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Supplementary Information

Polymer-Metal-Organic Framework Self-Assembly (PMOFSA) as a Robust One-Step Method to Generate Well-Dispersed Hybrid Nanoparticles in Water

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Contents

1. Characterization

Transmission electron microscopy (TEM)

Dry-state transmission electron microscopy (TEM) imaging was performed on either FEI TECNAI F20 microscope at an S3 acceleration voltage of 200 kV. All aqueous samples were diluted with deionized water and then deposited onto formvar-coated copper grids. Samples were directly diluted with milliQ water at the ratio of 1:100 and then deposited onto graphene oxide-coated copper grids. Samples were prepared as follows: 5 µL of solution were pipetted onto a formvar/carbon film-coated 400-mesh copper grid (Electron Microscopy Sciences). After 90 s, the solution was carefully absorbed at the base of the droplet using the edge of a filter paper, leaving behind the nanoparticles on the TEM grid.

Dynamic Light Scattering (DLS)

Dynamic light scattering (DLS) measurements were performed using a Malvern Zetasizer Nano S DLS instrument. Hydrodynamic diameters were calculated by the Malvern Zetasizer software package (version 7.13) from the Malvern Panalytical Company, using the classical assumptions. For M-PEGx-TMAn and M-PEG$_{5k}$-PO$_3$ samples with n =1, 5, 10 and 15 (see Table S1), an amount of deionized water was added to samples directly obtained from the synthesis until the final volume fraction was 1:50, 1:4, 1:4 and 1:4, respectively. For M-808-PEG$_{5k}$-TMAn samples with n =1, 5, 10 and 15 (see Table S1), an amount of deionized water was added to samples directly obtained from the synthesis until the final volume fraction was 1:300. The clear suspension was sonicated in a water bath for about half an hour, left to stand for about 15 min, then M-PEGx-TMAn and M-PEG$_{5k}$-PO$_3$ samples with n =5, 10 and 15, filtrated through a 0.45 µm PTFE filter (PHENEX) before use.

Small-angle neutron scattering (SANS)

Small-angle neutron scattering (SANS) measurements were performed at the Institute of Lau Langevin (ILL), Grenoble, France on the D11 spectrometer. The experimental scattering vector q ($q=(4\pi/\lambda)\sin(\theta/2)$) range was $1.2.10^3 < q$ (Å^{-1}) < 0.27, and was covered by 4 sample-to-detector distances (three distances at 1.7 m, 5.5 m and 20 m at the neutron wavelength of 6 Å as well as 38 m at 13 Å). The samples were loaded into Hellma quartz cells with a 2 mm optical path length. Scattering intensities from solutions were corrected for empty cell scattering, solvent scattering, and sample transmission. $I(q)$ is in absolute scale (cm^{-1}). All the solutions were prepared at a concentration of 10 g L^{-1} in H_2O and then dialyzed against D_2O.

Size exclusion chromatography (SEC), NMR, FTIR

Molecular weight determination of the precursor copolymers was obtained using size exclusion chromatography (SEC) in DMF as the eluent. SEC analyses were performed on a Shimadzu instrument fitted with mixed-C columns and RI. Molecular weight distributions (M_w/M_n) were calculated using poly(ethylene glycol) (PEG) standards. All ^{1}H, ^{13}C and ^{19}F NMR spectra were recorded on a Bruker 400 MHz FT NMR spectrometer. Samples were prepared in deuterated chloroform ($CDCl_3$) and their signals referenced to residual non-deuterated signals of the solvent. The spectra were analyzed using MestReNova 12.0.4 (Mestrelab Research S.L.). FTIR spectra were recorded on an Agilent Cary 630 FT-IR spectrometer.

Powder X-ray Diffraction (PXRD)

Powder X-ray Diffraction (PXRD) diffractograms were recorded on a high-throughput Bruker D8 Advance diffractometer working in transmission mode with a focusing Göbel mirror producing CuK_α radiation ($\lambda = 1.5418$ Å) and equipped with a LynxEye detector, in a 2θ range from 1.6 to 30°. Samples were freeze-dried before being cast as powders onto zero background plates. The simulated data of MIL-100(fe) was downloaded from Cambridge Crystallography Data Center (CCDC) and the powder pattern was calculated by Mercury software.

X-ray Photoelectron Spectroscopy (XPS)

X-ray Photoelectron Spectroscopy (XPS) analysis were carried out using a Thermo Scientific™ K-Alpha™ XPS System. A monochromatic Al-Kα source (1486.7 eV) and a charge neutralizer were used for all samples. The XPS data were analyzed using the Avantage software (version 5.9918) package from Thermo scientific Company.

2. Materials and Methods

Dichloromethane (DCM), N,N-dimethylformamide (DMF) and diethyl ether were obtained from Carlo Erba. 4-Dimethylaminopyridine (DMAP) was purchased from Aldrich, with a purity of 99%. N,N'-Dicyclohexylcarbodiimide (DCC) and phosphoryl chloride ($POCl_3$), with a purity of 99%, was purchased from Alfa Aesar. Trimesic acid (TMA), PEG of molecular weights 2000, 5000 and 10000 (PEG2k, PEG5k and PEG10k) and iron (III) nitrate nonahydrate (≥ 98% purity) were purchased from Sigma-Aldrich. Zr_6 cluster and formic acid were provided by ENS (CNRS), All reagents were used as received.

2.1. Synthesis of PEG10k-TMA, PEG5k-TMA, and PEG2k-TMA

Synthesis of PEG10k-TMA. In a round-bottle flask, 1.5 g of commercial PEG-OH of Mn 10000 (PEG10k, 0.15 mmol)) and trimesic acid (130 mg, 0.6 mmol) were dissolved in 20 mL dimethylformamide (DMF). After the reaction mixture had become completely colorless, 80 mL dichloromethane (DCM) were added. After stirring for 2h, 4-dimethylaminopyridine (7.3 mg, 0.06 mmol) and N, N'-dicyclohexylcarbodiimide (120 mg, 0.6 mmol) were added under stirring. The resulting mixture was stirred for 4 additional days at room temperature, then concentrated under reduced pressure. The resulting liquid was precipitated in ice-cold diethyl ether under stirring, the solid being recovered by filtration. It was further purified by three additional precipitations in dichloromethane.

Synthesis of PEG5k-TMA. In a round-bottled flask, 3.0 g of PEG-OH of M_n 5000

(PEG5k, 0.60 mmol) and 0.50 g of trimesic acid (2.38 mmol, 3.97 eq.) were dissolved in a mixture of 20 mL DMF and 80 mL DCM. After 2h, 4-dimethylaminopyridine (29 mg, 0.24 mmol) and N,N'-dicyclohexylcarbodiimide (500 mg, 2.4 mmol) were added upon stirring. The mixture was stirred for 4 days at room temperature, and then concentrated under reduced pressure. The resulting liquid was precipitated in ice-cold diethyl ether under stirring, the solid being recovered by filtration. It was further purified by three additional precipitations in dichloromethane.

PEG_{2k}-TMA was obtained using the same procedure, except for the initial molar ratio of the reagents and catalysts, i.e., 3.0 g of PEG-OH of M_n 2000 (PEG2k, 1.5 mmol) and 1.3 g of trimesic acid (6.2 mmol, 4.1 eq.) for 20 mL DMF and 80 mL DCM, 73 mg of 4-dimethylaminopyridine (0.6 mmol) and 1.2 g of N,N'-dicyclohexyl carbodiimide (5.8 mmol).

PEG_{2k}-TMA (see also fig. S1): ^1H NMR (400 MHz, CDCl3) δ/ppm: 3.38 (s, 3H, O-CH_3), 3.55(s, 4H, O-CH_2-CH_2), 4.52 (s, 2H, CH_2-CH_2-COOH), 8.88 (s, 3H, Ph). PEG_{5k}-TMA (see also fig. S2): ^1H NMR (400 MHz, $CDCl_3$) δ/ppm: 3.34 (s, 3H, O-CH_3), 3.61(s, 4H, O-CH_2-CH_2), 4.49 (s, 2H, CH_2-CH_2-COOH), 8.84 (s, 3H, Ph). SEC analyses are provided in Fig. S3. PEG_{10k}-TMA (see also fig. S3): 1H NMR (400 MHz, CDCl3) δ/ppm: 3.32 (s, 3H, O-CH_3), 3.59(s, 4H, O-CH_2-CH_2), 4.46 (s, 2H, CH_2-CH_2-COOH), 8.83 (d, J = 8.3 Hz, 3H).

2.2. Synthesis of PEG5k-PO_3.

The following procedure was modified based on the literature.[1] PEG5k-OH (10.0 g, 2 mmol) was dissolved in dichloromethane (100 mL) and triethylamine (2.79 mL, 20 mmol) was added to the mixture at -5°C (liquid nitrogen/saturated NaCl solution), followed by the addition of 700 µL of a $POCl_3$. The reaction mixture was maintained at room temperature for 3h. Water (40 mL) was subsequently added, and the solution was further stirred for an additional 1 h. The combined yellow organic phases were washed with 40 mL water twice, the water phase was extracted with DCM (100 mL), and finally dried over anhydrous magnesium sulfate. After evaporation of the DCM solvent, the yellow solid (8.2 g, 82% yield) was dried overnight in a fume hood. ^1H NMR (400 MHz, deuterium oxide) δ 4.00 (s, 2H), δ 3.85 (s, 2H), δ 3.67 (s, 536H), 3.35 (s, 3H). ^{31}P NMR (162 MHz, deuterium oxide) δ 0.30.

2.3. Synthesis of the MOF and Polymer-MOF Nanoparticles

2.3.1. *Synthesis of MIL-100 (Fe)*

Fe $(NO_3)_3$•$9H_2O$ (7.2 mg, 0.018 mmol) and trimesic acid (TMA) (2.5 mg, 0.012 mmol) were mixed in a 1 mL vial, dissolved in 0.9 mL Milli-Q water, stirred at 600 rpm, and heated at 60°C for 24 h. The resulting suspensions was centrifuged to remove the unreacted ligands and redispersed in water, then dialyzed against Milli-Q water for 3 days using a dialysis membrane with a cut-off of 6-8 kDa MWCO and 2-3 water changes per day. The resulting liquid samples were directly used for TEM and DLS characterizations. Freeze-drying was used to obtain the solid samples necessary for the FTIR, XPS, and XRD characterizations.

2.3.2. *Synthesis of MOF-PEG$_n$-OHn Samples by in situ Self-Assembly as Illustrated by M-PEG$_{2k}$-OH10 and M-PEG$_{5k}$-OH10 Samples*

Fe $(NO_3)_3$•$9H_2O$ (7.2 mg, 0.018 mmol), trimesic acid (TMA) (2.5 mg, 0.012 mmol) and either PEG2k-OH (100 mg, 0.05 mmol) or PEG5k-OH (100 mg, 0.02 mmol) were mixed in a 1 mL vial, dissolved in 0.9 mL Milli-Q water, stirred at 600 rpm, and heated at 60°C for 24 h. The resulting suspensions were dialized against Milli-Q water for 3 days using a dialysis membrane with a cut-off of 6-8 kDa MWCO and 2-3 water changes per day. The resulting liquid samples were directly used for TEM and DLS characterizations. Freeze-drying was used to obtain the solid samples necessary for the FTIR, XPS, and XRD characterizations.

2.3.3. *Synthesis of Other M-PEG$_{2k}$-OHn and M-PEG$_{5k}$-OHn Samples*

The same procedure was used for samples *M-PEG$_{5k}$-n* where $n = 1$, 5 and 20 (instead of 10) (see Table S1), except that volumes of 9.9, 1.9 and 0.4 mL Milli-Q water, respectively, were used instead of 0.9 mL as in the above procedure.

2.3.4. *Synthesis of MOF-PEG$_{5k}$-PO$_3$n Samples by in situ Self-Assembly as Illustrated by MOF-PEG$_{5k}$-PO(OH)$_2$10 Samples*

Fe $(NO_3)_3$•$9H_2O$ (7.2 mg, 0.018 mmol), trimesic acid (TMA) (2.5 mg, 0.012 mmol) and *PEG$_{5k}$- PO$_3$* (100 mg, 0.019 mmol) were mixed in a 1 mL vial, dissolved in 0.9 mL Milli-Q water, stirred at 600 rpm, and heated at 60°C for 24 h. The resulting suspensions were dialized against Milli-Q water for 3 days using a dialysis membrane with a cut-off of 6-8 kDa MWCO and 2-3 water changes per day.

2.2.5. *Synthesis of Other MOF-PEG$_{5k}$- PO$_3$nSamples*

The same procedure was used for *M-PEG$_{5k}$- PO$_3$n* samples where $n = 1$, 5 and 15 (instead of 10) (see Table S1), except that volumes of 9.9, 1.9 and 0.57 mL Milli-Q water, respectively, were used instead of 0.9 mL as in the above procedure.

2.3.6. *Synthesis of MOF-PEG$_n$-TMAn Samples by in situ Self-Assembly as Illustrated by M-PEG$_{2k}$-TMA10, M-PEG$_{5k}$-TMA10 and M-PEG$_{10k}$-TMA10 samples*

Fe $(NO_3)_3$•$9H_2O$ (7.2 mg, 0.018 mmol), trimesic acid (TMA) (2.5 mg, 0.012 mmol) and either PEG$_{2k}$-TMA (100 mg, 0.045 mmol) or PEG$_{5k}$-TMA (100 mg, 0.019 mmol) or PEG$_{10k}$-TMA (100 mg, 0.01 mmol) were mixed in a 1 mL vial, dissolved in 0.9 mL Milli-Q water, stirred at 600 rpm, and heated at 60°C for 24 h. The resulting suspensions were dialized against Milli-Q water for 3 days using a dialysis membrane with a cut-off of 6-8 kDa MWCO and 2-3 water changes per day.

2.3.7. *Synthesis of other M-PEG$_{2k}$-TMAn, M-PEG$_{5k}$-TMAn and M-PEG$_{10k}$-TMAn Samples*

The same procedure was used for samples *M-PEG$_{2k}$-TMAn, M-PEG$_{5k}$-TMAn and M-PEG$_{10k}$-TMAn* where *n* = 1, 5 and 15 (instead of 10) (see Table S1), except that volumes of 9.9, 1.9 and 0.57 mL Milli-Q water, respectively, were used instead of 0.9 mL as in the above procedure.

2.3.8. *Synthesis of MOF-808 and M-808-PEG$_{5k}$-TMAn Samples by in situ Self-Assembly.*

The procedure was modified from the literature.[2] Zr_6 oxoclusters (0.75 g, 1.37 mmol) were dispersed in formic acid (3.75 mL) under vigorous stirring. Milli-Q water (6.25 mL) was subsequently added, and the reaction mixture was stirred until it became completely transparent. The resulting solution was then injected into five 10 mL vials (2 mL solution per vial). Trimesic acid (37.5 mg, 0.178 mmol) along with several contents of PEG$_{5k}$-TMAn, where *n* = 1, 5, 10 and 15 (see Table S1) were then added into 2 mL pre-dispersed Zr6 solution, and the reaction was stirred for 24 h at 60°C. The resulting suspensions were dialized against Milli-Q water for 3 days using a dialysis membrane with a cut-off of 6-8 kDa MWCO and 2-3 water changes per day. The resulting liquid samples were directly used for TEM and DLS characterizations. Centrifugal washing and vacuum drying were used to obtain the solid samples necessary for the XRD characterizations.

2.3.9. *Sample Preparation for Characterization*

The resulting liquid samples were directly used for TEM and DLS characterizations. Freeze-drying was used to obtain the solid samples necessary for the FTIR, XPS, and XRD characterizations.

3. Figures and Tables

Figure S1. *^{1}H NMR spectra of PEG$_{2k}$-TMA, PEG$_{5k}$-TMA and PEG$_{10k}$-TMA in CDCl$_3$.*

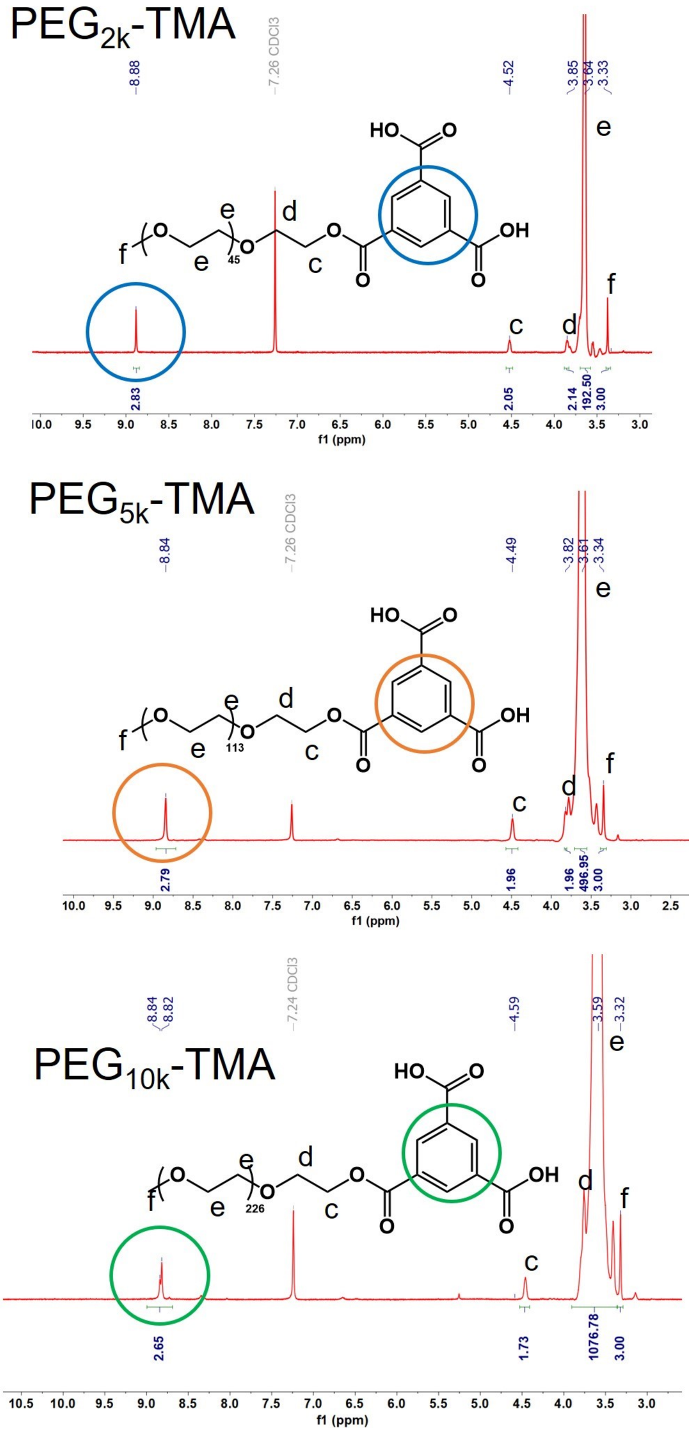


Figure S2. *^{1}H and ^{31}P NMR spectra of PEG$_{5k}$-PO$_3$ in D$_2$O.*

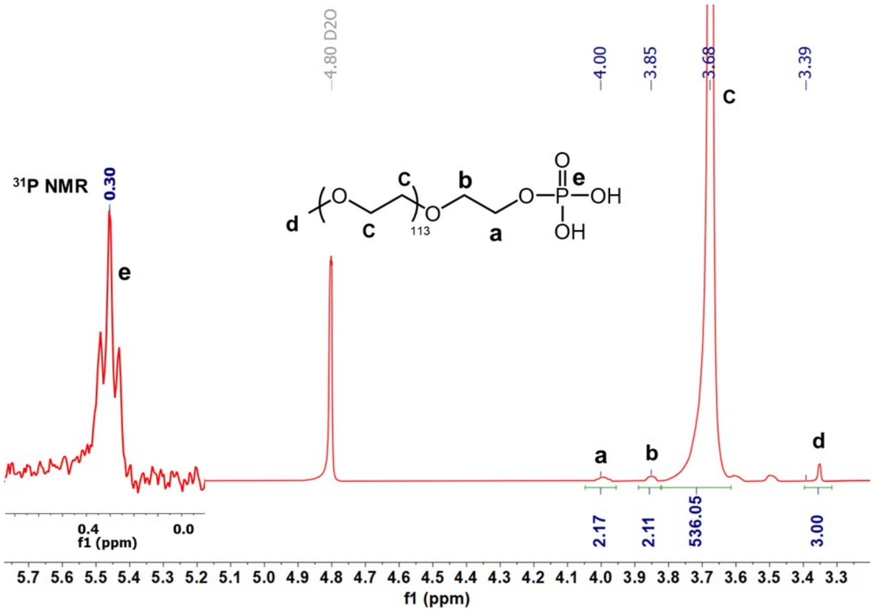


Figure S3. *SEC RI traces of PEG2k, PEG$_{2k}$-TMA, PEG5k, PEG$_{5k}$-PO$_3$, PEG$_{5k}$-TMA, PEG10k and PEG$_{10k}$-TMA. GPC analyses were performed in DMF and provided relative molecular weights with respect to PEG standards.*

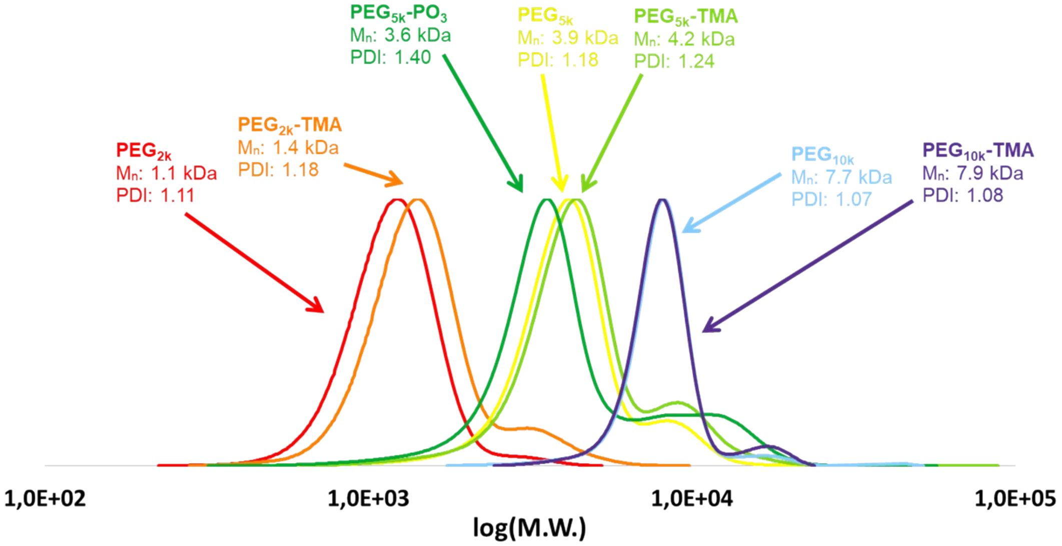


Figure S4. *TEM of M-PEG5k-OH10 and M-PEG2k-OH10*

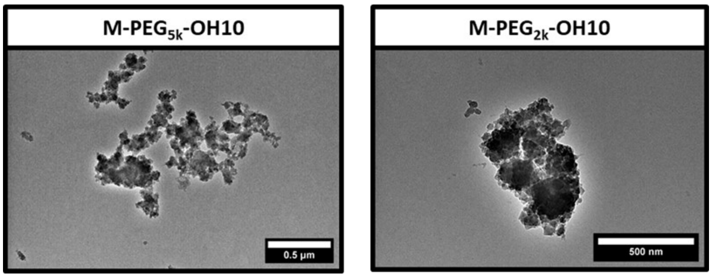


Table S1. *Summary of polymer-MOF nanoparticles size parameters as obtained by DLS*

Sample #	**Polymer wt-%**	**Mean diameter (nm)**	**Polydispersity index**
M-PEG$_{10k}$-TMA15	15.0	82	0.31
M-PEG$_{10k}$-TMA10	10.0	114	0.26
M-PEG$_{10k}$-TMA5	5.0	103	0.23
M-PEG$_{10k}$-TMA1	1.0	336	0.64
M-PEG$_{5k}$-TMA15	15.0	51	0.61
M-PEG$_{5k}$-TMA10	10.0	37	0.50
M-PEG$_{5k}$-TMA5	5.0	85	0.44
M-PEG$_{5k}$-TMA1	1.0	168	0.43
M-PEG$_{5k}$-PO$_3$15	15.0	26	0.57
M-PEG$_{5k}$-PO$_3$10	10.0	46	0.52
M-PEG$_{5k}$-PO$_3$5	5.0	60	0.29
M-PEG$_{5k}$-PO$_3$1	1.0	200	0.61
M-PEG$_{2k}$-TMA15	15.0	24	0.46
M-PEG$_{2k}$-TMA10	10.0	16	0.20
M-PEG$_{2k}$-TMA5	5.0	41	0.55
M-PEG$_{2k}$-TMA1	1.0	142	0.33
M-808-PEG$_{5k}$-TMA15	15.0	381	0.045
M@PEG$_{5k}$-TMA10	10.0	308	0.55
M@PEG$_{2k}$-TMA10	10.0	237	0.64
M@PEG$_{5k}$-PO$_3$10	10.0	170	0.30
M-808@PEG$_{5k}$-TMA10	10.0	1030	0.34

Figure S5. *Visual appearance of the dispersion state one day after the synthesis using standard experimental conditions: (from left to right) MIL-100 (Fe), M-PEG$_{2k}$-TMA10 and M-PEG$_{5k}$-TMA10 nanoparticles.*

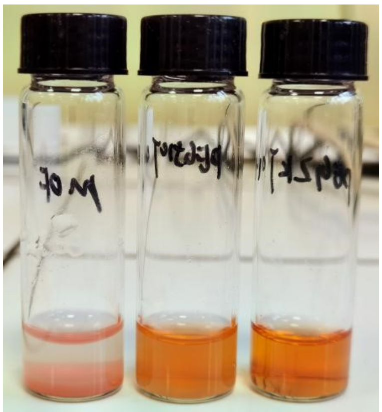


Figure S6. *Evolution of the hydrodynamic diameter (d_{hyd}) for PMOF particles synthesized in the presence of PEG-TMA polymer ligands (2k, 5k and 10k) and PEG-PO$_3$ (5k) as a function of the PEG weight percentage in the initial PEG : water mixture.*

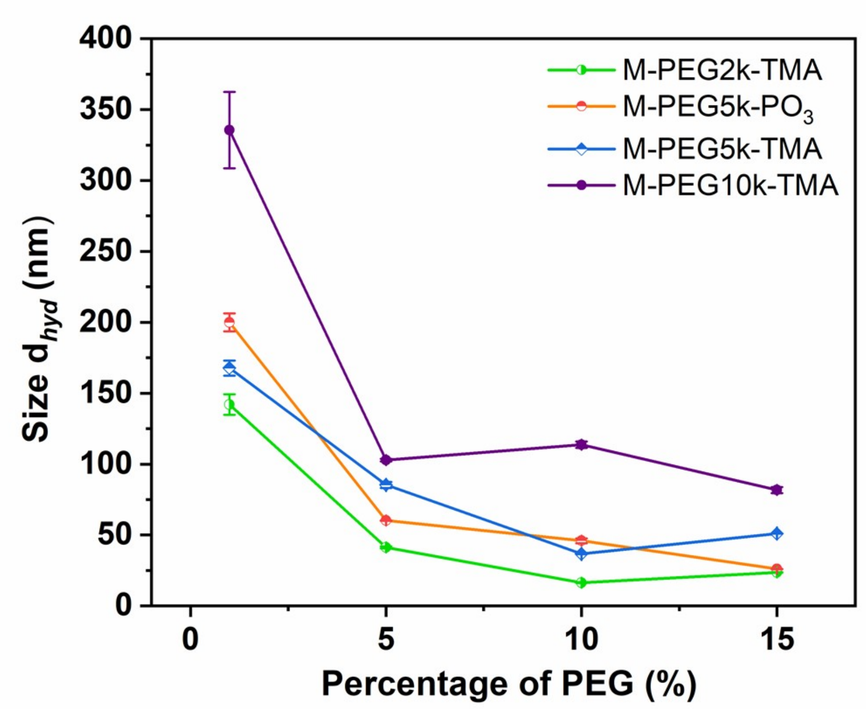
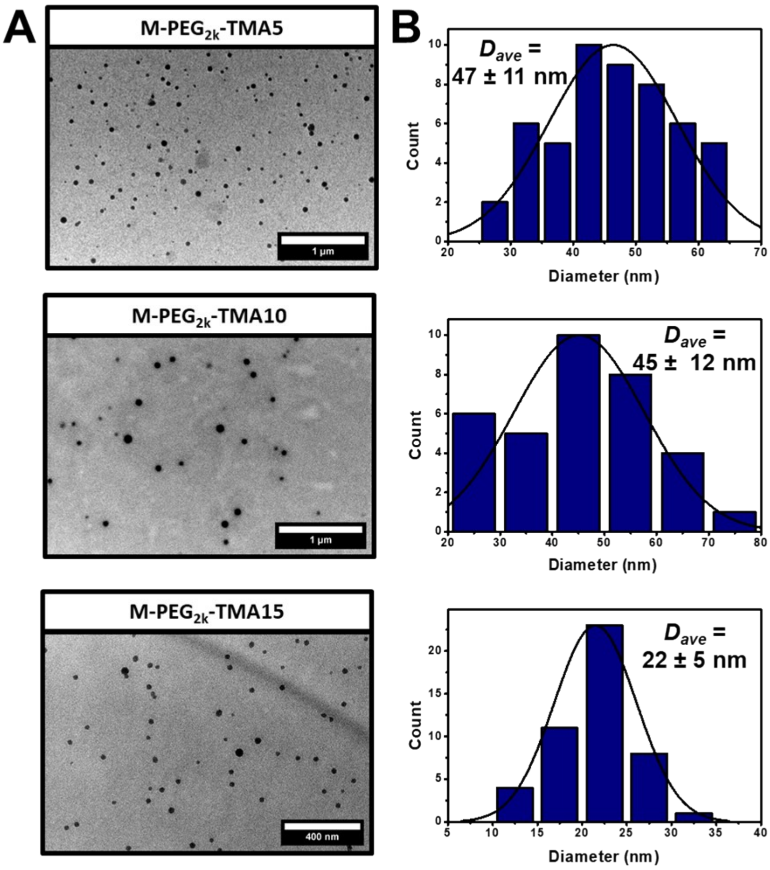


Figure S7. *A) Representative dry-state TEM images of purified particles; B) histograms of particle size distribution obtained from particle analysis on TEM images. In each case, from 30 up to 60 particles were analyzed.*



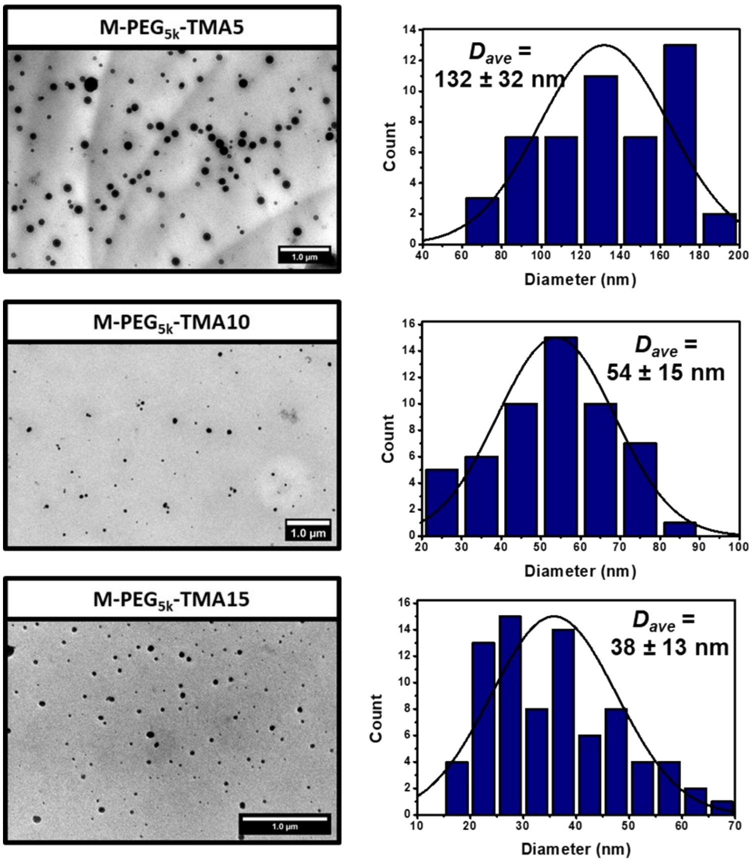


Table S2. *SANS fits results of M-PEG$_{2k}$-TMA10 and M-PEG$_{5k}$-TMA10.*

	M-PEG$_{5k}$-TMA$_{10}$	**M-PEG$_{2k}$-TMA$_{10}$**
D$_{core}$ (nm)	10.1 (+/- 0.3)	9.2 (+/- 0.4)
R$_{g,PEG}$ (nm)	3.56 (+/- 0.08)	2.23 (+/- 0.05)
d$_{penetration}$ (nm)	-0.18	-0.25

Note: Signal intensities were fitted using the Sasview software, with a model corresponding to a sphere covered by a polymer layer and dispersed in a good solvent. The scattering length density for the solvent, MOF and polymer are $\rho_{solv} = 6.2 \times 10^{-6}$ Å^{-2}; $\rho_s = 1.4 \times 10^{-6}$ Å^{-2}; and $\rho_l = 0.8 \times 10^{-6}$ Å^{-2}, respectively.

Figure S8. *(from bottom to top) PXRD diffractograms of simulated MIL-100 (Fe), as prepared MIL-100 (Fe), M-PEG$_{2k}$-TMA10 and M-PEG$_{5k}$-TMA10.*

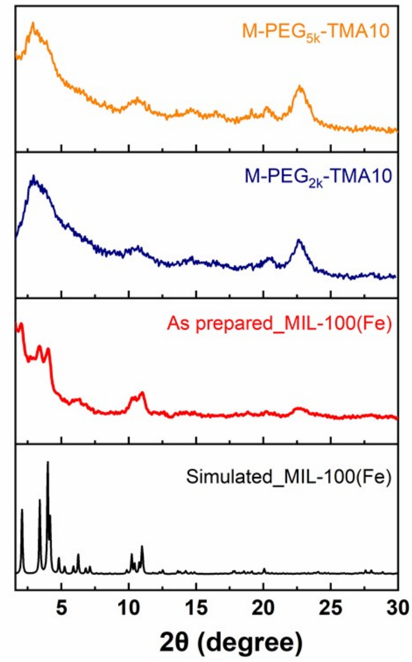


Figure S9. *(A) XPS survey spectra and high-resolution XPS spectra of MIL-100(Fe) and M-PEG2k-TMA10; (B) Fe 2p of native MIL-100(Fe) and M-PEG2k-TMA10; (C) C 1s of MIL-100(Fe); (D) C 1s of MIL-100(Fe); (E) C 1s of M-PEG2k-TMA10; (F) O 1s of M-PEG2k-TMA10.*

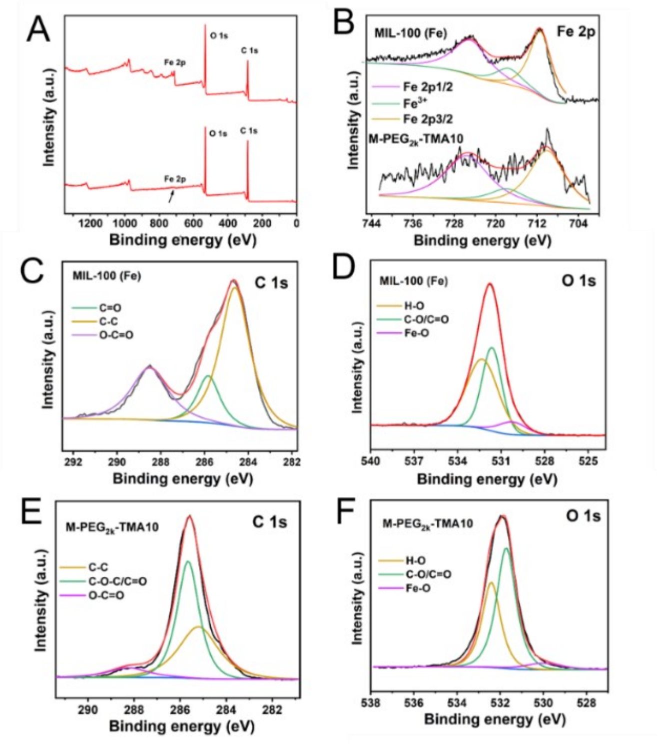


Figure S10. *ATR-FTIR spectra of the MIL-100 (Fe) (bottom, black curve), M-PEG$_{2k}$-OH10 (middle, red curve), and M-PEG$_{2k}$-TMA10 (top, blue curve) solid samples obtained after the treatments summarized in the experimental section to obtain solid powders. The assignments of the main bands are indicated in the figure.*

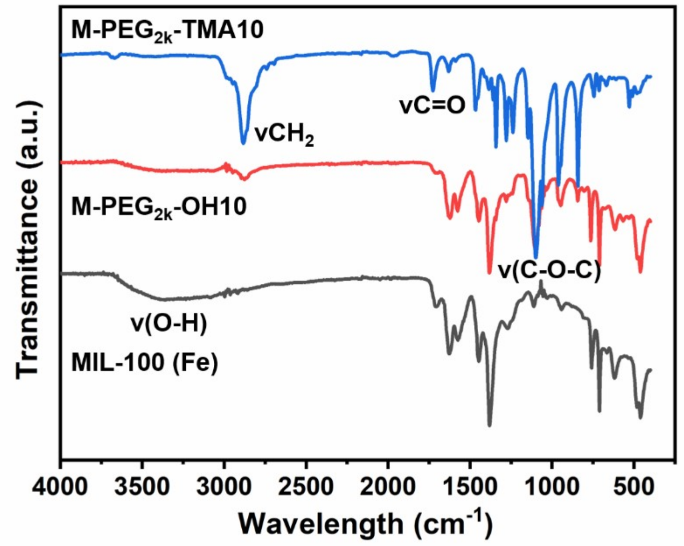


Figure S11. *DLS volume-averaged distribution for M-PEG2k-TMA10 particles synthesized at 60°C and 80°C, respectively (after a 1:4 dilution of the initial reaction mixture and filtration, see experimental section). Attempts at 20 and 40°C led to very large distributions whose parameters could not be reliably measured by our DLS equipment.*

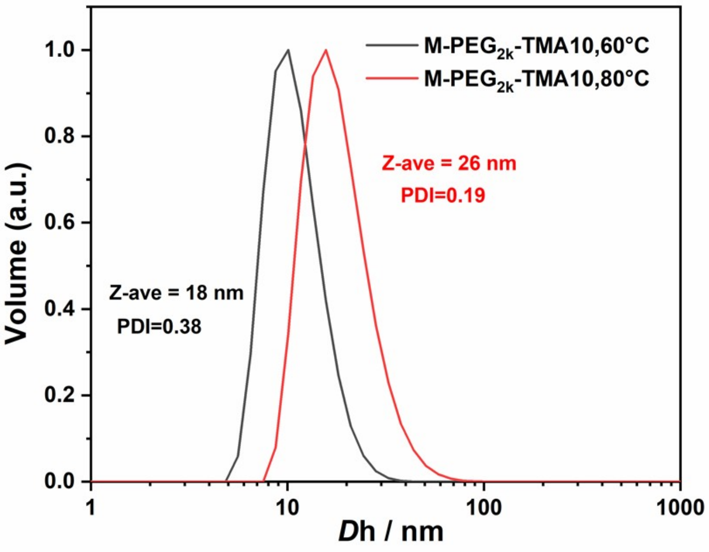


Figure S12. *DLS volume-averaged distribution of initial M-PEG$_{2k}$-TMA10 solution and different cycle of redispersion of M-PEG$_{2k}$-TMA10 dry powders obtained after freeze-drying.*

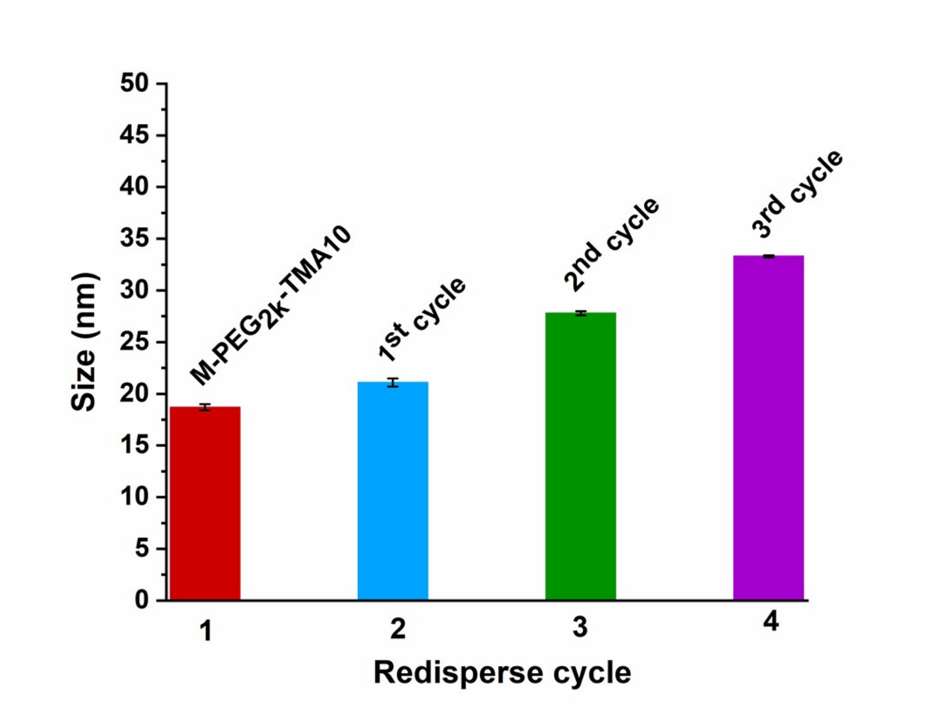


Figure S13. *N$_2$ adsorption-deposition isotherms (77K) of pristine MIL-100(Fe) obtained by vacuum drying (VAC) and freeze-drying (FD), M-PEG2k-TMA10 and M-PEG5k-TMA10 obtained by freeze-drying (FD). Two activation temperature were utilized, 60°C and 150°C.*

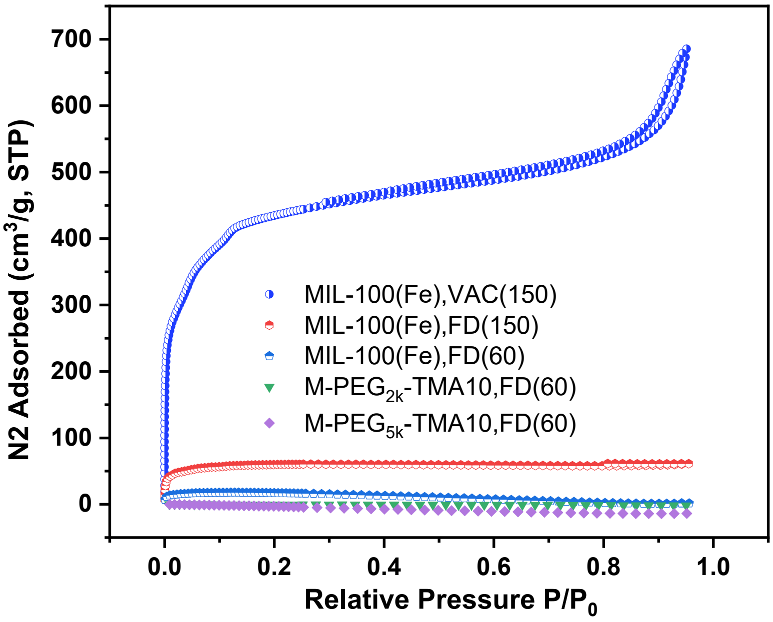
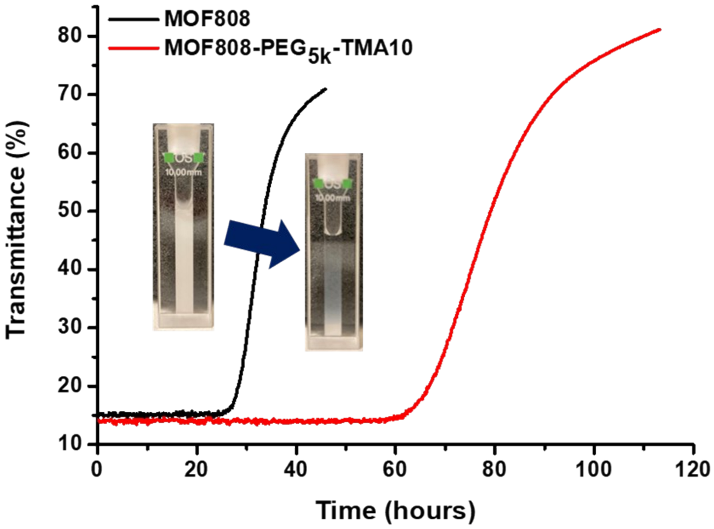


Figure S14. *Turbidity measurements of aqueous solutions of MOF808 and MOF808-PEG$_{5k}$-TMA10 as measured by UV/Vis spectroscopy at 600 nm.*



[1] X. Chen, Y. Zhuang, N. Rampal, R. Hewitt, G. Divitini, C. A. O'Keefe, X. Liu, D. J. Whitaker, J. W. Wills, R. Jugdaohsingh, J. J. Powell, H. Yu, C. P. Grey, O. A. Scherman, D. Fairen-Jimenez, *Journal of the American Chemical Society* **2021**, *143*, 13557-13572.

[2] S. Dai, C. Simms, I. Dovgaliuk, G. Patriarche, A. Tissot, T. N. Parac-Vogt, C. Serre, *Chemistry of Materials* **2021**, *33*, 7057-7066.