Generation of a solid Brønsted acid site in a chiral framework†

Michael J. Ingleson, Jorge Perez Barrio, John Bacsa, Calum Dickinson, Hyunsoo Park and Matthew J. Rosseinsky*

Received (in Cambridge, UK) 29th November 2007, Accepted 15th January 2008
First published as an Advance Article on the web 14th February 2008
DOI: 10.1039/b718443c

Protonation of chiral porous materials introduces a Brønsted acid centre, the structure of which is unique to the heterogeneous phase requiring pore wall confinement for stable isolation.

Zeolitic materials are important industrial heterogeneous catalysts, however their application in asymmetric transformations has been limited by the scarcity of chiral zeolite phases.[1,2] The requirement for new chiral porous catalytic materials may be fulfilled by metal organic frameworks (MOFs), with an increasing number of enantiopure materials reported,[3–6] including examples both porous and robust.[7–12] Excluding several notable exceptions,[13–15] realising both chirality and enantioselective catalytic activity with MOFs remains a formidable challenge. The synthetic conditions for MOF formation are in conflict with the requirements for catalytically active sites due to coordinative saturation at all metal centres (eliminating metal Lewis acidity), inaccessibility of the Lewis basic sites (involved in bonding to the metal) and absence of Brønsted acid sites (candidate low pK_a moieties are deprotonated by the unavoidable presence of Lewis basic ligands). An alternative approach to the synthesis of catalytically active MOFs, which reduces the probability for catalyst deactivation, is to introduce the active site after the construction of the framework; as exemplified by the work of Lin *et al.*[16] We were interested in using this methodology to introduce a Brønsted acid site into a homochiral MOF that would be of sufficiently low pK_a to be an effective catalyst. To date there has been only one reported chiral, Brønsted acidic MOF that is catalytically active (albeit with enantiomeric excesses (ee) $< 5\%$).[17] Here we report a fully reversible, post-synthetic, acid functionalisation of a homochiral, porous MOF family. This introduces Brønsted acidic centres that are heterogeneous asymmetric catalysts for organic transformations. The catalysts presented are novel as they are not heterogenised homogeneous catalysts;[18] in fact, homogeneous phase analogues are inaccessible. Stable catalyst isolation is dependent on active group confinement in the MOF scaffold wall.

The amino acid-based open framework Ni(L-asp)bipy$_{0.5}$, **1** (L-asp = L-aspartate, bipy = 4,4′-dipyridyl), is an ideal starting material for protonation studies, as it possesses permanent porosity, homochirality and excellent chemical and thermal stability.[9] A suspension of **1** in anhydrous Et_2O upon treatment with HCl in ether led to the isolation of the protonated phase Ni(L-asp)bipy$_{0.5}$(HCl)$_{0.9}$(MeOH)$_{0.5}$, **2**. EDX analysis confirmed this assignment with a Ni : Cl ratio consistently close to 1 : 1,† whilst the degree of solvation was elucidated by a combination of micro- and thermogravimetric (TG) analysis.† Powder X-ray diffraction (pXRD) confirmed the crystallinity of **2**, with only minor differences observed on comparison to the parent material **1**, confirming comparable framework connectivities.† Anhydrous conditions are essential for the isolation of **2**; an analogous reaction performed with HCl in the aqueous phase led to partial dissolution of the nickel salt and no resultant framework material. Despite various approaches the pXRD continually revealed two minor impurity phases; one phase is unreacted **1**, the other (which can be synthesised as the major product by use of 5 eq. of HCl in anhydrous ether for 120 h) is Ni(bipy)Cl_2,[19] consistent with an 'over-protonation' of the framework by excess acid. Optimised conditions of 1.2 equivalents of HCl (per Ni) in anhydrous ether and 18 h reaction time minimise both impurities. Infrared (IR) spectroscopy is particularly informative in identifying the site of protonation. In non-protonated **1**, the νCO_2^- symmetric and asymmetric stretches are in the range 1650 to 1300 cm^{-1} as expected,[20,21] on protonation the analogous region now includes a stretch at 1720 cm^{-1} (Fig. S3†) fully consistent with a protonated COOH νC=O stretch.[29] The 1 : 1 Ni : Cl EDX ratio confirms addition of one equivalent of H^+ (per aspartate) to the entire framework, precluding the presence of the COOH moiety in the IR as a minor impurity. TG analysis for **2** revealed a two stage mass loss before framework decomposition, an initial rapid solvent loss followed by gradual loss of HCl (from 130 to 200 °C); the combined mass loss of 14.0% approaches that predicted from the analysed composition (15.1%). Microanalysis post TG and pXRD confirms the regeneration of **1** by HCl loss. HCl removal can also be achieved chemically by action of the small, non-nucleophilic base Et_2NH to regenerate **1**. Desolvated **2**, though non-porous to CO_2 (at −78 °C and 25 °C) and H_2 (−196 °C), does adsorb MeOH at 25 °C, albeit at a slow rate.† The chloride counterion, with a van der Waals radius of 1.75 Å,[26] is of sufficient diameter to hinder the transport of even the smallest molecules through the narrow (3.2 Å by 4.3 Å) pores.[9] The selective porosity observed for **2** is attributed to the superior hydrogen bonding properties of MeOH, enabling it to overcome the framework···anion interactions and access the interior pores. In combination the analytical data clearly defines **2** as a new material produced by HCl introduction into the open framework structure of **1**. The detailed outcome

Department of Chemistry, University of Liverpool, Liverpool, UK L69 7ZD. E-mail: m.j.rosseinsky@liv.ac.uk; Fax: +44 151 794 3598; Tel: +44 151 794 3504

† Electronic supplementary information (ESI) available: Full experimental information, data and crystallographic details for all compounds. CCDC 662349–662350. See DOI: 10.1039/b718443c

corresponds to full proton transfer from HCl to a framework aspartate carboxylate group (either α or β) forming a COOH moiety that by its confinement within the pore wall is still tethered to the metal centre. The chloride conjugate base is located within the channels, demonstrated by a dramatic decrease in the porosity of **2** (in comparison to **1**). Framework **2** is a rare example of a post-synthesis chemically modified MOF[23] that can be shuttled, reversibly, between protonated and non-protonated states with no framework degradation. It was of interest to determine if the acidic sites in **2** were of sufficient strength to be active as a Brønsted acid catalyst. The test reaction examined was the methanolysis of *rac*-propylene oxide (PO) expected to yield 2-methoxy-1-propanol and 1-methoxy-2-propanol. Framework **2** is active for this conversion (albeit with limited turnover numbers at 25 °C and 48 h),† with catalyst activity limited by its effectively non-porous nature. With the low activity observed for **2**, a related material with larger pores was targeted to improve reactant adsorption kinetics (and increase active site accessibility) with the Cl^- counterion no longer effectively blocking the channel.

A new family of materials closely related to **1**, Cu(asp)$L_{0.5}$·(guests) (L = bipy, **3**, L = bpe, **4**) can be readily accessed phase pure by standard solvothermal methods.† The structure (Fig. 2 shows the bpe congener **4**) of both is similar to that previously reported for **1**, correspondingly consisting of neutral chiral M(asp) layers bridged by the *trans* disposed bipyridyl ligands. The major noteworthy distinction between the Ni and Cu congeners is the Jahn–Teller distortion around the d^9 octahedral Cu centre elongating the 'axial' Cu–O bonds. The bond lengthening observed around the metal in **3** and **4** reduces the thermal stability (framework decomposition temperature ~190 °C in **3** and **4**, compared with >300 °C for **1**).† Chiral gas chromatography (GC) confirmed the enantiopurity of the starting amino acid is delivered to the products **3** and **4** (>95% ee) by this route when either D- or L-aspartate is used as the starting material. Frameworks **3** and **4** are robust to guest loss and are truly porous, **4** for example reversibly adsorbs 6.5 wt% of methanol at 25 °C.† PLATON[24] revealed 22.1% solvent accessible volume for **3** and 25.2% for **4** (compared to 23.1% for **1**).[9] Framework **4** is highly significant to this study as it is an analogue of **1** but with larger pores. The channel topology of **4** is defined by pore windows of 4.1 × 4.3 Å, and elongated pores of 8.6 × 3.2 Å, arising from the increased interlayer separation of the bpe pillared framework (compared to a continuous channel, 4.3 by 3.2 Å in **1**). Protonation studies using HCl in Et_2O under anhydrous conditions revealed that **4** is considerably more sensitive to acid stoichiometry and reaction time than the Ni analogue, **1**, consistent with a less robust phase. Careful control of reaction time and stoichiometry led to the successful isolation of the protonated material Cu(L-asp)$bpe_{0.5}$(HCl)(H_2O), **5** (H_2O is adsorbed from atmospheric moisture, confirmed by micro- and TG analysis; observed 5.3% mass loss, predicted for 1 H_2O 5.2%).† The ratio of Cu : Cl obtained by EDX is constantly close to 1 : 1, consistent with this formulation. Again IR spectroscopy is the most useful diagnostic tool for identifying the position of protonation, with a signal at 1720 cm^{-1} observed in the protonated framework **5** that is not present in the parent material **4** supporting the formation of a COOH moiety fully analogous to the Ni system (Fig. 1). Again, the COOH group cannot arise

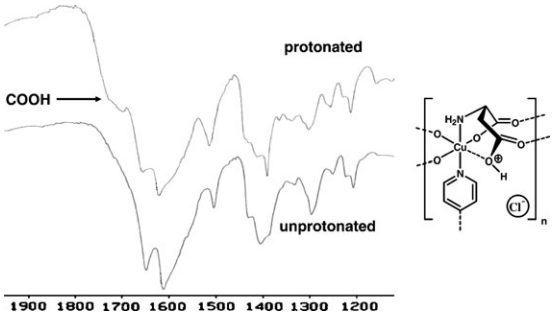


Fig. 1 Left, COOH region of the IR spectra before and after protonation of Cu(asp)$bpe_{0.5}$. Right, Cu environment showing the protonation position, β-carboxylate depicted protonated arbitrarily.

from a minor impurity due to the stoichiometric, 1 : 1 inclusion of H^+ per metal centre (by EDX) combined with the micro-analysis.† The similarity in the pXRD patterns of **4** and **5**† confirms closely related framework connectivities, precluding any cleavage of aspartate to metal bonding as observed in the homogeneous phase.[25–27] There is an unavoidable minor impurity in the synthesis of **5**, that increases with any over-equivalence of HCl used; we tentatively formulate this impurity as Cu(bpe)Cl_2 based on comparison to the Ni system, though it does not correspond to the reported literature phase.[28] The impurity can be strictly kept to a minimum (<5%) through the use of an exact stoichiometric equivalence of HCl and a reaction time of 1 h. The porosity of **5** was confirmed by MeOH uptake, whilst its porosity to propylene oxide (catalysis starting material) was confirmed by TG and micro-analysis on a desolvated sample of **5** soaked in propylene oxide overnight.† **5** however is non porous to CO_2 (−78 °C) frustrating attempts to probe the acid strength of the protonated site *via* IR studies.[20] The νC=O stretch of adsorbed acetone was also uninformative, obscured in the carboxylate region of **5**.[29]

Catalysis studies performed using **5** for the methanolysis of PO demonstrated a significant increase in turnover frequency (compared to **2**),† as anticipated on increasing the pore dimensions. Catalysis utilising **5** is unambiguously heterogeneous (the filtered supernatant is inactive, precluding catalysis by leeched HCl); catalysis is occurring in the pores, not just at

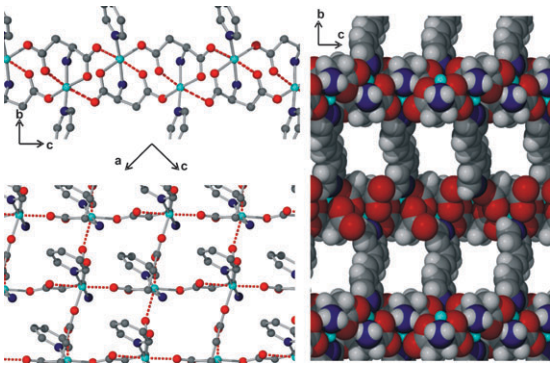
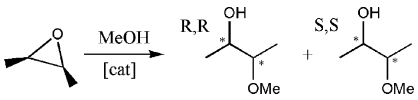


Fig. 2 Left, Cu(asp) 2D layer in **4** dashed red lines emphasise Jahn–Teller elongated Cu–O bonds. Right, cross sectional view down the *a* axis of **4** (solvent removed for clarity) displaying the 1D porous channels between chiral Cu(asp) layers. Red = O, dark blue = N, cyan = Cu, dark grey = C, light grey = H.

Table 1 Catalysis results for methanolysis of *cis*-2,3-epoxybutane



[Cat][a]	Temperature/°C	Yield (%)[b]	ee[c]	TOF[d]
5 (L-asp)	25	59	+10	4.8
6 (D-asp)	25	65	−6	4.7
5 (L-asp)	0	30	+17	2.6
6 (D-asp)	0	32	−13	2.7
H_2SO_4	25	100	+2	—

[a] Catalysts are activated overnight *in vacuo* before suspension in 5 ml dry MeOH under argon. [b] Combined *R*,*R* and *S*,*S* produced after 48 h from 10 mg of **5** (or **6**) by GC. [c] ees were assessed using chiral GC and are fully reproducible; negative signs signify the alternate enantiomer is in excess. [d] TOF units, mol^{-1} day^{-1}.

the surface (the observed turnover from the attempted methanolysis of a significantly bulkier epoxide (2,3-epoxypropyl)-benzene was effectively zero).† The protonated material **5** is the active catalyst with both the impurity phase, 'Cu(bpe)Cl_2' and the parent material **4** inactive (in separate control experiments). Framework **5** is returned essentially intact (by pXRD) after catalysis, with IR spectroscopy confirming the persistence of the COOH functionality. Furthermore, pore confined HCl is not the catalyst with significantly different observed selectivities (for homogeneous HCl compared to **5**).† Racemic starting materials (PO and *trans*-2,3-epoxybutane) produced effectively racemic products, with no evidence for any enantioselective reagent sorption.[9] A racemisation step in the catalysis is precluded by a test reaction using chirally pure *S*-PO, producing single enantiomer products.†

We next examined if any enantioselectivity is observed during the methanolysis of the *meso* compound, *cis*-2,3-epoxybutane. This would arise from a different mechanism to the selective sorption of chiral reagents. Indeed, the methanolysis of *cis*-2,3-epoxybutane (Table 1) to give (*R*,*R*)- and (*S*,*S*)-3-methoxybutan-2-ol catalysed by **5** at 25 °C proceeded with modest ee. This increased when the catalysis was repeated at 0 °C (to 17%). Importantly, methanolysis catalysed by a framework constructed with D-aspartate, Cu(D-asp)$bpe_{0.5}$(HCl)(H_2O), **6**, resulted in the opposite enantiomer dominating as expected. Methanolysis catalysed by sulfuric acid[30] (and HCl)† resulted in an effectively racemic mixture (<3% ee) of products. Whilst the ee generated is modest (a maximum of 17%) it is a rare example of enantioselective catalysis by a porous MOF material. The catalytic reactions chosen were enforced by the limited pore size inherent in these materials (imposing a starting material size restriction); we acknowledge the excellent homogeneous catalysts available for these reactions, but that does not diminish their validity as proof of Brønsted acid strength of the synthetically generated acid centre in these frameworks.

The protonated frameworks **2**, **5** and **6** are MOFs that have been chemically transformed to introduce a novel, catalytically active site, a distinct process to the heterogenisation of an existing homogeneous catalyst. It is important to re-emphasise that these catalysts are inaccessible in the homogeneous phase where protonation leads to either dissociation of the COOH group from the metal centre, or protonation (and dissociation) of the NH_2 site.[25–27] It is only the confinement of the aspartate moiety in the extended MOF structure that allows for the protonation of one of the two carboxylate groups per aspartate ligand whilst anchoring the resulting Brønsted acidic –COOH group to the metal centre. This is essential as the strong acidic nature of **5** (required for catalysis) arises only from the continual binding of the COOH to Cu, increasing proton acid strength *via* the stabilisation of the conjugate base through stronger coordination to the metal.

In conclusion, we report the rational, post-synthesis modification of a porous, homochiral MOF leading to a functional Brønsted acidic material that is active as a uniquely heterogeneous (inaccessible in the solution phase) asymmetric catalyst. Current work is targeting the functionalisation of chiral materials with significantly larger pore windows, allowing for increased catalytic reaction scope.

Notes and references

1 M. E. Davis and R. F. Lobo, *Chem. Mater.*, 1992, **4**, 756.
2 J. M. Newsham, M. M. J. Treacy, W. T. Koestier and C. B. deGruyter, *Proc. R. Soc. London, Ser. A*, 1988, **420**, 375.
3 S. Thushari, J. A. K. Cha, H. H.-Y. Sung, S. S.-Y. Chui, Andy L.-F. Leung, Y.-F. Yen and I. D. Williams, *Chem. Commun.*, 2005, 5515.
4 J. Weng, M. Hong, Q. Shi, R. Cao and A. S. C. Chan, *Eur. J. Inorg. Chem.*, 2002, 2553.
5 B.-Y. Lou, R.-H. Wang, D.-Q. Yuan, B.-L. Wu, F.-L. Jiang and M.-C. Hong, *Inorg. Chem. Commun.*, 2005, **8**, 971.
6 E. V. Anokhina and A. J. Jacobson, *J. Am. Chem. Soc.*, 2004, **126**, 3044.
7 D. Bradshaw, T. J. Prior, E. J. Cussen, J. B. Claridge and M. J. Rosseinsky, *J. Am. Chem. Soc.*, 2004, **126**, 6106.
8 N. G. Pschirer, D. M. Ciurtin, M. D. Smith, U. H. F. Bunz and H.-C. zur-Loye, *Angew. Chem., Int. Ed.*, 2002, **41**, 583.
9 R. Vaidhyanathan, D. Bradshaw, J.-N. Rebilly, J. P. Barrio, J. A. Gould, N. G. Berry and M. J. Rosseinsky, *Angew. Chem., Int. Ed.*, 2006, **45**, 6495.
10 E. V. Anokhina, Y. B. Go, Y. Lee, T. Vogt and A. J. Jacobson, *J. Am. Chem. Soc.*, 2006, **128**, 9957.
11 D. N. Dybtsev, M. P. Yutkin, E. V. Peresypkina, A. V. Virovets, C. Serre, G. Ferey and V. P. Fedin, *Inorg. Chem.*, 2007, **46**, 6843.
12 D. N. Dybtsev, A. L. Nuzhdin, H. Chun, K. P. Bryliakov, E. P. Talsi, V. P. Fedin and K. Kim, *Angew. Chem., Int. Ed.*, 2006, **45**, 916.
13 J. S. Seo, D. Whang, H. Lee, S. I. Jun, J. Oh, Y. J. Jeon and K. Kim, *Nature*, 2000, **404**, 982.
14 S.-H. Cho, B. Ma, S.-B. T. Nguyen, J. T. Hupp and T. E. Albrecht-Schmitt, *Chem. Commun.*, 2006, 2563.
15 S. Hasegawa, S. Horike, R. Matsuda, S. Furukawa, K. Mochizuki, Y. Kinoshita and S. Kitagawa, *J. Am. Chem. Soc.*, 2007, **129**, 2607.
16 C.-D. Wu, A. Hu and W. Lin, *J. Am. Chem. Soc.*, 2005, **127**, 8940.
17 O. R. Evans, H. L. Ngo and W. Lin, *J. Am. Chem. Soc.*, 2001, **123**, 10395.
18 P. McMorn and G. J. Hutchings, *Chem. Soc. Rev.*, 2004, **33**, 108.
19 N. Masciocchi, P. Cairati, L. Carlucci, G. Mezza, G. Ciani and A. Sironi, *J. Chem. Soc., Dalton Trans.*, 1996, 2739.
20 A. Vimont, J.-M. Goupil, J.-C. Lavalley, M. Daturi, S. Surble, C. Serre, F. Millange, G. Ferey and N. Audebrand, *J. Am. Chem. Soc.*, 2006, **128**, 3218.
21 D. H. Williams and I. Fleming, *Spectroscopic Methods in Organic Chemistry*, McGraw-HillPublishing Company, Maidenhead, 1995.
22 A. Bondi, *J. Phys. Chem.*, 1964, **68**, 441.
23 Z. Wang and S. M. Cohen, *J. Am. Chem. Soc.*, 2007, **129**, 12368.
24 A. L. Spek, *J. Appl. Crystallogr.*, 2003, **36**, 7.
25 H. Schmidbaur, I. Bach, J. Riede, G. Muller, J. Helbig and G. Hopf, *Chem. Ber.*, 1987, **120**, 867.
26 R. Barfod, L. Bendahl, A. Hammershoi, D. Kjaergaard-Jensen, A. M. Sargeson and A. C. Willis, *J. Chem. Soc., Dalton Trans.*, 1999, 449.
27 L.-P. Lu, M.-L. Zhu and P. Yang, *Acta Crystallogr., Sect. C: Cryst. Struct. Commun.*, 2004, **60**, m21.
28 Z.-G. Li, J.-W. Xu, H.-Q. Jia and N.-H. Hu, *Acta Crystallogr., Sect. C: Cryst. Struct. Commun.*, 2006, **62**, m205.
29 A. Panov and J. J. Fripiat, *Langmuir*, 1998, **14**, 3788.
30 G. K. Helmkamp and H. J. Lucas, *J. Am. Chem. Soc.*, 1952, **70**, 951.