ChemComm

RSCPublishing

COMMUNICATION

View Article Online
View Journal

Cite this: DOI: 10.1039/c3cc45310c

Received 14th July 2013,
Accepted 31st August 2013

DOI: 10.1039/c3cc45310c

www.rsc.org/chemcomm

Published on 02 September 2013. Downloaded on 26/09/2013 09:07:48.

A new copper-based metal–organic framework as a promising heterogeneous catalyst for chemo- and regio-selective enamination of β-ketoesters†

Ying Zhao,[ab] Dong-Sheng Deng,[b] Lu-Fang Ma,*[b] Bao-Ming Ji[b] and Li-Ya Wang*[bc]

Assembly of 5-nitro-1,2,3-benzenetricarboxylic acid (H_3nbta) with Cu^{II} in the presence of 1,3-bis(1,2,4-triazol-1-yl)propane (1,3-btp) leads to a new metal–organic framework, [Cu(Hnbta)(1,3-btp)]·$2H_2O$ (A_1), which is shown to be an efficient and recyclable heterogeneous catalyst for enamination of β-ketoesters with excellent product yields and selectivity.

There is much interest in the design of hybrid materials for selective and multi-step catalytic processes. Currently, the study on MOFs as catalysts is one of the hot topics.[1] Compared with conventional homogeneous catalysts, MOFs as heterogeneous catalysts have many advantages, including separation and recovery, disposal of spent catalysts, and so on.[2] Generally, to design and synthesize catalytically active MOFs, coordinatively unsaturated metal centers are often used because they may exhibit Lewis acidity and associated catalytic functionality, well-organized and well-maintained active sites and thus are expected to be effective heterogeneous catalysts.[3] On the other hand, Cu(II) ions exhibit dynamic Jahn–Teller distortion[4] and can provide open Lewis acid sites which are effective for catalysis of various organic reactions such as azide–alkyne cycloaddition, oxidative coupling reaction, ring opening of epoxides, Henry reaction, Diels–Alder reaction, *etc.*[5] As is well known, β-enaminoesters are key skeletons of some biologically natural products such as therapeutic agents[6] and synthons of different important antibacterial, anti-inflammatory, and antitumour agents.[7] Therefore, many efficient strategies have been established to obtain these compounds.[8] Among these, the condensation of β-dicarbonyl compounds with amines was the best synthetic method. Consequently, various catalysts including $InBr_3$, $Sc(OTf)_3$, $Zn(OAc)_2·6H_2O/MgSO_4$, $Si(OEt)_4$, $NaAuCl_4$, $ZrOCl_2·8H_2O$, $Ca(CF_3COO)_2$, and so on[9] have been employed to promote this reaction. However, the reaction occurs often under homogeneous conditions, which would lead to several problems, such as difficulty in separation and recovery and disposal of spent catalysts. Therefore, a process featuring an efficient and easy-to-handle catalytic system in combination with a reusable and eco-friendly catalyst would be highly desirable. Until now, no MOFs have been reported as effective heterogeneous catalysts for condensation of β-dicarbonyl compounds with amines. Here, we report a new 3D complex, [Cu(Hnbta)(1,3-btp)]·$2H_2O$ (**A_1**), which displays remarkable capability for heterogeneous selective enamination of β-ketoesters with excellent product yields and selectivity.

Reaction of 5-nitro-1,2,3-benzenetricarboxylic acid (H_3nbta, 0.1 mmol) and 1,3-bis(1,2,4-triazol-1-yl)propane (1,3-btp, 0.1 mmol) with Cu(II) acetate at 130 °C for 3 days under hydrothermal conditions generates blue crystalline product [Cu(Hnbta)(1,3-btp)]·$2H_2O$ (**A_1**).‡ Single-crystal X-ray analysis reveals that compound **A_1** crystallizes in the orthorhombic form with a chiral space group $P2_12_12_1$.§ The Flack parameter of 0.007(12) demonstrates the homochirality of the single crystal. The randomly selected single crystals from the same batch show that spontaneous resolution occurs here and the bulk sample is racemic.

The asymmetric unit of **A_1** contains one crystallographically independent Cu^{II} ion, one Hnbta, one 1,3-btp and two free water molecules, as shown in Fig. S1, ESI.† The Cu1 center is coordinated by two nitrogen atoms of two 1,3-btp [Cu1–N2 = 2.001(2) and Cu1–N7B = 2.003(2) Å] and four oxygen atoms of two Hnbta [Cu1–O1 = 1.966(18), Cu1–O2 = 2.667(2), Cu1–O5A = 2.716(2) and Cu1–O6A = 1.953(18) Å], showing a distorted [4+2] octahedral geometry. The Cu1–O2 and Cu1–O5A bond lengths are much longer, suggesting negligible interaction. The 2-carboxylic group of Hnbta remains undeprotonated and is free of coordination. Each Hnbta takes a μ_2-bridging mode to coordinate two Cu(II) ions *via* its two carboxylic groups in bis-monodentate modes. Thus the Cu(II) ions are connected by Hnbta to produce a 1D chain along the *b* axis. These polymeric chains are arranged at parallel levels and are further cross-linked to one another by bridging 1,3-btp into

---

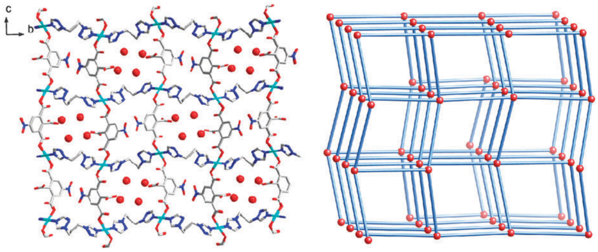
[a] *College of Chemistry and Molecular Engineering, Zhengzhou University, Zhengzhou 450001, P. R. China*

[b] *College of Chemistry and Chemical Engineering, Luoyang Normal University, Luoyang 471022, P. R. China. E-mail: mazhuxp@126.com*

[c] *College of Chemistry and Pharmaceutical Engineering, Nanyang Normal University, Nanyang 473061, P. R. China. E-mail: wlya@lynu.edu.cn*

† Electronic supplementary information (ESI) available: An X-ray crystallographic file in the CIF format, NMR data, and additional structural figures, some of the results of preparation of different β-enaminoesters in the presence of various catalysts, PXRD and TGA curves. CCDC 926307. For ESI and crystallographic data in CIF or other electronic format see DOI: 10.1039/c3cc45310c

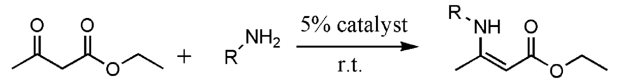
Published on 02 September 2013. Downloaded on 26/09/2013 09:07:48.

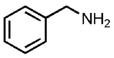
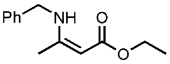
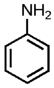
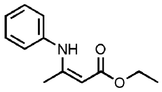
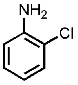
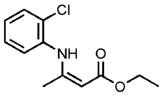
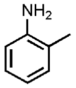
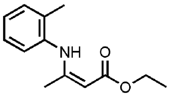
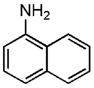
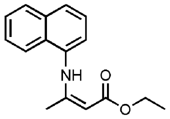
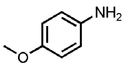
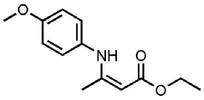
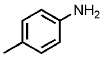
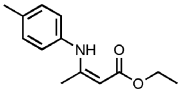
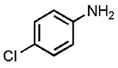
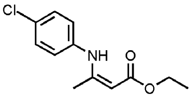
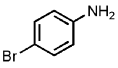
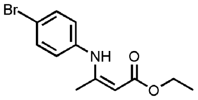
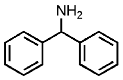
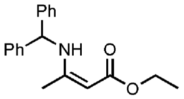
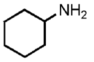
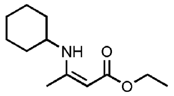


(a) (b)

Fig. 1 (a) Perspective view of the 3D network showing its two types of rectangular channels. (b) Schematic view of the 4-connected framework with a diamond topology, blue bonds represent the 1D chains, while red spheres represent the Cu atoms.

Table 1 Synthesis of different β-enaminoesters using A_1 as catalyst under solvent-free conditions



Entry	Amine	Product	Time (h)	Yield[a] (%)
1			0.5	97
2			1	93
3			2	92
4			2	92
5			2	91
6			1	94
7			1	95
8			1	94
9			1	96
10			2	92
11			2	95

[a] Isolated yield. Selectivity% for each reaction: 100%.

a 3D network with a 4-connected **dia** topology (see Fig. 1a and b), featuring two types of rectangular channels (see Fig. S2, ESI†). The nitro groups of Hnbta protrude inside the voids of one type of channel and another type of channel encapsulates free water molecules as guest molecules. Two crystallographically unique free water molecules are observed in the unit of $\mathbf{A_1}$, which are stabilized by maintaining hydrogen bonds to the carboxylic oxygen atoms of Hnbta in the hydrophilic channel. The effective free volume of $\mathbf{A_1}$ was calculated by PLATON analysis to be 11.9% of the crystal volume (251.6 out of the 2105.3 Å^3 unit cell volume).

Thermogravimetric analysis (TGA, see Fig. S3, ESI†) of $\mathbf{A_1}$ indicates that the first weight loss of 7.1% (calculated: 6.8%) corresponds to the loss of two free water molecules. From *ca.* 200 °C, the expulsion of organic components occurs. The pure compound $\mathbf{A_1}$ was confirmed by powder X-ray diffraction (PXRD) measurement in which diffraction peaks of experimental data are in agreement with the simulated data from single-crystal X-ray data (see Fig. S4, ESI†). After a sample of $\mathbf{A_1}$ was treated under vacuum at 120 °C for 4 h, a PXRD analysis of the resultant crystalline solid $\mathbf{A_1}'$ showed a sharp diffraction pattern similar to that of the as-synthesized sample (see Fig. S4, ESI†). This indicates that the framework is maintained after removal of the free water molecules. Furthermore, the desorption process was also monitored by TGA. The TGA curve of $\mathbf{A_1}'$ shows no weight loss up to 200 °C.

Recent studies have shown that coordinatively unsaturated copper sites can exhibit interesting catalytic activities.[3] To evaluate the catalytic activity of $\mathbf{A_1}$, the reaction of ethyl acetoacetate with benzyl amine was performed under solvent free conditions at room temperature for 0.5 h, which generated the corresponding product in excellent yield (Table 1, entry 1). In order to further explore the versatility of $\mathbf{A_1}$ as catalyst and the effect of substrates on the condensation reaction, different types of amines with different molecular dimensions were used as substrates under solvent-free conditions. The results are summarized in Table 1. All condensation reactions between ethyl acetoacetate and various amines including aromatic (entries 1–10) and aliphatic (entry 11) were completed within 0.5–2 h at room temperature to afford β-enaminoesters in excellent yields (up to 97%). Further, it is noted that all of these reactions display excellent chemoselectivity. The nucleophilic reactant amine only reacts with the ketone part of the β-ketoesters. And reaction with the ester part was not observed in all cases to give the corresponding amide.

In order to confirm the role of catalyst, a blank reaction was performed under similar reaction conditions with benzyl amine and ethyl acetoacetate. At room temperature, no β-enaminoester was observed even after stirring for a long reaction time (24 h). However, at 80 °C, the reaction can proceed to afford a mixture with 76% conversion with low selectivity, which contains imine (62.6%), amide (8.2%) and only 29.2% selectivity of β-enaminoester (see Scheme S1, ESI†). The result clearly shows the role of $\mathbf{A_1}$ as catalyst in the activation of the carbonyl group and the orientation of the reaction toward the desired enaminoester.

Secondly, to prove the heterogeneous mechanism of the condensation catalyzed by $\mathbf{A_1}$, the catalyst was filtered off after

This journal is © The Royal Society of Chemistry 2013

Published on 02 September 2013. Downloaded on 26/09/2013 09:07:48.

15 min reaction time and stirring of the filtrate continued under the same conditions. The result confirms the assumption of a heterogeneous mechanism since neither additional ethyl acetoacetate is consumed nor the product is formed after filtration. A plausible mechanism of enamination of β-ketoester reactions is that unsaturated Cu(II) acts as a Lewis acid active site.[5] Finally, for a more comprehensive study of the catalytic activity of **A**$_1$ in the condensation of β-ketoesters with primary amines, a recycling test with three consecutive runs was performed (see the experimental section). As mentioned before, a product yield of 97% is achieved in the first run after 0.5 h. In the second and the third run the product yields, determined after the same reaction time (0.5 h), decrease to 95% and 93%, respectively. The PXRD patterns of the recovered **A**$_1$ suggest that its structure is well maintained after several cycles of reactions (see Fig. S4, ESI†).

In summary, we have reported a pertinent method for preparation of β-enaminoesters by condensation of β-ketoesters with primary amines under solvent-free conditions at room temperature with **A**$_1$ as a novel heterogeneous catalyst. Compared with the reported homogeneous catalysts for the condensation reaction, **A**$_1$ has some fascinating features because of its low environmental impact, recovery and reusability, and high chemo-selectivity. To our knowledge, this is the first report on selective enamination of β-ketoesters performed using Cu(II) with unsaturated coordination spheres as active sites.

This work was supported by the National Natural Science Foundation of China (21073082, 21271098 and 21272109), and sponsored by the Program for New Century Excellent Talents in University (NCET-11-0947), Innovation Scientists and Technicians Troop Construction Projects of Henan Province (134100510011) and the Program for Science & Technology Innovation Talents in Universities of Henan Province (2011HASTIT027).

Notes and references

‡ Synthesis of **A**$_1$: [Cu(Hnbta)(1,3-btp)]·2H_2O. A mixture of H_3nbta (0.1 mmol, 25.5 mg), 1,3-btp (0.1 mmol, 17.8 mg), Cu(OAc)$_2$·H_2O (0.1 mmol, 19.8 mg) and H_2O 12 mL was placed in a Teflon-lined stainless steel vessel, heated to 130 °C for 3 days, and then cooled to room temperature for over 24 h. Blue block crystals of **A**$_1$ were obtained. Yield: 18.5 mg, 51% (based on Cu). Elemental analysis (%): calcd for $C_{16}H_{17}CuN_7O_{10}$ C 36.20, H 3.23, N 18.47; found C 36.29, H 3.15, N 18.40. IR (cm^{-1}): 3118 m, 1723 s, 1574 s, 1537 s, 1432 m, 1338 s, 1132 m, 995 m, 734 s, 665 m.

§ Crystal data for **A**$_1$: $C_{16}H_{17}CuN_7O_{10}$, M = 530.91, orthorhombic, space group $P2_12_12_1$, a = 5.7467(5) Å, b = 17.9631(16) Å, c = 20.3944(19) Å, V = 2105.3(3) Å^3, Z = 4, S = 1.057, Flack parameter = 0.007(12), D_c = 1.675 g cm^{-3}, F(000) = 1084, μ = 1.109 mm^{-1}, 3809 reflections were used in the refinement. R_{int} = 0.0277, R_1 = 0.0277, and wR_2 = 0.0696 for [$I > 2\sigma(I)$], and R_1 = 0.0326, wR_2 = 0.0719 for all data, $\Delta\rho_{max}$ = 0.241 e Å^{-3}, $\Delta\rho_{min}$ = −0.246 e Å^{-3}. Single crystal X-ray diffraction analysis of **A**$_1$ was carried out on a Bruker APEX II CCD diffractometer equipped with graphite monochromated Mo-Kα radiation (λ = 0.71073 Å) using the ϕ/ω scan technique at room temperature. A total of 3809 reflections were used in the refinement for **A**$_1$. The structure was solved by direct methods with SHELXS-97. The hydrogen atoms were included in the final refinement by use of geometrical restraints and assigned with isotropic displacement factors. The hydrogen atoms of water molecules were located by different maps and the bond length of O–H was restrained to 0.85 Å and the bond angle was 107° and then refined by a riding mode with U_{eq} = 1.5U_{eq}(O). A full-matrix least-squares refinement on F^2 was carried out for the non-H atoms using SHELXL-97. A *typical procedure for catalytic studies*: In a typical experiment 1 mmol ethyl acetoacetate, 1 mmol amine and 0.05 mmol **A**$_1$ were stirred at room temperature for appropriate time. At the end of the reaction, 10 mL of distilled water was added to the residue. After the catalyst was filtered off, the filtrate was extracted with ethyl acetate (3 × 10 mL). The organic layer was dried over $MgSO_4$. The solvent was removed under reduced pressure; pure β-enaminoester was obtained by column chromatography over the silica gel using hexane/ethyl acetate as an eluent. All isolated pure products were fully characterized by ^{1}H and ^{13}C NMR or otherwise compared with the known compounds. The recovered catalyst was washed with ethyl acetate, dried, and reused without further purification or regeneration. Moreover, the recovered catalysts were characterized by powder X-ray diffraction and showed identical results to those of the fresh samples.

1 (*a*) L. Ma, C. Abney and W. Lin, *Chem. Soc. Rev.*, 2009, **38**, 1248–1256; (*b*) J. Kim and M. Movassaghi, *Chem. Soc. Rev.*, 2009, **38**, 3035–3050; (*c*) F. Song, C. Wang, J. M. Falkowski, L. Ma and W. Lin, *J. Am. Chem. Soc.*, 2010, **132**, 15390–15398; (*d*) L.-X. Shi and C.-D. Wu, *Chem. Commun.*, 2011, **47**, 2928–2930; (*e*) X. Jing, C. He, D. Dong, L. Yang and C. Duan, *Angew. Chem., Int. Ed.*, 2012, **51**, 10127–10131; (*f*) Y.-X. Tan, Y.-P. He and J. Zhang, *Chem. Mater.*, 2012, **24**, 4711–4716; (*g*) H.-X. Li, W. Zhao, H.-Y. Li, Z.-L. Xu, W.-X. Wang and J.-P. Lang, *Chem. Commun.*, 2013, **49**, 4259–4261.

2 (*a*) M. Banerjee, S. Das, M. Yoon, H. J. Choi, M. H. Hyun, S. M. Park, G. Seo and K. Kim, *J. Am. Chem. Soc.*, 2009, **131**, 7524–7525; (*b*) S. Horike, M. Dinca, K. Tamaki and J. R. Long, *J. Am. Chem. Soc.*, 2008, **130**, 5854–5855; (*c*) Z. Xu, Q. Wang, H. Li, W. Meng, Y. Han, H. Hou and Y. Fan, *Chem. Commun.*, 2012, **48**, 5736–5738; (*d*) M. Yoon, R. Srirambalaji and K. Kim, *Chem. Rev.*, 2011, **112**, 1196–1231.

3 (*a*) H. R. Moon, N. Kobayashi and M. P. Suh, *Inorg. Chem.*, 2006, **45**, 8672–8676; (*b*) B. Chen, M. Eddaoudi, T. M. Reineke, J. W. Kampf, M. O'Keeffe and O. M. Yaghi, *J. Am. Chem. Soc.*, 2000, **122**, 11559–11560; (*c*) S. Kitagawa, S.-i. Noro and T. Nakamura, *Chem. Commun.*, 2006, 701–707; (*d*) A. Dhakshinamoorthy, M. Alvaro and H. Garcia, *Chem.–Eur. J.*, 2010, **16**, 8530–8536; (*e*) A. Corma, M. Iglesias, F. X. Llabrés i Xamena and F. Sánchez, *Chem.–Eur. J.*, 2010, **16**, 9789–9795; (*f*) J. Kim, S. Bhattacharjee, K.-E. Jeong, S.-Y. Jeong and W.-S. Ahn, *Chem. Commun.*, 2009, 3904–3906; (*g*) D. Sarma, K. Ramanujachary, N. Stock and S. Natarajan, *Cryst. Growth Des.*, 2011, **11**, 1357–1369; (*h*) D. Shi, Y. Ren, H. Jiang, J. Lu and X. Cheng, *Dalton Trans.*, 2013, **42**, 484–491.

4 M. A. Halcrow, *Chem. Soc. Rev.*, 2013, **42**, 1784–1795.

5 (*a*) J. Park, J.-R. Li, Y.-P. Chen, J. Yu, A. A. Yakovenko, Z. U. Wang, L.-B. Sun, P. B. Balbuena and H.-C. Zhou, *Chem. Commun.*, 2012, **48**, 9995–9997; (*b*) S.-K. Yoo, J. Y. Ryu, J. Y. Lee, C. Kim, S.-J. Kim and Y. Kim, *Dalton Trans.*, 2003, 1454–1456; (*c*) D. A. Evans, S. J. Miller, T. Lectka and P. von Matt, *J. Am. Chem. Soc.*, 1999, **121**, 7559–7573; (*d*) Y. Gong, T. Wu, P. G. Jiang, J. H. Lin and Y. X. Yang, *Inorg. Chem.*, 2012, **52**, 777–784; (*e*) D. Jiang, T. Mallat, F. Krumeich and A. Baiker, *J. Catal.*, 2008, **257**, 390–395; (*f*) I. H. Hwang, J. M. Bae, W.-S. Kim, Y. D. Jo, C. Kim, Y. Kim, S.-J. Kim and S. Huh, *Dalton Trans.*, 2012, **41**, 12759–12765.

6 A.-Z. A. Elassar and A. A. El-Khair, *Tetrahedron*, 2003, **59**, 8463–8480.

7 (*a*) N. N. Salama, K. R. Scott and N. D. Eddington, *Biopharm. Drug Dispos.*, 2004, **25**, 227–236; (*b*) N. D. Eddington, D. S. Cox, M. Khurana, N. N. Salama, J. P. Stables, S. J. Harrison, A. Negussie, R. S. Taylor, U. Q. Tran, J. A. Moore, J. C. Barrow and K. R. Scott, *Eur. J. Med. Chem.*, 2003, **38**, 49–64; (*c*) A. P. Marcus and R. Sarpong, *Org. Lett.*, 2010, **12**, 4560–4563.

8 (*a*) A. R. Katritzky, A. E. Hayden, K. Kirichenko, P. Pelphrey and Y. Ji, *J. Org. Chem.*, 2004, **69**, 5108–5111; (*b*) D. S. Reddy, T. V. Rajale, K. Shivakumar and J. Iqbal, *Tetrahedron Lett.*, 2005, **46**, 979–982.

9 (*a*) Z.-H. Zhang, L. Yin and Y.-M. Wang, *Adv. Synth. Catal.*, 2006, **348**, 184–190; (*b*) J. S. Yadav, V. N. Kumar, R. S. Rao, A. D. Priyadarshini, P. P. Rao, B. V. S. Reddy and K. Nagaiah, *J. Mol. Catal. A: Chem.*, 2006, **256**, 234–237; (*c*) R. K. Vohra, J.-L. Renaud and C. Bruneau, *Collect. Czech. Chem. Commun.*, 2005, **70**, 1943–1952; (*d*) Y. Zhao, J. Zhao, Y. Zhou, Z. Lei, L. Li and H. Zhang, *New J. Chem.*, 2005, **29**, 769–772; (*e*) A. Arcadi, G. Bianchi, S. D. Giuseppe and F. Marinelli, *Green Chem.*, 2003, **5**, 64–67; (*f*) Z.-H. Zhang, T.-S. Li and J.-J. Li, *Catal. Commun.*, 2007, **8**, 1615–1620; (*g*) M. A. Harrad, R. Outtouch, M. Ait Ali, L. E. Firdoussi, A. Karim and A. Roucoux, *Catal. Commun.*, 2010, **11**, 442–446.