Modulated Formation of MOF-5 Nanoparticles—A SANS Analysis

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ABSTRACT: MOF-5 nanoparticles were prepared by mixing a solution of \([\text{Zn}_4\text{O}(\text{C}_6\text{H}_5\text{COO})_6]_n\) with a solution of benzene-1,4-dicarboxylic acid in DMF at ambient conditions. The former species mimics as a secondary building unit (SBU), and the latter acts as linker. Mixing of the two solutions induced the formation of MOF-5 nanoparticles in dilute suspension. The applied conditions were identified as suitable for a closer investigation of the particle formation process by combined light and small angle neutron scattering (SANS). Scattering analysis revealed a significant impact of the molar ratio of the two components in the reaction mixture. Excessive use of the building unit slowed down the process. A similar effect was observed upon addition of 4n-decylbenzoic acid, which is supposed to act as a modulator. The formation mechanism leads to initial intermediates, which turn into cubelike nanoparticles with a diameter of about 60–80 nm. This initial stage is followed by an extended formation period, where nucleation proceeds over hours, leading to an increasing number of nanoparticles with the same final size of 60–80 nm.

INTRODUCTION

Metal–organic frameworks (MOFs), also called porous coordination polymers (PCPs), represent a subclass of coordination polymers with a very robust three-dimensional lattice-like structure. This feature generates a large internal surface, which predestines MOFs for a variety of potential applications. Examples are the use as gas storage tanks with bulk materials, as gas separation materials based on MOF membranes, and as heterogeneous catalysts whereby their superiority is caused by the fact that they can easily be separated from the products and thus can be recovered for new production cycles. The catalyst may preferentially be designed as micrometer or even nanometer sized particles. Besides, MOFs have a great potential to administer drugs on specific sites at a suitable dose. It is at hand that MOF materials applied as drug carriers, or in gas separation membranes, require a rational design of colloidal MOF material, including a controlled formation of MOF particles. Such a control has to consider particle size, size distribution, but also the suppression of interpenetrating networks, a phenomenon especially known for framework systems with large pores. A prerequisite for any control of the particle morphology is a detailed knowledge of the mechanism of nucleation and growth of MOF nanoparticles.

MOF particles can be formed with a number of different techniques. Early strategies to obtain high quality crystalline material were predominantly based on solvothermal synthesis in a solution of all necessary constituents. A drawback of these procedures is the rather long preparation time of half a day or longer. Meanwhile, various attempts have been published to speed up the synthesis of MOF material and to better control the formation process and the resulting particle size of nanoscaled MOF material. Application of microwave treatment during the solvothermal process decreased the preparation time considerably and led to a decrease of crystal size with either decreasing component concentrations or decreasing crystallization time. Similar progress has been achieved with the application of ultrasound to a solution prepared at ambient conditions.

Further progress was achieved by discovering that a simple mixing of appropriate components or building units in solution at ambient conditions may result in MOF materials. In particular, choosing metal ion components that mimic the secondary building units of the final MOF material proved particularly advantageous. For example, the Be and Co isotypes of the well-known Zn-based MOF-5, \([\{\text{Zn}_n\text{O}(\text{BDC})_m\}_n\] (BDC = benzene-1,4-dicarboxylate), were accessible only by using this so-called controlled secondary building unit (SBU) approach. This discovery did not only minimize the preparation time but also opened up a new route to the preparation of MOF nanoparticles. Despite this considerable progress, the control of particle size and its distribution remains an open issue, which attracts increasing attention.

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The identification of suitable modulators which will influence the speed of particle formation as well as the shape of the growing MOF particles may offer the possibility to capture particles with a distinct size and morphology. In an early feasibility study, perfluoromethylbenzenecarboxylate (PFMBC) was identified as a promising coordination reagent, which is able to trap MOF-5 nanoparticles if the PFMBC is added during the course of particle formation.\(^\text{16}\) Shortly thereafter, Kitagawa and co-workers\(^\text{17}\) succeeded to direct the growth of \([\text{Cu}_2(\text{NDC})(\text{DABCO})]_2\) MOF particles (with NDC \(= 1,4\)-naphtalene dicarboxylate and DABCO \(= 1,4\)-diazabicyclo-[2,2,2]octane) in dependence on the amount of additional added acetic acid, which acts as coordination modulator. This influences the coordination equilibria during the growth, forcing small nanocrystals to an oriented attachment since faces of the nanocrystals are selectively blocked by the modulator. A similar strategy was applied by Oh et al.,\(^\text{18}\) who succeeded to block the growth rate of distinct crystal facets, thus also directing the growth toward anisotropically shaped MOF crystals. In these contributions,\(^\text{17,18}\) no direct in situ monitoring of the particles was performed. The characterization of the particle shape and size was carried out by means of TEM measurements.

Further progress to a better control of the particle features clearly needs more detailed investigations on the nucleation and growth processes of MOF (nano) crystals. Various techniques are available to monitor and analyze such processes in situ. One promising technique is light scattering, as this is noninvasive as long as the scattering particles do not absorb the light. In particular, time-resolved static light scattering (TR-SLS) turned out to offer a powerful tool to follow processes from a few minutes on. The first application of this “new” technology in the field of MOF growth demonstrated that MOF-5 formation under solvothermal conditions exhibited a relatively fast nucleation, which was succeeded by a growth step of the particles.\(^\text{19}\) The latter step could successfully be followed by TR-SLS for more then 10 min, and as mentioned above, the growth could be stopped upon the addition of PFMBC.\(^\text{16}\) Two further investigations were devoted to the formation of HKUST-1 \([\text{Cu}_3(\text{BTC})_2]\) (BTC = benzene, 1,3,5-tricarboxylic acid) in a water–ethanol mixture\(^\text{19}\) and to ZIF-8 in methanol,\(^\text{15,20}\) respectively. The formation of HKUST-1 was induced by cooling a supersaturated and thermally pretreated solution of Cu(NO\(_3\))\(_2\) and BTC to room temperature. During the first 10 min, particle growth was overlaid by an ongoing nucleation process. While particle growth stopped at a size close to 400 nm, nucleation still produced new particles even after 25 min.\(^\text{19}\) The formation of ZIF-8 was initiated by simply mixing solutions of Zn(NO\(_3\))\(_2\) and 2-methylimidazole. In this case, ZIF-8 nanoparticles with a size of 50 nm formed rapidly during the first minutes and TR-SLS could only indicate the increase of the number of particles. The nanoparticles started to agglomerate after a few minutes, once its content seemed to be large enough.\(^\text{13}\)

Meanwhile, the technique of mixing component solutions at ambient conditions to generate MOF nanoparticles had been successfully extended also to the preparation of MOF-5\(^\text{20}\) and shall be applied in the present work to investigate the impact of a modulator molecule on the growth process. The two components are \([\text{Zn}_\text{nO}(\text{C}_\text{nH}_\text{mCOO})_\text{n}]\), providing the secondary building unit (and henceforth being abbreviated as SBU), and benzene-1,4-dicarboxylic acid (BDC), which acts as the linker. In addition, 4n-decylbenzoic acid (DBA) is used as a growth modulator in order to control the formation of MOF-5 nanoparticles. The choice of a molecule with a long alkyl-chain as a modulator was based on the large neutron scattering contrast of its alkyl-chain moiety, which enables, in principle, a selective addressing of these molecules in the composite system of MOF-5 and modulator. The particle formation process is induced simply via mixing a solution of the SBU in DMF with a solution of BDC in DMF. The focus of the present work lies on the investigation of the resulting growth mechanism of MOF-5 particles with and without modulator molecules and of the morphological nature of the nucleated MOF-5 particles. The work is based on a joint application of TR-SLS and small angle neutron scattering (SANS). Light scattering will enable us to follow the evolution of global dimensions with time, and SANS will extend the local resolution of the particle shape analysis down to less than 1 nm and offer the chance to selectively address specific compartments of the particles if heterogeneities occur. Selective addressing with SANS is made possible by contrast variation via deuterium–hydrogen exchange in the organic residues of MOF-5. These joint experiments shall present insight into the particle formation mechanism induced upon direct mixing of suitable component solutions in comparison to the solvothermally induced process\(^\text{21}\) and into characterization of the morphology of the MOF-5 nanoparticles. In addition, they will give a first rationale on how to modulate or even stop the growth of MOF-5 nanoparticles in a controlled manner.

### EXPERIMENTAL PART

**Materials.** Benzene-1,4-dicarboxylic acid, \(\text{C}_\text{nH}_\text{m}(\text{COOH})_\text{2}\) (BDC) (98+%), was purchased from Alfa Aesar (Massachusetts), and deuterated \(\text{C}_\text{nD}_\text{m}(\text{COOH})_\text{2}\) (\(\text{d}_\text{1}-\text{BDC}\)) (99+%%) was purchased from Merck (Darmstadt, FRG). The molecular precursor \([\text{Zn}_\text{nO}(\text{C}_\text{nH}_\text{mCOO})_\text{n}]\) of the secondary building unit was synthesized according to a literature procedure.\(^\text{22}\) 4n-Decylbenzoic acid (DBA) (+99%) was purchased from ABCR (Karlsruhe, FRG). \(\text{N,N}\)-Dimethylformamide (DMF) served as the solvent. \(\text{H}_\text{2}-\text{DMF}\) (99%) was supplied by Merck (Darmstadt, FRG), while \(\text{D}-\text{DMF}\) (99,5%) was obtained from Deutero (Kastellaun, FRG).

**Sample Preparation.** All experiments with a SBU to linker ratio of 1:1 were based on two starting solutions: (i) 0.0055 g of benzene-1,4-dicarboxylic acid (BDC) dissolved in 10 mL of DMF and (ii) 0.03347 g of preformed secondary building unit \([\text{Zn}_\text{nO}(\text{C}_\text{nH}_\text{mCOO})_\text{n}]\) (SBU) dissolved in 10 mL of DMF. The molar concentration for both components in the starting solutions was \(3.33 \times 10^{-3}\) mol/L. Two milliliters of each solution was precleaned by passing it through a 1.2 μm filter to remove any dust particles while successively injecting it into the scattering cell. Addition of SBU solution as the second component set time zero for the reaction. Five minutes after mixing BDC and SBU, 20 μL of the third component, 4n-decylbenzoic acid (DBA) dissolved in DMF at a concentration of 0.667 mol/L, was added. The experiments with a SBU to linker ratio of 1:3 were carried out with a procedure similar to the route described for the 1:1 ratio. In the case of the 1:3 ratio, a precooled solution of 0.005 mmol of SBU solvent in 3 mL of DMF was added to 3 mL of the precooled BDC solution (0.015 mmol of BDC in 3 mL of DMF). Again, the addition of SBU to the BDC solution set time zero for the reaction. The molar concentrations for the components in the final solutions were 1.6710^{-3} mol/L (SBU) and 5 \(\times 10^{-3}\) mol/L (BDC), respectively. SANS experiments were performed at SBU/BDC/
Table 1. Model Independent Parameters Extracted from the SANS Experiments Performed at Variable Contrast and at Variable DBA Content

<table>
<thead>
<tr>
<th>solvent composition</th>
<th>66% H$_7$-DMF/34% D$_7$-DMF</th>
<th>100% H$_7$-DMF</th>
</tr>
</thead>
<tbody>
<tr>
<td>ratio SBU/BDC/DBA</td>
<td>1:1:2</td>
<td>1:1:10</td>
</tr>
<tr>
<td>age of sample, h</td>
<td>17.28</td>
<td>15</td>
</tr>
<tr>
<td>$(\text{d}I/\text{d}q)_w$ cm$^{-1}$</td>
<td>1.83</td>
<td>1.56</td>
</tr>
<tr>
<td>$R_p$, nm</td>
<td>26.4</td>
<td>28.8</td>
</tr>
<tr>
<td>invariant $Q_w$ nm$^{-1}$</td>
<td>0.00454</td>
<td>0.00600</td>
</tr>
<tr>
<td>$(\text{d}I/\text{d}q)_w/Q \sim V_g$</td>
<td>403</td>
<td>488</td>
</tr>
<tr>
<td>$10^3Q^2/(\text{d}I/\text{d}q)_w \sim N$</td>
<td>1.13</td>
<td>1.23</td>
</tr>
</tbody>
</table>

DBA ratios of 1:1:2, 1:1:5, and 1:1:10. Preparation of the samples for the SANS experiments has been made accordingly, except for the fact that each sample was investigated in H$_7$-DMF and in mixed H$_7$-DMF/D$_7$-DMF. Use of two solvents differing in their degree of deuteration enabled us to tune the scattering contrast of MOF-5. An overview on all SANS samples is given in Table 1.

**Time-Resolved Static Light Scattering (TR-SLS).** TR-SLS was performed with a home-built multangle goniometer described by Becker and Schmidt.$^{22}$ Cylindrical quartz glass cuvettes with a diameter of 20 mm from Hellma (Mu¨hlheim, Germany) served as scattering cells. The goniometer was equipped with a He–Ne laser operating at a wavelength of 632.8 nm. It enabled simultaneous recording of the scattering intensity at 2 times 19 scattering angles arranged symmetrically on both sides of the laser beam. The angular regime covered a range of 25.84° ≤ θ ≤ 143.13°. Recording of an angular dependent curve was completed after 2 ms. 1000 successive recordings were added to form one measurement requiring 2 s in total. The time interval between the start of two successive measurements was 10 s. All experiments were performed at room temperature.

Scattering curves were processed by means of the Rayleigh ratio $\Delta R_p$ of the MOF-5 particles, which was calculated from the difference between the Rayleigh ratio of the particle dispersion and of the pure solvent at variable scattering angles θ. It is composed of three factors.

$$\Delta R_p = K c M_w P(q) \cdot S(q)$$  \hspace{1cm} (1)

In eq 1, c is the concentration of monomeric units given by the formula [Zn$_4$O(BDC)$_3$] in g/L. In the case of the nonstoichiometric ratio, the concentration of MOF-5 was calculated with respect to BDC, the component used in nonstoichiometric ratio, the concentration of MOF-5 was calculated with the Avogadro number $N_A$, with the laser wavelength $\lambda = 632.8$ nm, with the refractive index $n = 1.43$ of pure DMF (20 °C), and with $dn/dc$ the refractive index increment of MOF-5 in DMF. The lack of a $dn/dc$ value forced us to apply a default value of $dn/dc = 0.1$ mL/g. This still reproduces the correct order of magnitude of mass values and gives correct relative values.

Scattering curves were evaluated according to the Zimm approximation$^{23}$

$$\frac{Kc}{\Delta R_0} = \frac{1}{M_w} \left[ 1 + \frac{R_g^2}{3q^2} \right] + A_2$$  \hspace{1cm} (4)

with $A_2 \equiv 0$ corresponding to $S(q) \equiv 1$ in eq 1.

An example for a run with a molar ratio of SBU/BDC/DBA of 1:1:0 is given in Figure 1. Relative $M_w$ values can be extracted from the intercept of eq 4, and values for the z-averaged squared radius of gyration $R_g^2$ are accessible from the slope in eq 4.

**Dynamic Light Scattering (DLS).** Time-resolved DLS experiments were performed using a model 5000E compact goniometer system from ALV-Laser Vertriebsgesellschaft (Langen, Germany), equipped with a 200 mW Nd:YAG laser operating at a wavelength of $\lambda = 532$ nm. The concentrations of the reagents for SLS and DLS experiments were identical.

Correlation functions were detected in single channel correlation mode during 30 s. The cumulant method$^{24}$ with linear and quadratic terms of the correlation time $\tau$ was used for evaluation.

$$\ln(g_1(\tau)) = \ln A - \Gamma \tau + \frac{H_2}{2} \tau^2$$  \hspace{1cm} (5)

In eq 5 $\ln(g_1(\tau))$ is the logarithm of the electric field correlation function with the z-averaged decay constant $\Gamma, A$ is
the amplitude, and $\mu_2$ is the second cumulant providing information on the polydispersity of the sample. The $z$-averaged translational diffusion coefficient $D_z$ was calculated according to eq 6

$$D_z = \frac{1}{q^2} \Sigma \frac{I(q) - I_{Cd}}{I_{HC} - I_{Cd}}$$ (6)

Time-resolved DLS experiments forced us to fix the scattering angle at 30°. At this relatively small angle, the extracted diffusion coefficient $D_z(\theta=0^0)$ is expected to be close to the true value of the diffusion coefficient $D_z(\theta=0^0)$, since the averaged particle radii remained well below 100 nm.

According to the Stokes–Einstein relation, $D_z$ can be transformed into a hydrodynamically effective radius $R_h$ according to

$$R_h = \frac{k_BT}{6\pi\eta D_z}$$ (7)

with $k_B$ the Boltzmann constant, $T$ the absolute temperature, and $\eta$ the viscosity of the solvent in mPa·s.

**Small Angle Neutron Scattering (SANS).** The SANS experiments were performed at the Institut Laue-Langevin (ILL), Grenoble, France, using the instrument D11. All experiments were carried out at a sample-to-detector distance of 1.2, 8, or 28 m using a neutron wavelength of 6 Å. This results in a range of the scattering vector $q$ of 0.00254 Å$^{-1}$ ≤ $q$ ≤ 0.51836 Å$^{-1}$. The SANS intensity signals were radially averaged and normalized by using water as a secondary calibration standard. Radially averaged data $I_r$ were corrected for sample thickness and transmission via

$$\frac{d\Sigma}{d\Omega} = \frac{I_r - I_{Cd}}{I_{HC} - I_{Cd}}$$

leading to scattering curves in units of absolute scattering cross section. The indices in eq 8 denote standard (H$_2$O), empty cell (EC), cadmium (Cd), and sample (S), corresponding to solvent or solution, respectively. The cadmium measurement provides the electronic background and $d$ is the sample thickness. Cells from Hellma (type 404-QS) with $d = 1$ mm were used for all measurements. ($d\Sigma/d\Omega)_{H_2O} = 0.983$ cm$^{-1}$ is the differential scattering cross section for water at $\lambda = 6$ Å. The term $(1 - n_t)$ takes into account the correction for dead time losses, with $n_t$ representing the integral count rate of each measurement and $r$ the dead time. The transmission $T_x$ of any sample $x$ was determined by dividing the measured intensity of the beam at $q = 0$ attenuated by any sample ($I_x$) by the measured intensity of the incident beam ($I_0$):

$$T_x = \frac{I_x(q = 0)}{I_0(q = 0)}$$ (9)

The excess signal from the MOF-5 particles was isolated by subtracting the average of the angular independent signal ($d\Sigma/d\Omega$)$_{1.2m}$ in the range 0.06177 Å$^{-1}$ ≤ $q$ ≤ 0.2464 Å$^{-1}$ (measured at 1.2 m) from the solution data ($d\Sigma/d\Omega$)$_{solution}$. The value of ($d\Sigma/d\Omega$)$_{1.2m}$ included the scattering signal from nonreacted SBU and linkers as well as from solvent:

$$\left(\frac{d\Sigma}{d\Omega}\right)_{MOF} = \left(\frac{d\Sigma}{d\Omega}\right)_{solution} - \left(\frac{d\Sigma}{d\Omega}\right)_{1.2m}$$ (10)

A model independent analysis of the scattering curves included a Guinier approximation and the evaluation of the invariant. The scattering curves were approximated by quadratic Guinier fits according to eq 11

$$\ln \left(\frac{d\Sigma}{d\Omega}\right)_{MOF} = \ln \left(\frac{d\Sigma}{d\Omega}\right)_{q=0} + \frac{R_h^2}{3} q^2 + K\Omega^4$$ (11)

with ($d\Sigma/d\Omega$)$_{q=0}$ the extrapolated intensity at $q = 0$, $R_h^2$ the squared $z$-averaged radius of gyration, and $K\Omega$ the coefficient of the $q^4$-term. The invariant $Q$ was calculated as the area under the curve $4\pi q^2 (d\Sigma/d\Omega)_{MOF}$ vs $q$ according to

$$Q = 4\pi \int (\frac{d\Sigma}{d\Omega})_{MOF} q^2 dq$$ (12)

The parameter $Q$ corresponds to the concentration of the MOF-5 particles. The missing initial part of the scattering curve was approximated by a triangle (see Figure 2).

![Figure 2. Kratky curve of the experiment with SBU/BDC/DBA molar ratio 1:1:2 in a H$_7$-DMF(66%)/D$_7$-DMF(34%) solvent mixture. Inset: quadratic Guinier evaluation of the same experiment. The example illustrates the calculation of the two model independent parameters $Q$ and $R_h$.](image)

Deuterated BDC ($D_2$-BDC) and hydrogenated DBA were used for all SANS experiments. The final concentrations of BDC and SBU were 1.67 × 10$^{-3}$ mol/L, corresponding to the conditions identified by SLS and DLS as the most suitable ones for SANS. Two different types of experiments, each with three different final concentrations of DBA, corresponding to 2-fold, 5-fold, or 10-fold excess compared to BDC, were conducted. An H$_7$/D$_7$ solvent mixture was used for the first type of experiments, designed to match as closely as possible the scattering contrast of the MOF-5 particles (core is matched). A rationale for the corresponding composition (66% H$_7$-DMF and 34% D$_7$-DMF) is given in the Supporting Information. For the second type of experiments, 100% H$_7$-DMF as a solvent was used, which predominantly matches the contrast of the hydrogenated coordination modulator (shell is matched).
Transmission Electron Microscopy (TEM). Typically, 0.25 mL of a DMF solution of the SBU-like material [Zn₈O(C₆H₅COO)₆] (0.005 mmol) was transferred to 2.75 mL of a DMF solution of H₂BDC (0.005 mmol). Five minutes after mixing BDC and SBU, the capping agent was added. Afterward, one drop of the reaction mixture was directly transferred to a TEM grid. After the evaporation of the solvent, one additional drop was placed on the TEM grid. This procedure was repeated 4 times. The preparation was carried out under inert conditions. All TEM measurements were performed on a Philips CM200 equipped with a LaB₆ gun operating at 200 kV at low dose conditions and long exposure times.²⁸

Theoretical Form Factor Calculations. Theoretical form factors of polydisperse cubes $P(q)$ were calculated according to eq 13

$$P(q) = \frac{\int_0^{V_{\text{max}}} \text{SZ}(V) V P_V(q) \, dV}{\int_0^{V_{\text{max}}} \text{SZ}(V) \, dV}$$

(13)

where $P_V(q)$

$$P_V(q) = \frac{\sin(qav \cdot \sin \alpha \cos \beta)}{qav \cdot \sin \alpha \cos \beta} \times \frac{\sin(qav \cdot \sin \beta)}{qav \cdot \sin \beta} \frac{\sin(qav \cdot \cos \alpha)}{qav \cdot \cos \alpha} \sin \alpha \, d\alpha \, d\beta$$

(14)

is the form factor of a cube²⁹ with the volume $V$ and the edge half length $a_v$. $\text{SZ}(V)$ is the Schultz–Zimm distribution of the cube volume $V$ given as the weight fraction³⁰

$$\text{SZ}(V) = \left(\frac{V}{V_0}\right)^{z+1} \frac{z^2}{(z+1)!} \left(1 - \frac{V}{V_0}\right)^z$$

(15)

with $V_0$ the number averaged volume, $\Gamma(z+1)$ the gamma function, and $z$ the characteristic polydispersity parameter. At given parameters $V_0$ and $z$, an upper limiting value $V_{\text{max}}$ was applied in eq 13 such that at least 99.99% of the distribution is covered by this limit. The parameter $z$ is related to the polydispersity index DPI according to $z = 1/(\text{DPI} - 1)$. The polydispersity index DPI is defined as the ratio of the weight-averaged particle volume $V_w$ and the number averaged particle volume $V_n$

$$\text{DPI} = \frac{V_w}{V_n}$$

RESULTS AND DISCUSSION

Usually, detection of a single scattering curve of dilute systems with SANS requires minutes or hours. Hence, a sample investigated with SANS must be stable, or at least change insignificantly over the measuring time. In the present work, SLS and DLS experiments were carried out to identify suitable conditions for SANS experiments. For this purpose, diluted suspensions of MOF-5 nanoparticles were produced by the reaction of BDC and SBU. The concentration of SBU was set to $1.67 \times 10^{-3}$ mol/L. Proper evaluation of a potential impact of the modulator DBA on the process requires reference experiments on pure DBA in DMF. Such reference experiments are necessary since pure DBA may already self-assemble in DMF, leading to a significant scattering pattern from DBA aggregates, which overlap with the scattering signal from MOF-5 nanoparticles. Fortunately, corresponding reference experiments both with light and neutrons revealed no significant contribution from DBA below $q \sim 2$ nm$^{-1}$. Details are outlined in the Supporting Information. Hence, distortion of the successively detected scattering signals by independent DBA aggregates can be ruled out.

In a first set of light scattering experiments, the molar ratio of the two components SBU/BDC = 1:3 was investigated in the absence of DBA. A fast growth of particles leading to the formation of a bidisperse system with a rapidly growing fraction of larger particles with $R_g$ up to 1 μm was observed. The addition of DBA up to a ratio of 1:3:6 did not significantly slow down this process. All experiments of this set turned out to be poorly reproducible and, hence, not to be suitable for any further scattering analysis.

Successively, the growth of MOF-5 particles was followed at a decreased SBU/BDC ratio of 1:1, with the concentration of SBU being kept the same as in the case of the experiments at the ratio 1:3. Additionally, experiments without and with DBA at a 2-fold excess compared to BDC were performed. In both cases, the growth process could successfully be slowed down. Results of the measurements are given in Figures 3 and 4.

![Figure 3. Results of TR-SLS measurements. The symbols represent experiments with a molar ratio SBU/BDC/DBA equal to 1:1:0 (■), i.e. without modulator, and experiments with a molar ratio SBU/BDC/DBA equal to 1:1:2 (□).](image-url)
Apparently, a fast process which cannot be resolved by our experiments generates large particles during the first minute. Further insight in this initial stage can be expected from a time-resolved SAXS experiment on the process induced with a stopped-flow device. The successive decrease of the size may result from a densification or from a partial redissolution of large particles or simply due to a lowering of the average mass value by the generation of a large amount of smaller particles. This decrease is followed by a period where the particle size hardly changed anymore. While in the presence of DBA the final plateau value was approached after passing a shallow minimum, this plateau value was approached immediately after the 2 h of decrease in the absence of the modulator. This indicates an ongoing nucleation of particles, which grow fast and approach a final size close to \( R_g \approx 35 \) nm. A similar behavior, where particle formation proceeds via an increase of the number of particles with a fixed final size, has been observed for ZIF-8.\(^{13}\) This pattern had been inferred from the fact that such a formation hardly affects \( z \)-averages like \( R_g^2 \) or \( R_x \), but still causes an increase of the weight averaged particle mass \( M_w \). This is due to the fact that \( z \)-averages are higher moments than weight averages and therefore approach limiting values prior to the weight averages.\(^{13,20,31}\)

As seen from SLS measurements performed in the presence of DBA, the apparent mass evolves more slowly compared to the experiment without additive, whereas the final particle size remains unaffected. This suggests that DBA predominantly modifies the nucleation step. It is an open question in this context whether DBA adheres to the growing nanoparticles, thereby forming a core–shell structure. The excess of the SBU-like material should result in particles which are capped by \( \text{Zn}_2\text{O} \) units; thus, DBA should favorably interact with these species. In order to support this hypothesis, we applied a contrast variation in SANS, which may enable revelation of the inner structure of these nanosized objects.

These were carried out in two types of SANS measurements (summarized in Table 1). The first type was performed in a solvent mixture (66 mol % \( \text{H}_7\text{-DMF} \), 34 mol % \( \text{D}_7\text{-DMF} \), which is supposed to match the MOF-5 core. The second type was carried out in pure \( \text{H}_7\text{-DMF} \), which is expected to match a potential shell based on the modifying agent DBA with its alkyl chains. Three different modifying agent concentrations, corresponding to a 2-fold, 5-fold, or 10-fold excess compared to the BDC, were performed at each scattering contrast. All samples were measured within a time interval of 5–22 h established by SLS as suitable because no significant change in size was observed anymore beyond 5 h. The results of the experiments are given in Figures 5 and 6 and in Table 1. Both figures clearly indicate a significant decrease of the scattering intensity in the \( \text{H}_7\text{-DMF/} \text{D}_7\text{-DMF} \) mixture in accordance with the anticipated matching of the MOF-5 contrast. However, as will be outlined below, this difference does not suffice to unambiguously prove the existence of a DBA shell.

A model independent analysis of the scattering curves already leads to three highly valuable parameters: The \( z \)-averaged mean square radius of gyration \( R_g^2 \) and the intercept of the scattering curve \( (d\Sigma/d\Omega)_{\Omega=0} \) are established by SLS as suitable because no significant change in size was observed anymore beyond 5 h. The results of the experiments are given in Figures 5 and 6 and in Table 1. Both

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**Figure 4.** Hydrodynamically effective radius from DLS at \( \theta = 30^\circ \) for experiments with (□) and without (●) modulator performed with the same two samples as used in Figure 3.

**Figure 5.** SANS curves at different DBA concentrations. Curves plotted with hollow symbols represent experiments in \( \text{H}_7\text{-DMF/(66\%)} / \text{D}_7\text{-DMF(34\%)} \) (lowered contrast of MOF-5 cores), and curves plotted with filled symbols represent experiments in pure \( \text{H}_7\text{-DMF} \) (lowered contrast of DBA shells). The symbols denote the following SBU/BDC/DBA ratios: (□, ■) 1:1:2; (○, ●) 1:1:5, (▲, △) 1:1:10. The numbers are multiples of the BDC concentration of \( 1.67 \times 10^{-3} \) mol/L.

**Figure 6.** Kratky representation of SANS curves given in Figure 5. The symbols denote the following SBU/BDC/DBA ratios: (□, ■) 1:1:2; (○, ●) 1:1:5, (▲, △) 1:1:10. The numbers are multiples of the BDC concentration of \( 1.67 \times 10^{-3} \) mol/L.
The size of the particles obtained from the Guinier evaluation was within the narrow regime of 23 nm < R_g < 29 nm for all experiments and does not significantly vary during the time window of 5 h < t < 22 h. This may indicate that the particles stop to grow at a similar size in all experiments. The intercepts of the scattering curves (d\(\sum/d\Omega\))_q at q = 0 are 1.6–3 times larger for shell matched experiments than for the respective core matched experiments. The same tendency is observed for the invariant Q, whose values are 3.0–3.8 times larger for shell matched experiments. Under the assumption of similar particle size distributions within each pair of experiments performed in the two different scattering contrasts, this decrease indeed indicates that the scattering contrast in 66% H_7–DMF/34% D_7–DMF is weaker than that in pure H–DMF. However, the decrease may be too small and does not enable unambiguous deduction of the formation of a thin layer of DBA. A shell of 1 nm layer thickness would lead to a factor of 10 rather than 3, to give but an example. Also, we have to keep in mind that the decrease observed with the present experiments does not prove entire matching of the scattering contrast of MOF-5 cores in the H_7–DMF/D_7–DMF-mixture.

Our theoretical estimation of the match point may only be a poor estimation due to the uncertainty in the established partial specific volume of MOF-5 particles in DMF and/or due to a variation of the H_7–DMF/D_7–DMF composition of the solvent mixture in the pores of MOF-5 compared to the solvent mixture in the bulk phase.

Despite the fact that the issue of a DBA shell has to remain unsettled, the present SANS data recorded at two different scattering contrasts bear significant insight into the nanoparticle formation and morphology. First and foremost, the parameters outlined in Table 1 do not seem to correlate with the amount of modifying agent. However, such a correlation may be overlaid by a variation of those parameters with the age of the sample, which was identical neither in the three experiments in 66% H_7–DMF/34% D_7–DMF nor in the three experiments in pure H–DMF. In fact, the invariant Q and with it the number density of particles N increases with the age of the sample except for the experiment 1:1:10 in 66% H_7–DMF/34% D_7–DMF. More importantly, the size and the particle volume essentially remained constant. This indicates an ongoing nucleation which generates particles approaching their final dimensions extremely fast. Most likely, the modulator does not interfere with the growth of individual particles but rather influences the nucleation, in line with the hypothesis inferred already from the time-resolved light scattering results.

Further information on particle morphology can be expected from a discussion of the overall trends of the scattering curves. A suitable theoretical model to be compared with the present experiments is a polydisperse cube, which corresponds to a limiting case of the model of rectangular parallelepipeds developed by Mittelbach and Porod.29 In Figure 7 experimental form factors of the 1:1 ratio at three different modifier concentrations in pure H_7–DMF (Figure 7A) and mixed H_7–DMF/D_7–DMF (Figure 7B) are compared with theoretical form factors of polydisperse cubes at polydispersity indices DPI of 1.2, 1.5, 2, 3, and 10. The form factors are plotted as normalized Kratky plots u^2P(u) vs u with u = qR_g, where

\[
P(u) = \frac{(d\sum/d\Omega)_{\text{MOF}}}{(d\sum/d\Omega)_{q=0}}
\] (17)

Figure 7. Graph A indicates experiments in pure H_7–DMF (lowered contrast of DBA modulator), and graph B represents experiments in H_7–DMF (66%)/D_7–DMF (34%) (lowered contrast of MOF-5).

Experimental curves are compared with theoretical model curves of polydisperse cubes.29 The polydispersity index DPI was varied as follows: 1.2, 1.5, 2, 3, and 10, whereby the values of the curves increase with the DPI. Curves are plotted as normalized Kratky plots u^2P(u) vs u with u = qR_g.

For compact structures such as spheres, cubes, or highly branched polymers, Kratky-plots show a characteristic peak located close to \(q \sim 1/R_g\).32

Several features become transparent. Once normalized, all three curves fall on top of each other, indicating that the amount of modifying agent has no significant impact on the particle shape. Also, there is no significant difference between the scattering curves recorded in H_7–DMF (66%)/D_7–DMF (34%) and the curves recorded in pure H_7–DMF. Both series of experiments exhibit a fair agreement with the model form factors of polydisperse cubes, showing the characteristic maximum. This also supports the finding that the experiments performed in the H_7–DMF (66%)/D_7–DMF (34%) mixture did not lead to entirely matched MOF-5 particles with only shells of modulator molecules to be seen. Finally, the experimentally observed Kratky peaks seem to be slightly larger than those predicted by polydisperse cubes. Even a drastic increase of the polydispersity does not entirely account for this small discrepancy. A more detailed and quantitative analysis of the form factors is in progress and will be presented in a forthcoming contribution.

Besides the characterization by means of light scattering and neutron scattering techniques, careful TEM measurements were carried out in order to prove the presence of phase pure MOF-5 material.

TEM measurements revealed very strong faceting with strict rectangular angles (Figure 8a) and a size between 50 and 100 nm for the vast majority of the MOF-5 crystals. Rarely, larger crystals with a size up to 150 nm were found. The shape of the crystals in projection was usually squared or close to squared. The acquired electron diffraction pattern of a single MOF-5 crystal in the [001] zone axis orientation (Figure 8b) identifies the material as crystalline MOF-5. The crystals were unusually stable to the electron beam, allowing the observation of diffraction spots up to approximately 1 min. Usually, MOF-5 reflections disappear within several seconds after exposure to the electron beam. The electron diffraction pattern of many
Initial light scattering revealed that a variation of the stoichiometric ratio of the SBU and linker BDC is an efficient tool to control the formation process. A decrease of the amount of linker from the stoichiometric ratio of SBU/BDC = 1:3 to the ratio SBU/BDC = 1:1 corresponding to an excess of the SBU caused a significant deceleration of the process. An instantaneous formation of particles with a radius of gyration of 80 nm, followed by a comparatively fast decrease in size, eventually led to particles with an averaged radius of gyration of 40 nm. It is noteworthy that the scattering signal and with it the averaged particle mass increased throughout all this time; albeit, this increase slowed down in the course of the process. Such trends of data from scattering experiments (decrease of size or its leveling off while the mass is still increasing) are unexpected only at first sight. They can be nicely reconciled with the following particle formation mechanism. Mixing of the two component solutions instantaneously initiates polymerization. The growth of individual particles is fast with respect to the time of the entire experiments. During the course of formation, the fast growth of individual particles is accompanied by an ongoing nucleation, which persistently generates new nanoparticles, all having the same final size of 30 nm < Rg < 40 nm.

Addition of 4n-decylbenzoic acid to the solution with a ratio of SBU/BDC = 1:1 weakened the formation of the initial large-sized particles and slowed down the formation process further, as reflected by the evolution of the apparent particle mass. However, no effect could be discerned on the average size of the final particles (light scattering) nor on its morphology (SANS). Since the modulator does not modify the nature of the final particles, the observed moderation is likely to be due to an interference with the nucleation of new particles.

On the basis of the light scattering results, a time window between 5 h < t < 20 h was selected to analyze the intermediate stages of the particle formation by means of small angle neutron scattering. To this end, a sample with an SBU/BDC ratio of 1:1 was investigated at three different contents of the modulator. Two different scattering contrasts had been applied for the MOF-5 particles. The SANS experiments confirmed the formation of stable nanoparticles with a final average size of Rg ≈ 30 nm. The H2-DMF/D7-DMF solvent mixture designed to match the scattering contrast of MOF-5 indeed exhibited a considerably lower scattering signal of the nanoparticles. However, proof of the existence of a layer of modulator enveloping the MOF-5 nanoparticles could not be given with the present contrast varying SANS experiment. Independent TEM studies combined with electron diffraction measurements of the as-synthesized nanoparticles supported formation of nanosized cubic MOF-5 crystallites.

As already inferred from light scattering results, SANS indicated that the amount of modulator had no impact on the size and shape of the resulting particles. Only the age of the samples achieved during the SANS analysis slightly influenced the intensity, which increased the older the samples became. The latter again supports the hypothesis of a formation mechanism where an ongoing generation of new nanoparticles all growing rapidly and all approaching a constant final size extends over several hours. A first analysis of the scattering curves revealed close similarity to the curves calculated for the fast growth of individual particles is accompanied by an ongoing nucleation, which persistently generates new nanoparticles, all having the same final size of 30 nm < Rg < 40 nm.

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Similar in situ scattering experiments, where particle formation had been induced by an extended period of heating of a solution of Zn(NO3)2 and linker diethylformamide, led to an entirely different particle formation pattern. In this
solvothermally pretreated solution, particle growth was extremely slow, taking an extended period of time of up to an hour, and thus differs significantly from the process under present consideration. Growth of individual particles in the present case is much shorter and not discernible and in addition is overlaid by continuous nucleation. Apparently, the instantaneous mixing of preformed secondary building units provides monomers "ready-to-react" and generates a large degree of supersaturation, which causes persistent nucleation and growth of finitely sized particles. The finite size can easily be explained by the excess of SBU, which eventually leads to a much lower number of nuclei successively incorporate polymerizable material and, hence, to a much lower number of nuclei. This low number of nuclei successively incorporate newly formed SBU and thus grow to much larger particles.

ASSOCIATED CONTENT

Supporting Information

Reference experiments (SLS and SANS) on pure 4-n-decylbencoic acid solutions in DMF; estimation of the solvent composition in a mixture of H7-DMF/D7-DMF with a match-point for the neutron scattering contrast with MOF-5. This provision of beam time at D11 by the ILL is gratefully acknowledged. C.W. and D.Z. are grateful for support by the Ruhr University Research School and by the Priority Program 1362 "Metal Organic Frameworks" of the German Research Foundation (DFG).

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Notes

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