaptopropyl) trimethoxysilane (0.95 mL, 5.0 mmol) in 10.0 mL of methanol was added dropwise. The mixture was protected from light and stirred under nitrogen at room temperature overnight. The reaction was quenched and the solvent was evaporated under vacuum. The solid product was dissolved in a small amount of methanol, followed by ethyl ether precipitation. The purified product (5.14 g, yield = 74.7%) was collected by filtration and dried under vacuum. <sup>1</sup>H-NMR (300 MHz; D<sub>2</sub>O) δ 0.79 (*t*, 2H, CH<sub>2</sub>(1)), 1.83 (*q*, 2H, CH<sub>2</sub>(2)), 2.81 (*t*, 2H, CH<sub>2</sub>(3)), 3.03 (*t*, 2H, CH<sub>2</sub>(5)), 3.27 (*t*, 2H, CH<sub>2</sub>(4)), 3.60 (*s*, 7H, OCH<sub>3</sub>).

1. Carlsson, J.; Drevin, H.; Axen, R. *Biochem. J.* **1978**, *173*, 723–737.

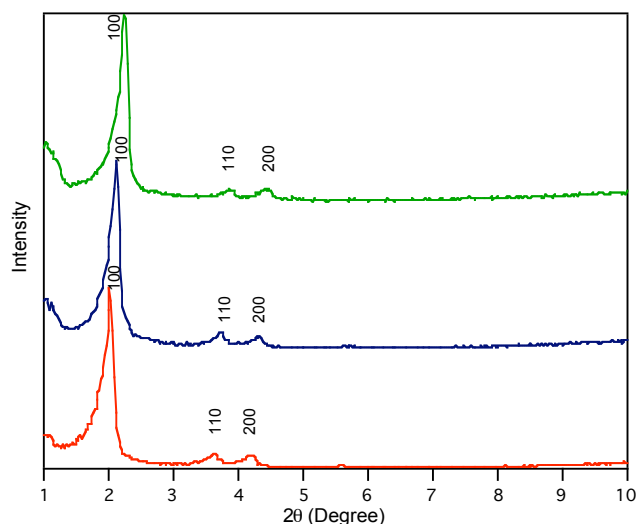
### C. Synthesis of MSN materials

Three organically functionalized mesoporous silica materials, MSN-COOH, MSN-SO<sub>3</sub>H, and MSN-SH, were prepared by adding an ethanolic solution (2 mL, 2.24 mmol) of CDSP-TMS, SDSP-TMS, and the commercially available MP-TMS, respectively, to an aqueous solution (480 mL) of CTAB (2.74 mmol), NaOH (7.00 mmol), and TEOS (22.40 mmol) at 80°C. The reaction mixture was stirred for 2 h. The solid products were isolated by filtration and washed thoroughly with methanol. The surfactant-removed materials were obtained by refluxing 1 g of the MSN material in 170 mL of methanolic solution of HCl (1 M) for 12 h. The resulting surfactant-removed material was isolated by filtration, washed extensively with methanol, and dried under vacuum.

To obtain mesoporous silica material with free thiol groups, the surfactant extracted MSN material was added to 100.0 mL of 5% NaHCO<sub>3</sub>(aq) containing a disulfide reducing agent, dithiothreitol (DTT) (1.88 g, 12.2 mmol). The mixture was stirred at room temperature for 4 h. The white product was then filtered and washed with water and methanol, following by vacuum drying.

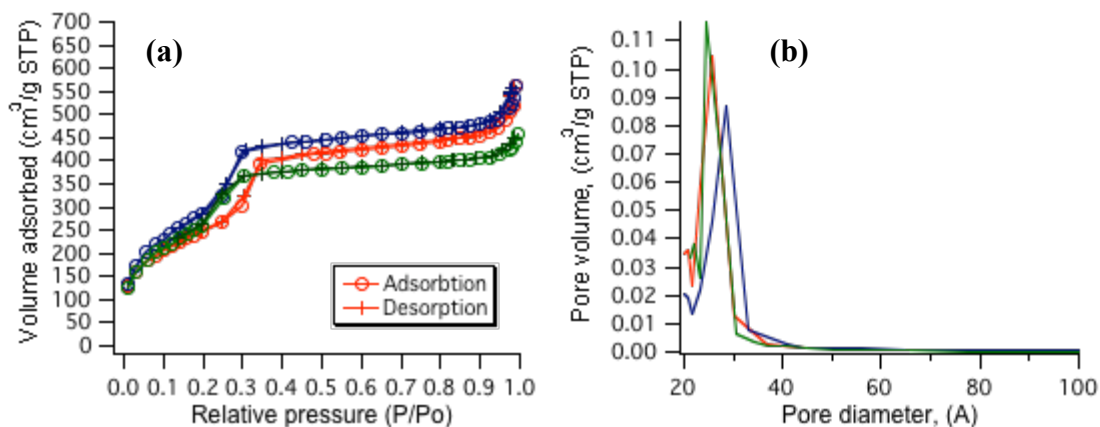
### D. Characterization of the Organic Functionalization of the MSN Materials

**D.1** Powder XRD diffraction patterns of MSN-COOH, MSN-SO<sub>3</sub>H, and MSN-SH are summarized in Table S1. The data were collected on a Scintag XRD 2000 X-Ray diffractometer using Cu K $\alpha$  radiation. Low angle diffraction with a  $2\theta$  range of 1 to 10° was used to investigate the long-range order of the materials. The well-resolved diffraction patterns characteristic of hexagonal MCM-41 silicas, including (100), (110), and (200) peaks with the spacing ratio of  $1:\sqrt{3}:\sqrt{4}$ , were observed in MSN-SH, MSN-COOH and MSN-SO<sub>3</sub>H materials as shown in Fig. S2.



**Fig. S2.** Powder XRD diffraction patterns of the MSN-SH (green), MSN-COOH (red) and MSN-SO<sub>3</sub>H (blue) materials after treatment with disulfide reducing agent (DTT).

**D.2** Surface area (SA) and Median Pore Diameter (MPD) were measured using a Micromeritics ASAP2000 sorptometer. Samples were degassed at 90 °C for 1 h and at 150 °C for 4 h. Nitrogen adsorption and desorption isotherms of the MSN materials were obtained at –196 °C. Specific surface areas and pore size distributions were calculated using the Brunauer-Emmett-Teller (BET) and Barrett-Joyner-Halenda (BJH) method, respectively.



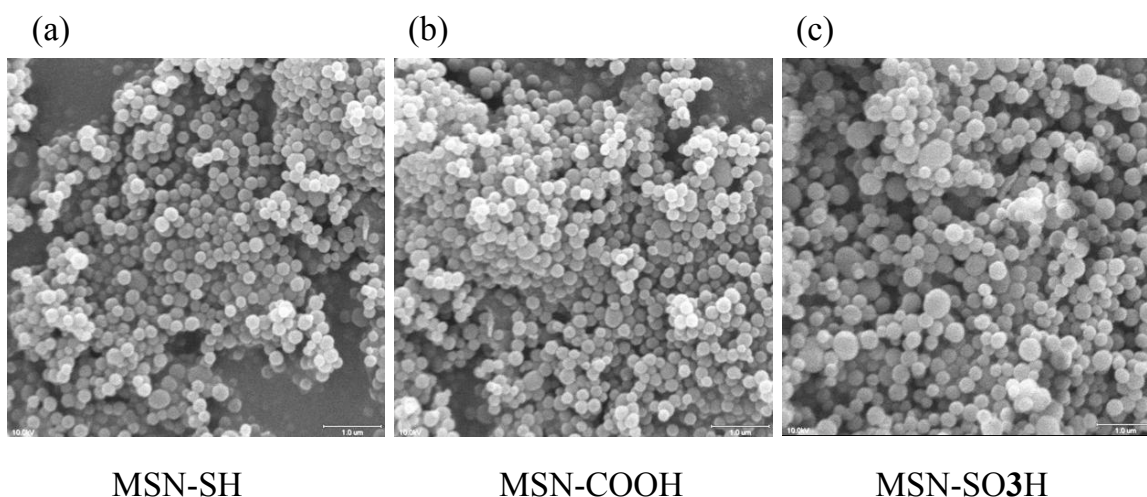
**Fig. S3.** (a) Nitrogen sorption isotherms of the MSN-SH (green), MSN-COOH (red) and MSN-SO<sub>3</sub>H (blue) materials after treatment with disulfide reducing agent (DTT). (b) Pore size distributions of the MSN-SH, MSN-COOH and MSN-SO<sub>3</sub>H materials.

**Table S1.** Structural properties of the organically functionalized MSN materials.

	Powder XRD			Nitrogen Sorption Isotherms		
	Low angle			BET	BET	BJH
	(Silica) (Å)			surface area	pore volume	pore diameter
	$d_{100}$	$d_{110}$	$d_{200}$	(m <sup>2</sup> /g)	(mL/g)	(Å)
MSN-SH	39.8	22.9	19.9	999	0.793	25.8
MSN-COOH	40.5	22.8	20.1	920	0.657	27.3
MSN-SO <sub>3</sub> H	43.8	24.4	20.9	863	0.755	28.1

\*Nitrogen sorption isotherms of the three MSN materials exhibited a sharp step starting at ca.  $p/p_0 = 0.38$ , as shown in Fig. S3a with reversible type IV isotherms. (The inflection point is attributed to the commencement of pore filling from which the pore diameter can be roughly estimated).

**D.3** Particle morphology of these MSN materials was determined by scanning electron microscopy (SEM) using a JEOL 840A scanning electron microscope with 10 kV accelerating voltage and 0.005 nA of beam current for imaging. For obtaining the transmission electron microscopy (TEM) micrograph displayed in the main text, a small aliquot was taken from a suspension of MSN in methanol, and placed in a lacey carbon-coated TEM grid, which was pulled through the suspension and allowed to dry in air. The specimen was given no further treatment, as it appeared stable under beam bombardment.



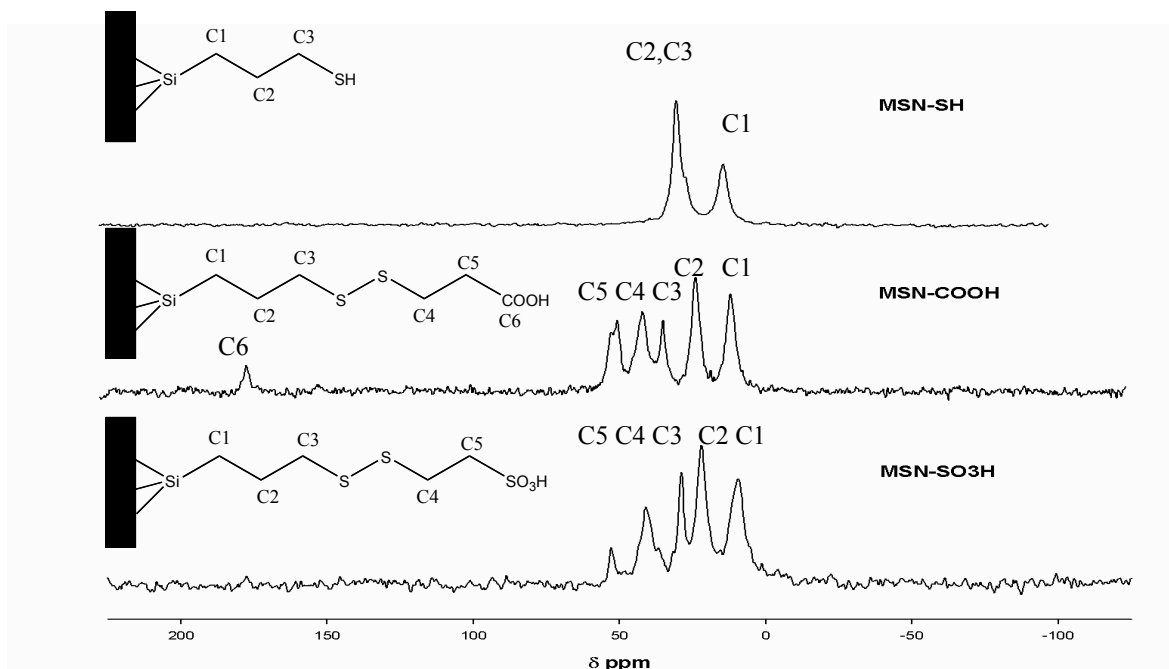
**Fig. S4.** SEM images of MSN-SH (a), MSN-COOH (b) and MSN-SO<sub>3</sub>H (c). All three materials exhibited spherical particle morphology, with an average particle diameter of 200 nm. All images are presented using the same magnification (scale bar = 1 μm).

**D.4** TGA curves were recorded using a TA Instruments TGA 2950 thermogravimetric analyzer with a temperature ramp of 5° C/min under continuous flow of nitrogen (100 mL/min). The percentage of weight loss when heating the samples of MSNs in the range of 1-1000°C is concluded in Table S2. In general, three or four distinct weight loss TGA profiles were found, including methanol, organic functional groups, and a small weight loss due to the dehydration of the surface hydroxyl groups.

**Table S2. TGA results of the materials after DTT cleavage**

Material	% weight loss
M-SH	9.620
M-COOH	12.98
M-SO <sub>3</sub> H	15.25

**D.5** The  $^{13}\text{C}$  spectra shown in the Fig. S5 confirm the presence of the three organic functional groups in the MSN materials before the disulfide bond reductions. Solid-state  $^{13}\text{C}$  CP-MAS NMR spectra were obtained at 75.47 Mhz on a Bruker MSL300 spectrometer equipped with Bruker 4mm rotor MAS probe. Magic-angle sample spinning rate was maintained at 10 KHz. The NMR spectra consisted of between 2,000 and 6,000 acquisitions with cross polarization times of 3ms and pulse repetition times of 15s. All chemical shifts reported are referenced to liquid  $\text{SiMe}_4$  (TMS).



**Fig. S5.** Solid state  $^{13}\text{C}$  CP-MAS NMR spectra of the MSN-SH (up), MSN-COOH (middle) and MSN-SO<sub>3</sub>H (bottom).

**E. Quantification of chemically accessible surface-functionalized thiol coverage.**

All experiments were performed in triplicate, by reacting a predetermined amount of material (in the range of 20 to 25 mg) with a methanolic solution of excess 2, 2'-dipyridyl disulfide (44 mg, 0.2 mmol dissolved in 5 mL methanol).