

Electronic Supplementary Information

Degradation of ZIF-8 in Phosphate Buffered Saline Media

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Methods and Instrumentation

Materials

2-methylimidazole (HmIM) was purchased from Tokyo Chemical Industry (TCI). Zinc acetate dihydrate ($\text{Zn}(\text{OAc})_2 \cdot 2\text{H}_2\text{O}$) was obtained from Sigma-Aldrich. Sodium chloride (NaCl), potassium chloride (KCl), and potassium dihydrogen phosphate (KH_2PO_4) were purchased from Carl Roth. Disodium hydrogen phosphate dehydrate ($\text{Na}_2\text{HPO}_4 \cdot 2\text{H}_2\text{O}$) was obtained from Honeywell Riedel-de Haën. All reagents and chemicals were used as received without further purification.

Phosphate Buffered Saline (PBS) was prepared according to the literature procedure: NaCl (8 g, 0.137 M), KCl (0.2 g, 2.7 mM), $\text{Na}_2\text{HPO}_4 \cdot 2\text{H}_2\text{O}$ (1.77 g, 10 mM), KH_2PO_4 (0.24 g, 1.8 mM) were dissolved in 800 mL of distilled water, the solution was adjusted to pH 7.4 using NaOH (1M), and diluted to 1000 mL with distilled water.

FT-IR spectroscopy

FT-IR spectra were recorded on a Bruker ALPHA spectrometer using the ATR accessory with a diamond window in the range of $\tilde{\nu}$ 500 – 4000 cm^{-1} .

Gas Chromatography-Mass Spectrometry (GC-MS) analysis of 2-methylimidazole

The GC-MS analyses of the mother liquors were carried out on a gas chromatographic system with a single quadrupole mass selective detector (Shimadzu QP 2010 Ultra, Shimadzu Europe GmbH, Duisburg, Germany) with an AOC 5000 autosampler.

Aliquots of one microliter was injected in split mode (split ratio 1:20) at 250°C injection port temperature with a specific liner for aqueous injection (4 mm precision liner, Topaz, Restek, Belfonte, USA).

Separation was done on a polar column (Phenomenex ZB Wax 20 m*0.18 mm inner diameter and 0.18 μm film thickness, Phenomenex LTD, Aschaffenburg, Germany) with the following temperature ramp starting at 60°C (1 min) and ramped to 240°C with a temperature ramp of 15°C min^{-1} . Helium was used as carrier with a linear velocity of 35 cm/s in the constant flow mode. The quadrupole was operated in the scan mode with a scan range from 50–150 amu with a scan rate of 5 scans per second. Interface and ion source temperature were set to 230°C and 200°C respectively. Multiplier voltage was reduced by 200 voltage relative to tune value to avoid detector saturation.

Six different standard solutions of 2-methylimidazole (1 mM, 2 mM, 3 mM, 4 mM, 5 mM, and 6 mM) were analyzed with the established GC-MS method to generate the corresponding calibration curve. The repeatability of the analytical method was tested by conducting three repeated analyses of the standard solutions.

^{31}P Nuclear Magnetic Resonance Spectroscopy (NMR)

^{31}P NMR spectrum of the PBS (10 mM) prepared in D_2O was collected on a 200 MHz Bruker spectrometer (time = 0). Afterwards, the micro-ZIF-8 particles (0.5 mg mL^{-1}) were soaked into this sample, and the corresponding ^{31}P NMR spectra were recorded at different incubation times (1 h and 24 h).

To explain the decrease in signal associated with PBS without any newly appearing resonances we performed a titration experiment with Na_2HPO_4 and ZnCl_2 . To facilitate NMR detection we increased the concentration of phosphate in solution to ca. 100 mM.

We prepared an NMR sample containing 113 mM phosphate (11.2 mg Na_2HPO_4 in 700 μL D_2O , pH \approx 8) and stepwise added 20 μL of an 878 mM solution of ZnCl_2 in D_2O . This results in Zn^{2+} concentrations of 0, 24, 47, and 69 mM. A ^{31}P spectrum was recorded after each addition (Figure S1). After adding Zn^{2+} the solution becomes immediately cloudy. The

line shape is deteriorated and the ^{31}P integral steadily decreases. Due to different counterions, concentration and pH the ^{31}P shift may be different compared to the PBS experiment. Importantly, no new resonances appear in the spectrum.

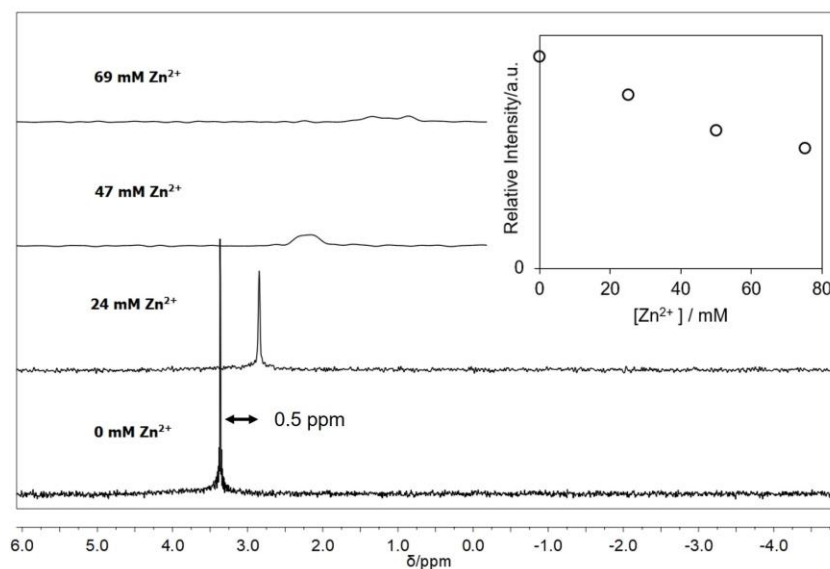


Figure S1. NMR ^{31}P control experiment to prove the decrease of the phosphate signal due to the formation of insoluble zinc phosphate by-products.

AFM experimental section

AFM samples were prepared as follows. The ZIF-8 polycrystalline film was prepared by inducing the growth of ZIF-8 on a Bovine Serum Albumin (BSA) film supported on Si (100). The BSA film was obtained with the following procedure: first Si was treated in basic Piranha solution at 60°C for 30 minutes and then exposed to a toluene solution of (3-Aminopropyl)triethoxysilane (APTES, 10 μL in 5 mL). Then, APTES-functionalized Si was exposed to a mixture of BSA (1 mg in 0.5 mL of 15 mM MES buffer at pH=6) and 1-Ethyl-3-(3-dimethylaminopropyl)carbodiimide (EDC, 1 mg in 100 μL of 15 mM MES buffer at pH=6) at RT for 2 h. The sample was then rinsed and stored in fresh 15 mM MES buffer at 4°C. The polycrystalline ZIF-8 film was grown by exposing the BSA/APTES film to 1 mL of a freshly prepared 40 mM of $\text{Zn}(\text{OAc})_2 \cdot 2\text{H}_2\text{O}$ and 0.64 mM of HmIM water solution at RT for 30 minutes. Finally, the sample was rinsed with ethanol and dried under Nitrogen flux. AFM experiments were performed using an Asylum Research (Oxford Instruments) model Cypher ES in tapping mode, with blueDrive photothermal excitation. The probes used were Olympus Instruments AC 40 silicon nitride cantilevers with silicon

tips. Images of the ZIF-8 crystals were recorded at a scanning rate of 2Hz in a closed liquid cell with perfusion ports. The measurements were first stabilized against a background solution of DI water adjusted to pH 7.4 using NaOH (1M). This procedure is necessary in order to obtain a stable tip-sample contact under flux. A buffer solution of PBS (1X) was then added through the perfusion ports at a rate of 50 $\mu\text{L min}^{-1}$ while the topography of the crystals was imaged continuously for 25 minutes. The frame rate shown in the video (movie.mp4) is 40x faster than the recorded one. The slight changes observed during the first frames (in water) are due to fluctuations in the tip-sample contact during the stabilization scans. Once the PBS solution was added, it is possible to observe a drastic modification in the topography of the ZIF-8 crystal attributed to the degradation process.

Powder X-ray diffraction (PXRD)

PXRD patterns of the micro- and nano-ZIF-8 samples were collected on a Rigaku powder diffractometer equipped with D/teX Ultra 250 detector and using $\text{CuK}\alpha$ radiation ($\lambda = 1.5406 \text{ \AA}$). The scan speed was 3 deg min^{-1} and the step 0.01° .

Scanning electron microscopy (SEM)

SEM micrographs were collected using Tescan VEGA 3 SEM with tungsten source filament working at 20 kV. The samples were deposited on conductive carbon tape and subsequently coated with Au. The EDX elemental mapping was performed using a Zeiss Sigma 300 VP (Field Emission Gun) with an Oxford X-Max^N 80mm² EDX Detector.

Time-resolved Small Angle X-Ray Scattering (SAXS)

Time-resolved SAXS have been collected on the SAXS beamline at the ELETTRA synchrotron light source. We operated at photon energy of 8 keV covering the range of momentum transfer, $q = 4\pi \sin(\theta)/\lambda$, between 0.12 and 6.3 nm^{-1} . The stability of the MOF was monitored by measuring the MOF suspension in a 1 mm glass capillary. All the experiments were performed at RT. The acquisition started 15 minutes after the dispersion of ZIF-8 in PBS with a time resolution of 3 minutes (detector: Pilatus3 1M, Dectris Ltd, Baden, Switzerland; sample to detector distance: 1260 mm, as determined with a silver behenate calibration sample). Prior the experiment, PBS 10 mM solution was measured in order to assess and subtract the background from the data. The resulting two-dimensional images were radially integrated to obtain a 1D pattern of normalized intensity versus scattering vector q .

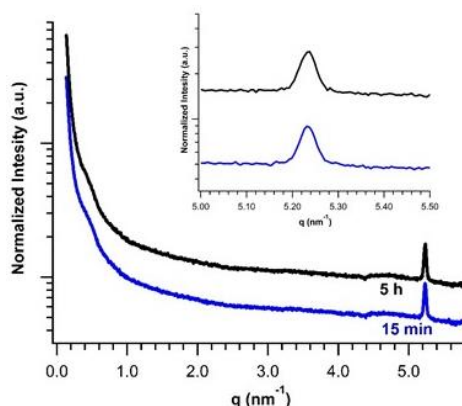


Figure S2. Time-resolved solution SAXS of nano-ZIF-8 particles dispersed in DI water. The intensity of the (011) diffraction peak of sod-ZIF-8 particles dispersed in DI water is almost unchanged after a 5 h exposure and this is highlighted in the inset.

Determination of the concentration of Zn^{2+} in the mother liquors by Inductively Coupled plasma-optical emission spectroscopy (ICP-OES)

The Zn concentration in micro-ZIF-8 and nano-ZIF-8 was quantified using axially viewed ICP-OES (Ciros Vision EOP, Spectro, Germany) after dilution with 1 mol L^{-1} nitric acid. The Zn (II) 213.856 nm emission line was used.

Table S1. Amount of Zn^{2+} released in the mother liquors (expressed in ppm of Zn^{2+} and % Zn^{2+}) after the incubation process of micro- and nano-ZIF-8 particles in PBS (1X)

Sample micro-ZIF-8 particles	$[\text{Zn}^{2+}]$ (mg/L)	% Zn^{2+}	Sample nano-ZIF-8 particles	$[\text{Zn}^{2+}]$ (mg/L)	% Zn^{2+}
Blank	0.028	0.019	Blank	0.03	0.021
1 h in PBS	0.052	0.036	1 h in PBS	0.074	0.052
3 h in PBS	0.068	0.047	24 h in PBS	0.082	0.057
6 h in PBS	0.072	0.050	72 h in PBS	0.082	0.057
24 h in PBS	0.074	0.052	-----	-----	-----

Synthesis and characterization of micro- and nano-ZIF-8 particles

Micrometric particles of ZIF-8 (micro-ZIF-8) were prepared as reported in the literature. Briefly, an aqueous solution of $\text{Zn}(\text{OAc})_2 \cdot 2\text{H}_2\text{O}$ (15 mL, 120 mM) was added to an aqueous solution of 2-methylimidazole (30 mL, 960 mM). The final concentrations of $\text{Zn}(\text{OAc})_2 \cdot 2\text{H}_2\text{O}$ and HmIM after mixing were 40 mM and 640 mM, respectively; keeping a molar ratio $\text{HmIM}/\text{Zn}^{2+} = 16$. The reaction mixture was left under static conditions at room temperature for 24 h. Afterwards, the precipitates were collected by centrifugation (13, 400 rpm for 10 min). The supernatant was removed, and the sample was washed three times with H_2O and ethanol to remove the unreacted precursors. The micro-ZIF-8 particles

were re-dispersed in water, obtaining a suspension with a concentration of 27.61 mg/mL (stock suspension **A**).

The nanometric particles of ZIF-8 (nano-ZIF-8) were obtained following a procedure similar to the above-mentioned one, keeping a molar ratio $\text{HmIM}/\text{Zn}^{2+} = 16$. Nevertheless, in this case the final concentration of $\text{Zn}(\text{OAc})_2 \cdot 2\text{H}_2\text{O}$ and HmIM after mixing were 80 mM and 1280 mM, respectively. The nano-ZIF-8 particles were re-dispersed in water, obtaining a suspension with a concentration of 36.75 mg mL^{-1} (stock suspension **B**).

The particle size and morphology of both samples (Suspensions **A** and **B**) were assessed by scanning electron microscopy (SEM); whereas the crystallinity and phase purity of the bulk samples were confirmed by powder X-ray diffraction (PXRD).

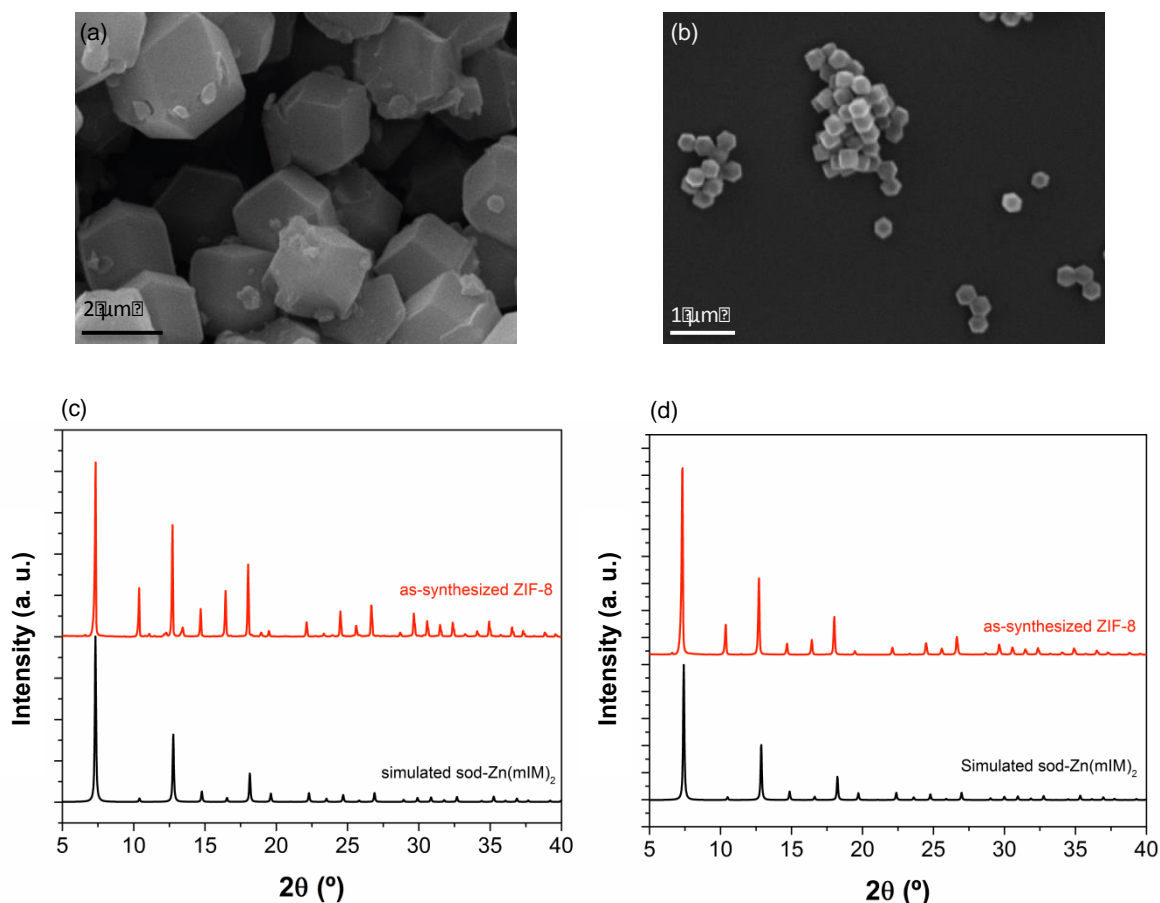


Figure S3. Structural and morphological characterization of the as-synthesized micro- and nano-ZIF-8 particles. (a) SEM micrograph of the micro-ZIF-8 (ca 2 μm) particles with rhombic dodecahedron crystal morphology. (b) SEM image of the nano-ZIF-8 (ca 250 nm) particles. (c) PXRD pattern of the as-synthesized micro-ZIF-8 particles and its comparison with the simulated diffraction pattern for the sodalite polymorph. (d) Comparative PXRD patterns between the as-synthesized nano-ZIF-8 particles the simulated one for sod-Zn(mIM)₂.

Degradation of micro-ZIF-8 particles

A suspension of micro-ZIF-8 particles (0.5 mg mL^{-1}) was prepared adding $724 \text{ }\mu\text{L}$ of the stock suspension **A** into 40 mL of PBS. Such micro-ZIF-8 particles were incubated in the buffer media at $37 \text{ }^\circ\text{C}$ for 1 h, 3 h, and 24 h. Afterwards, the solid was collected by filtration under vacuum using WHATMAN® Anodisc membranes (pore size: $0.02 \text{ }\mu\text{m}$). The collected solids, at different degradation times, were analyzed by infrared spectroscopy (FTIR-ATR), PXRD, and SEM, to demonstrate the progressive formation of zinc phosphates. Additionally, the mother liquors were analyzed by GC-MAS to determine the concentration of 2-methylimidazole released during the degradation process.

Table S2. Relative intensity of micro-ZIF-8 particles as a function of incubation time in PBS

Sample	$I_{\text{ZIF-8}(011)}$	$I_{\text{TiO}_2(101)}$	$I_{\text{ZIF-8}(011)}/I_{\text{TiO}_2(101)}$	% $I_{\text{ZIF-8}(011)}$
Blank	27249.17	3877.5	7.03	100
1 h in PBS	7143.53	3877.5	1.84	26.2
3 h in PBS	4328.77	3877.5	1.12	15.5
6 h in PBS	3962.65	3877.5	1.02	15.9
24 h in PBS	2947.57	3877.5	0.76	10.8

Degradation of nano-ZIF-8 particles

A suspension of nano-ZIF-8 particles (0.5 mg mL^{-1}) was prepared adding $544 \text{ }\mu\text{L}$ of the stock suspension **B** into 40 mL of the corresponding Buffer (PBS). Such nano-ZIF-8 particles were incubated in the buffer media at $37 \text{ }^\circ\text{C}$ for 1 h, 24 h, and 72 h. Afterwards, the solid was collected by filtration under vacuum using WHATMAN® Anodisc membranes (pore size: $0.02 \text{ }\mu\text{m}$). The collected solids, at different degradation times, were analyzed by infrared spectroscopy (FTIR-ATR), PXRD, and SEM, to demonstrate the progressive formation of zinc phosphates. Additionally, the mother liquors were analyzed by GC-MAS to determine the concentration of 2-methylimidazole released during the degradation process.