Supporting information for

A Toolbox for the Synthesis of Multifunctionalized Mesoporous Silica Nanoparticles for Biomedical Applications

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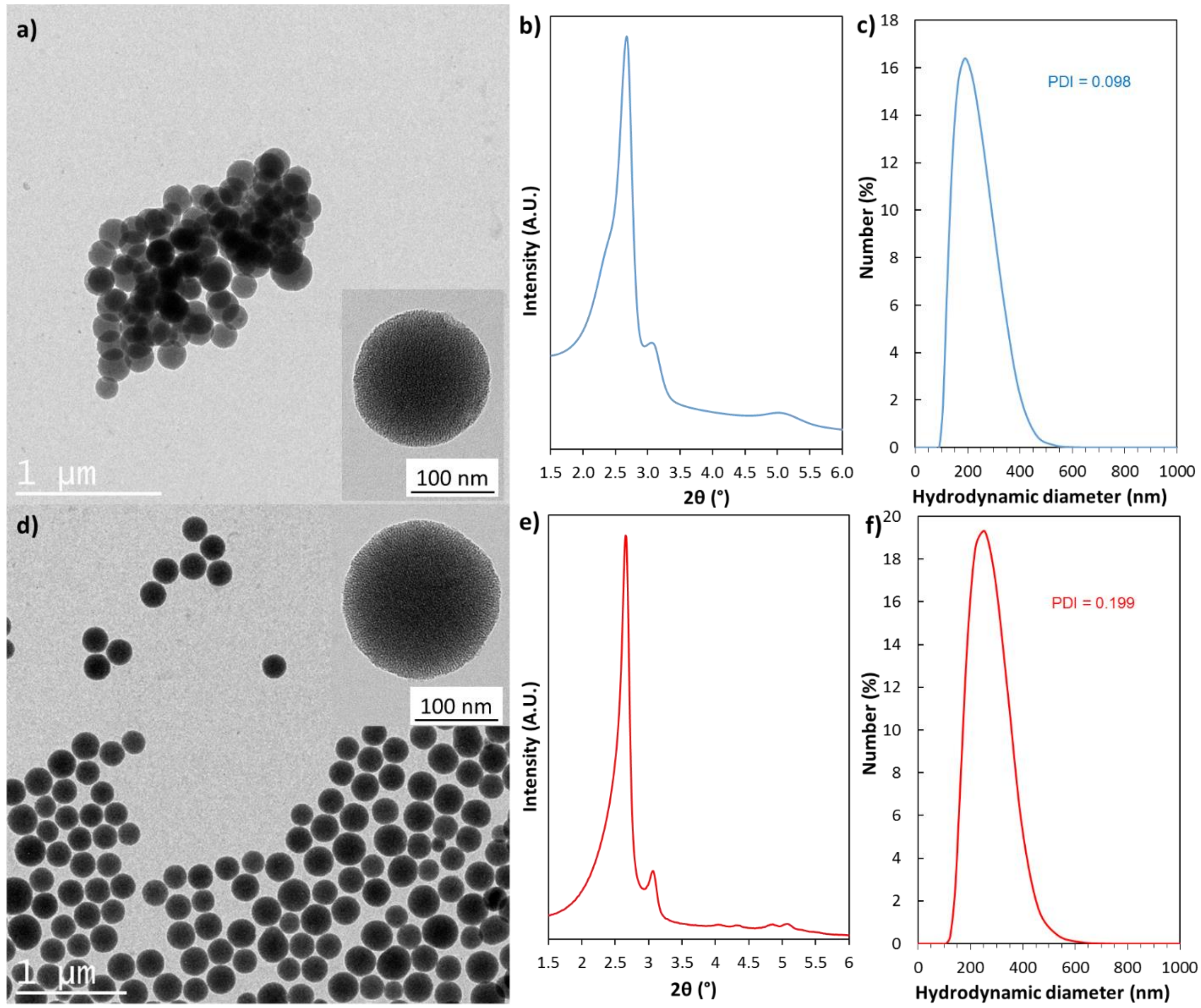

Figure S1. TEM images, low-angle XRD patterns and number-weighted hydrodynamic diameter distributions in water as determined by DLS analyses of (a, b, c) calcined and (d, e, f) extracted MSNs.

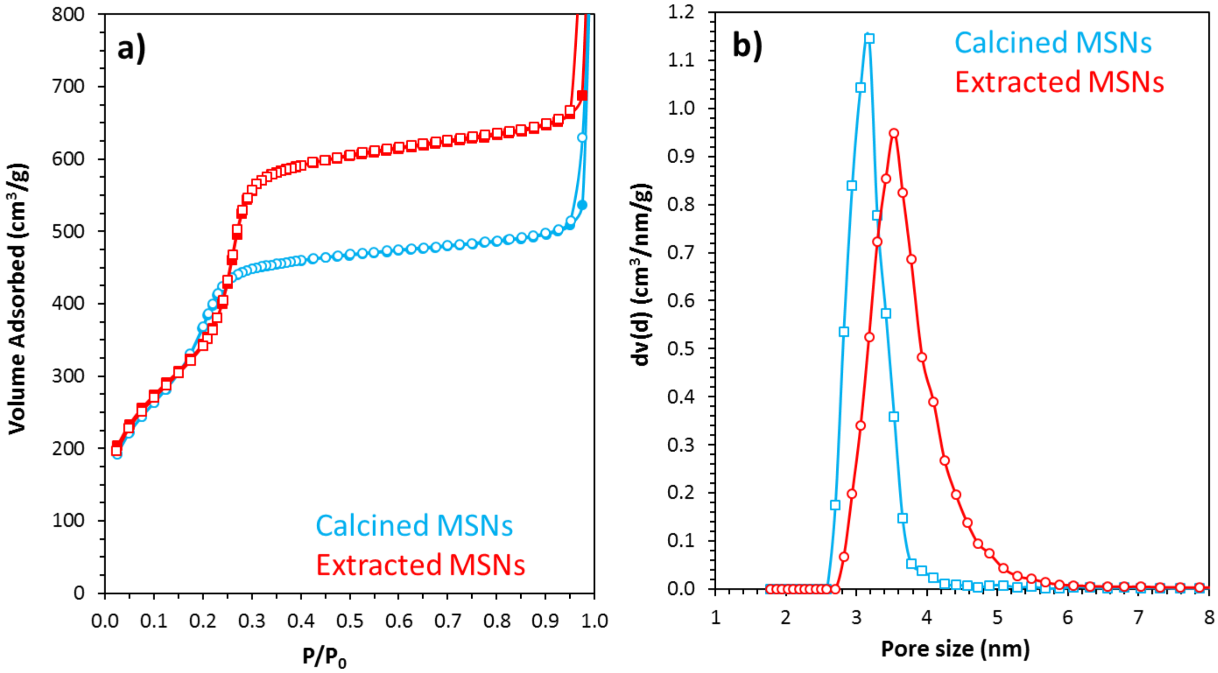

Figure S2. a) N_2 adsorption-desorption isotherms at -196 °C and b) corresponding NLDFT pore size distributions of calcined and extracted MSNs.

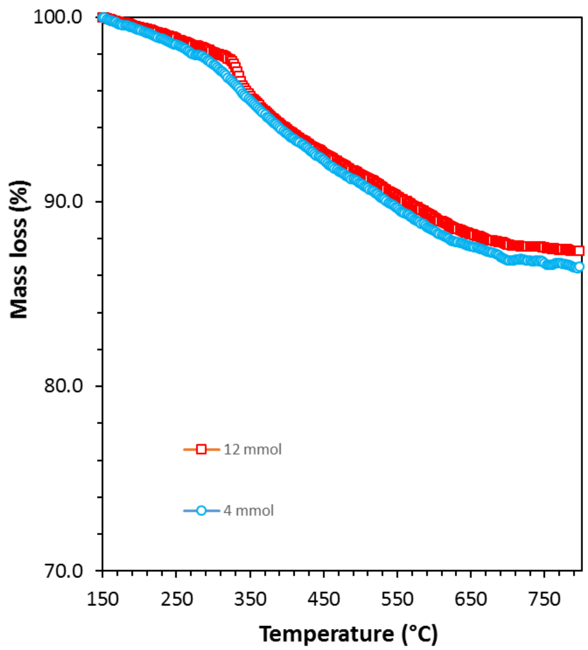

Figure S3. TGA data of post-grafted (PG) APTS-particles with different quantities of aminosilane on calcined MCM-48 MSNs.

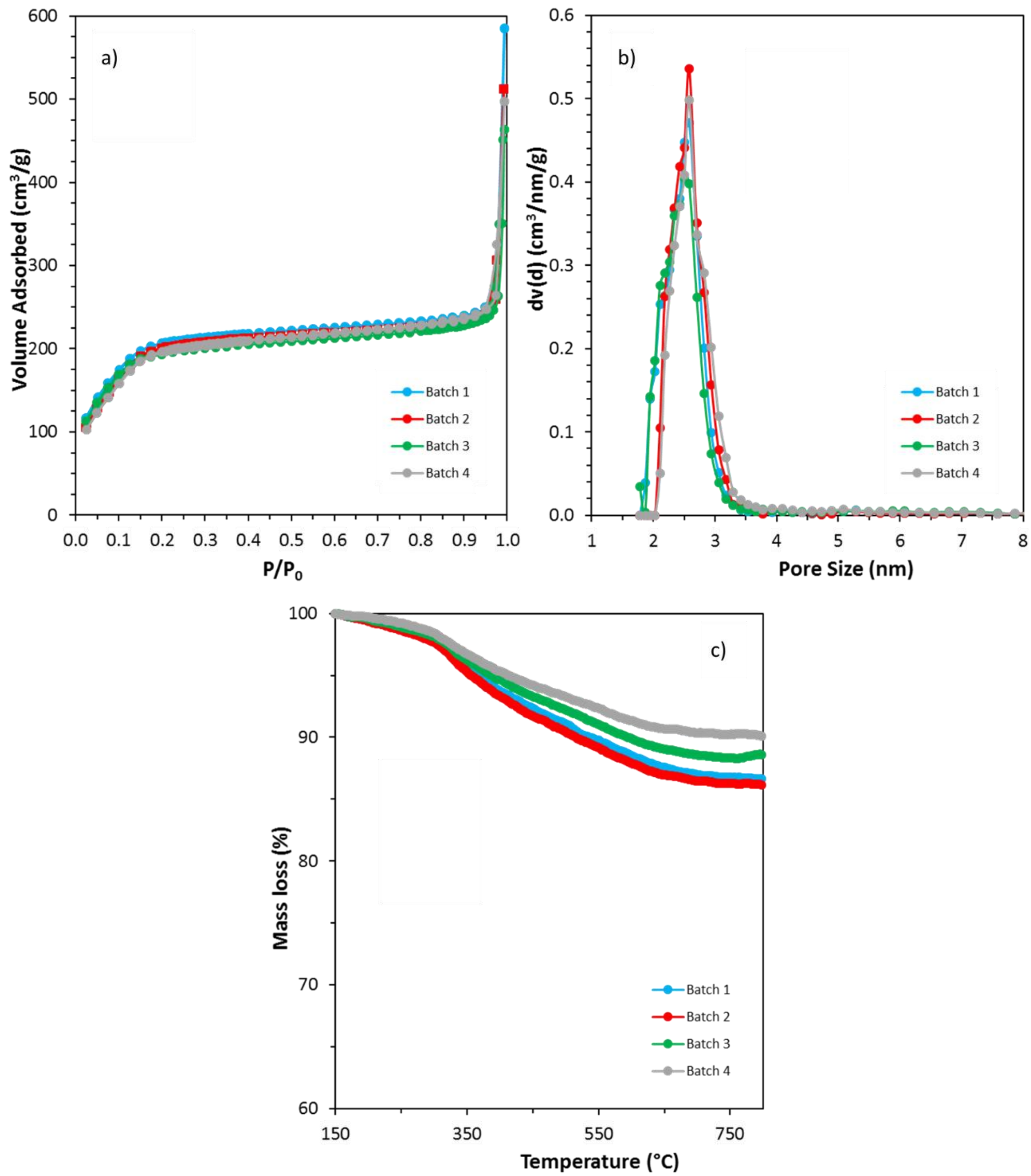

Figure S4. a) N_2 adsorption-desorption isotherms at -196 °C, b) corresponding NLDFT pore size distributions, and c) TGA plots of NH_2-MSNs-PG in quadruplicates.

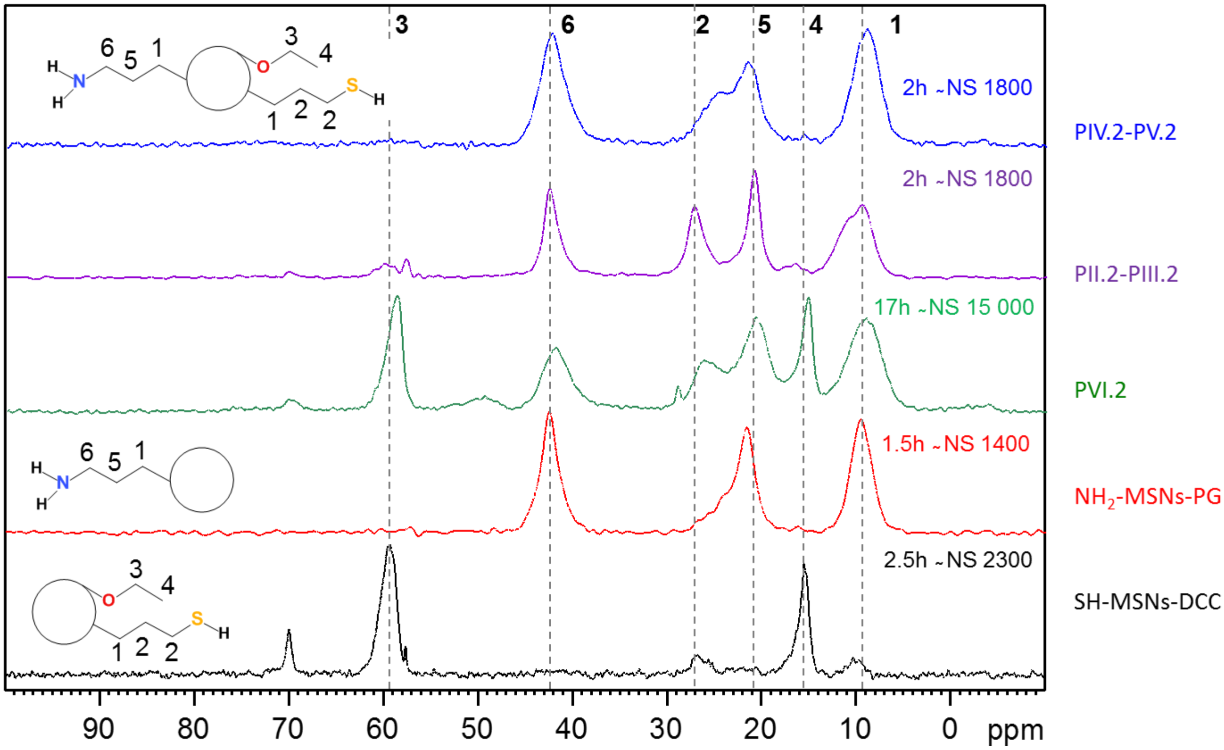

Figure S5. ^{13}C CP/MAS solid state NMR spectra of various functionalized MSNs.

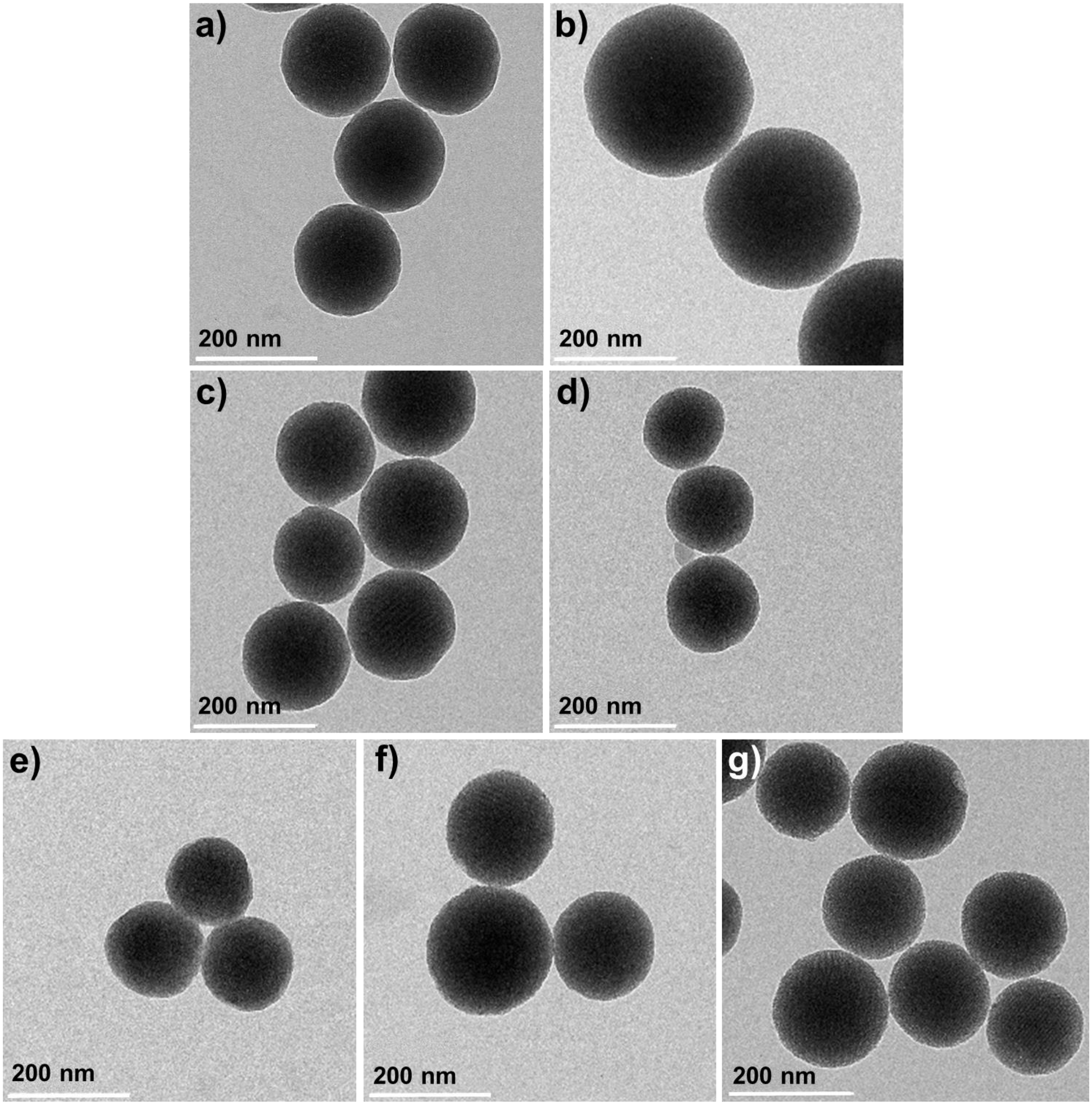

Figure S6. Magnified TEM images of amine- and thiol-functionalized MSNs obtained following the different synthesis pathways, a) PII-2 - PIII-2, b) PIV-2 – PV-2, c) PVI-2, d) PVII-2, e) PVIII-2, f) PIX-2 – PX-2, and g) PXI-3.

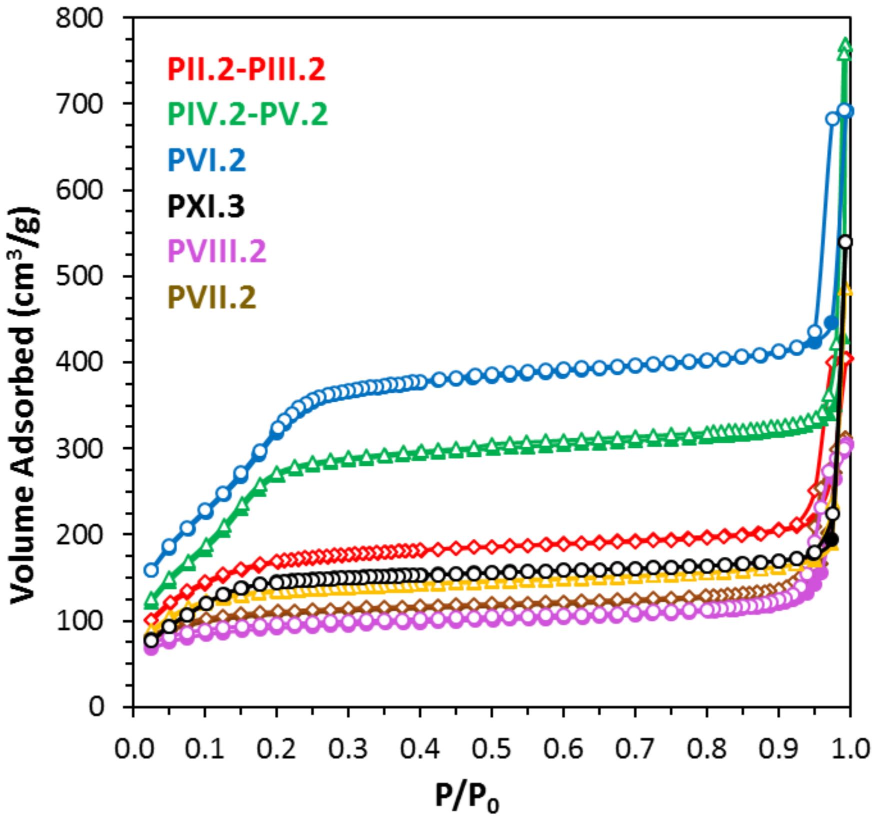

Figure S7. N_2 adsorption-desorption isotherms measured at -196 °C for the MSN samples from line 2 or 3 of Scheme 1.

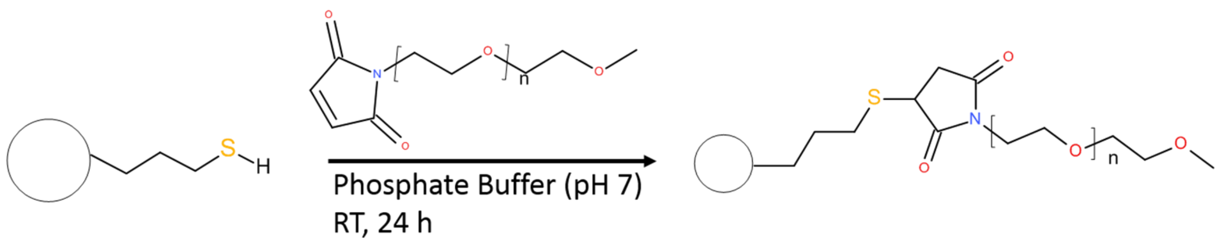

Figure S8. Reaction scheme of thiol-MSNs PEGylation.

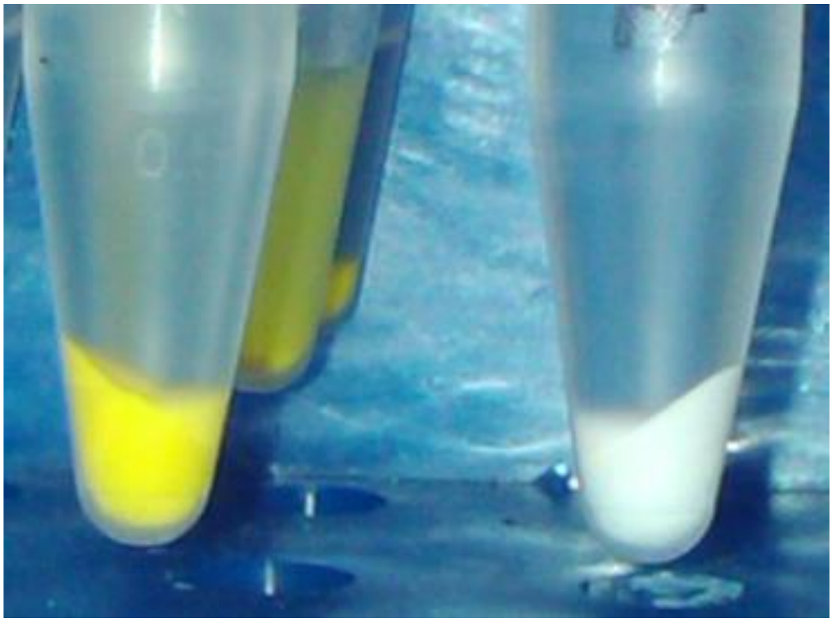

Figure S9. Visual comparison of functionalized MSNs synthesized according to pathway PV-3, with and without fluorescein maleimide.

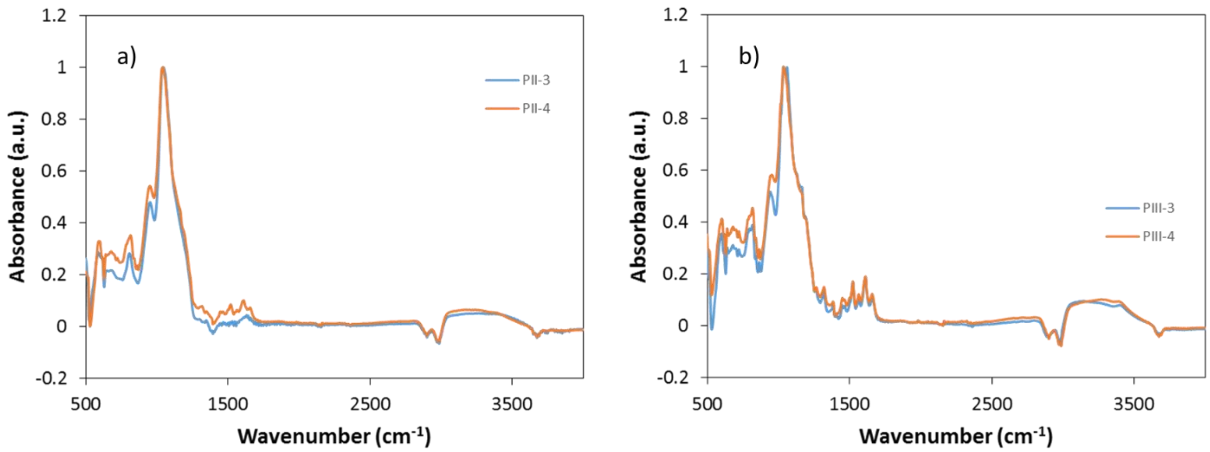

Figure S10. IR (ATR) measurements for a) pathway II and b) pathway III. For each spectrum, the absorbance is normalized to its maximum.

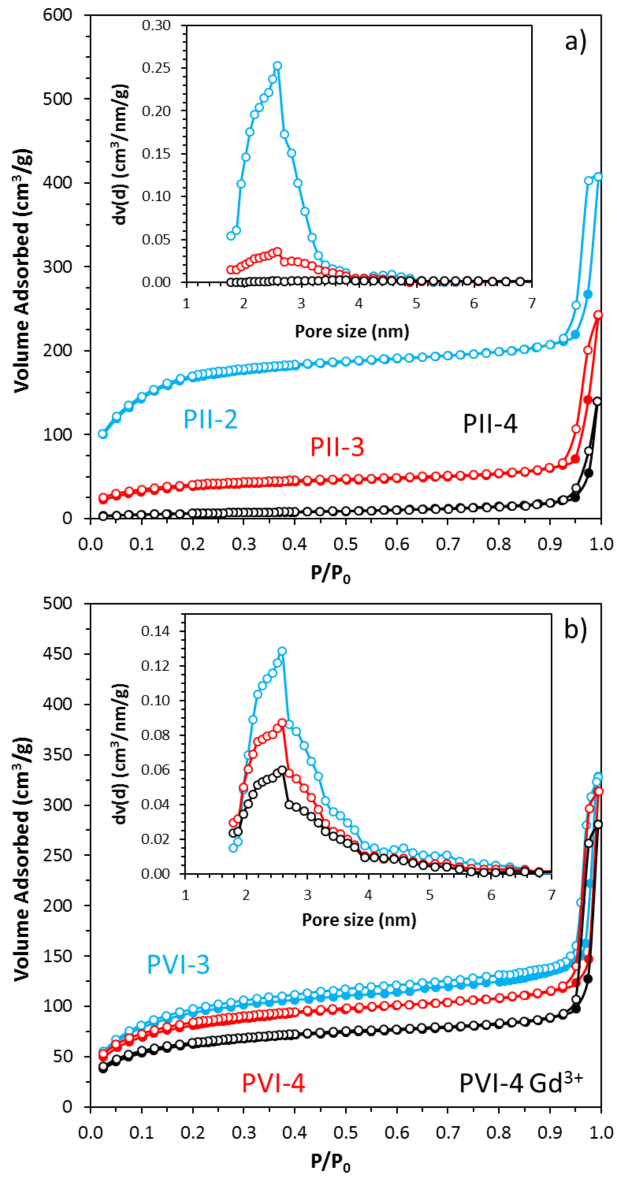

Figure S11. N_2 adsorption (plain symbols) – desorption (open symbols) isotherms at -196 °C and corresponding NLDFT PSD (insets) of MSNs functionalized using the synthesis pathways a) PII and b) PVI.

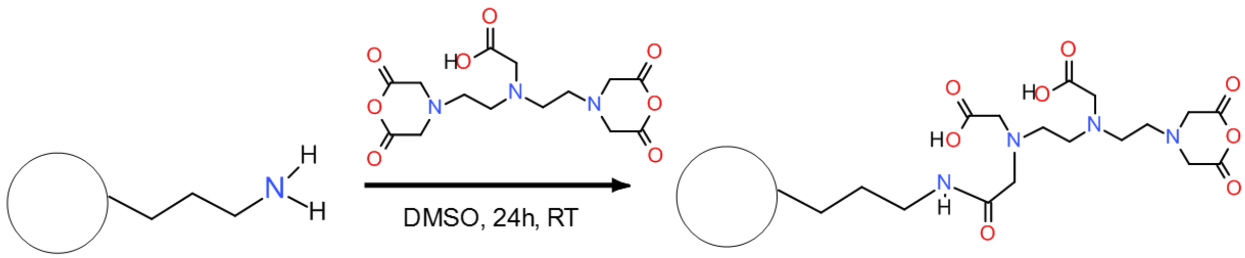

Figure S12. Reaction scheme of DTPA grafting onto NH_2-MSNs.

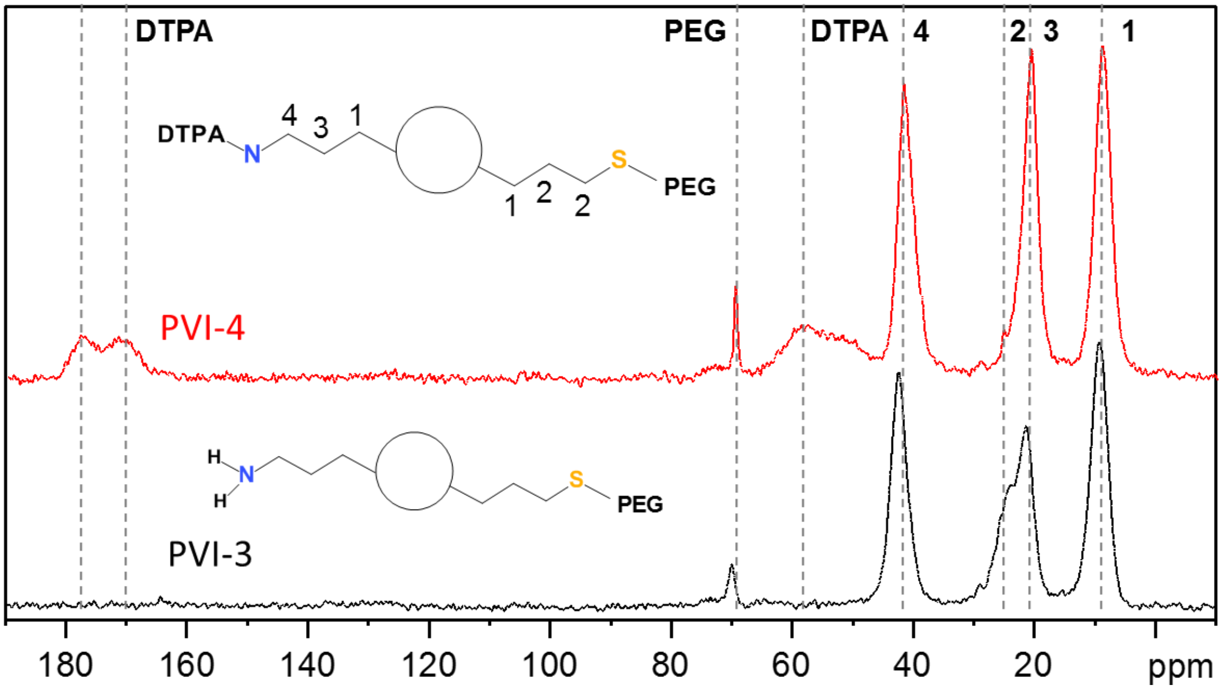

Figure S13. ^{13}C CP solid state NMR spectra of functionalized MSNs synthesized via pathway PVI at different steps.

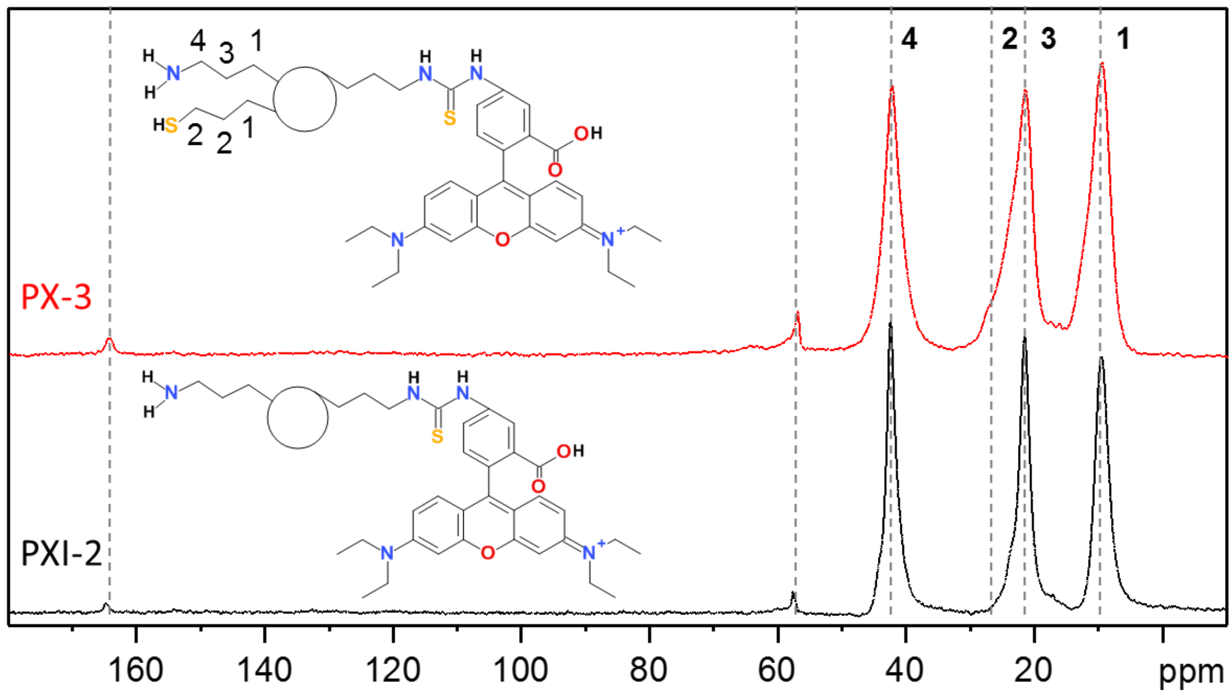

Figure S14. ^{13}C CP solid state NMR spectra of functionalized MSNs after rhodamine grafting performed according to pathways PX and PXI.

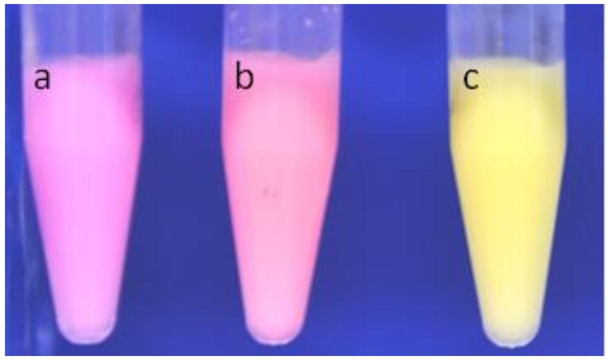

Figure S15. Photos of functional MSNs (PVI-4) following reactions with different fluorophores: a) Rhodamine B isothiocyanate, b) rhodamine B isothiocyanate and fluorescein-5-maleimide, and c) fluorescein-5-maleimide.

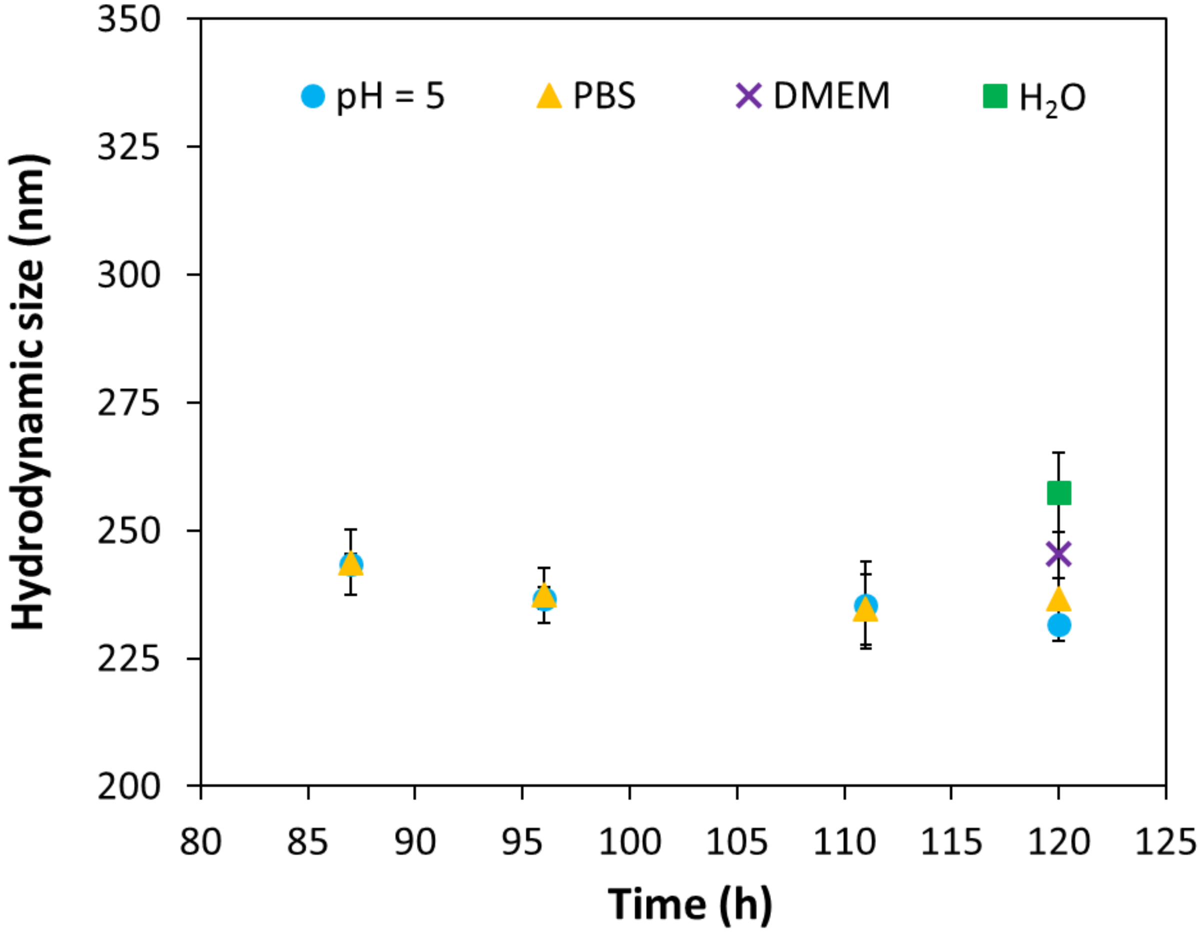

Figure S16. Hydrodynamic diameters of MSNs synthesized according to PVI-4 in different media and at different pH over time.

Table S1. N_2 physisorption at -196 °C data of the different samples at all the different steps mentioned in Scheme 1, a) BET specific surface area in m^2g^{-1}, b) Total pore volume in cm^3g^{-1} and c) NLDFT desorption mode pore size in nm, cursive values in parentheses = including Gd.

a)	Step 1	Step 2	Step 3	Step 4	b)	Step 1	Step 2	Step 3	Step 4	c)	Step 1	Step 2	Step 3	Step 4
Pathway I	1090 ± 74		195			0.92 ± 0.08		0.13			3.4 ± 0.1		2.6	
Pathway II		747 ± 190	146	23			0.42 ± 0.14	0.11	0.04			2.6 ± 0.3	2.6	--
Pathway III		747 ± 190	124 ± 58	62			0.42 ± 0.14	0.10 ± 0.04	0.07			2.6 ± 0.3	2.6	--
Pathway IV	1090 ± 74	771 ± 84	253 *(187)*	297		0.92 ± 0.08	0.46 ± 0.08	0.20 *(0.11)*	0.17		3.4 ± 0.1	2.9 ± 0.2	2.6 *(1.9)*	--
Pathway V	1090 ± 74	771 ± 84	311 ± 60	255 *(322)*		0.92 ± 0.08	0.46 ± 0.08	0.36 ± 0.06	0.30 (*0.33*)		3.4 ± 0.1	2.9 ± 0.2	3.0 ± 0.2	-- *(2.6)*
Pathway VI		811 ± 209	358	307 (*235*)			0.45 ± 0.13	0.20 ± 0.03	0.19 (*0.15*)			2.7 ± 0.2	2.6	2.6 *(2.6)*
Pathway VII	549 ± 78	312 ± 171	281 ± 12			0.34 ± 0.07	0.27 ± 0.10	0.27 ± 0.05			2.6 ± 0.0	2.5 ± 0.2	2.6 ± 0.0	
Pathway VIII	526 ± 31	321 ± 156	230 ± 47			0.31 ± 0.07	0.27 ± 0.08	0.19 ± 0.05			2.6 ± 0.0	2.5 ± 0.2	2.6 ± 0.0	
Pathway IX	781 ± 141	576 ± 113	281			0.38 ± 0.05	0.30 ± 0.03	0.20			2.5 ± 0.2	2.5 ± 0.2	2.6	
Pathway X	781 ± 141	576 ± 113	74	70		0.38 ± 0.05	0.30 ± 0.03	0.08	0.08		2.5 ± 0.2	2.5 ± 0.2	2.6	--
Pathway XI	781 ± 141	658	593	329		0.38 ± 0.05	0.31	0.27	0.25		2.5 ± 0.2	2.6	2.6	2.6

Table S2. Elemental analysis (EA) of the various MSNs materials (see Scheme 1), in molar ratios of a) C:N, b) C:S, and c) N:S. Cursive values in parentheses = including Gd.

a)	Step 1	Step 2	Step 3	Step 4	b)	Step 1	Step 2	Step 3	Step 4	c)	Step 2	Step 3	Step 4
Pathway I	--		153.1			12.2		110.9				0.7	
Pathway II		6.8	12.3	25.0			8.1	13.5	28.8		1.2	1.1	1.2
Pathway III		6.8	17.9	39.3			8.1	23.2	36.7		1.2	1.3	0.9
Pathway IV	--	4.3	3.9 *(4.3)*	4.4		12.2	26.4	60.9 *(43.4)*	44.3		6.2	15.6 *(10.1)*	10.0
Pathway V	--	4.3	4.2	4.0 *(4.7)*		12.2	26.4	22.7	53.8 *(30.2)*		6.2	5.4	13.4 *(6.4)*
Pathway VI		8.0	21.1	13.3 *(14.6)*			10.2	27.0	22.4 *(27.0)*		1.3	1.3	1.7 *(1.8)*
Pathway VII	4.0	6.1	11.0			--	11.3	14.9			1.9	1.4	
Pathway VIII	3.8	6.0	11.0			--	8.7	12.2			1.4	1.1	
Pathway IX	3.2	3.8	4.5			--	23.2	23.0			6.1	5.1	
Pathway X	3.2	3.8	4.5	5.3		--	23.2	11.7	12.1		6.1	2.6	2.3
Pathway XI	3.2	4.0	3.8	5.5		--	--	31.5	34.9		--	8.3	6.4

Table S3. Elemental analysis (EA) of the various MSNs materials (see Scheme 1), in mmol g^{-1} of a) carbon, b) hydrogen, c) nitrogen, and d) sulfur.

a)	Step 1	Step 2	Step 3	Step 4	b)	Step 1	Step 2	Step 3	Step 4	c)	Step 1	Step 2	Step 3	Step 4	d)	Step 1	Step 2	Step 3	Step 4
Pathway I	5.2		13.9			25.7		39.0			--		0.1			0.4		0.1	
Pathway II		6.1	9.7	16.8			33.2	31.8	33.3			0.9	0.8	0.7			0.8	0.7	0.6
Pathway III		6.1	13.9	20.3			33.2	32.9	33.2			0.9	0.8	0.5			0.8	0.6	0.6
Pathway IV	5.2	8.8	10.4 *(11.7)*	11.7		25.7	36.2	36.8 *(37.4)*	37.4		--	2.1	2.7 *(2.7)*	2.7		0.4	0.3	0.2 *(0.3)*	0.3
Pathway V	5.2	8.8	7.5	9.4 *(10.4)*		25.7	36.2	30.9	33 1 *(33.9)*		--	2.1	1.8	2.3 *(2.2)*		0.4	0.3	0.3	0.2 *(0.3)*
Pathway VI		4.2	10.6	10.3 *(10.9)*			32.2	35.0	31.2 *(34.2)*			0.5	0.5	0.8 *(0.7)*			0.4	0.4	0.5 *(0.4)*
Pathway VII	3.8	5.8	8.1			30.3	30.8	26.6			1.0	1.0	0.8			--	0.5	0.6	
Pathway VIII	3.3	5.3	8.1			30.4	28.8	26.6			0.9	0.9	0.7			--	0.6	0.7	
Pathway IX	5.0	5.8	6.2			31.5	33.4	28.6			1.6	1.5	1.4			--	0.3	0.3	
Pathway X	5.0	5.8	7.4	8.0		31.5	33.4	30.0	30.6		1.6	1.5	1.6	1.5		--	0.3	0.6	0.7
Pathway XI	5.0	5.0	5.6	7.1		31.5	28.7	28.1	26.4		1.6	1.5	1.5	1.3		--	--	0.2	0.2

Table S4. Mass loss (150 – 800 °C) in % of the different samples at all the different steps analyzed by TGA. Cursive values in parentheses = including Gd.

	Step 1	Step 2	Step 3	Step 4
Pathway I	12 ± 1		32	
Pathway II		14 ± 4	22	36
Pathway III		14 ± 4	32	34
Pathway IV	12 ± 1	16 ± 3	23(*25*)	19
Pathway V	12 ± 1	16 ± 3	16 ± 1	21(*21*)
Pathway VI		14 ± 3	25	26(*25*)
Pathway VII	13 ± 1	14 ± 2	17	
Pathway VIII	13 ± 2	14 ± 2	17	
Pathway IX	12 ± 2	13 ± 2	12	
Pathway X	12 ± 2	13 ± 2	14 ± 2	17
Pathway XI	12 ± 2	10 ± 2	13 ± 1	12