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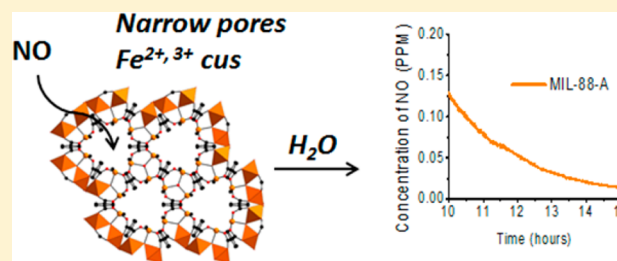
Nitric Oxide Adsorption and Delivery in Flexible MIL-88(Fe) Metal–Organic Frameworks

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S Supporting Information

ABSTRACT: Adsorption and release of the biologically active nitric oxide (NO) was evaluated over a series of highly flexible iron(III) dicarboxylate MOFs of the MIL-88 structure type, bearing fumaric or terephthalic spacer functionalized or not by polar groups (NO₂, 2OH). As evidenced by *ex situ* X-ray powder diffraction and *in situ* IR spectroscopy, it appears that if the contracted dried forms of MIL-88 do not expand their structures in the presence of NO, the combination of very narrow pores and trimers of iron polyhedra leads to the adsorption of significant amounts of NO either physisorbed (very narrow pores) and/or chemisorbed [iron(II) or iron(III) coordinatively unsaturated metal sites (CUS)]. The delivery of NO under vapor of water or in simulated body fluid does not exceed 20% range of the total adsorbed amount probably due to a partial release that occurs between the adsorption/desorption setup and the chemiluminescence release tests. Some of these solids nevertheless exhibit a significant release at the biological levels over a long period of time (>16 h) that make these biocompatible and biodegradable MOFs of interest for the controlled release of NO.

KEYWORDS: nitric oxide, metal organic frameworks, iron carboxylates, flexibility, infrared spectroscopy,



■ INTRODUCTION

Metal–organic frameworks (MOFs) are attracting an ever-increasing interest due to their wide-ranging and sometimes unique properties.^{1,2} MOFs have the potential to be used in many applications from the storage or separation of fluids for environmental benefit to clean energy applications,³ and there is emerging research to show that MOFs could also be used in healthcare.⁴ MOFs are typically constructed from metallic clusters, chains, or layers combined with organic linkers to produce crystalline frameworks that show some of the highest porosities of all known porous solids, together with pore sizes in the range of 0.3 to 6 nm. This combination of high surface area and tunable pore size allows MOFs to be considered ideal for gas storage applications. Indeed, many MOFs have recently been shown to store and release large amounts of gas for a wide variety of applications.⁵ Most MOFs are crystalline solids that are connected by strong metal–ligand bonds, which can confer a rigid structure and often leads to a permanent porosity to the material. However, there are notable exceptions that show breathing-like qualities/properties with frameworks being able to reversibly adapt their pore size according to an external stimulus (pressure, temperature, guest...),⁶ often leading to dramatic effects on adsorption and release properties.⁷ Two

typical examples of highly flexible MOFs are the two series of iron(III) dicarboxylates denoted MIL-88^{8–10} and MIL-53^{11–13} (MIL stands for Materials from Institut Lavoisier). If the impact of flexibility of MIL-53 derivatives,¹⁴ bearing various metals or functional groups, has been so far extensively studied for several applications,¹⁵ then this is not the case for their MIL-88 polymorphs. These solids of general formula M^{III}₃OX(solv)₂{–O₂C–R–CO₂–}₃ (M = Fe or Cr; R = organic spacer; X = F, OH, Cl or –O₂C–CH₃), can be obtained either through a direct solvothermal approach or through a controlled SBU route using preformed trimeric iron acetate [Fe^{III}₃O(OAc)₆] clusters. Their three-dimensional framework is constructed from trimers of oxocentered iron(III) octahedra and dicarboxylate aliphatic or aromatic linkers (Figure 1). This delimits an acs net built up of trigonal bipyramidal cages of trimers between which microporous channels are lying along the *c*-axis (Figure 2). The absence of any linkages between the trimers within the (ab) plane is at the origin of the flexible character of these solids. The unit cell volume undergoes a

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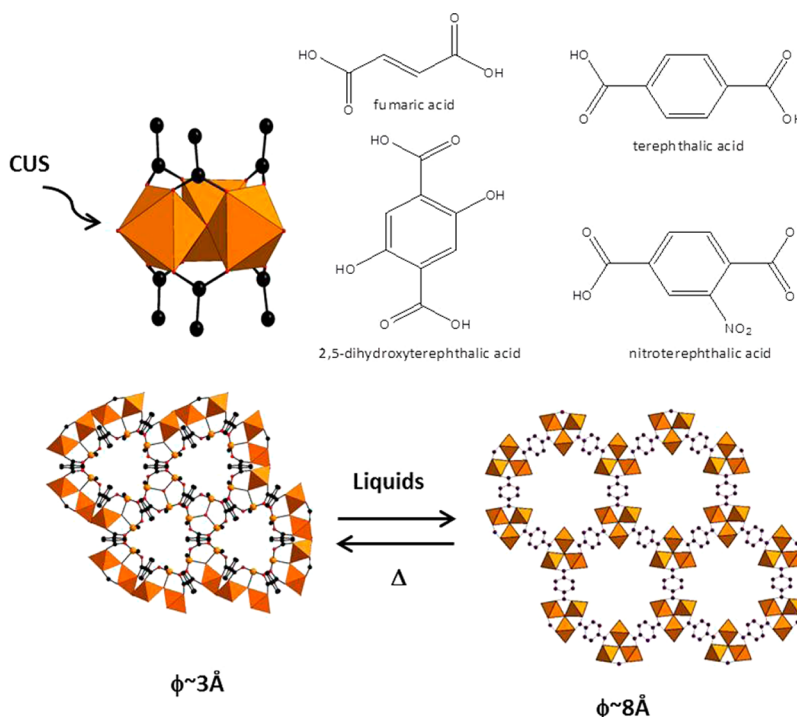


Figure 1. Top: view of the trimers from MIL-88s (left) and the constitutive linkers (right). Bottom: view of the structure of MIL-88B, along the *c* axis, in its dried form (left) and MIL-88B in its open form (right). Metal polyhedra (and iron atoms) and carbon atoms are in orange and black, respectively (hydrogen atoms have been omitted). For a better understanding, iron polyhedra from the inner pores have been represented using ball and sticks mode (note that the position of the OH counteranion could not be determined).

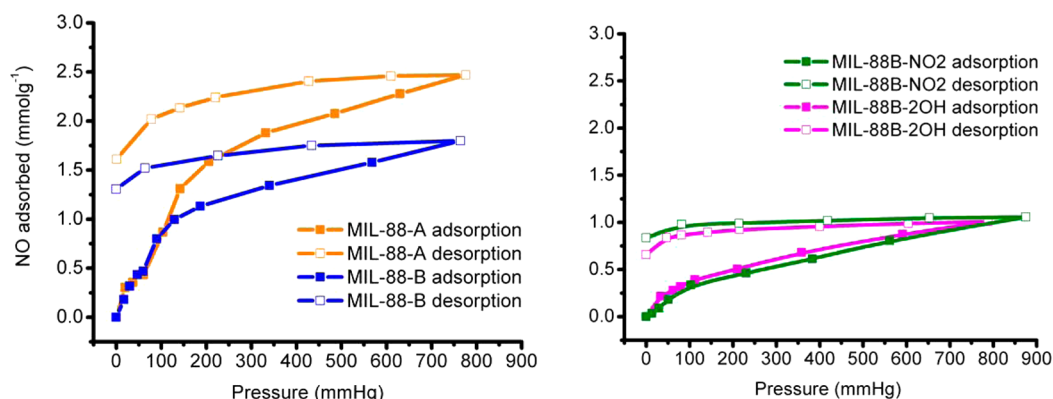


Figure 2. NO adsorption-desorption isotherms at 303 K of selected MIL-88 samples.

reversible expansion from the closed (dehydrated) to the open (fully solvated) forms, with enormous changes in the unit cell volume, from 85% for the iron fumarate MIL-88A(Fe) to more than 230% for the largest analogue chromium 4,4'-benzene dicarboxylate MIL-88D.⁹ As a consequence, the dried forms exhibit very low surface area to nitrogen at 77 K. By introducing functional groups, it is nevertheless possible to lower the intraframework interactions and allow a significant adsorption of guest species and with this tuning, make easier the breathing behavior.¹⁶ However, systematic studies of the sorption properties of these solids are still very scarce, being only related to the liquid phase selective reopening of the pores.¹⁰

Biomedical applications on MOFs can be placed into two categories. The first one consists of using MOFs themselves as active materials either based on bioactive cations such as Gd, Mn, or Fe (well-known for their interesting imaging properties)^{17,18} or therapeutically active linkers.¹⁹ The second method

involves using the MOF porosity as a storage medium for the delivery of appropriate therapeutic agents such as drugs^{4,21,22} or biologically active gases (NO, CO, H₂S, ...).^{23,24}

Recently, there has been increased interest in nitric oxide (NO) gas since it was discovered to play an important role in the regulation of various parts of the body, including cardiovascular, nervous, and immune systems.²⁵ Therefore, delivery of biologically significant amounts of this gas would be attractive for many *in vitro* and *in vivo* applications, including wound healing, antithrombotic, and antibiotic-based remedies.^{26,27} Due to the nature of NO, release from a material would cause only local effects (not systemic), which is an advantage due to the reduction of unwanted side effects.^{27b} Over recent years, there have been ever-increasing efforts to produce NO-releasing materials, such as polymers,^{28–31} functionalized silica nanoparticles,^{32,33} and zeolites,^{34,35} all dispensing different amounts of NO and at different rates.

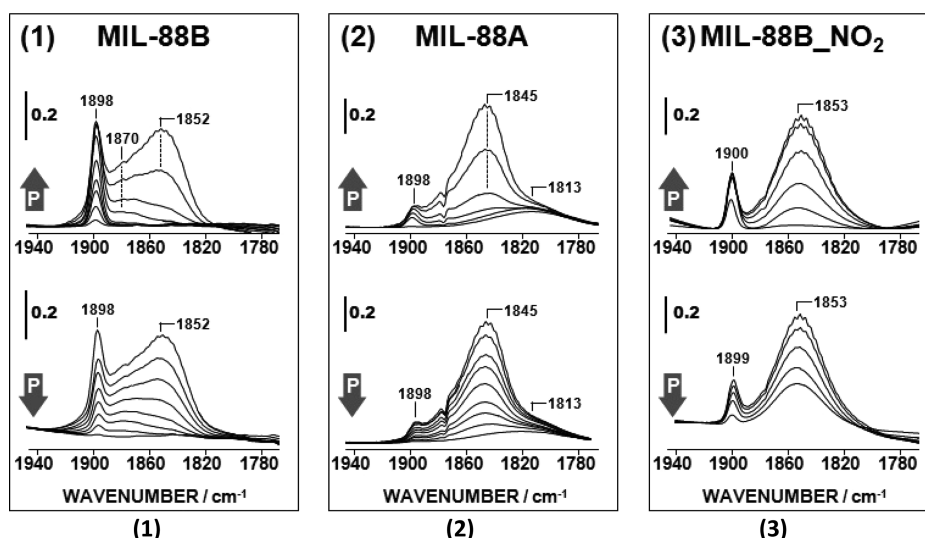


Figure 3. IR spectra of NO adsorbed at 298 K on (1) MIL-88B; (2) MIL-88A; (3) MIL-88B-NO₂ (previously activated at 423 K for 3 h under secondary vacuum). Upper part: adsorption; lower part: desorption.

Obviously, before any material is used for healthcare/medicinal purposes, it has to be thoroughly tested in terms of toxicology and stability. So far, most results dealing with the use of MOFs for the delivery of NO have dealt with Ni-, Co-, and Cu-based MOFs,^{23,24} which are generally thought of as toxic metals (although one must remember that the NO is likely to be the most toxic species present). However, recent toxicology studies have shown no detrimental effect resulting from the *in vivo* intravenous administration of high doses of nanoparticles of several iron polycarboxylate MOFs bearing different linkers.^{4,36} It is noteworthy that two of these solids correspond to the hydrophilic iron fumarate MIL-88A and the hydrophobic iron tetramethylterephthalate MIL-88B(Fe)-4CH₃. Thus, compositions and biodegradability of the MIL-88(Fe) structures seem favorable in terms of toxicology as they contain iron as the metal source, which is substantially less toxic when compared to some of the other metals in MOFs studied for NO applications so far (e.g., cobalt). Actually, current prescribed medicines that have the same chemical composition as MOFs have been approved for medical use. For example, an iron fumarate (i.e., same composition as MIL-88A(Fe)) has been approved as an oral iron supplement (trade name Ferrets).

In addition, it appears that trimer-based Cr or Fe MOFs such as MIL-100, MIL-101, or MIL-126, rigid micro- or mesoporous MOFs with large pore volumes and high surface areas, can reversibly coordinate polar or quadrupolar small gas molecules such as CO or CO₂.³² Thus, one can expect that all trimer based polycarboxylate MOFs possess similar accessible Lewis acid sites. In the case of iron trimers MOFs, another interesting property lies in the controlled reducibility of part of the iron(III) centers into Fe(II) CUS, which is also highly in favor of stronger interactions with unsaturated molecules through a back-donation effect.³⁷ Thus, following our recent demonstrations of potential NO storage and release from various rigid MOFs,^{23,24} we describe here the adsorption and release of biologically active NO from a series of iron based MIL-88(Fe) solids, bearing or not functional groups, combined to an *ex situ* XRPD analysis of some of the NO loaded samples as well as an investigation into the way in which NO interacts with the Fe atom in these MOFs using *in situ* IR studies.

RESULTS

A series of Fe-based MIL-88A, MIL-88B, MIL-88B-NO₂, and MIL-88B-2OH solids were synthesized at the gram scale and fully characterized (see Supporting Information, SI)¹⁶ before any adsorption experiments were carried out. Figure 1 shows the structure of both MIL-88A and MIL-88B (excluding guest solvent molecules). If the MIL-88 solids do not exhibit any significant BET surface area in presence of nitrogen (77K), when functional groups are however grafted, this partially decreases the extent of pore contraction, leading to a progressive increase in the accessible pore size, and thus surface area.¹⁶

Prior to the adsorption of nitric oxide, the sorption properties of MIL-88s in the presence of simple gases (CO₂ and CH₄) were investigated at high pressure at room temperature on MIL-88A(Fe) and MIL-88D(Cr) solids. It appears (Figure S1 of the SI) that only very limited amounts of gases are adsorbed in both cases, with however a higher amount for the larger analogue MIL-88D. This clearly suggests that adsorption occurs probably only within the very narrow pores of the dried forms with almost no breathing of the framework. Unlike its MIL-53 polymorphs wherein intraframework ligand interactions occur between consecutive dicarboxylate linker (dimers), trimers of organic spacers are present within the framework of MIL-88s solids that would render more difficult the pore opening from an energy point of view, particularly for small gas molecules that weakly interact with the pore walls.

Adsorption–Desorption of NO. The MIL-88 compounds were in a second step subjected to NO gravimetric adsorption measurements (see SI). MIL-88 solids were outgassed at 150 °C under primary vacuum (except for the less stable MIL-88B-2OH at 80 °C). MIL-88A shows a ~33% drop in mass before exposure to NO, which correlates well with thermogravimetric analysis (TGA; Figure S3 of the SI), where a plateau after 150 °C indicates that all guest solvent molecules (including bound species) are removed. The remaining MIL-88 compounds showed on the whole similar behavior, indicating that all solvent molecules were removed prior to NO adsorption. NO adsorption isotherms can be seen in Figure 2. MIL-88A adsorbed the largest amount of NO, 2.5 mmol·g⁻¹, followed by

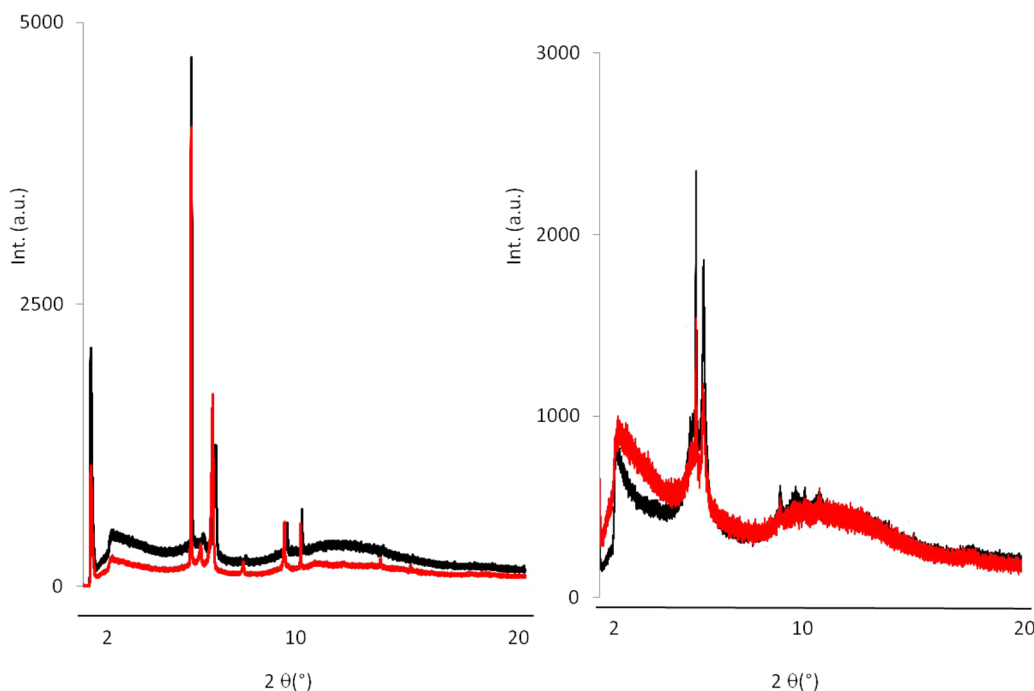


Figure 4. XRPD of MIL-88B-NO₂ (left) and MIL-88B-2OH (right) at 303 K before (black) and after (red) adsorption of NO ($\lambda \approx 0.827439$ Å).

MIL-88B at ~ 1.6 mmol·g⁻¹, and the functionalized MIL-88Bs both at ~ 1 mmol·g⁻¹.

Nonetheless, the shape of all of the adsorption isotherms is in agreement with compounds not fully saturated with NO. In addition, our equipment only measures up to 2 atm of NO for safety reasons, which would explain this phenomenon.

In the curves for MIL-88A and B, a jump can be observed between 50 and 100 mmHg, which could be due to a “gate opening” effect,⁵ possible for flexible structures and known for MIL-88 type structures which exhibit closed pores, i.e., with free aperture around 3 Å upon thermal activation. The desorption curve of the isotherm shows a large hysteresis, which would be consistent with the free release of physisorbed NO, demonstrated in previous NO studies,^{24,25} and the binding of NO chemisorbed to open iron accessible metal sites. The amount of adsorbed NO is lower than that of the exceptional storage capacity of the CPO-27 materials (up to 7 mmol·g⁻¹).¹² Nonetheless, it is still comparable to that of Zn-Zeolite A, which adsorbs ~ 1.5 mmol·g⁻¹ of NO.³⁰

Infrared Spectroscopy. In order to get some insight on the adsorption sites of NO within these iron carboxylate MOFs, *in situ* infrared (IR) spectroscopy under different NO pressure have been monitored. The IR spectra of the different MIL-88 solids have been recorded after introduction of increasing pressure of NO into the IR cell at 298 K, from 1 to 760 mmHg (Figures 3 and 4). As expected, adsorbed NO gives rise to $\nu(\text{NO})$ bands below 1900 cm⁻¹. For instance, the spectra of MIL-88B after introduction of the first doses ($P = 1$ to 50 Torr) display a $\nu(\text{NO})$ at 1898 cm⁻¹ which is pressure-dependent (Figure 3). This band is assigned to Fe³⁺: NO species formed by NO interacting with Fe³⁺CUS (CUS: Coordinatively Unsaturated metal Sites).³⁷ At higher pressure, a second and broader band develops at 1870 cm⁻¹ and then a third one occurs, centered at 1852 cm⁻¹. Desorption experiments show that the band at 1852 cm⁻¹ is the first one to disappear, and can be assigned to physisorbed NO species. This is followed by the decrease of the band intensity at 1870 and 1898 cm⁻¹.

Concerning the 1870 cm⁻¹ band, it appears only when the intensity of the 1898 cm⁻¹ band is strong. Therefore, it could involve coordination on Fe³⁺ sites, a possibility being the formation of Fe³⁺: ON species.³⁸

A similar behavior is observed for the modified MIL-88-NO₂ solid. The first $\nu(\text{NO})$ band lies at 1900 cm⁻¹, corresponding once again to NO coordinated on Fe³⁺ CUS, followed by another one at 1853 cm⁻¹ which becomes rather strong at higher pressure [Figure 3(3)]. This latter band is less sensitive to the desorption step, compared to the case of MIL-88 A and MIL-88B, since it is well detected even after evacuation during 30 min.

Concerning MIL-88A, most of the NO is physisorbed since the band at about 1900 cm⁻¹ is weak [Figure 4(2)]. However, one can observe right after the first NO dose the appearance of a broad weak band at 1800 cm⁻¹ which persist under vacuum. To assign such a band, an experiment has been performed on MIL-88B-2OH activated at 150 °C, temperature for which reduction of Fe³⁺ into Fe²⁺ occurs as shown by Mössbauer experiments [to be published]. NO adsorption leads then to one band at 1800 cm⁻¹ whose intensity is hardly affected by evacuation (Figure S3 of the SI). It characterizes NO adsorption on Fe²⁺ CUS. Note that the experimental conditions used for the determination through chemiluminescence of adsorption–desorption isotherms are different, with an activation at 353 K overnight under primary vacuum of MIL-88B-2OH, since trials performed at 423 K led to the destruction of the unstable sample, instead of 423 K and secondary vacuum during a few hours for the IR analysis. Such discrepancies make thus less exploitable any comparison of both adsorption and desorption results using these two different techniques.

One could mention in the case of MIL-88B and MIL-88B-NO₂ that no interaction with Fe²⁺ CUS are observed, which indicates that at 150 °C under secondary vacuum, no reduction of iron(III) CUS has started.

Table 1. Comparison of Theoretical and Experimental (Chemiluminescence) Amount of Adsorbed NO in Various MIL-88 Materials (The Anions Considered for the Calculation Are OH Groups)

solids	theoretical number of CUS per trimer ^a (2 CUS per trimers)	total amount of adsorbed NO ^a (gravimetry)	amount of NO adsorbed on CUS Fe ³⁺ (IR measurements) ^a	total release of NO (wet gas) ^a	total release of NO (PBS) ^a
MIL-88-A	3.8	2.5	0.06	0.12	0.30
MIL-88-B	3	1.6	0.2	0	0
MIL-88-B-NO ₂	2.5	1	0.18	0.14	
MIL-88-B-2OH	2.6	1		0.12	0.13

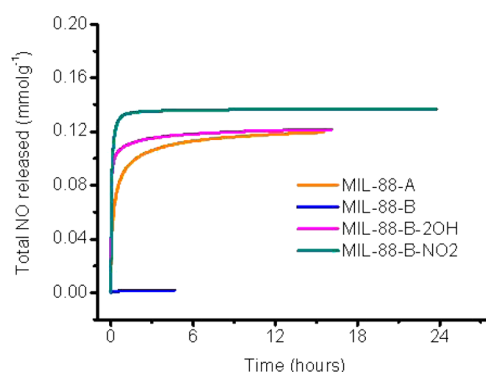
^aexpressed in mmol per gram of solid.

Besides, considering that the molar absorption coefficient of the $\nu(\text{NO})$ band at 1898 cm^{-1} of $\text{NO}:\text{Fe}^{3+}$ species is equal to $3.5\text{ cm}^2\text{ mol}^{-1}$,³⁹ one can roughly estimate the number of Fe^{3+} sites accessible to NO under $P_{\text{NO}} = 1\text{ bar}$ or 760 mmHg . Noteworthy, this gives values equal to 0.2, 0.18, and 0.065 mmol g^{-1} in the case of MIL-88B, MIL-88B-NO₂, and MIL-88A, respectively (Table 1).

XRPD Analysis. To get some insights on the consequences of NO adsorption on the breathing of MIL-88's samples, *ex situ* XRPD analysis of the MIL-88B-NO₂ and MIL-88B-2OH samples loaded with NO were carried out using Synchrotron radiation facility. It appears (Figure 4) that very limited breathing of the structure occurs upon exposure to NO. The Bragg peaks positions are almost identical as the one of the dried samples. However, one can clearly see significant changes in their relative intensity, particularly for the main Bragg peaks at low angle. This is in agreement with the adsorption of NO molecules without however any pore expansion and also corresponds on the whole to the amount of CO₂ adsorbed at room temperature but at higher pressures; NO usually interacts with unsaturated metal sites on a much pronounced manner than CO₂ and thus is adsorbed at much lower pressure than CO₂. As a confirmation, *in situ* IR NO adsorption experiments reveal, through the comparison of the spectra of the different MIL-88 material under various NO pressures, no shift of skeletal bands occurs whatever the NO pressure introduced, in particular those due to carboxylate groups or benzene rings, sensitive to the pore opening.²⁰

Release of NO. As previously mentioned, it is not only the amount of adsorbed gas that is important for particular biological applications relating to NO, but also the amount released and the duration of that release which determines if individual MOFs are suitable for further investigation. As such, release experiments were carried out on the MIL-88 compounds to determine if the NO stored in the framework could be completely released using moisture (H₂O vapor) as a trigger. Following the same activation procedure as mentioned above, the NO-loaded samples were stored under a dry atmosphere before being placed in the sample holder. Once exposed to the "wet gas" of the apparatus, the water molecule should replace the NO on each Fe atom, and the NO should be released and quantifiably calculated using the intensity of chemiluminescence on reaction of ozone with released NO (see SI).

Figures 5 and 6 show the concentration release profile and the total amount of NO released from the MIL-88 compounds. Except for the MIL-88B solid, the graphs show that the vast majority of the NO is released within the first hour of the experiment. Very small amounts of NO were however released from the MIL-88B.

**Figure 5.** Total NO release from MIL-88 samples exposed to wet nitrogen ($T = 303\text{ K}$).

Nonetheless, the compounds are still releasing biologically significant quantities (10 parts per billion (ppb)) of NO up to 16 h after starting (in the case of MIL-88A). Ultimately, the compounds are releasing values of NO that are 1 order of magnitude lower than the amount initially adsorbed. Note that a similar behavior has been previously observed in HKUST-1 (a Cu-based MOF), where the framework adsorbed 3 mmol g^{-1} but only released 2 μmol of NO per g of sample.²⁴

The flowing gas technique is useful as a guide for the amount of NO released in medical situations with minimal water presence, for example applying an NO-loaded MOF to the skin. However, for antithrombotic or antibiotic systemic used, NO will be released under serum conditions. For this experiment, MIL-88s were loaded in the same manner as before but, in addition to the wet gas, the sample was also exposed to phosphate buffered saline (PBS 0.02 M at $\text{pH} = 7.4$, $37\text{ }^{\circ}\text{C}$ or 310 K), which mimics physiological solutions and leads, as shown previously for MIL-88A and MIL-100, to a progressive full degradation of all the iron(III) polycarboxylate MOFs.³⁶ As expected, the NO is released far quicker in solution compared to the wet gas (Figures 6 and 7), as the water molecules should immediately remove all of the NO molecules attached to the iron metal sites. These results indicate that, again, not all of the adsorbed NO is released, even when exposed to a solution even if, in the case of MIL-88A a significant improvement of total amount of NO released. Figure 8 shows that MIL-88A releases 0.3 mmol g^{-1} of NO under buffer conditions, whereas it only releases 0.12 mmol g^{-1} when the wet gas is used. The materials are still releasing biologically relevant amounts of gas after more than 24 h. Increases are also seen for the other MIL-88 compounds.

DISCUSSION

MIL-88 solids possess a high theoretical number of metal sites due to their oxocentered trimers of iron(III) octahedra building

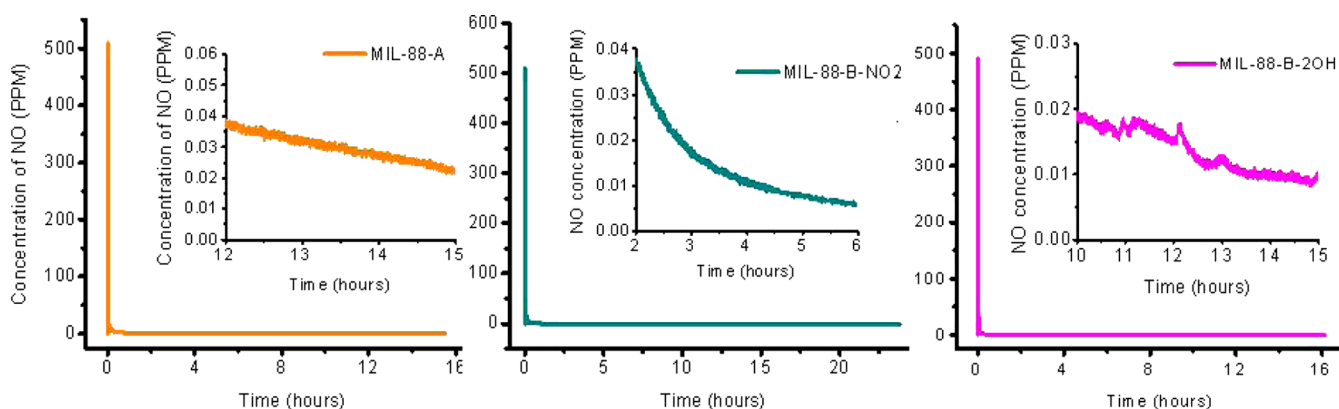


Figure 6. Kinetics of release at 298 K under wet gas of NO from the MIL-88s samples. Insets have been included to highlight the delivery at biological levels of the samples.

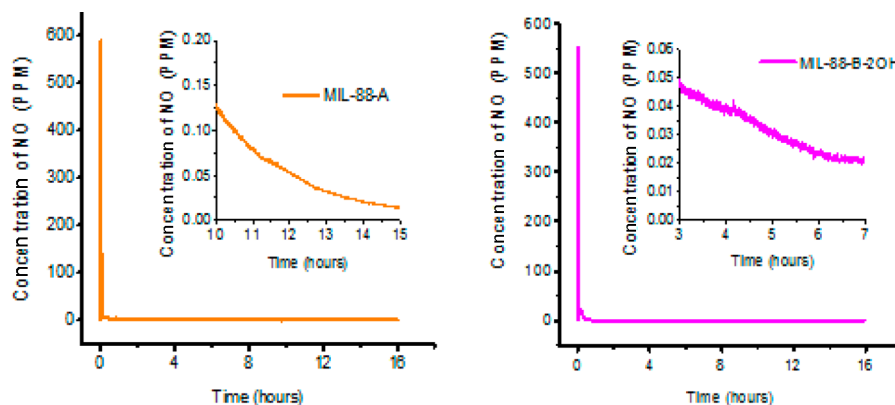


Figure 7. Kinetics of release at 298 K of NO from selected MIL-88s samples immersed in PBS. Insets have been included to highlight the delivery at biological levels of the samples.

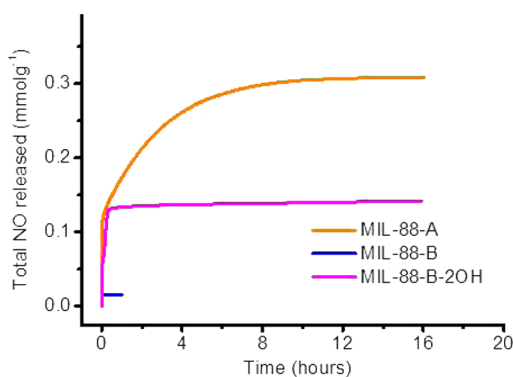


Figure 8. Total NO release at 310 K from MIL-88 samples dispersed in PBS.

units. IR experiments show that the activation mode used for the samples leads to a full removal of the free water molecules, as well as the coordinated water, leaving the dehydrated structure and CUS allowing the NO binding. IR spectroscopy has evidenced the coordinatively unsaturated Fe^{3+} or Fe^{2+} CUS³⁶ as the preferential binding sites for NO during adsorption studies. If one considers previous results obtained with MIL-100(Cr) and MIL-100(Fe), then only two iron atoms per trimer exhibit accessible metal sites, the third iron atom being coordinated with the anion (OH, Cl, acetate...), this would give a theoretical amount of iron CUS of 3.8, 3.0, 2.6, and 2.5 $\text{mmol} \cdot \text{g}^{-1}$ for respectively MIL-88A, MIL-88B, MIL-

88B-2OH, and MIL-88B- NO_2 . The lower obtained NO loading capacities (Table 1) are far below from the theoretical values. In particular, the *in situ* IR experiments indicate that the adsorbed amounts of NO on Fe^{3+} CUS are significantly lower than the theoretical values (Table 1). The total amount of adsorbed NO determined by gravimetry is much higher than that of NO coordinated on Fe^{3+} CUS, concluding therefore that a large amount of NO is physisorbed. *Ex situ* XRPD analysis reveals that NO adsorption occurs without any pore expansion. Therefore, considering the fact that the MIL-88 samples chosen here exhibit closed pores after dehydration (which leads to very narrow pores), one can estimate that NO diffuses hardly within the very narrow pores to bind on the strongest sites, i.e., the Lewis acid sites. Furthermore, due to this contraction, a fraction of the iron CUS is probably not accessible to NO, in agreement with the lower NO adsorbed amount detected by IR. One cannot also exclude the presence of chemisorbed or physisorbed NO at the external surface of the particles, associated to the absence of pore opening under NO atmosphere.

The comparison between the NO adsorption and desorption by IR experiments shows a different behavior. During the adsorption step, NO preferentially adsorbs on Fe^{3+} (or Fe^{2+}) CUS and then physisorption occurs. Upon the desorption steps, both species desorb simultaneously, whereas Fe^{3+} (or Fe^{2+}): NO species are expected to be the more stable and therefore being desorbed later. This result suggests that Fe^{3+} (or Fe^{2+}) species are more accessible to NO molecules

(external surface or entrance of the pores), whereas NO physisorption would rather occur inside the narrow pores, in agreement with the narrow porosity of MIL-88 solids (diffusion effect).¹⁶

Therefore, both a full degree of chemisorption and increased physisorption could be achieved by using functionalized MIL-88 solids that bear bulkier groups (CH_3 , 2CH_3 , 4CH_3 , or 2CF_3)¹⁶ in order to make diffusion of NO easier within the pores. An obvious alternative would also be to consider the use of porous rigid Fe trimer based MOFs. However, such simple, biocompatible, biodegradable and cheap MIL-88 solids are still of interest due to their important and controlled release at the biologically relevant level.

IR results concerning the NO adsorption on the partially reduced MIL-88-2OH sample show that NO strongly adsorbs on Fe^{2+} CUS (Figure S4 of the SI). Figure 2 relative to MIL-88A presenting a weak amount of both Fe^{2+} and Fe^{3+} CUS shows a preferential NO adsorption on Fe^{2+} leading to coordinated species, which persist even after long evacuation under secondary vacuum. This suggests that in order to increase the amount of strongly bounded NO, it would be worth trying to obtain a higher amount of $\text{Fe}(\text{II})$ CUS. Such materials have recently been synthesized.³⁷

One should point out that there is a much lower amount of NO released, observed by chemiluminescence after storage, compared to the total experimental value. Under wet atmosphere, MIL-88A releases indeed only about 5% of the total amount adsorbed, while MIL-88B- NO_2 and MIL-88B-2OH both release about 14% of the total adsorbed NO. IR spectroscopy results lead however to values, for the NO bounded to the Fe CUS, closer to those deduced from the release tests (chemiluminescence). Thus, even if one cannot exclude that the frameworks retain a large portion of the NO (i.e., water does not compete for bound NO completely), it is likely that only the strongest adsorbed NO (chemisorbed or physisorbed) NO is observed during the chemiluminescence tests, the less strongly physisorbed one being lost prior to the release tests. This is confirmed by the higher but still very low released NO (in comparison with the adsorbed capacity) in presence of PBS solution, phosphate groups competing by the iron CUS coordination.

The absence of NO release from MIL-88B in the presence of either water flow or PBS suggests a full desorption of the NO before the release tests, as supported by IR NO desorption experiments in which physi- and chemisorbed NO molecules are released almost simultaneously.

CONCLUSION

Significant amounts of the biologically active gas NO can be adsorbed at room temperature from a series of nontoxic and biodegradable highly flexible iron(III) dicarboxylate MIL-88 samples. Loading capacities, which are lying within the 1–2.5 $\text{mmol}\cdot\text{g}^{-1}$ range, are far below the theoretical values (2.5–3.6 $\text{mmol}\cdot\text{g}^{-1}$; Table 1). This is mainly due to the low accessibility of the pores due to the absence of any breathing of the structure under such conditions which then remain closed, preventing NO to diffuse easily within the pores and bind to the accessible iron metal sites. IR spectroscopy shows that NO either chemisorbs on Fe^{3+} or Fe^{2+} CUS, depending on their availability or accessibility, as well as physisorbs within the very narrow accessible pore volume.

Release amounts, either in the presence of wet gas or in simulated body fluid (PBS), are even lower, close to a few tenth

of a $\text{mmol}\cdot\text{g}^{-1}$, which is probably due to desorption of physisorbed NO prior to the release tests, but still sufficient enough to ensure a significant release at the biological level over prolonged periods of time.

Finally, MOFs have already been tested for use in NO therapies, but they are typically composed of relatively toxic metals (e.g., Co, Ni, Cu) that could pose a hazard due to leaching or degradation of the framework. Since iron is much less toxic compared to other metals, the MIL-88 solids would be more ideally suited for such applications.

Other iron MOFs are currently being under investigation for an optimization for this NO controlled release application.

ASSOCIATED CONTENT

Supporting Information

Absorption/desorption experiments; CO_2 and CH_4 high pressure excess adsorption isotherms of MIL-88A and MIL-88D at 303 K (Figure S1); XRPD patterns of MIL-88 samples (Figure S2); TGA under air atmosphere of MIL-88 samples (Figure S3); IR spectra of NO adsorbed at 298 K on MIL-2OH (Figure S4); and complete references (PDF). This material is available free of charge via the Internet at <http://pubs.acs.org>.

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Notes

The authors declare no competing financial interest.

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