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Spray-drying synthesis of MOFs, COFs and related composites

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Conspectus

Metal-Organic Frameworks (MOFs) and Covalent-Organic Frameworks (COFs) are among the most attractive porous materials today. They exhibit outstanding porosity for countless applications such as gas storage, CO₂ capture, gas separation, sensing, drug delivery and catalysis. Moreover, researchers have recently begun to combine MOFs or COFs with other functional materials to obtain composites that boast the respective strengths, and mitigate the respective weaknesses, of each component, enabling enhanced performance in many of the aforementioned applications. Accordingly, development of methods for fabrication of MOFs, COFs and related composites is important for facilitating adoption of these materials in industry. One promising synthetic technique is *spray-drying*, which is already well-integrated in manufacturing processes for diverse sectors. It enables rapid, continuous and scalable production of dry micro-spherical

powders in a single step, leading to lower fabrication costs and shorter production times compared to traditional methods.

In this Account, we outline our ongoing work on spray-drying synthesis of crystalline porous MOFs, COFs and related composites. Versatile and tunable, spray-drying can be adapted to perform reactions involving Coordination and Covalent Chemistry for the synthesis of micrometer spherical beads/superstructures of MOFs and COFs. Likewise, MOF- and COF-based composites can be synthesized using similar conditions as those for pure MOFs or COFs, through the simple introduction of additional functional materials into the feed precursor solution or colloid. Interestingly, spray-drying can also be done in water, thus providing the basis for its use as a scalable green method for industrial fabrication of these materials. To date, spray-drying has already been scaled-up for pilot production (kilogram scale) of MOFs.

Graphic:



1. Introduction

Spray-drying is an industrial technique designed to rapidly process solutions into powders. The principle underlying spray-drying was first described in 1872 by Samuel Percy in a patent entitled “Improvement in Drying and Concentrating Liquid Substances by Atomization”.¹ What distinguishes this technique from other drying processes is that it breaks the precursor solution into small aerosol droplets, which are subsequently contacted with a hot gas stream. The higher surface-area-to-volume ratio of the aerosol droplets compared to the bulk solution promotes rapid evaporation and precipitation of the solute within the aerosol droplet. For example, a cubic meter of liquid forms approximately 2×10^{12} uniform, 100 μm -sized droplets (total surface area: $\approx 60,000 \text{ m}^2$).² Interestingly, spray-drying was not industrialized until WWII, when it was harnessed in continuous production to reduce the weight of supplies such as milk powders and dried food. Since then, it has been widely used for production of dried pharmaceuticals; bone and tooth amalgams; beverages; flavors; milk and egg products; soaps and detergents; and many other products.³ Later, the possibility to control the co-precipitation of two components within a single aerosol droplet was exploited to fabricate capsules in which a “wall” material, generally a polymer, precipitates around the core component during aerosol drying.⁴

Greater understanding of spray-drying mechanisms, and development of new microscopic techniques, have enabled further extension of spray-drying to new applications. For example, close observation of the powders processed by spray-drying revealed that they typically comprise spherical amorphous microparticles. Thus, spray-drying can be employed to miniaturize active compounds for functional gains such as augmented solubility or dispersibility.⁵ All these features have been used extensively by

the pharmaceutical industry to make spray-drying-based formulations of active pharmaceutical ingredients: for instance, to achieve superior aqueous solubility or better pharmacokinetics compared to the corresponding bulk powders.

By the 1990s, spray-drying had become well-established in the chemical, food and pharmaceutical industries, yet was rarely used in academia or basic research. However, a turning point came with seminal works by Baskaran et al.,⁶ who spray-dried hydrolyzed silicon alkoxide-surfactant solutions to prepare mesoporous powders, and by Brinker *et al.*, who combined sol-gel chemistry with one-step drying to induce assembly of silica-surfactant micellar species in a process called *evaporation induced self-assembly* (EISA).⁷ They obtained materials that exhibit hierarchical porosity generated through organization of the assembled inorganic precursors. Thus, Brinker and co-workers demonstrated that spray-drying could be used to engineer new materials based on the premise that each aerosol droplet is a confined microreactor that undergoes well-controlled physical and chemical transformations. Researchers later employed controlled precipitation to assemble hierarchical particles of materials such as inorganic nanoparticles, zeolites and nanotubes.⁸⁻
¹¹ Furthermore, the amenability of spray-drying to materials synthesis was further demonstrated in the capture, and shaping into microparticles, of a metastable phase of sodium zinc carbonate salt that, once isolated, could undergo efficient template-based conversion into ZnO porous nanoparticles.¹² Since 2013, our group has expanded the scope of chemistries accessible in aerosol droplets beyond precipitation and assembly, to include coordination chemistry and covalent chemistry. Accordingly, we have repeatedly demonstrated that spray-drying is a straightforward method for fabrication of crystalline

porous nano-structured materials such as Metal-Organic Frameworks (MOFs), Covalent Organic Frameworks (COFs) and various composites thereof.

2. General Strategies for Spray-Drying Synthesis

Spray-drying is based on atomization of a feed solution into aerosol droplets that are subsequently brought into contact with each other and suspended within a hot gas stream, which induces solvent evaporation (Figure 1). The dried particles are transported to a collector, generally located at the bottom of a gas-stream cyclone generated by an aspirator located downstream of the outlet filter. This arrangement prevents particles from entering the exhaust gas. Importantly, the whole process can be run continuously in a closed loop, which is advantageous both technically and environmentally. Atomization of the feed can be considered the central step of spray-drying. While atomization can be performed by forcing the solution to pass through a membrane, using oscillatory discs, or using ultrasounds, the most common approach for atomizing precursor solutions entails breaking them up with a stream of hot gas (N_2 or compressed air) via a two-fluid nozzle comprising two concentric channels (Figure 2a). When the precursor solution is pumped into the inner channel, it encounters the gas stream that has been flowing through the second channel, thereby creating a shear field that atomizes the solution into droplets. Typically, before the atomization step, the precursor feed is introduced into the nozzle via simple peristaltic-pump tubing. This direct injection strategy is straightforward and convenient for precursor solutions that do not undergo any undesired reactions before spray-drying. However, some precursor solutions are unstable because they contain highly reactive reagents. In these cases, the precursor solutions must first be mixed shortly before or immediately after atomization, which can be done by either of two methods: i) use of T-junction that combines

two independently pumped solutions into a single mixed solution that is immediately introduced into the nozzle (Figure 2b); or ii) use of a three-fluid nozzle, which can simultaneously atomize two independent solutions via three concentric channels: one for each liquid solution and one for the gas stream. In this latter configuration, the two solutions are only mixed when they are already atomized via collision of the aerosol droplets in the drying chamber (Figure 2c). Alternatively, some precursor solutions must first be activated thermally before they can undergo chemical reaction. This can be resolved by a continuous flow-assisted approach, whereby a continuous-flow reactor is coupled to the entrance of the spray dryer (Figure 2d). In this mode, the precursor solution is pumped and directed into a continuous coil flow reactor encased in a thermostatic oil tank, where it is heated at a certain temperature. Then, the pre-heated (activated) solution is automatically injected into the spray-drier at the same feed rate, since the outlet of the continuous coil flow reactor is connected directly to the nozzle of the spray-dryer.

3. Synthetic parameters

In spray-drying synthesis, the principal parameters to be controlled are: i) the *feed rate* at which the liquid precursor feed is injected into the spray-drying equipment; ii) the *flow rate* used to atomize the liquid droplets; iii) the *inlet temperature* (T_{inlet}), which is the temperature of the gas used to dry the aerosol droplets; and iv), in the case of the continuous flow-assisted method, the *coil-flow reactor temperature* (T_{coil}). Researchers must achieve a delicate balance of these parameters. For instance, increasing the feed rate can augment the production rate, but this comes at the cost of increased energy demands for atomization and drying (*i.e.* higher flow rate and inlet temperature). Importantly, adjusting these parameters

not only dictates the quality and the production rate of the final product, but also influences the morphology and size of the product, as we discuss below.

4. Spray-Drying for Coordination Chemistry

4.1. Spray-drying synthesis of MOFs

In 2013, our group published the first report of a spray-drying synthesis of coordination compounds, describing a general method for spray-drying of MOFs.¹³ In this work, we showed that MOFs could be produced easily, rapidly and continuously via direct spray-drying of the MOF precursor solution. This approach relies on the formation and further drying of micrometric droplets containing the metal salt and the organic linker. Rapid evaporation of the solvent induces formation, at the air-liquid interface, of MOF nanocrystals that, upon drying, accumulate and merge into compact/hollow spherical MOF superstructures/beads (Figure 3). We first illustrated this simple approach by producing the archetypical MOF HKUST-1, by injecting directly into the spray-dryer, a solution of $\text{Cu}(\text{NO}_3)_2 \cdot 2.5\text{H}_2\text{O}$ and trimesic acid (BTC) (3:2 molar ratio) in DMF/EtOH/ H_2O (1:1:1) solvent mixture. The dried HKUST-1 powder was produced in the form of hollow spherical micron-size superstructures built-up from MOF nanocrystals (Figure 3a). Similarly, our group and others have since used this strategy to produce a wide range of MOFs with different characteristics, such as dimensionality, metal ions and/or clusters, and organic linkers, and coordination compounds with other functionalities such as thermochromism or spin crossover (SCO), revealing the broad scope of this method (Table 1).¹⁴⁻¹⁷

[ENREF 5](#) [ENREF 9](#)

Although the aforementioned general approach is very wide in scope, the specific conditions (*e.g.* temperature, time or solvents) of some MOF syntheses demand novel

strategies or, at the very least, major adaptations of existing ones. In this regard, a critical aspect of spray-drying synthesis of MOFs is control over reaction kinetics. On one hand, reaction conditions that promote rapid crystallization upon mixing of the reagents can lead to formation of amorphous phases or unwanted species before spray-drying even begins. Contrarily, synthesis of MOFs that require longer reaction times may result in low yields and/or afford materials with poor sorption capabilities, due to the fast drying kinetics of the process. As we discussed in the previous section, the flexibility of spray-drying allows for broad modification of synthetic conditions.

4.1.1. MOFs with fast crystallization kinetics: use of T-junction connectors or three-fluid nozzles

A potential problem in spray-drying is rapid precipitation of solids upon contact of the MOF precursor mixtures before spray-drying even begins, which can lead to undesired byproducts or to large MOF crystals that can block the spray nozzle. This problem can be resolved through use of a T-junction connector or a three-fluid nozzle (Figure 2), attachments that shorten the contact time between the precursor solutions. For example, our group used these attachments to produce IRMOF-3 and MOF-5 (T-junction connector) and ZIF-8, Cu-PB and SIFSIX-1-Zn (three-fluid nozzle) (Table 1).^{13,18} Moreover, because of the short contact time between precursors, T-junction connectors and three-fluid nozzles can both be used with precursor mixture solutions that promote or accelerate MOF formation: for instance, when using bases to deprotonate an organic ligand. Following this approach, spray-drying synthesis of MIL-88A was optimized to a yield of 40% by the addition of NaOH to the ligand solution using a three-fluid nozzle.¹³

4.1.2. MOFs with slow crystallization kinetics: use of spray-drying, continuous flow-assisted synthesis

Direct injection is not convenient for the synthesis of MOFs comprising high-nuclearity clusters such as zirconium-oxo-hydroxo clusters, due to the longer reaction times usually required. In 2016, we optimized spray-drying synthesis of various MOFs of this class, including several UiO-66-type MOFs, Fe-BTC/MIL-100 and $[\text{Ni}_8(\text{OH})_4(\text{H}_2\text{O})_2(\text{L})_6]_n$ (where L = 1H-pyrazole-4-carboxylic acid) (Table 1) by adding a continuous-flow reactor at the entrance of the spray-dryer to induce nucleation before spray-drying.¹⁹ We called this method spray-drying, continuous flow-assisted synthesis. This approach usually affords compact, spherical, micron-size MOF beads, contrary to the hollow ones typically obtained by the synthetic methods that we described in the previous sections. We have attributed this difference chiefly to formation of the primary nuclear suspension inside the coil-reactor, rather than within the drying chamber. In spray-drying, the hot air stream inside the drying chamber shrinks the microdroplets. During drying, the precursor concentration is increased at the surface until MOF nanoparticles begin to crystallize. In conventional approaches, this leads to formation of hollow superstructures comprising MOF nanocrystals (Figure 3a). However, when a continuous-flow reactor is used, a uniform cluster concentration and solution temperature are reached before spray-drying. Therefore, MOF nanoparticles begin to form as soon as the solution is sprayed within the hot drying chamber, thereby favoring uniform crystallization inside the microdroplets and ultimately dictating formation of dense beads or superstructures (Figure 3b).

4.1.3. Green synthesis of MOFs by spray-drying: use of water as solvent

Spray-drying is already well-integrated in many industrial sectors. However, for it to become a scalable, sustainable and cost-effective industrial process for MOF fabrication, the organic solvents typically used in research laboratories (*e.g.* DMF, which is expensive, toxic, flammable and teratogenic) must be replaced by water. In this context, in 2018, we demonstrated the aqueous based synthesis of two UiO type MOFs, UiO-66-NH₂ and Zr-fumarate (also known as MOF-801), through the spray-drying, continuous flow-assisted method. It is well known that modulators (*i.e.* monocarboxylic acids) capable to compete with linkers for metal coordination can influence the reaction kinetics and therefore, the nucleation and growth of MOFs. Thus, by controlling the modulator amount, we were able to optimize aqueous production (acetic acid concentration: 30%) of spherical microscale beads of UiO-66-NH₂ (BET surface area: 1270 m²/g), producing them on a 40-gram scale in 85% yield.²⁰ This demonstration established the basis for using spray-drying as a scalable green method for continuous one-step fabrication of shaped MOF microbeads (*vide supra*).

5. Spray-drying for Covalent Chemistry

5.1. Spray-drying covalent chemistry and functionalization of MOFs

Once we had acquired a certain level of experience in spray-drying synthesis of MOFs, we sought to extend our methodology beyond coordination chemistry. Thus, we began to explore spray-drying for synthesis of functional materials assembled by linking organic building units via covalent bonds. We began with formation of species made by Schiff-base condensation reactions. This type of reaction is suitable for spray-drying, since water, which is generated as a side-product during formation of the condensation product,²¹ can be removed during atomization to drive the equilibrium in the forward direction, according to Le Chatelier's principle.²² To prove the feasibility of performing this reaction by spray-

drying, we first synthesized a series of imines by reacting 2-aminoterephthalic acid (NH₂-BDC) with different aldehydes. By atomizing ethanolic suspensions containing both amine and aldehyde reagents in a molar ratio of 1:3 (NH₂-BDC/aldehyde), using a two-fluid nozzle at an inlet temperature of 130 °C, we obtained the desired imines in high conversion rates (up to 92%). This inlet temperature was crucial to ensure evaporation of ethanol as well as to force evaporation of the water molecules formed during the Schiff-base condensation reaction, thereby favoring formation of the imine bond.²³ Encouraged by these results and considering that the Schiff-base condensation between an amine and an aldehyde is among the most common reactions in covalent post-synthetic modifications of MOFs, we then demonstrated spray-drying for post-synthetic modifications of amine- and aldehyde-terminated MOFs (Figure 4a). Spray-drying enabled high post-functionalization/conversion efficiencies while maintaining the crystallinity of the parent MOF. Firstly, we functionalized UiO-66-NH₂ by atomizing a suspension of this MOF and several aldehydes (4-pyridinecarboxaldehyde, 2-pyridinecarboxaldehyde and salicylaldehyde) using a two-fluid nozzle at an inlet temperature of 130 °C. Remarkably, we obtained conversion efficiencies up to 20% within 2 seconds of reaction. Similarly, we performed post-synthetic modifications of aldehyde-terminated ZIF-90 with butylamine (42% conversion) or hexamethylenediamine (HDMA; 70% conversion). In the latter case, we found that the aldehyde groups of ZIF-90 were post-synthetically cross-linked by the diamine HDMA molecule, closing its pores and leading to a drastically (93%) smaller surface area than in the starting ZIF-90.²³

5.2. Spray-drying synthesis of COFs

Having explored spray-drying syntheses and post-synthetic modifications of MOFs, we next turned to Covalent-Organic Frameworks (COFs), beginning with imine-based COFs. Importantly, COFs must be synthesized under thermodynamic control.^{24,25} However, and as we mentioned above, the rapid drying of microdroplets in the spray-dryer favors formation of kinetic products rather than thermodynamic ones. In this sense, Dichtel *et al.*²⁶ reported that amorphous imine-based polymers could be crystallized via dynamic covalent chemistry. Thus, our group showed that spherical superstructures made from the assembly of imine-based COF nanocrystals could be obtained by combining spray-drying with dynamic covalent chemistry. In this methodology, the first step is formation of amorphous imine-based polymer spheres (kinetic product) by spray-drying, followed by crystallization of the spheres (thermodynamic product) via dynamic covalent chemistry, whereby the original size and morphology of the amorphous spheres is preserved (Figure 4b). Using this approach, we synthesized the imine-based COF-TAPB-BTCA by reacting 1,3,5-benzenetricarbaldehyde (BTCA) with 1,3,5-tris-(4-aminophenyl)benzene (TAPB). Briefly, the amorphous imine-based polymer spheres were obtained after separate atomization of a solution of BTCA in a mixture of DMSO and acetic acid (9:1 v/v), and a solution of TAPB in DMSO, using a three-fluid nozzle at an inlet temperature of 200 °C. Then, the dry powder was dispersed in a mixture of 1,4-dioxane/mesitylene/water/acetic acid and heated at 80 °C for 192 h. After this two-step process, we obtained crystalline, hollow imine-based COF-TAPB-BTCA superstructures (BET surface area: 911 m²/g). We later extended this approach to synthesize COF-LZU1 (BET surface areas: 319 m²/g) and COF-TAPB-PDA (BET surface areas: 1162 m²/g) superstructures.²⁷

6. Spray-Drying for Porous Composite Materials

Beyond synthesis of pure MOF and COF beads, researchers have also investigated spray-drying to prepare composites of MOFs or COFs with other functional materials.²⁸⁻³³ Such composites offer the respective strengths, and mitigate the respective weaknesses, of each component, enabling enhanced performance, multifunctionality and even new physical or chemical properties. Moreover, the resulting composites can be structured into more sophisticated architectures and can be shaped into forms matched to specific applications. Our group reported the spray-drying synthesis of various MOF- and COF-based composites using the same conditions as those for pure MOF or COF beads, except that we introduced an additional functional material into the reactions (Figure 5). Among the advantages of synthesizing such composites by spray-drying rather than by other methods (*e.g.* impregnation, gas-phase infiltration or co-precipitation), is that by controlling the composition of the initial feed, one obtains greater control over the composition of the final products. Furthermore, as opposed to other methods, spray-drying enables *in-situ*, one-step fabrication of these composites directly in their dried form.

6.1. Spray-drying synthesis of MOF-derived composites

6.1.1. MOFs as matrices

Using MOFs as porous matrices to host functional materials is a convenient way to prevent the guest materials from aggregating or from degrading in harsh environments; to regulate their release in a controlled/sustained manner; and to improve their adsorption capacity or selectivity.³⁴⁻³⁶ In germinal work from 2013, we explored the capability of spray-drying to generate composites by simultaneously encapsulating guest cargo within HKUST-1 superstructures.¹³ Initially, we investigated a solution-based approach using sodium chloride (NaCl) as guest cargo, due to its high solubility and facile crystallization. Spray-

drying of a solution containing the two MOF precursors and dissolved NaCl afforded micrometric NaCl@HKUST-1 composites, in which cubic NaCl crystals were found only inside the HKUST-1 superstructure (Figure 5c). Moreover, we employed spray-drying to fabricate MOF-based composites starting from emulsions or suspensions. In the first case, compounds that are immiscible with the MOF precursor solution were trapped inside the spherical MOF superstructure by spray-drying an oil-in-MOF precursor solution emulsion, in which the guest materials had been dissolved in the oil, as demonstrated for a pyrene@HKUST-1 composite (Figure 5e). Alternatively, we demonstrated that suspensions of colloidal particles could be combined with the MOF precursor solution to encapsulate suspended species. The first example comprised entrapment of magnetic Fe₃O₄ nanoparticles inside HKUST-1 superstructures to form Fe₃O₄@HKUST-1 composites (Figure 5a), which exhibited utility for magnetic solid-phase removal of pollutants (*e.g.* dibenzothiophene). This foundational study revealed the great potential of spray-drying for creating MOF-based composites with a broad array of guest materials.³⁷⁻³⁹ Recently, we have developed novel, more-effective methods to achieve spray-drying fabrication of functional composites with other MOFs, as we described in the previous sections. For example, we employed continuous flow spray-drying to synthesize Zr-based UiO-66 MOFs and several new related composites for diverse applications. Thus, we incorporated inorganic nanoparticles (INPs) into dense UiO-66-type beads by spray-drying suspensions of the INPs (*e.g.* Pd, Pt, Au, CeO₂ and hybrid core-shell Au/CeO₂ NPs) and UiO-66-type precursors (Figure 5b). Some of these composites exhibited remarkable catalytic activity for CO oxidation at low temperatures: for instance, one Au/CeO₂@UiO-66 composite enabled total CO conversion at temperatures as low as 100 °C.³⁷ Others, like CeO₂@UiO-

66-SH, efficiently and simultaneously remove multiple heavy metals from samples of polluted water, including As(III and V), Cd(II), Cr(III and VI), Cu(II), Pb(II) and Hg(II).³⁸

As illustrated by our example of NaCl@HKUST-1 composites, soluble inorganic salts can be readily incorporated into spray-drying syntheses of MOFs. We followed a similar strategy to confine hygroscopic CaCl₂ into the dense superstructures of UiO-66 beads. The resulting CaCl₂@UiO-66 composites (Figure 5d), commonly named as *composite salt in porous matrix* (CSPM) materials, demonstrated superior water-uptake relative to UiO-66 alone, yet did not lead to dissolution of the salt in the adsorbed water. Indeed, these new adsorbents exhibited high adsorption capacity and stability after several cycles of water sorption/desorption. We also demonstrated that these MOF-based composites are promising candidates for adsorption chillers. In fact, a composite comprising UiO-66 and CaCl₂ (53% w/w) exhibits a specific cooling power of 631 W kg⁻¹ and a coefficient of performance of 0.83, comparable to the values for the best solid adsorbents reported to date.⁴⁰

6.1.2. MOFs as guest cargo

For use of MOFs in adsorption applications, a critical property to address is their low hydrolytic stability.⁴¹ A strategy to protect MOFs from hydrolysis is to encapsulate them into other materials: for example, MOFs can be encapsulated into organic polymers to produce MOF@polymer composites. In 2015, our group reported the spray-drying encapsulation of crystals of the water-labile MOF HKUST-1 into hydrophobic polystyrene (PS) microspheres to afford HKUST-1@PS composite microspheres.⁴² The rapid one-step method entailed continuous spray-drying of a suspension of HKUST-1 crystals mixed with a solution of PS (Figure 5f). Among the main advantages of this approach is that it does not

require any additional purification or filtration steps, as the products are obtained directly as pure dry solids. Adsorption studies on the HKUST-1@PS composites revealed that optimizing the MOF/polymer ratio is crucial for balancing porosity and protection (from hydrolysis), as the non-porous PS coating reduces access of water molecules to MOF pores. As we previously commented, in spray-drying, the composition of the final product can be finely tuned by simply adjusting the composition of the feed-mixture. Thus, after evaluating different compositions for our HKUST-1@PS composites, we found that a MOF content of 63% w/w offers the optimal balance between porosity and protection. Interestingly, researchers have used spray-drying to coat pre-synthesized MOF crystals with different materials for distinct purposes. For instance, Li *et al.* reported the synthesis of MOF-GO (GO = graphite oxide) yolk-shell superstructures, based on spray-drying of a suspension of Cu(BDC) crystals and GO in aqueous polyvinylpyrrolidone (PVP).⁴³ The resultant Cu(BDC)@GO composites (Figure 5g) readily dispersed in water, owing to the hydrophilic GO coating. Similarly, our group recently employed spray-drying to coat MOF crystals with porous COF,⁴⁴ obtaining MOF@COF composites whose sorption capacities are superior to those of either component (*vide infra*).

6.2. Spray-drying of COF-derived composites

Analogously to MOF-based composites, COF-based composites can marry the advantages of COFs to those of other functional materials. For instance, COFs can act as dispersive and protective porous matrices due to their excellent thermal and chemical stabilities, which are critical features for certain applications.^{28,45} [ENREF 17](#) Our group has demonstrated spray-drying synthesis of COF-based composites and proven that COF-based composites can be used as vehicles for hosting and releasing guest cargo. For instance, we encapsulated

the dye Rose bengal into COF-TAPB-BTCA superstructures, by spray-drying it with the initial COF solution precursor.²⁷ We then showed that incubation of the resultant Rose-bengal@COF-TAPB-BTCA composite (Figure 5j) in ethanol for several days leads to gradual release of the encapsulated dye from the COF superstructures. In another example, we showed that magnetic Fe₃O₄ nanoparticles could be encapsulated into COF-TAPB-BTCA superstructures (Figure 5i).²⁷ The resulting Fe₃O₄@COF-TAPB-BTCA composite retained the magnetic character of the nanoparticles, as confirmed by magnetic measurements. More recently, we reported that combination of MOFs and COFs via spray-drying yields a novel hierarchical composite.⁴⁴ This was the first published example in which pre-synthesized UiO-66-NH₂ and Zr-fumarate particles were dispersed into a spherical matrix comprising packed nanocrystals of COF-TAPB-BTCA. In this case, we employed spray-drying to encapsulate the MOF crystals into the amorphous, imine-based polymer superstructures. We then subjected these new materials to dynamic covalent chemistry conditions (see section 4.2, above), thereby transforming the amorphous polymer into COF-TAPB-BTCA crystals to obtain the corresponding MOF@COF composite (Figure 5h). Intriguingly, we discovered that the amorphous-to-crystalline transformation generated new pores at the MOF/COF interface. In fact, the newly-formed porosity strongly influenced the functionality of the composite. For example, the N₂-sorption and water-sorption capacities of the composite were each three-to-four-fold higher than the corresponding sums of the respective contributions from each component (MOF and COF).⁴⁴

7. Scale-up of Spray-Drying Methods for Industrial Applications

Over the past decade, MOFs have been proposed for industrial use, thanks to their revolutionary performance in applications such as gas storage,^{46,47} petrochemical separation,⁴⁸ CO₂ capture⁴⁹ and drug delivery.⁵⁰ However, commercial adoption of MOFs is currently precluded by a lack of cost-effective methods for industrial-scale synthesis and shaping of them. In this context, advances on large scale production of MOFs has been made using different methods, such as electrochemistry, solvothermal synthesis, continuous flow chemistry and mechanochemistry. However, an advantage of spray-drying is that it is a well-established technology in industry, and spray-driers are common pieces of factory equipment in many industrial domains such as the food and pharmaceuticals sectors. Moreover, spray-drying can readily be scaled-up to pilot production. In this context, in collaboration with Prof. David Farrusseng, Axel'One and the company MOFApps, and as part of the project ProDIA, our group recently demonstrated large-scale spray-drying production of the MOFs HKUST-1 and ZIF-8 at the Axel'One facilities, in Lyon, France (Figures 6a-c). To this end, we fabricated a certified spray-drying-based platform, called *ATEX*, which is equipped with tools and large vessels designed for large-scale studies of solids, including organics and organometallics. It also includes a pilot-scale spray-dryer (height: 10 m; diameter: 2 m). The pilot spray-drying tower can operate in open (air) or closed (nitrogen) configurations and is equipped with diverse nozzle systems, to enable adaptation to different feeds as well as control over aggregate size. The solvents employed are condensed, collected and reinjected into the drying chamber. Our first successful, large-scale, spray-drying production was of HKUST-1, in 2018 (Figures 6d-f). An aqueous slurry of HKUST-1 precursor (158 kg) was sprayed over 2 h, to afford 18 kg of HKUST-1 beads (bead size: up to 200 μm; yield: 99% w/w), corresponding to 95%

(w/w) solvent recovery. The global space-time yield was estimated to be 1,000 kg/m³·day. To remove solvent trapped in the micropores, the powder as received was activated in oven at 150 °C under N₂ flow, yielding high-quality material, as confirmed by X-ray diffraction. The BET surface area was measured as being above 1600 m²/g. More recently, we employed this platform to synthesize ZIF-8 beads on the kilogram scale.

8. Conclusions and outlook

Over the past decade, spray-drying has become increasingly valued as a method for synthesis of fine chemicals and advanced materials. Indeed, since our group's work in 2013, spray-drying synthesis of crystalline porous compounds such as MOFs, COFs and their corresponding composites has rapidly progressed. Unlike conventional methods, spray-drying enables production of dry micro-spherical powders in a fast, continuous and scalable manner, leading to lower fabrication costs and shorter production times. Additionally, due to its robustness and simplicity of operation, spray-drying is amenable to a nearly infinite variety of precursors, components and reaction conditions. Moreover, recent advances in large-scale spray-drying synthesis have brought industrial production within reach.

We anticipate that spray-drying will soon be expanded to synthesize other types of crystalline porous materials. For instance, preliminary experiments suggest that spray-drying can be used to fabricate hydrogen-bonded porous materials such as MPM-1-TIFSIX, via supramolecular assembly of [Cu₂(ADE)₄(TiF₆)₂] (ADE = adenine) paddlewheels.¹⁸ Moreover, we believe that spray-drying could be exploited to augment the complexity of synthesized porous beads. For example, early tests have revealed that spray-drying can be used to fine-tune the composition of the distinct MOFs within multi-variate UiO-66-type

MOF beads.¹⁹ Nevertheless, to advance MOFs, COFs and related composites from the laboratory to the market, greater research efforts are required to make spray-drying processes even greener, safer, cheaper and more amenable to pilot-scale.

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Troyano et al., Figure 1

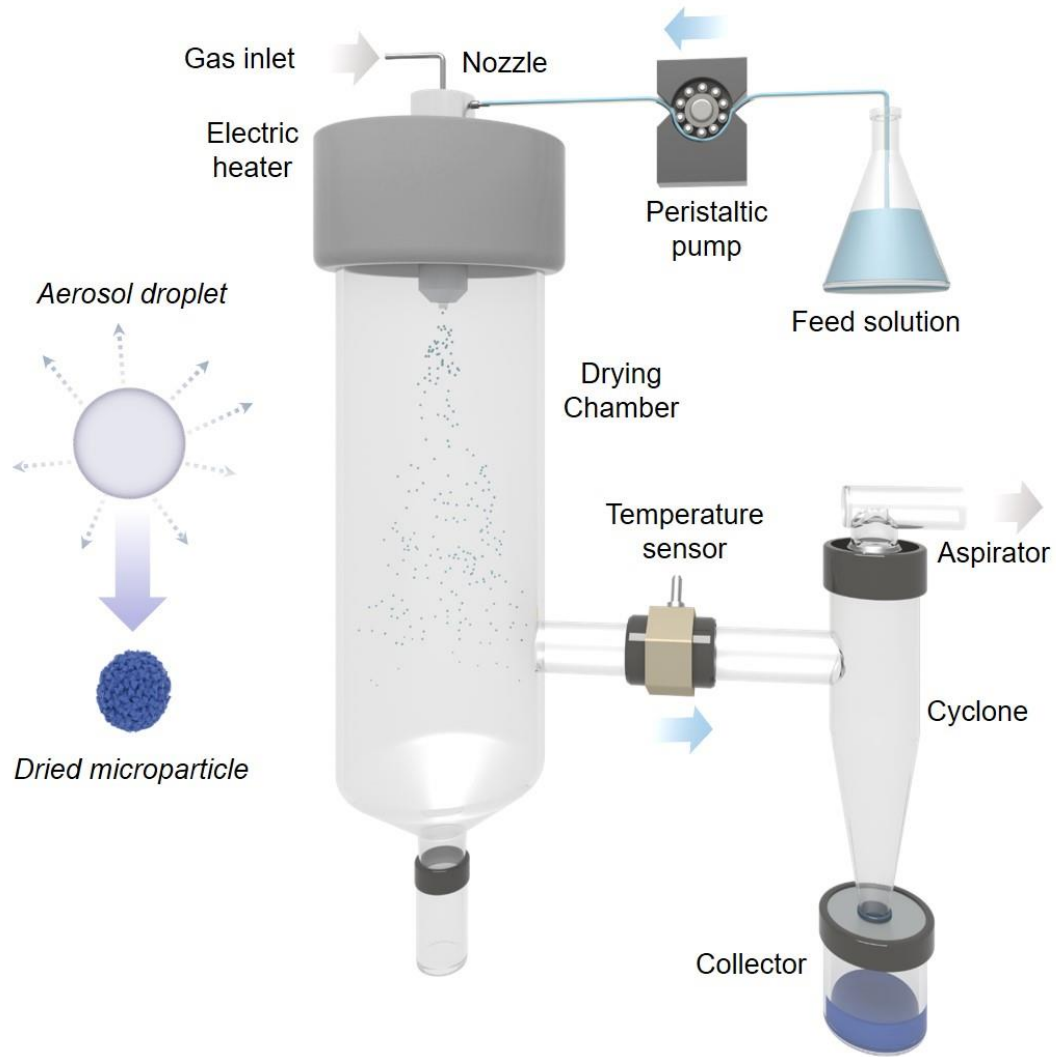


Figure 1. Schematic of the general spray-drying set-up.

Troyano et al., Figure 2

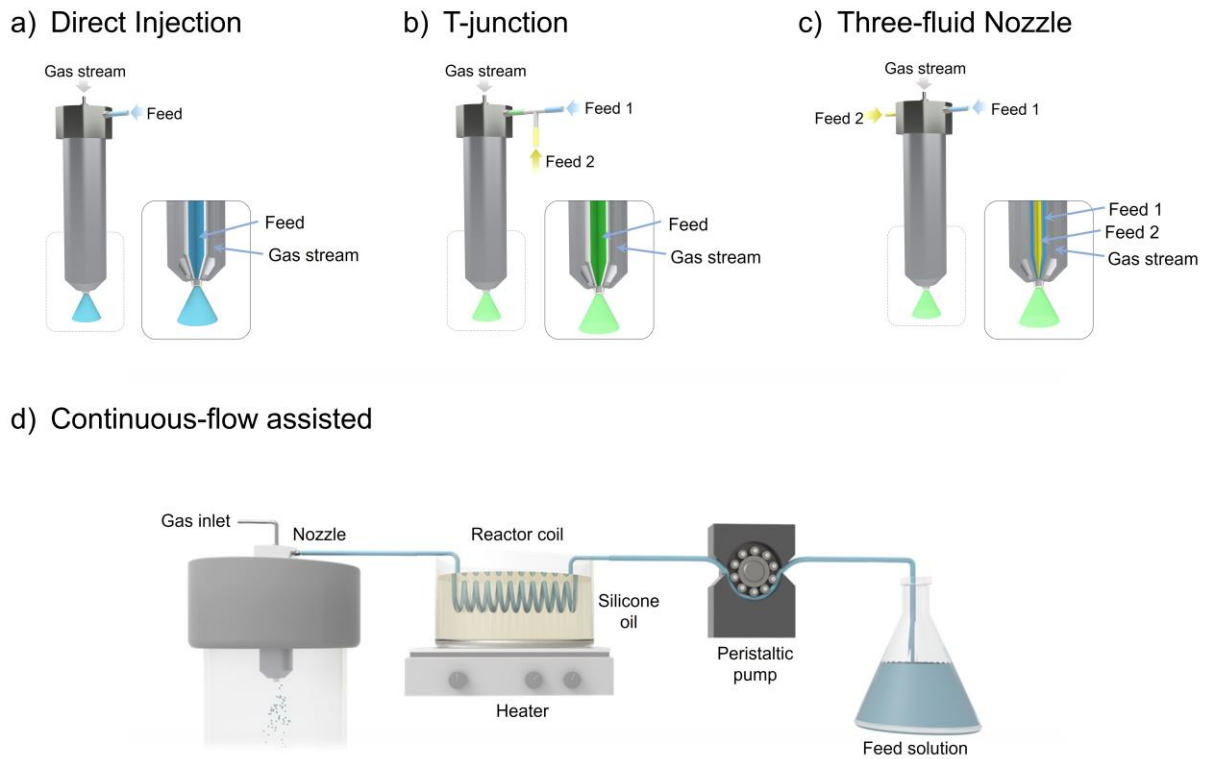


Figure 2. Schematic illustrating the synthetic versatility of spray-drying. a) Spray-drying of a feed solution by *direct injection* with a two-fluid nozzle; b) Spray-drying of two independent solutions mixed through a *T-junction* at the entrance of a two-fluid nozzle; c) Spray-drying of two independent solutions mixed at the tip of a *three-fluid nozzle* before atomization; and d) *Continuous flow-assisted* spray-drying.

Troyano et al., Figure 3

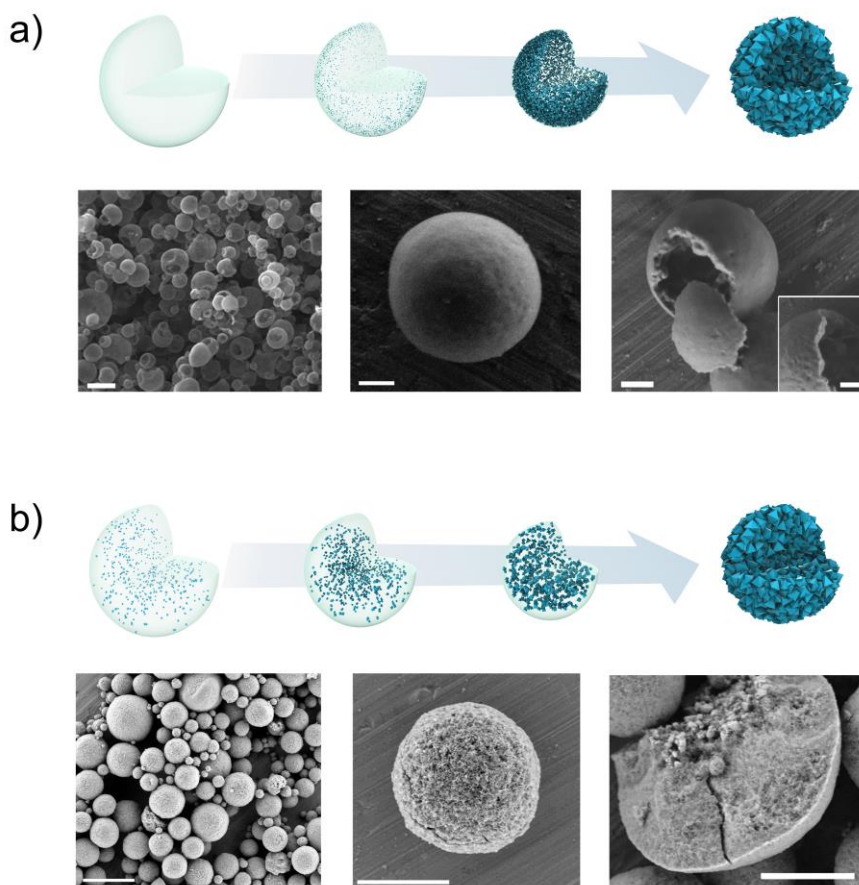


Figure 3. a) Proposed mechanism for the formation of hollow MOF superstructures by spray-drying: MOF precursors accumulate at the surface of an aerosol droplet, where they react to form nanoscopic crystals that pack densely into the final MOF shell (top). FESEM images of hollow HKUST-1 superstructures (bottom). Scale bars (from left to right) = 5 μm , 500 nm, 200 nm and 200 nm. b) Proposed mechanism for formation of MOF beads: MOF crystals in the aerosol droplet undergo homogenous crystallization to yield, once dried, dense spherical MOF beads (top). Representative images of UiO-66 beads. Scale bars (from left to right) = 5 μm , 2 μm and 2 μm .

Troyano et al., Figure 4

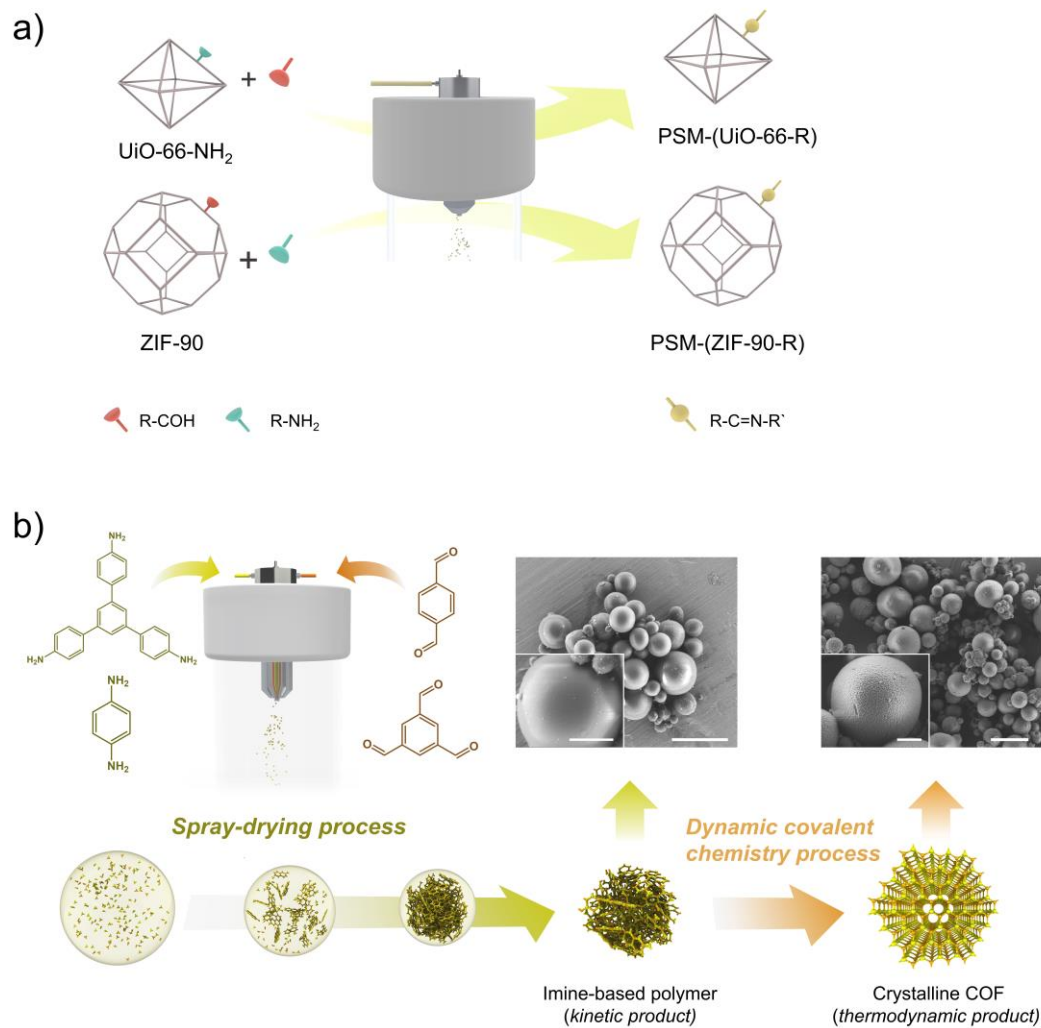


Figure 4. a) Schematic of spray-drying for post-synthetic functionalization of UiO-66-NH₂ and ZIF-90 *via* formation of imine bonds. b) Schematic of spray-drying synthesis (left) of spherical beads of amorphous imine-based polymers (center), and subsequent transformation of these beads into spherical crystalline COF beads, *via* covalent dynamic chemistry (right). Scale bars = 5 μm and 1 μm (inset).

Troyano et al., Figure 5

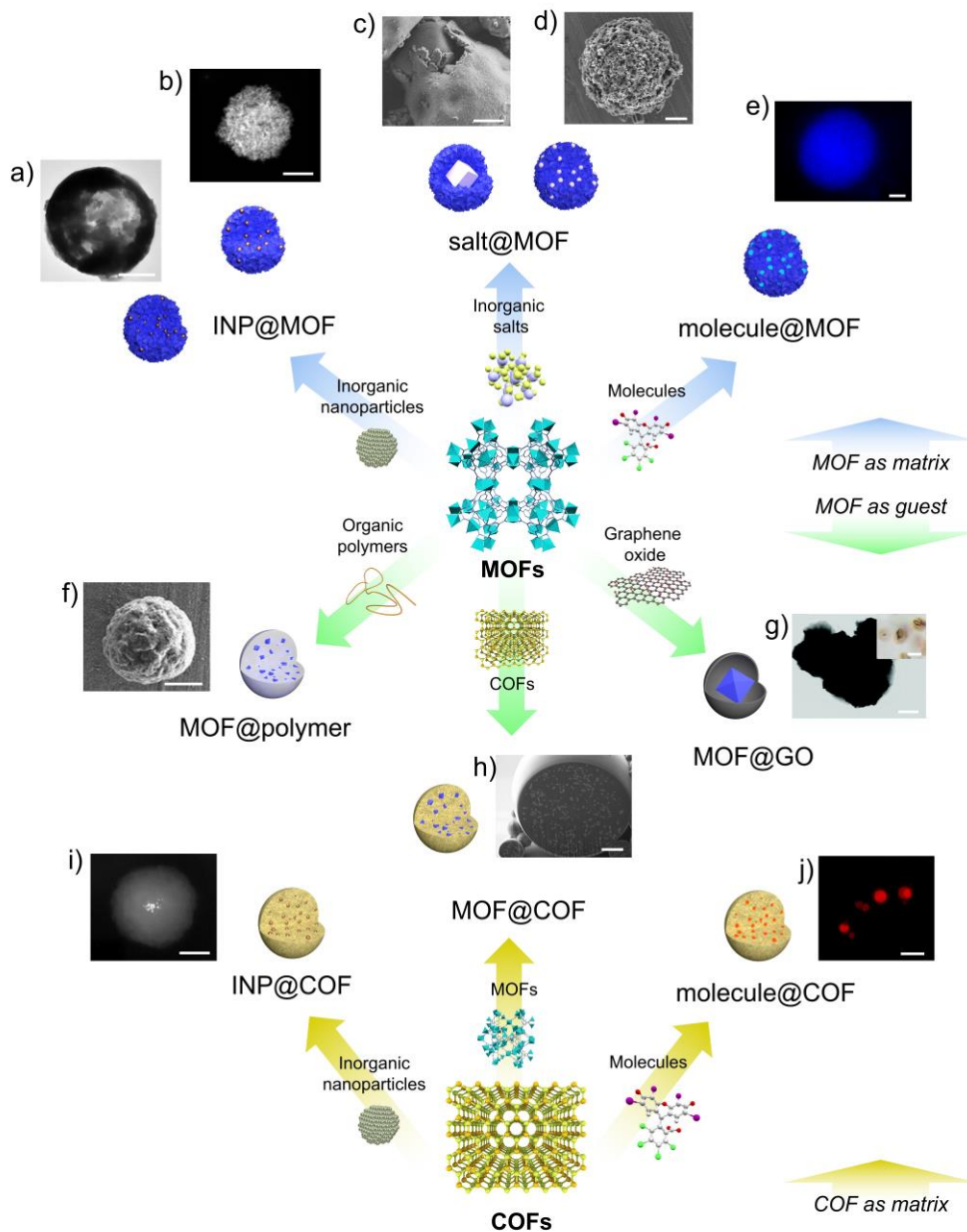


Figure 5. Illustration summarizing the various MOF- and COF-based composites synthesized by spray-drying: a-b) INP@MOF; c-d) salt@MOF; e) molecule@MOF; f) MOF@polymer; g) MOF@GO; h) MOF@COF; i) INP@COF and j) molecule@COF. Scale bars = 500 nm (a,b); 1 μm (c,d,e,g); 2 μm (f, h); and 100 nm (i); and 10 μm (j, g inset).

Troyano et al., Figure 6



Figure 6. Pictures of the Axel'One pilot-scale spray-dryer tower (a-c) and the produced HKUST-1 powder (d-e).

Table 1. Summary of reported MOFs and coordination polymers synthesized by spray-drying

	Precursors	Solvent(s)	T_{inlet} (T_{coil}) [°C]	Yield [%]	S_{BET} [m ² /g]	Shape	Ref.
<i>Direct injection</i>							
HKUST-1	Cu(NO ₃) ₂ , BTC	DMF/EtOH/water	180	70	1260	Hollow superstructures ; see Figure 3a	13
Cu-BDC	Cu(NO ₃) ₂ , BCD	DMF	180	70	543	Hollow superstructures	13
NOTT-100	Cu(NO ₃) ₂ , BPTC	DMF/water	180	54	1140	Hollow superstructures	13
MOF-14	Cu(NO ₃) ₂ , BTB	DMF/EtOH/water	180	30	-	Hollow superstructures	13
Zn-MOF-74	Zn(NO ₃) ₂ , DHBDC	DMF/water	180	50	-	Hollow superstructures	13
Mg-MOF-74	Mg(NO ₃) ₂ , DHBDC	DMF/EtOH/water	180	35	-	Hollow superstructures	13
Ni-MOF-74	Ni(NO ₃) ₂ , DHBDC	DMF/EtOH/water	180	40	-	Hollow superstructures	13
MIL-88B	FeCl ₃ , NH ₂ -BCD	DMF/MeOH/water	180	27	-	Hollow superstructures	13
ZIF-8 ^a	Zn(OAc) ₂ , 2-MIM	Water	180	-	1634	Beads	15 ENREF 1 2
ZIF-67 ^a	Co(OAc) ₂ , 2-MIM	Water	180	-	1861	Beads	15
Zn/Co-ZIF ^a	Zn(OAc) ₂ , Co(OAc) ₂ , 2-MIM	Water	180	-	1746	Beads	15
[Fe(NH ₂ trz) ₃]Br ₂ ·nH ₂ O	FeBr ₂ , NH ₂ -TRZ	Water	90	-	-	Beads	17
[Fe(NH ₂ trz) ₃](BF ₄) _n	Fe(BF ₄) ₂ , NH ₂ -TRZ	Ethanol; water	90	-	-	Beads	17
[Fe(Htrz) ₂ (trz)](BF ₄) _n	Fe(BF ₄) ₂ , HTRZ	Ethanol; water	90	-	-	Hollow superstructures	17

Tb _{0.914} Eu _{0.086} -PDA	Tb(NO ₃) ₃ , Eu(NO ₃) ₃ , PDA	DMF/water	180	55	-	Hollow superstructures	16
<i>T-junction</i>							
MIL-88A	FeCl ₃ , FUM	DMF/MeOH/water	180	40	-	Hollow superstructures	13
MOF-5	Zn(OAc) ₂ , BCD	DMF	180	60	1215	Hollow superstructures	13
IRMOF-3	Zn(OAc) ₂ , NH ₂ -BCD	DMF	180	70	-	Hollow superstructures	13
<i>3-fluid nozzle</i>							
ZIF-8	Zn(OAc) ₂ , 2-MIM	Water	180	10	941	Hollow superstructures	13
Cu-PB	Cu(NO ₃) ₂ , K ₃ Co(CN) 6	Water	180	20	617	Hollow superstructures	13
SIFSIX-3-Co	CoSiF ₆ , PYZ	MeOH	85	44	-	Hollow superstructures	18
SIFSIX-3-Ni	NiSiF ₆ , PYZ	MeOH	85	-	-	Hollow superstructures	18
SIFSIX-3-Cu	CuSiF ₆ , PYZ	MeOH	85	55	-	Hollow superstructures	18
SIFSIX-3-Zn	ZnSiF ₆ , PYZ	MeOH	85	57	-	Hollow superstructures	18
SIFSIX-1-Zn	ZnSiF ₆ , BPY	MeOH	85	40	1300	Hollow superstructures	18
TIFSIX-1-Cu	Cu(NO ₃) ₂ , BPY	MeOH	130	79	1650	Hollow superstructures	18
<i>Continuous-flow</i>							
UiO-66	ZrCl ₄ , BCD	DMF/water	180 (115)	70	1106	Beads; see Figure 3b	19
UiO-66-NH ₂	ZrCl ₄ , NH ₂ -BCD	DMF/water	180 (115)	67	752	Beads	19
UiO-66-NO ₂	ZrCl ₄ , NO ₂ -BCD	Acetic acid/water	180 (115)	62	679	Beads	19
UiO-66-Br	ZrCl ₄ , Br- BCD	DMF/water	180 (115)	68	527	Beads	19

UiO-66-(OH) ₂	ZrCl ₄ , (OH) ₂ - BCD	DMF/water	180 (115)	81	401	Beads	19
UiO-66-acetamido	ZrCl ₄ , acetamido- BCD	DMF/water	180 (115)	51	586	Beads	19
UiO-66-1,4-NDC	ZrCl ₄ , 1,4- NDC	DMF/water	180 (115)	45	431	Beads	19
UiO-66-2,6-NDC	ZrCl ₄ , 2,6- NDC	DMF/water	180 (115)	49	557	Beads	19
Fe-BTC/MIL-100	Fe(NO ₃) ₃ , BTC	DMF	180 (135)	78	1039	Beads	19
Ni ₈ (OH) ₄ (H ₂ O) ₂ (L) ₆	Ni(OAc) ₂ , PCA	DMF/water	180 (100)	60	377	Beads	19
UiO-66-NH ₂	ZrOCl ₂ , NH ₂ -BCD	Acetic acid/water	150 (90)	64	1261	Beads	ENREF 17 2 0
Zr-fumarate	ZrOCl ₂ , FUM	Acetic acid/water	140 (90)	58	664	Beads	20

^a Crystallized in a solvent after spray-drying. BTC = trimesic acid; BDC = terephthalic acid; BPTC = biphenyl-3,3',5,5'-tetracarboxylic acid; BTB = 1,3,5-tris(4-carboxyphenyl)benzene; DHBDC = 2,5-dihydroxy-terephthalic acid; 2-MIM=2-methylimidazole; R-TRZ = 4-R-substituted-1,2,4-triazole; PDA = 1,4-phenylenediacetic acid; FUM = fumaric acid; PYZ = pyrazine; BPY = 4,4'-bipyridine; NDC = naphthalenedicarboxylic acid; PCA = 1H-pyrazole-4-carboxylic acid.