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Heating and separation using nanomagnet-functionalized metal–organic frameworks†

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A magnetic functionalization of microcrystalline MOF particles was realized using magnetic iron oxide particles. Such magnetic MOFs can be separated using a static magnetic field after use in catalytic processes and heated by an external alternating magnetic field to trigger desorption of encaged drug molecules.

Porous metal–organic frameworks (MOFs) have gained considerable attention particularly in the last decade.¹ The modular building concept allows the creation of porous networks with specific surface areas unattained by traditional adsorbents, adjustable pore size, and surface functionality, leading to a wide variety of possible applications in gas storage,² separation,³ and heterogeneous catalysis.⁴

A key challenge for the design of advanced adsorbents is to introduce functional modules for *in vivo* detection, magnetically controlled movement, or external control of the adsorption capacity. Pressure induced gate opening due to structural transformations is an impressive step towards externally triggered adsorption phenomena in gate pressure MOFs.⁵ Quite recently the optically induced pore opening was proposed⁶ and the influence of a static magnetic field on the adsorption properties and crystallization of MOFs was studied *in situ*.⁷ However, the external manipulation of MOFs remains a challenge.

For magnetic manipulation, the use of intrinsic magnetic MOF properties seems limited due to the limited cooperative interactions in inorganic–organic networks. In the following we propose the integration of superparamagnetic functionality into MOF composites using iron oxide nanoparticles. Owing to a high magnetization, superparamagnetic functionalization enables rapid separation of the MOF catalyst from the reaction media in a static magnetic field, while in the absence of an external field no aggregation of the MOF composites is

observed due to zero magnetization. Hence another potential use for those magnetically functionalized, highly porous systems emerges. MOFs have been shown to be promising candidates for drug-delivery applications.⁸ Since superparamagnetic nanoparticles heat up in an alternating magnetic field,⁹ our magnetic functionalization approach allows to heat up the adsorbent and thus causes an externally triggered burst release. In consequence of the good dispersibility, magnetically functionalized MOFs allow for the combination of high drug loading capacities with a trigger mechanism which is easily activated from outside the organism.

Three MOFs, namely AlOH(ndc) (DUT-4), AlOH(bpdc) (DUT-5) and Cu₃(btc)₂ (HKUST-1), have been functionalized as model systems with superparamagnetic magnetite particles. The known affinity between magnetite surfaces and carboxylate groups¹⁰ of organic linker molecules is thereby used to stabilize magnetic nanoparticles against agglomeration. Additionally the coated particles are surface-activated and can act as seeds for the growth of metal–organic frameworks. Uncapped iron oxide nanoparticles have been prepared *via* a slightly modified coprecipitation procedure described in the literature.¹¹ The Al-based MOFs and the Cu₃(btc)₂ have been prepared according to methods developed recently,¹² magnetic functionalization was thereby achieved through the heteronucleation of the porous networks on the outer surface of the magnetic nanoparticles resulting in products entitled as M-DUT-4, M-DUT-5 and M-HKUST-1. Due to the rapid MOF particle growth, the magnetic nanoparticles are in this way embedded into polycrystalline MOF aggregates without altering their magnetic properties but forming a strong interaction between the two functional components. Fig. 1 shows that under the given reaction conditions a homogeneous green magnetic product is obtained in the case of M-HKUST-1 (light brown in the case of the Al-MOFs) consisting of crystalline Cu₃(btc)₂ and γ -Fe₂O₃ (maghemite) particles. The amount of magnetic particles in the composite can be adjusted by using different volumes of magnetite dispersion and ranges between 5 and 15 wt% for the prepared samples according to elemental analyses. Magnetic measurements show that superparamagnetism of the utilized magnetic particles is retained for the composite materials (see Fig. S4, ESI†). Superparamagnetism is crucial for biomedical applications, since a residual magnetization leads to aggregation and consequently to the formation of embolisms in the blood

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Fig. 1 X-Ray powder diffraction pattern of a magnetically functionalized $\text{Cu}_3(\text{btc})_2$ sample. The inset shows a photograph of M-HKUST-1 powder held by a small permanent magnet.

vessels. The specific surface areas of the magnetically functionalized MOFs were determined from nitrogen physisorption measurements at 77 K. High BET-surface areas of $1394 \text{ m}^2 \text{ g}^{-1}$, $1346 \text{ m}^2 \text{ g}^{-1}$ and $1248 \text{ m}^2 \text{ g}^{-1}$ are calculated for M-HKUST-1, M-DUT-4 and M-DUT-5, respectively. These values are only slightly below the literature data for the pure MOF materials. Additionally, the adsorption behavior at low pressures down to 10^{-6} atm was compared for M-DUT-4 and a pristine DUT-4 sample, showing only minor differences. Thus, it is clearly shown that the magnetic functionalization did not have an effect on the adsorption behavior besides a slightly lower specific surface area due to the incorporation of nonporous, nanoparticles with higher density (see inset, Fig. S5, ESI†). In addition, SEM micrographs of the samples show no change in the morphology of the MOFs after addition of magnetic nanoparticles to the reaction media as can be seen for (M-)HKUST-1 in Fig. 2a and b (Al-based MOFs see Fig. S6 and S7, ESI†). The inclusion of the magnetic particles into the MOF-matrix is supported by TEM investigations as can be seen in Fig. 2c. The darker areas of higher electron density are

Fig. 2 Scanning electron micrographs of an M-HKUST-1 sample (a), a nonmagnetic HKUST-1 reference sample (b) and a TEM image of an M-DUT-5 sample (c) showing the included magnetic nanoparticles (marked with arrow).

attributed to the iron oxide whereas the lighter areas represent the surrounding MOF matrix. The magnetic nanoparticles are embedded in between the MOF flake-like particles of DUT-5. The primary particle size of the included magnetic particles is about 10 to 20 nm, which is consistent with the values from the literature, and is thus too large to be incorporated inside the MOF micropores.¹¹

As expected, using polyfunctional stabilizers leads to agglomerates of the iron oxide nanoparticles of about 50 to 70 nm in size. This aggregation is also proven by dynamic light scattering (DLS) measurements of magnetite dispersions in solutions of polycarboxylic acids (see Fig. S8, ESI†).

Cyanosilylation of benzaldehyde using trimethylsilylcyanide (TMSCN) has proven to be a valuable test reaction for the Lewis acidity of metal-organic frameworks¹³ and was therefore used as a model reaction to demonstrate the suitability of magnetically functionalized MOFs for catalytic applications. Products obtained by cyanosilylation can be converted directly to cyanohydrins. These molecules are important precursors for the synthesis of fine chemicals or pharmaceuticals since a large number of different functional groups are accessible *via* conversion of cyanohydrins.¹⁴ As a representative, M-DUT-4 was tested in cyanosilylation of benzaldehyde (see ESI† for experimental details). In order to demonstrate efficient magnetic separation DUT-4 and M-DUT-4 were directly compared in the cyanosilylation (Fig. 3).

DUT-4 produces a quantitative yield after 12 hours, M-DUT-4 yields 79% of product after the same reaction time. Quantitative yields using M-DUT-4 are obtained after 24 hours. Differences in the catalytic performances can be assigned to the lower overall content of MOF in the M-DUT-4 catalyzed reaction ($\gamma\text{-Fe}_2\text{O}_3$ content 14.3 wt%, according to elemental analysis). A filtration test proved the heterogeneous nature of the reaction mechanism. The pristine DUT-4 sample had to be filtered off by a syringe filter ($0.45 \mu\text{m}$), while the M-DUT-4 catalyst could be separated by using a permanent magnet (Fig. S9, ESI†). Since filters rapidly block especially when fine powdered catalysts are used, the magnetic separation method has proven to significantly facilitate separation of the catalyst.¹⁵

Fig. 3 Product yield during cyanosilylation reaction of benzaldehyde using 4 mol% pristine DUT-4 (■) and 3.3 mol% magnetically functionalized M-DUT-4 (●). The open symbols and the dotted lines represent the yield after separation of the catalyst by either filtration or magnetic separation.

Fig. 4 Magnetic heating curve of 324 mg M-HKUST-1 in 30 ml of ethanol at 183 kHz and a field strength of 1.7 kA m^{-1} , giving a specific absorption rate (SAR) of 114.2 W g^{-1} based on the iron content ($\times$). The arrows indicate the initial release rates for ibuprofen at 20 and 40 °C, respectively.

As mentioned above, magnetic MOFs are promising candidates for drug delivery applications. Magnetic particles heat up in an alternating magnetic field,¹⁶ a phenomenon so far mainly studied for medical applications (hyperthermia).¹⁷ However, the high porosity and drug loading capacities, adaptable functionality and biodegradability render nanosized MOFs as highly promising drug delivery systems.¹⁸ The superparamagnetic functionalization described here introduces a new external trigger mechanism for MOFs as well as enhanced imaging capabilities and therefore further improves the functionality and versatility of MOF materials for drug delivery applications. In Fig. 4 the externally triggered heating of M-HKUST-1 is monitored at a frequency of 183 kHz and a magnetic field strength of 1.7 kA m^{-1} . A specific absorption rate (SAR) of 11.1 W g^{-1} (M-HKUST-1) was calculated from the slope of the curve which is equivalent to $105.7 \text{ W g}^{-1}(\text{Fe})$. This value is among the higher values reported in the literature, which can be explained by the nearly optimal size of the $\gamma\text{-Fe}_2\text{O}_3$ particles of about 16 nm, for which the highest SARs were experimentally observed.¹⁷

In addition, we have loaded the magnetic M-HKUST-1 with ibuprofen using a wet infiltration technique and measured the release of drug from the sample at different temperatures (see ESI† for detailed descriptions). The release rate of ibuprofen from the network can be significantly accelerated at higher temperature (Fig. 4). A supplementing concept to externally trigger the release mechanism is to use a thermally removable, pore-blocking capping agent, a concept recently developed for mesoporous silica nanoparticles.¹⁹ Another field of interest is targeted drug delivery, which is also well studied for silica based delivery systems.²⁰ Additionally, despite specific surface functionalizations an external static magnetic field could also be used for directed accumulation in certain body tissues if magnetic drug carriers are used. In our opinion the variety of possible capping mechanisms and the versatility in the MOF chemistry will lead to further improvements for MOF-based drug-delivery systems.

Summarizing, the superparamagnetic functionalization of metal–organic frameworks was demonstrated for the first time by integrating superparamagnetic iron-oxide nanoparticles into polycrystalline MOF aggregates. The concept allows the external manipulation of highly microporous MOFs for efficient catalyst separation. Furthermore magnetically induced heating introduces for the first time an external control to trigger the release rate of drugs by an alternating field, which is promising for biomedical applications.

Notes and references

- (a) O. M. Yaghi, M. O'Keeffe, N. W. Ockwig, H. K. Chae, M. Eddaoudi and J. Kim, *Nature*, 2003, **423**, 705; (b) G. Ferey, C. Mellot-Draznieks, C. Serre, F. Millange, J. Dutour, S. Surble and I. Margiolaki, *Science*, 2005, **309**, 2040; (c) S. Kaskel, in *Handbook of Porous Solids*, ed. K. S. W. Sing, F. Schüth and J. Weitkamp, Wiley-VCH, Weinheim, Germany, 2002, p. 1190.
- (a) M. Eddaoudi, J. Kim, N. Rosi, D. Vodak, J. Wachter, M. O'Keeffe and O. M. Yaghi, *Science*, 2002, **295**, 469; (b) N. L. Rosi, J. Eckert, M. Eddaoudi, D. T. Vodak, J. Kim, M. O'Keeffe and O. M. Yaghi, *Science*, 2003, **300**, 1127.
- (a) D. Farrusseng, C. Daniel, C. Gaudillere, U. Ravon, Y. Schuurman, C. Mirodatos, D. Dubbeldam, H. Frost and R. Q. Snurr, *Langmuir*, 2009, **25**, 7383; (b) J. R. Li, R. J. Kuppler and H. C. Zhou, *Chem. Soc. Rev.*, 2009, **38**, 1477.
- (a) L. Q. Ma, C. Abney and W. B. Lin, *Chem. Soc. Rev.*, 2009, **38**, 1248; (b) J. Lee, O. K. Farha, J. Roberts, K. A. Scheidt, S. T. Nguyen and J. T. Hupp, *Chem. Soc. Rev.*, 2009, **38**, 1450.
- (a) C. Serre, S. Bourrelly, A. Vimont, N. A. Ramsahye, G. Maurin, P. L. Llewellyn, M. Daturi, Y. Filinchuk, O. Leynaud, P. Barnes and G. Ferey, *Adv. Mater.*, 2007, **19**, 2246; (b) J. Seo, R. Matsuda, H. Sakamoto, C. Bonneau and S. Kitagawa, *J. Am. Chem. Soc.*, 2009, **131**, 12792; (c) N. Klein, C. Herzog, M. Sabo, I. Senkovska, J. Getzschmann, S. Paasch, M. R. Lohe, E. Brunner and S. Kaskel, *Phys. Chem. Chem. Phys.*, 2010, **10**, 11778.
- H. Sato, R. Matsuda, K. Sugimoto, M. Takata and S. Kitagawa, *Nat. Mater.*, 2010, **9**, 661.
- K. Hashikawa, S. Ogata, A. Hamasaki, S. Ozeki, at 10th International Conference on Fundamentals of Adsorption, book of abstracts, Awaji, Japan, 2010, p. 39.
- P. Horcajada, C. Serre, M. Vallet-Regi, M. Sebban, F. Taulelle and G. Ferey, *Angew. Chem., Int. Ed.*, 2006, **45**, 5974.
- (a) A. K. Gupta and M. Gupta, *Biomaterials*, 2005, **26**, 3995; (b) R. Hergt, S. Dutz, R. Müller and M. Zeisberger, *J. Phys.: Condens. Matter*, 2006, **18**, 2919.
- M. Klokkenburg, J. Hilhorst and B. H. Erne, *Vib. Spectrosc.*, 2007, **43**, 243.
- Y. S. Kang, S. Risbud, J. F. Rabolt and P. Stroeve, *Chem. Mater.*, 1996, **8**, 2209.
- (a) I. Senkovska, F. Hoffmann, M. Fröba, J. Getzschman, W. Böhlmann and S. Kaskel, *Microporous Mesoporous Mater.*, 2009, **122**, 93; (b) P. Krawiec, M. Kramer, M. Sabo, R. Kunschke, H. Frode and S. Kaskel, *Adv. Eng. Mater.*, 2006, **8**, 293.
- (a) M. Fujita, Y. J. Kwon, S. Washizu and K. Ogura, *J. Am. Chem. Soc.*, 1994, **116**, 1151; (b) K. Schlichte, T. Kratzke and S. Kaskel, *Microporous Mesoporous Mater.*, 2004, **73**, 81; (c) S. Horike, M. Dinca, K. Tamaki and J. R. Long, *J. Am. Chem. Soc.*, 2008, **130**, 5854.
- R. J. H. Gregory, *Chem. Rev.*, 1999, **99**, 3649.
- M. Feyen, C. Weidenthaler, F. Schüth and A. H. Lu, *Chem. Mater.*, 2010, **22**, 2955.
- A. Jordan, P. Wust, H. Fahling, W. John, A. Hinz and R. Felix, *Int. J. Hyperthermia*, 2009, **25**, 499.
- A. Figuerola, R. Di Corato, L. Manna and T. Pellegrino, *Pharmacol. Res.*, 2010, **62**, 126.
- (a) R. C. Huxford, J. Della Rocca and W. B. Lin, *Curr. Opin. Chem. Biol.*, 2010, **14**, 262; (b) S. R. Miller, D. Heurtaux, T. Baati, P. Horcajada, J. M. Greneche and C. Serre, *Chem. Commun.*, 2010, **46**, 4526.
- A. Schlossbauer, J. Kecht and T. Bein, *Angew. Chem., Int. Ed.*, 2009, **48**, 3092.
- J. M. Rosenholm, C. Sahlgren and M. Lindén, *Nanoscale*, 2010, **2**, 1870.