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High-Throughput Assisted Rationalization of the Formation of Metal Organic Frameworks in the Iron(III) Aminoterephthalate Solvothermal System

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Through the use of high-throughput methods, solvothermal reactions of $FeCl_3$ and 2-aminoterephthalic acid in protic as well as aprotic reaction media were systematically studied. Thus, the fields of formation of the isoreticular structures of MIL-53, MIL-88, and MIL-101 based on Fe(III) and aminoterephthalate could be identified for the first time. The resulting 3D framework materials with amino-functionalized pores have been characterized using X-ray diffraction; IR spectroscopy; and thermogravimetric, elemental, and energy dispersive X-ray analysis. Due to the applied high-throughput method, a high density of information was obtained in a short period of time, which allows the extraction of important reaction trends and contributes to a better understanding of the role of compositional as well as process parameters in the synthesis of inorganic−organic hybrid materials. We have found that the nature of the reaction medium has the most profound impact on structure formation. Furthermore, the concentration of the starting mixture (i.e., the solvent content) and the temperature have also been identified as key parameters for the formation of the different hybrid phases.

Introduction

Inorganic−organic hybrid compounds or MOFs (for metal−organic frameworks) have developed into an important class in the family of porous materials.[1−5] This is due to their interesting magnetic[6−8] or optical properties[9,10] and their potential application in the fields of gas separation[11,12] and storage,[13−16] catalysis,[17,18] and drug delivery.[19] The success of hybrid frameworks is based on the diversity of metal oxide clusters that can be connected with innumerous functionalized organic linkers. In the majority of these studies, the focus of interest is directed toward a detailed characterization of the product. The synthesis is only briefly

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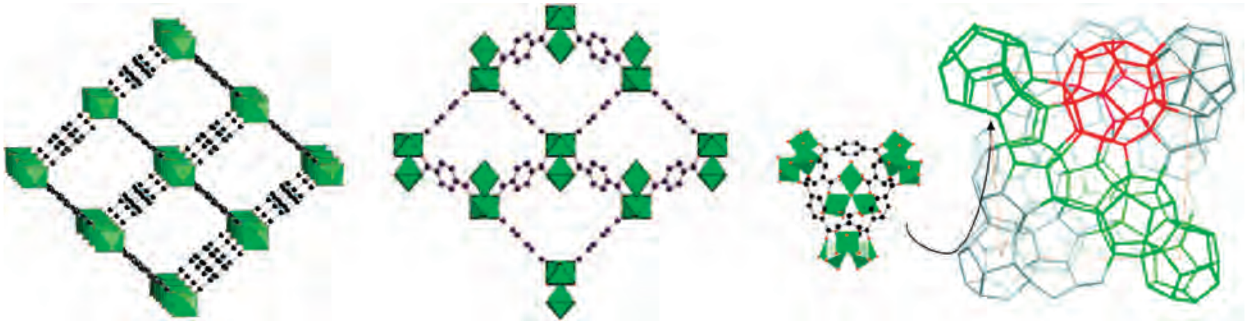

Figure 1. Structures obtained from the reaction of trivalent metals (Cr, Fe, and V) and terephthalic acid: MIL-47 and MIL-53 (left), MIL-88B (center), and MIL-101 (right).

described, and a systematic investigation of the reaction parameters is missing. As the synthesis of these hybrid solids is often very sensitive to small changes in compositional and process parameters, it is found to be hard to reproduce literature synthesis procedures. In addition, the chemistry of these hybrid solids is very rich, which makes it necessary to get deep insight into their chemical formation conditions for an understanding of the influence of each parameter on the final result.

In the field of metal carboxylates, the use of linear organic linkers, especially terephthalic acid (hereafter labeled H_2BDC), is very popular, since it leads to many open-framework structures with interesting features.[3] For instance, its combination with trivalent metal cations such as Al^{3+}, Cr^{3+}, Fe^{3+}, V^{3+}, Sc^{3+}, and In^{3+} under solvothermal synthesis conditions results in the formation of at least eight crystalline phases with very close chemical formulas but different structures: MIL-53 ($M(OH)BDC \cdot guest$),[20] MIL-68 ($M(OH)BDC \cdot guest$),[21] MIL-71 ($M_2(OH)_2F_2BDC \cdot guest$),[22] MIL-85 ($Fe_2O[O_2C\text{-}CH_3]_2BDC \cdot guest$),[23] MIL-88B [$M_3O(BDC)_3 \cdot X \cdot guest$],[24] MIL-101 [$Cr_3O(BDC)_3 \cdot X \cdot guest$],[25] $Sc_2(BDC)_3$,[26] and $In_2(OH)_3(BDC)_{1.5}$.[27] Of special interest are the materials MIL-53 and MIL-88B, which exhibit exceptional framework flexibility, and MIL-101, with an unusually large pore volume and surface area (Figure 1). These materials are currently tested for industrial applications, and therefore the use of nontoxic metal ions is of great interest.

To improve and adjust the properties of these MIL compounds, the chemical modification of their pore walls could be of great interest.[28] This could lead, for example, to more selective materials with a higher storage capacity in fields such as gas separation or gas storage. Such a modification can be accomplished by employing functionalized organic linker molecules, for example, amino-, methyl-, bromo-, or hydroxoterephthalic acid. The presence of the functional groups leads often to changes in the Brønsted/Lewis acid−base properties and the solubility of the starting materials. This can drastically affect the synthesis conditions. Thus, the synthesis conditions of the parent material (the isoreticular compound) cannot be transferred one-to-one to the new system, and a tedious trial and error technique is required to get the pure product. This is particularly true for the class of hybrid materials based on trivalent metals and terephthalic acid, mentioned above, which has already been shown to be a highly complex system. Large differences in the reaction conditions can also be expected when the metal ion is changed. Thus, for example, MIL-101 has only been obtained with Cr^{3+} ions up to now. The synthesis of Cr-containing MOFs necessitates much higher reaction temperatures (up to 220 °C) than the synthesis of corresponding Fe-containing MOFs.[25,23] Therefore, a drastic change of synthesis conditions has been expected in order to synthesize Fe-MIL-101_NH_2.

Whereas in the chemistry of microporous inorganic materials, the role of pH, Si/Al ratio, temperature, or synthesis time is now well understood,[29−32] such systematic investigations in the field of inorganic−organic hybrid compounds are still rare.[33−35] For this challenging task, high-throughput methods are the ideal tool, allowing a parallel investigation of many individual reaction mixtures under solvothermal conditions.[36,37] Compositional as well as process parameters can be systematically and efficiently explored. This approach leads to an accelerated discovery of new compounds and optimization of their synthesis, due to the large amount of data obtained in a short period of time. Not only are the fields of formation and best synthesis conditions obtained but, even more important, reaction trends

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are established. This high information density could also be used in the future to extract information on the physical chemistry of these systems.

Our first attempt, described here, relates to amino-functionalized terephthalic acid NH_2-H_2BTC as a ligand. It is one of the simplest aminodiacids, which are well-known to form zwitterions drastically depending on the pH conditions. The choice of NH_2-H_2BTC obviously complicates the investigation due to its intrinsic properties (complexation, protonation, etc.). For this reason, we have systematically investigated the reaction systems $FeCl_3$/2-aminoterephthalic acid (NH_2-H_2BDC)/NaOH/solvent applying high-throughput methods. This led to the formation of the NH_2-functionalized isoreticular compounds of MIL-53, MIL-88B, and MIL-101, that is, $Fe(OH)NH_2-BDC\cdot 0.3NH_2-H_2BDC$, $Fe_3O(solv)_3X(NH_2-BDC)_3\cdot m$solv ($X = Cl^-$, Br^-; solv = H_2O, DMF, CH_3OH, CH_3CN), and $Fe_3O(solv)_3Cl(NH_2-BDC)_3\cdot m$solv$\cdot n$guest (solv = H_2O, DMF; guest = NH_2-H_2BDC, HCl), respectively. We present here the results of our systematic studies, including the influence of compositional parameters, reaction temperature and medium, as well as the addition of HCl or HF to the reaction mixture.

Experimental Section

Chemicals. $FeCl_3\cdot 6H_2O$ (Riedel-de Haen, ≥99%), NH_2-H_2BDC (Fluka, ≥98%), NaOH (Merck, ≥99%), NaBr (Merck, ≥99%), HCl (Bernd Kraft GmbH Salze and Lösungen, ≥99%), HF (Merck, 99.9%), N,N-dimethyl-formamide (BASF, tech.), methanol (BASF, purum), and acetonitrile (Riedel-de Haen, ≥99%) were used as purchased.

Methods. The high-throughput X-ray analyses were carried out using a STOE high-throughput powder diffractometer equipped with a linear position sensitive detector. High-precision X-ray powder diffraction patterns were recorded with a STOE STADI P diffractometer equipped with a linear position sensitive detector using monochromated Cu $K\alpha_1$ radiation. IR spectra were recorded on an ATI Matheson Genesis in the spectral range 4000−400 cm^{-1} using the KBr disk method. Thermogravimetric (TG) analyses were carried out in the air (25 mL/min, 25−900 °C, 10 °C/min) on a NETZSCH-STA-449C (Fe-MIL53_NH_2) or under nitrogen (75 mL/min, 25−900 °C, 8 °C/min) on a Netzsch STA-409CD (Fe-MIL88B_NH_2 and Fe-MIL101_NH_2). Carbon, hydrogen, and nitrogen contents were determined by elemental analysis on an Eurovektor EuroEA Elemental Analyzer. Energy dispersive X-ray (EDX) analysis was performed on a Philips ESEM XL 30. NMR spectra were recorded on a Bruker Avance 400 pulse Fourier transform spectrometer. A single crystal of Fe-MIL-53_NH_2 was mounted with paratone oil on a nylon cryoloop and measured at 200 K on a X8 Bruker diffractometer. The structure was solved and refined by full-matrix least-squares techniques, based on F^2, using the SHELX software package.[38] All non-hydrogen atoms were refined anisotropically; hydrogen atoms were introduced at calculated positions (except on OH and NH_2 functionalities) and were not refined. Disordered NH_2-H_2BDC molecules occupying the pores were discarded using the SQUEEZE procedure.

Synthesis and Characterization

A scaleup of the high-throughput reactions was performed, and the following optimized procedures led to larger amounts of the title compounds. Furthermore, single-crystal growth as well as ion/solvent exchange experiments are described here. The high-throughput experiments are described in the High-Throughput Experimentation section.

Table 1. Summary of Crystal Data, Intensity Measurement, and Structure Refinement Parameters for Fe-MIL-53_NH_2, $Fe(OH)NH_2-BDC\cdot 0.3NH_2-H_2BDC$

empirical formula	$Fe(OH)[(OOC)_2NH_2-C_6H_3]\cdot 0.3(HOOC)_2NH_2-C_6H_3$
cryst syst	orthorhombic
space group	*Imma*
a [Å]	6.9177(14)
b [Å]	17.668(3)
c [Å]	12.120(3)
vol [10^6 pm^3]	1481.3(6)
Z	4
temperature [K]	200(2)
formula mass	306.33
density [g/cm^3]	1.1374
F(000)	621
cryst size (μm^3)	40 × 40 × 30
μ [mm^{-1}]	1.037
θ range [deg]	2.04 to 30.00
range in hkl	$-9 \leq h \leq +9$, $-24 \leq k \leq +24$, $-16 \leq l \leq +16$
total data collected	11476
data/restraints/parameters	1197/1/50
abs correction	semiempirical from equivalents
max. and min. transmission	0.7460, 0.6817
refinement	full-matrix least-squares on F^2
R(int)	0.0549
$R1$, w$R2$ ($I > 2\sigma(I)$)	0.0357, 0.1002
$R1$, w$R2$ (all data)	0.0516, 0.1043
goodness of fit	1.063
Δe min/max [eÅ^{-3}]	−0.379/0.629

Fe-MIL-53_NH_2, $Fe(OH)NH_2-BDC\cdot 0.3NH_2-H_2BDC$. Microcrystalline bulk material of $Fe(OH)NH_2-BDC\cdot 0.3NH_2-H_2BDC$ is obtained by hydrothermal reaction of a mixture of 480 mg (2.65 mmol) of 2-aminoterephthalic acid (NH_2-H_2BDC), 4.968 mL (0.994 mmol) of 0.2 M HF, 40 mL of H_2O, and 3.312 mL (1.325 mmol) of 0.4 M $FeCl_3\cdot 6H_2O$. The reaction mixture is heated at 150 °C for two days in an autoclave with a total reaction volume of 100 mL. After the workup, 203 mg (yield: 50%, based on Fe^{3+}) of microcrystalline Fe-MIL-53_NH_2 was obtained (elem anal. found: C, 40.88; H, 2.75; N, 5.99. Calcd: C, 40.77; H, 2.67; N, 5.94). Single crystals were grown from 40 mg (0.221 mmol) of NH_2-H_2BDC, 13.3 mL of H_2O, 1.104 mL (0.221 mmol) of 0.2 M HF, and 0.552 mL (0.221 mmol) of 0.4 M $FeCl_3\cdot 6H_2O$. Reactants were introduced in this order and heated in a stainless steel autoclave (30 mL total volume; 1 week heating to 110 °C, 2 weeks at 110 °C, 1 week cooling to room temperature). The pH before and after the synthesis was 1.

Single crystals were isolated from the reaction mixture and measured at 200 K. The crystal data for Fe-MIL-53_NH_2 are listed in Table 1; atomic coordinates and selected bond distances are given in the Supporting Information (Table S1). The comparison of the experimental and theoretical X-ray diffraction patterns deduced from single-crystal data indicates that this phase is crystalline-pure (Figure S1 in the Supporting Information). As already observed in other isoreticular compounds of MIL-53,[20,39] the pores in as-synthesized Fe-MIL-53_NH_2 are occupied by highly disordered 2-aminoterephthalic acid guests, leading to the chemical composition of $[Fe(OH)NH_2-BDC]\cdot 0.3NH_2-H_2BDC$. The amount of free carboxylic acid is lower than the one observed in the pure terephthalate-based MIL-53 ($M(OH)BDC\cdot 0.75H_2BDC$). As shown by Jacobson et al., the pores

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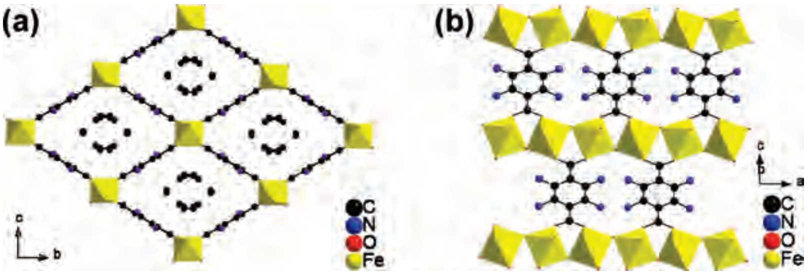

Figure 2. (a) View along and (b) perpendicular to (disordered NH_2-H_2BDC molecules have been omitted for clarity) the pore system in Fe-MIL53_NH_2. The FeO_6 octahedra are presented in yellow.

are in this case filled with chains of hydrogen-bonded H_2BDC molecules, weakly interacting with the hybrid network.[40] The amount of H_2BDC is related to the ratio between the H_2BDC length and the inorganic chain parameter. In our case, the NH_2-H_2BDC molecules may interact with the hybrid network through stronger hydrogen bonds involving the amino group ($N-H\cdots O$ or $O-H\cdots N$ interactions). This may lead to a disruption of the close-packed terephthalic chains, and therefore to a lower amount of guest molecules in the pores. These findings are confirmed by IR spectroscopy and EDX and TG analyses (Figures S2 and S3, Supporting Information).

Crystal Structure of Fe-MIL-53_NH_2, $Fe(OH)NH_2-BDC\cdot 0.3NH_2-H_2BDC$. The three-dimensional framework structure of Fe-MIL-53_NH_2 is built up from chains of corner-sharing Fe(III) octahedra connected by μ_2-OH and carboxylate groups. These chains are connected by aminoterephthalate ions to form a one-dimensional channel system along the *a* axis, occupied with hydrogen-bonded 2-aminoterephthalic acid molecules (Figure 2a). Due to the disorder of the NH_2 groups in the Fe-MIL-53_NH_2 framework, no symmetry reduction occurs (Figure 2b).

Fe-MIL-88B_NH_2, $Fe_3O(solv)_3Cl(NH_2-BDC)_3\cdot m$solv (solv = H_2O, DMF). For the synthesis of $Fe_3O(solv)_3Cl(NH_2-BDC)_3\cdot m$solv (solv = H_2O, DMF) from DMF, typically, 1.0 g (5.52 mmol) of NH_2-H_2BDC is dissolved in 7.5 mL of DMF, and a solution of 2.984 g (11.04 mmol) of $FeCl_3\cdot 6H_2O$ in 7.5 mL of DMF is added. The reaction mixture is heated to 170 °C for 24 h in an autoclave with a total volume of 30 mL. The brown reaction product is filtered off, washed with DMF, and dried at room temperature (yield: 3.59 g, 63.5% based on NH_2-BDC). The Cl^- ions of $Fe_3O(solv)_3Cl(NH_2-BDC)_3\cdot m$solv can be removed by ion exchange. The Br-containing Fe-MIL-88B_NH_2 was obtained by immersing 300 mg of the as-synthesized Cl material in 250 mL of a 1 M aqueous NaBr solution and stirring at room temperature overnight. The product was recovered by filtration, and the exchange procedure was repeated twice. Finally, the product was washed with deionized water, until no Br^- ions could be detected in the filtrate (elem anal. found: C, 28.10; H, 4.16; N, 4.15. Calcd: C, 28.09; H, 3.93; N, 4.10).

Depending on the reaction medium employed and the drying conditions, Fe-MIL-88B_NH_2 exhibits different powder patterns reflecting the high flexibility of the framework.[41] For the unambiguous identification of the different Fe-MIL-88B_NH_2 forms, they must be converted into the water-exchanged form, whose X-ray pattern stays unchanged under an air atmosphere (Figure S4, Supporting Information). Since no single crystals of Fe-MIL-88B_NH_2 could be obtained so far, the structure was refined from laboratory X-ray powder diffraction data collected on the water-and ion-exchanged form. The powder X-ray diffraction pattern of Fe-MIL-88B_NH_2 was collected on a STOE STADI P diffractometer equipped with a linear position sensitive detector using monochromated Cu Kα_1 radiation. The cell parameters and atomic positions of the chromium terephthalate analogue Cr-MIL88B were used as starting parameters for the structure refinement. After a pattern matching was performed with Fullprof2k within the WinPLOTR software package,[42,43] the structure refinement of Fe-MIL-88B_NH_2 proceeded without any difficulties. Successive Fourier differences were performed to locate the bromide ion, the amino group, and the free water molecules present in the pores. The final structure was refined using Fullprof2k employing soft distances and angle constraints. Full details of the structure determination are reported in the Supporting Information. Bond valence calculations confirm the trivalent oxidation state of the iron atoms.[44] The formula deduced from the structure determination for Fe-MIL-88B_NH_2 is $Fe_3O(OH_2)_3BR(NH_2-BDC)_3\cdot 9.5H_2O$. The final agreement factors are satisfactory (Table 2).[45] The corresponding Rietveld plot is shown in Figure S5 and atomic coordinates are given in Table S2 in the Supporting Information. The deduced chemical composition is in agreement with IR spectroscopy and EDX and TG analyses (Figures S3 and S6, Supporting Information).

Table 2. Crystal Data for Fe-MIL-88B_NH_2, $Fe_3O(OH_2)_3Br(NH_2-BDC)_3\cdot 9.5H_2O$

empirical formula	$Fe_3O(OH_2)_3Br[(OOC)_2NH_2-C_6H_3]_3\cdot 9.5\ H_2O$
cryst syst	hexagonal
space group	*P*6$_3$/*mmc* (no. 194)
molar mass [$g\cdot mol^{-1}$]	1025.2
a [Å]	11.108(1)
c [Å]	19.093(1)
V [Å^3]	2040.0(3)
no. of reflns	274
radiation (Cu Kα_1), λ [Å]	1.5406
2θ range [deg]	6−80
R_p	0.229
R_F	0.112
R_{wp}	0.113
R_B	0.103

Crystal Structure of Fe-MIL-88B_NH_2, $Fe_3O(OH_2)_3Br(NH_2-BDC)_3\cdot 9.5H_2O$. Fe-MIL-88B_$NH_2$ is built up from trimers of μ_3-O-bridged Fe(III) octahedra, which are connected by NH_2-BDC molecules. Thus, a 3D framework with cages (Figure 3a) and 1D channels along the *c* axis is formed (Figure 3b). The bromine anions are disordered within the channel system, and H bonds with the amino groups of NH_2-BDC are formed (N−Br distance: 2.72 Å). Two different types of noncoordinating water

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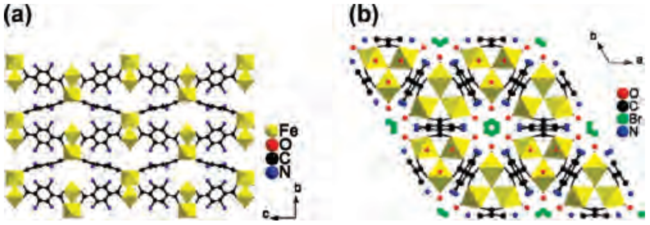

Figure 3. Projection of the structure of Fe-MIL-88B_NH$_2$ (a) along the a axis (Br$^-$ anions and water molecules have been omitted for clarity) and (b) along the c axis. The FeO$_6$ octahedra are presented in yellow.

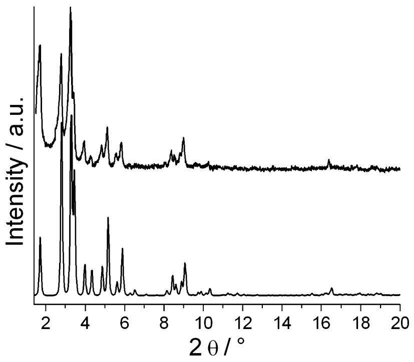

Figure 4. Experimental XRD-powder pattern of Fe-MIL-101_NH$_2$ (top) and theoretical pattern of Cr-MIL-101 (bottom).[19]

molecules are present in the structure. These are located in the cages and the channels, respectively, and are involved in strong H-bonding.

Fe-MIL-101_NH$_2$, Fe$_3$O(solv)$_3$Cl(NH$_2$−BDC)$_3$·$m$solv·$n$guest (solv = H$_2$O, DMF; guest = NH$_2$−H$_2$BDC, HCl). Fe$_3$O(solv)$_3$Cl(NH$_2$−BDC)$_3$·$m$solv·$n$guest (solv = H$_2$O, DMF; guest = NH$_2$−H$_2$BDC, HCl) is typically synthesized from a mixture of 0.225 g (1.242 mmol) of NH$_2$−H$_2$BDC in 7.5 mL of DMF with a solution of 0.675 g (2.497 mmol) of FeCl$_3$·6H$_2$O in 7.5 mL of DMF. After thermal treatment in a stainless steel autoclave (30 mL total volume) for 24 h at 110 °C, the reaction product is recovered by filtration, washed with DMF, and then dried at ambient conditions (0.93 g Fe-MIL-101_NH$_2$; the yield could not be determined due to the large amount of solvents in the highly porous structure). The formation of the MIL-101 structure is confirmed by excellent agreement of the experimental X-ray powder pattern with the theoretical powder pattern of Cr-MIL-101 (Figure 4).[20] EDX analyses of different samples of Fe-MIL-101_NH$_2$ show varying molar ratios of Fe/Cl higher than 1/3, indicating different degrees of protonation of the amino groups. This is due to sample preparation (molar ratios) and the workup procedure. The IR spectrum shows no band due to the presence of free NH$_2$−H$_2$BDC molecules in the pores (Figure S3, Supporting Information).

In order to prove the incorporation of the 2-aminoterephthalic acid into the framework, a sample of Fe-MIL-101_NH$_2$ was hydrolyzed by stirring in 1 M NaOH at 60 °C overnight. The Fe(OH)$_3$ was filtered off, and the yellow solution was acidified with 0.5 M HCl. The recrystallized NH$_2$−H$_2$BDC was characterized by NMR. ^{1}H NMR (400 MHz, DMSO): δ 6.98 (dd, 1H, $^3J = 8.3$ Hz, $^4J = 1.7$ Hz,); 7.31 (d, 1H, $^4J = 1.7$); 7.72 (d, 1H, $^3J = 8.3$). ^{13}C NMR (101 MHz, DMSO): δ 169.51, 167.62, 151.54, 135.63, 131.96, 117.99, 115.23, 113.11.

Results and Discussion

High-Throughput Experimentation. Our high-throughput methodology is based on the 96-well plate format, which allows the parallel study of up to 48 individual reaction mixtures at a time with an individual reaction volume of up to 250 μL.[29] Since the syntheses of MIL-53, MIL-88B, and MIL-101 were carried out under rather dilute conditions, we employed our 24-multiclave with a higher individual reaction volume (up to 2 mL) in order to obtain sufficient amounts of reaction products for the characterization. All high-throughput experiments were carried out in a custom-made 24-reactor system with Teflon inserts and a total volume of 3 mL. The thermal treatment was performed in a convection oven. The reaction products were recovered by filtration, washed with the corresponding reaction medium, and dried at room temperature. In the course of this study, 38 high-throughput experiments comprising a total number of 912 individual reaction mixtures in four different protic as well as aprotic reaction media with varying polarity (methanol, acetonitrile, DMF, and water) were performed. In the following, the influence of the solvent, temperature, molar ratios of starting compounds, and concentration of the reaction mixture as well as the addition of HF or HCl on the product formation in the system FeCl$_3$/NH$_2$−H$_2$BDC/NaOH is discussed. In some cases, due to the poor solubility of NH$_2$−H$_2$BDC in water and acetonitrile, the reaction products contain recrystallized NH$_2$−H$_2$BDC, which for clarity is not shown in the crystallization diagrams. In a typical high-throughput experiment, the molar ratio NH$_2$−H$_2$BDC/FeCl$_3$ was varied from 0.5 to 2 in six steps, and the molar ratio NaOH/FeCl$_3$ was varied from 0 to 1.5 in four steps, leading to 24 different reaction mixtures (i.e., Figure 5a). The results of the high-throughput experiments are based on powder X-ray diffraction and are presented in the crystallization diagrams. The molar ratios and the exact amounts of starting materials for the reported high-throughput experiments are given in the Supporting Information.

Results of the High-Throughput Studies

Acetonitrile as a Reaction Medium. The system FeCl$_3$/NH$_2$−H$_2$BDC/NaOH in acetonitrile was studied in two high-throughput experiments (110 and 160 °C). In addition to Fe-MIL-88B_NH$_2$, an X-ray amorphous product is obtained in some reactions (Figure 5). The system is drastically influenced by the reaction temperature. At 110 °C, MIL-88B crystallizes only in the presence of larger amounts of NaOH, whereas at 160 °C, the reverse situation occurs. A possible explanation of these findings can be provided by looking at the two domains delimited by the bisectrix of the diagram. This line corresponds approximately to a molar ratio of [NaOH/FeCl$_3$]/[NH$_2$−H$_2$BTC/FeCl$_3$] = 1. Thus, it is close to the semineutralization of the acid (i.e., the buffer region) where the molar ratio of (NH$_2$−H$_2$BDC)/(NH$_2$−HBDC$^-$) is around 1. At 110 °C, the crystallization of MIL-88 occurs above this line, and at 160 °C, it is below. At 110 °C, more NaOH is necessary for providing the required amount of aminoterephthalate ions needed for the formation of MIL-88; at 160 °C, such an excess is not necessary. This may relate to the equilibrium of deprotonation of the aminoterephthalic acid ($NH_2{-}H_2BDC \rightleftharpoons NH_2{-}HBDC^- + H^+$). Increasing the reaction temperature or adding a base shifts

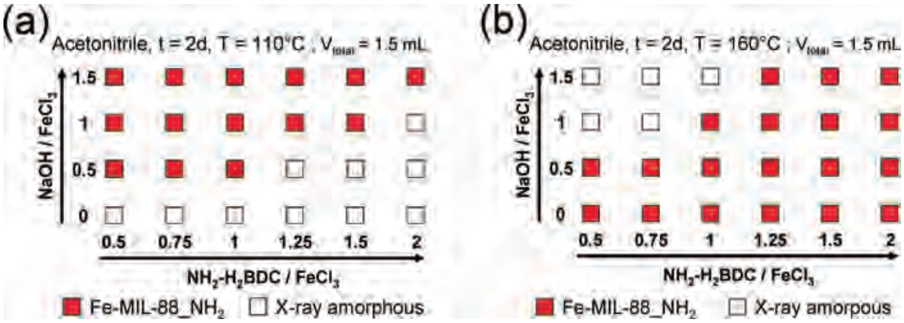

Figure 5. Crystallization diagrams for the high-throughput investigation of the system $FeCl_3/NH_2-H_2BDC/NaOH$ in acetonitrile at 110 °C (a) and 160 °C (b) based on powder XRD measurements.

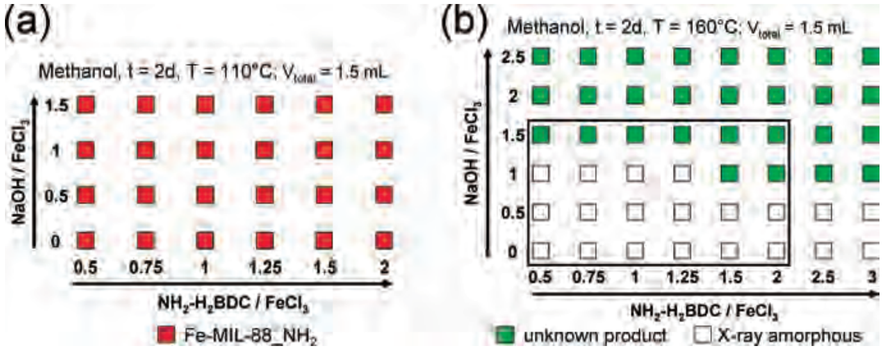

Figure 6. Crystallization diagrams for the high-throughput investigation of the system $FeCl_3/NH_2-H_2BDC/NaOH$ in methanol at 110 °C (a) and 160 °C (b) based on powder XRD measurements. The framed area corresponds to the parameter space investigated in the first high-throughput experiment at 160 °C, and the remaining molar compositions were investigated in an additional experiment.

the equilibrium toward the dissociated products. Thus, at 110 °C, the dissociation is too weak to provide enough anions for the appearance of MIL-88, and NaOH has to be added.

Methanol as a Reaction Medium. Three high-throughput experiments were performed to investigate the system $FeCl_3/NH_2-H_2BDC/NaOH$ in methanol. The first experiment was carried out at 110 °C. The molar composition of the reaction mixtures has no influence on the product formation, and exclusively Fe-MIL-88B_NH$_2$ is observed (Figure 6a). In contrast to the reactions performed in acetonitrile, the increased reaction temperature (160 °C) leads in most cases to an X-ray amorphous product (marked section in Figure 6b). At a molar ratio of $NaOH/FeCl_3 \geq 1.5$, a poorly crystalline phase is observed. EDX, elemental, and thermogravimetric analyses, as well as IR-spectroscopy, indicate that an iron aminoterephthalate with a methanolate group directly present in the framework has been produced (Figure S8, Supporting Information). Jacobson and co-workers reported previously the solvothermal synthesis of an iron terephthalate of a MIL-53 structure type with a bridging DMF group which replaces the OH group from the chains of MIL-53;[46] we therefore propose that our new phase, of composition $Fe(OCH_3)[NH_2-BDC]$, might be related to Fe-MIL-53_NH$_2$. However, due to its low crystallinity, no structural analysis is feasible. Since the phase appears at the boundary of the investigated parameter space, in a third high-throughput experiment, the compositional parameter space was expanded in order to learn more about the unknown compound and, furthermore, to look for additional phases. The reaction trend observed in the previous experiment was verified (Figure 6b), and solids with identical powder patterns corresponding to the assumed iron aminoterephthalate methanolate were obtained.

The drastically different behavior of the reaction system observed by changing the nature of the solvent must be due to the reactive species in solution. At 110 °C, the dissociation of NH_2-H_2BTC in methanol is sufficiently high to lead to the formation of Fe-MIL-88_NH$_2$. At 160 °C, the nature of the solvent leads to a striking difference. Indeed, it is well-known that methanol dissociates ($ROH \rightleftharpoons RO^- + H^+$) under certain conditions. From the present results, it seems clear that such a dissociation occurs at high temperatures. Therefore, a competition arises between the NH_2-BTC^{2-} and RO^- ions regarding the reaction with Fe^{3+}. As RO^- can also act as a strong ligand, its reaction with Fe^{3+} leads to a new solid in which both of the ligands are present. That rules out the existence of the Fe-MIL-88_NH$_2$ at these conditions.

DMF as a Reaction Medium. The complexity of the system increases when DMF is used. Fe-MIL-101_NH$_2$ appears in addition to Fe-MIL-88B_NH$_2$. High-throughput experiments at three different temperatures were carried out (110, 170, and 185 °C; Figure 7). In the absence of NaOH, Fe-MIL-101_NH$_2$ is the only phase formed at temperatures up to 170 °C. It seems that a higher concentration of aminoterephthalate ions favors the formation of Fe-MIL-88B_NH$_2$, while without NaOH, Fe-MIL-101_NH$_2$ is formed. Accordingly, at 185 °C, only Fe-MIL-88B_NH$_2$ is observed.

After the identification of the fields of formation of Fe-MIL-88B_NH$_2$ and Fe-MIL-101_NH$_2$, focused experiments were performed for the scaleup synthesis employing more

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(46) Whitfield, T. R.; Wang, X.; Liu, L.; Jacobson, A. J. *Solid State Sci.* **2005**, *7*, 1096.

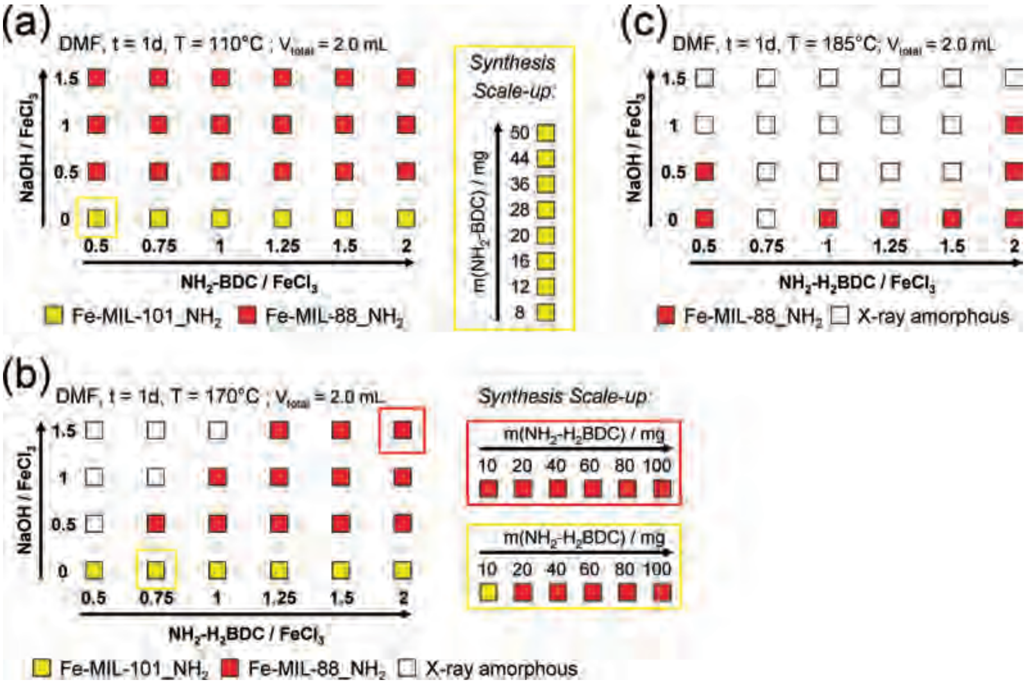

Figure 7. Crystallization diagrams for the high-throughput investigations of the system $FeCl_3/NH_2-H_2BDC/NaOH$ in DMF at 110 °C (a), 170 °C (b), and 185 °C (c) based on powder XRD measurements. The highlighted compositions in the crystallization diagrams refer to the molar ratios realized in the corresponding synthesis scaleup studies.

concentrated reaction mixtures. The two different molar ratios of $NH_2-H_2BDC/FeCl_3/NaOH$ that led to the formation of Fe-MIL-101_NH$_2$ (0.75:1:0) and Fe-MIL-88B_NH$_2$ (2:1:1.5) at 170 °C were chosen, and the overall concentration of the reaction mixtures was varied. This was done using six different amounts of NH_2-BDC (six steps between 10 and 100 mg) in a total volume of 1.5 mL and keeping the molar ratios described above constant. Whereas the synthesis of Fe-MIL-88B_NH$_2$ can be scaled up using more concentrated synthesis mixtures without any obvious change in crystallinity, the study of the synthesis scaleup of Fe-MIL-101_NH$_2$ shows that the desired product can only be obtained at the lowest concentrations. From as little as 20 mg of NH_2-H_2BDC, Fe-MIL-88B_NH$_2$ is formed (Figure 7b, right-hand side). However, Fe-MIL-101_NH$_2$ was successfully synthesized at lower temperatures (110 °C), and no influence of the concentration on the product formation was observed up to 50 mg of NH_2-H_2BDC per 1.5 mL of DMF (Figure 7a, right-hand side). This is in accordance with the concentration changes of NH_2-BDC^{2-} with the temperature and the addition of NaOH.

Water as a Reaction Medium. Water is the only reaction medium in which all three title compounds have been observed. While at 160 °C, only Fe-MIL-53_NH$_2$ is observed (Figure 8a), a decrease of the reaction temperature to 110 °C (Figure 8b) leads under otherwise identical reaction conditions to the formation of Fe-MIL-101_NH$_2$ and Fe-MIL-53_NH$_2$. The former is exclusively observed at low pH, namely, from reaction mixtures with low molar ratios of $NH_2-H_2BDC/FeCl_3$ and $NaOH/FeCl_3$. In contrast to the reactions performed in the other reaction media, the main phase in this system is Fe-MIL-53_NH$_2$.

Since for applications the synthesis of large amounts of Fe-MIL-101_NH$_2$ from water instead of DMF would be advantageous, a high-throughput experiment for the synthesis scaleup was performed. For the molar ratio of $NH_2-H_2BDC/FeCl_3/NaOH$ = 0.5:1:0, the overall concentration was increased in eight steps, referring to an amount of 6−25 mg of NH_2-H_2BDC (1.5 mL total volume of liquid; 110 °C, 1 day). The following conclusions can be drawn from these results: (a) for dilute conditions, a mixture of Fe-MIL-53_NH$_2$ and Fe-MIL-101_NH$_2$ is observed as soon as the amount of the acid is larger than 6 mg; (b) medium concentrations lead to mixtures of all three title compounds MIL-101, MIL-53, and MIL-88; (c) at higher concentrations, like in the case of DMF/170 °C, Fe-MIL-88B_NH$_2$ appears as a pure phase.

Therefore, the effect of the addition of the strong acid HCl on product formation was investigated in a subsequent experiment. The resulting crystallization diagram is shown in Figure 8c. For the reaction mixtures without HCl (bottom row), the results from the first high-throughput experiment (Figure 8b) were basically reproduced. Surprisingly, the addition of HCl leads to a mixture of Fe-MIL-53_NH$_2$ and Fe-MIL-88B_NH$_2$. Finally, at even lower pH, X-ray amorphous solids are isolated.

Finally, the effect of the addition of the weak acid HF, which is well-known to act as a mineralizing agent,[27] was studied at 110 °C (Figure 8d). Here, the fluorine ion has a strong effect on the crystallization process since the addition of HF favors the exclusive formation of Fe-MIL-53_NH$_2$. From previous structural studies, it was known that F^- and OH^- ions participate in a statistical distribution as bridging ligands between two octahedra of the chains of the structure, whereas they are terminal in MIL-88 and MIL-101. In the present system, it seems that the coexistence of the amino groups on the ligand with F^- ions in the solution strongly

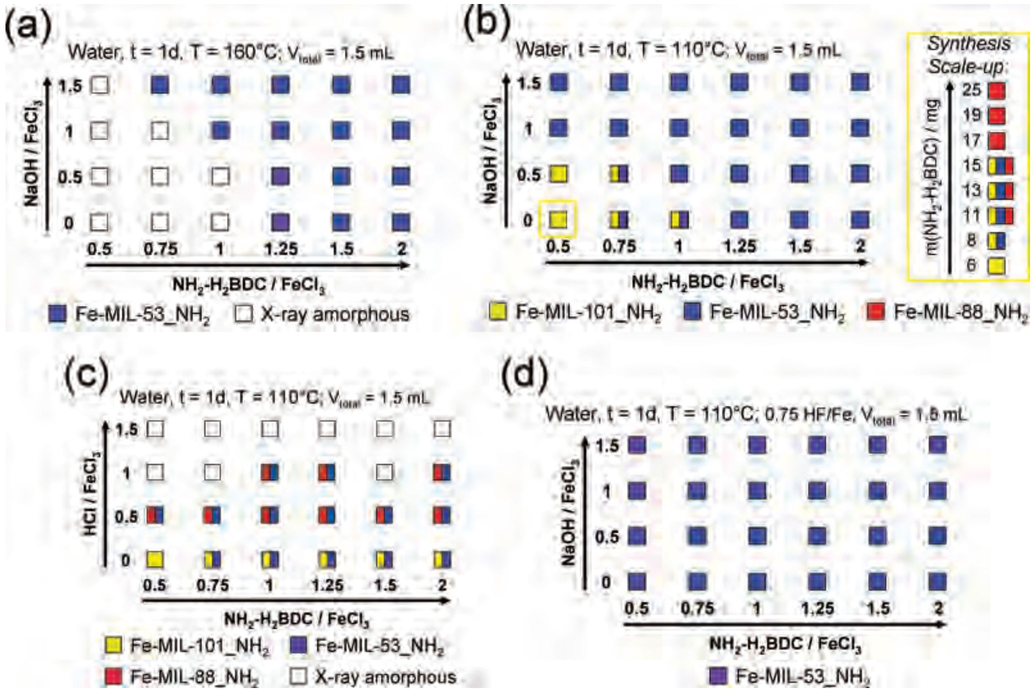

Figure 8. Crystallization diagrams for the high-throughput investigations of the system FeCl$_3$/NH$_2$−H$_2$BDC/NaOH at 160 °C (a) and 110 °C (b) in water. The system FeCl$_3$/NH$_2$−H$_2$BDC/HCl in water was investigated at 110 °C (c). Furthermore, the results of the study of the influence of the addition of HF to the synthesis mixtures are given (d). The highlighted composition in the crystallization diagram (b) refers to the molar ratio employed in the corresponding synthesis scaleup study. All crystallization diagrams are based on powder XRD measurements.

favors a bridging role for the latter and therefore privileges the formation of MIL-53.

Discussion of the High-Throughput Studies. While the synthesis of the Fe-containing MIL-53 and MIL-88 with terephthalic acid has been reported preciously,[40,47] the amino-functionalized compounds were obtained for the first time. With Fe-MIL-101_NH$_2$, an isoreticular MIL-101 compound was obtained which contains a nontoxic metal center. This could have an important impact on the possible application of this highly porous compound. Comparing the large number of results obtained from the high-throughput experiments in the different reaction media, important reaction trends can be deduced. The reaction medium has the most profound impact on product formation, due to solubility, polarity, and acid−base (protolysis) properties. The other important parameter is the reaction temperature.

With acetonitrile, only Fe-MIL-88B_NH$_2$ was observed within the investigated parameters independently of the reaction temperature. Reactions in methanol yield Fe-MIL-88B_NH$_2$ at lower temperatures and an up-to-now unidentified iron aminoterephthalate methanolate at higher temperatures. With DMF as the reaction medium, only structures based on iron trimers, that is, Fe-MIL-88B_NH$_2$ and Fe-MIL-101_NH$_2$, are observed. This fact illustrates the higher stability of the iron trimer in DMF compared with other polar solvents. At higher temperatures, Fe-MIL-88B_NH$_2$ is the stable phase, indicating that it is the thermodynamically stable compound. At lower temperatures, the basicity of the reaction medium seems to be the structure determining factor. The observation that Fe-MIL-53_NH$_2$ is not formed in DMF is supported by the fact that the reaction of as-synthesized Fe-MIL-53_NH$_2$ in DMF (160 °C, 2 d) leads to the formation of Fe-MIL-88B_NH$_2$ (Figure S9, Supporting Information). Fe-MIL-88B_NH$_2$ is also formed upon thermal treatment of a sample of the iron aminoterephthalate methanolate in DMF (160 °C, 2d; Figure S8a, Supporting Information). These results further support the hypothesis that in DMF Fe-MIL-88B_NH$_2$ is the thermodynamically favored phase.

For a better understanding, reactions of amino-terephthalic and terephthalic acid were compared. When iron and terephthalic acid (1,4-H$_2$BDC) are used in DMF, the kinetically and thermodynamically stable phases are MIL-88B, which forms at low temperatures (<100 °C), and MIL-53, which forms at higher temperature (150 °C, Figure S10, Supporting Information). This is in contrast to the amino-terephthalic system where only hybrid phases based on the trimer are formed. Thus, the stability of the phases depends not only on the nature of the solvent, but also on the nature of the organic linker. In DMF, more basic reaction conditions lead only to the formation of MIL-88 structures, both for amino-terephthalic and terephthalic acid. While at low temperatures (T < 100 °C) MIL-88 is formed, at higher temperatures the more basic reaction conditions lead to X-ray amorphous products.

A striking result of the study is the concentration-dependency of the product formation. This parameter is usually not taken into account for the synthesis of hybrid compounds, and to the best of our knowledge this effect has not been systematically investigated before. Thus, in two cases (in H$_2$O at 110 °C and in DMF at 170 °C), for identical process parameters and molar ratios of the starting compounds, the concentration of the reaction mixture determines

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(47) Surblé, S.; Serre, C.; Mellot-Draznieks, C.; Millange, F.; Férey, G. *Chem. Commun.* **2006**, 284.

product formation. Whereas under dilute synthesis conditions Fe-MIL-101_NH_2 is formed, higher concentrations lead to Fe-MIL-88B_NH_2. When H_2O is used at low concentrations, the formation of Fe-MIL-101_NH_2 is in competition with the formation of Fe-MIL-53_NH_2. This might be due to the fact that, in water, Fe-MIL-101_NH_2 is the kinetically favored phase, whereas Fe-MIL-53_NH_2 is the thermodynamically stable compound. This is supported by the fact that, for identical concentrations at higher temperatures, pure Fe-MIL-53_NH_2 is observed. The addition of HF to the synthesis mixture exclusively leads to the formation of Fe-MIL-53_NH_2. Surprisingly, upon acidification by the addition of HCl, the formation of mixtures of Fe-MIL-88B_NH_2 and Fe-MIL-53_NH_2 is observed. This is in contrast to observations in DMF, where the increase of the basicity leads at a given reaction temperature to the formation of Fe-MIL-88B-NH_2. It remains to be explored whether chloride anions can act as a template in the synthesis of Fe-MIL-88B_NH_2.

Conclusion

Using our high-throughput methodology, we synthesized the isoreticular compounds of MIL-53, MIL-88B, and MIL-101 based on 2-aminoterephthalic acid and Fe(III), namely, Fe-MIL53_NH_2, Fe-MIL88B_NH_2, and Fe-MIL101_NH_2, respectively. These compounds are of great interest due to the amino-functionalization of the pore walls. The systematic investigation of parameter space allows for the identification of their fields of formation in different reaction media, and due to the large amount of data, reaction trends could be deduced. While the reaction medium and the reaction temperature play the most important role in product formation, the molar ratio $NH_2-H_2BDC/FeCl_3$ is less important. Remarkably, the overall concentration of the reaction mixture can be a decisive factor for product formation. To the best of our knowledge, such a result is unprecedented for the inorganic−organic hybrid compounds and should be taken into account for the study of other systems. Ongoing research is concerned with the investigation of the reaction time as a variable. Furthermore, the exploration of the properties of the title compounds in terms of inclusion chemistry, gas sorption, and gas storage is in progress, and the results will be published soon.

Supporting Information Available: Atomic coordinates and bond distances for Fe-MIL53_NH_2 and Fe-MIL88B_NH_2. TG curves for Fe-MIL53_NH_2, Fe-MIL88B_NH_2, and Fe-MIL101_NH_2. Powder pattern, IR spectrum, and TG data for the iron aminoterephthalate methanolate. Molar ratios and exact amounts of starting compounds of all high-throughput experiments. This material is available free of charge via the Internet at http://pubs.acs.org. CCDC 647506 (Fe-MIL53_NH_2) and CCDC 647646 (Fe-MIL88B_NH_2) contain the supplementary crystallographic data for this paper. These data can be obtained free of charge from the Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.

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