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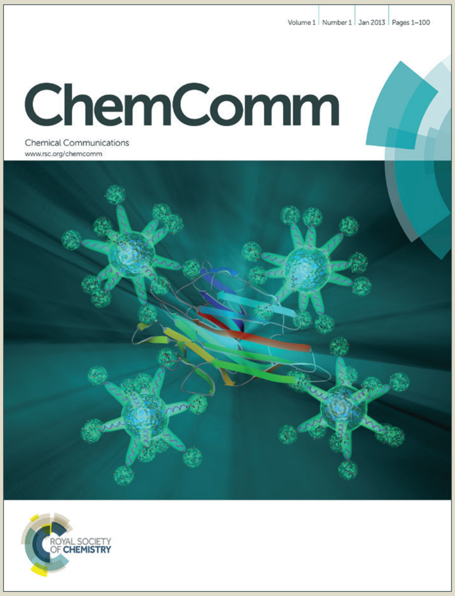

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Straightforward Installation of Carbon-Halogen, Carbon-Oxygen and Carbon-Carbon Bonds within Metal–Organic Frameworks (MOF) via Palladium-Catalysed Direct C-H Functionalization†

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Tao Liu[a+], Da-Qiang Li[a+], Si-Yu Wang,[a] Yong-Zhou Hu,[a] Xiao-Wu Dong,[*a] Xin-Yuan Liu,[*b] and Chi-Ming Che[c,d]

The straightforward C-H functionalization of UiO-67-dcppy materials was realized by a Pd-catalysed PSM. This novel protocol provides an efficient method for the synthesis of various functionalized MOFs, which have shown promising adsorbent ability in removing phenolic contaminates from water.

Crystalline metal–organic frameworks (MOFs) have become particularly attractive for a range of wide applications such as gas storage,[1a,b] separation,[1c] biomedicine,[1d] heterogeneous catalysis,[1e] and other technologies.[1f,g] The development of efficient methods for the construction of various types of functionalized MOFs is highly important.[2] Recently, post-synthetic modifications (PSM) of known MOFs have emerged as important tools for broader introduction of functional groups into MOFs,[3] in particular, which have also been achieved to produce functional materials with improved catalytic[4] and gas sorption properties.[5] Despite these advancements in PSM approaches, a large proportion of these methods depend on the interconversions of functional groups (*e.g.* amine,[6a,b] hydroxyl,[6c] azide,[6d] and aldehyde[6e]), which are greatly limited by the requirement of pre-formed functionality of MOFs, thereby promoting us to develop novel PSM methods for the straightforward functionalization of MOFs.

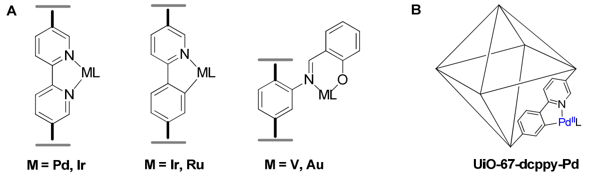
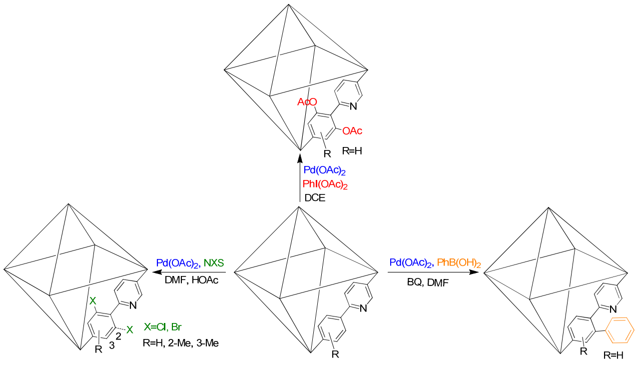


Fig. 1 (A) The post-synthetic cyclometalation in previous work; (B) the proposed cyclopalladation intermediate within UiO-67-dcppy.

Recently, MOFs with open coordination sites have been shown to efficiently bind to various metal ions via PSM protocol, providing a useful platform for the development of coordination chemistry and heterogeneous catalysts (Fig. 1A).[7] In particular, the usage of 2-phenylpyridine-5,4'-dicarboxylic acid (H_2dcppy) as a building block is much more preferable for the preparation of efficient single-site MOF catalysts through the organometallic cyclometalation (*i.e.* iridium and ruthenium).[8] However, to our knowledge, the C-H functionalization of MOFs assisted by a directing group with transition metal catalysis is not disclosed so far.

Although Glorius and co-workers have recently reported pioneering work on the direct palladium-catalysed C-H phenylation of an indole-derived UMCM-1-type MOF,[9] there are still some challenges needing to be addressed, such as the limited scope in terms of MOFs (only one example) and the long reaction time (seven days). Therefore, based on the mode of cyclometalation within MOFs and owing to the use of 2-phenylpyridine as effective directing group in Pd-catalysed C–H activation in homogenous systems,[10] we envisioned that MOFs bearing 2-phenylpyridine as a building linkage would be the potential precursor for C−H functionalization via cyclopalladation intermediate (Fig. 1B). Herein, we reported the first example of a convenient PSM protocol of UiO-67-dcppy materials via a facile palladium-catalysed carbon-halogen, carbon-oxygen and carbon-carbon bond-forming functionalization, affording chemically stable, highly porous and functionally diverse collection of MOFs (Scheme 1).

To validate the feasibility of the proposed PSM process, three Zr-cluster-based MOFs bearing 2-phenylpyridine moiety (*i.e.* UiO-67-dcppy, 2-Me-UiO-67-dcppy and 3-Me-UiO-67-dcppy) were synthesized via solvothermal reaction,[11] since this class of MOFs have exhibited particularly attractive features including chemical and thermal stability and large apparent surface areas.[12] Powder X-Ray diffraction (PXRD) and Brunauer–Emmett–Teller (BET) surface analyses clearly demonstrate that the resultant UiO-67-type materials are highly porous crystalline which are isostructural with UiO-67 materials (Fig. S1† and Table S2†).[12] Then, these UiO-67-dcppy materials were used as substrates for Pd-catalysed C-H activation/C-X (halogenation) according to reported procedures for homogenous C-H activation reactions.[13] The reaction of UiO-67-dcppy and *N*-bromosuccinimide (NBS) using 20 mol% of $Pd(OAc)_2$ as the catalyst with acetic acid as the additive was conducted in acetonitrile at room temperature for 24 hours (Table S3†, entry 1)



Scheme 1. PSM of UiO-67-dcppy materials via Pd-catalysed C-H activation.

and afforded desired brominated product (2-Br-UiO-67-dcppy) on a proximal C-H site of 2-phenylpyridine, albeit with low conversion (16%), which was quantified and characterized using ^{1}H NMR analysis of digested solution. Next, the screening of solvents (*i.e.* 1,4-dioxane, DCE, DMF, Table S3†) for the reaction reveals that DMF was the optimal one, affording a good yield of 2-Br-UiO-67-dcppy (21%) and 2,6-diBr-UiO-67-dcppy (75%) (Table S3†, entry 6 and Fig. 2). On the contrary, no desired product was observed in absence of Pd catalysis, indicating that palladium is essential for this reaction (Table S3†, entry 4). The different loadings of Pd(OAc)$_2$ were examined, and found that 20 mol% of Pd(OAc)$_2$ gave the best result. In addition to NMR analysis, other evidences for successful bromination on UiO-67-dcppy were provided by the presence of typical C-Br stretching vibrations (783 cm^{-1}) in IR spectra (Fig. S2†) and molecular ion peak of [Hdcppy-Br]$^-$ (*m/z* 320) and [Hdcppy-diBr]$^-$ (*m/z* 400) in negative mass spectra of digested solution.

Most importantly, the superior catalytic C-H bromination performance and reactivity of UiO-67-dcppy derivatives was observed as compared with that of H$_2$dcppy as the substrate under the homogeneous reaction conditions (42% yield of 2-Br-H$_2$dcppy without 2,6-diBr-H$_2$dcppy) (Fig. S3†). It should be noted that no brominated product was obtained by using non-porous amorphous Zr-based powder (Fig. S1† and Table S2†)[14] as the substrate under the standard conditions (Fig. S3†). Such drastic difference could be attributed to their intrinsic topology and porosity for efficiently substrate and catalysis binding and interaction in the porous cage.[15]

Table 1 The Pd-catalysed C-X (*i.e.* Cl and Br), C-O and C-C bond-forming functionalization of UiO-67-dcppy materials.

Entry	UiO-67-dcppy materials	Substrate	Yield (%)^e	
			mono-	*di-*
1^a	UiO-67-dcppy	NBS	21	75
2^b	UiO-67-dcppy	NCS	26	70
3^a	2-Me-UiO-67-dcppy	NBS	46	/
4^a	3-Me-UiO-67-dcppy	NBS	85	/
5^b	2-Me-UiO-67-dcppy	NCS	68	/
6^c	UiO-67-dcppy	PhI(OAc)$_2$	/	75
7^d	UiO-67-dcppy	PhB(OH)$_2$	20	/

[a] UiO-67 materials (0.1 mmol), Pd(OAc)$_2$ (20 mol%), NBS (0.5 mmol) and HOAc (0.5 mmol) in DMF (1.0 mL) at r.t. (~25 °C) for 24 hours; [b] UiO-67 materials (0.1 mmol), Pd(OAc)$_2$ (20 mol%), NCS (0.5 mmol) and HOAc (0.5 mmol) in DMF (1.0 mL) at 60 °C for 24 hours; [c] UiO-67-dcppy (0.1 mmol), Pd(OAc)$_2$ (20 mol%), PhI(OAc)$_2$ (0.5 mmol) in DCE (1.0 mL) at 80 °C for 12 hours; [d] UiO-67-dcppy (0.1 mmol), Pd(OAc)$_2$ (30 mol%), BQ (0.3 mmol), PhB(OH)$_2$ (0.3 mmol), DMF (1.0 mL) at 100 °C for 24 hours; [e] The conversion was determined by ^{1}H NMR analysis of digested solution.

To further investigate the scope of application, we set out to explore the scope of this protocol with respect to chlorinated agent (*N*-chlorosuccinimide, NCS) and other UiO-67-dcppys. To our delight, a good yield of desired chlorinated products 2-Cl-UiO-67-dcppy (26%) and 2,6-diCl-UiO-67-dcppy (70%) on a proximal C-H site of 2-phenylpyridine were obtained with NCS as chlorinated agent at 60 °C (Table 1, entry 2 and Fig. 2). Moreover, mono-halogenated products of 2-CH$_3$-UiO-67-dcppy and 3-CH$_3$-UiO-67-dcppy with up to almost complete regioselectivity were afforded with 2-Me-6-Br-UiO-67-dcppy, 3-Me-6-Br-UiO-67-dcppy and 2-Me-6-Cl-UiO-67-dcppy in good yields of 46%, 85% and 68%, respectively (Table 1, entry 3-5 and Fig. 2). The highly regioselective features of C-H halogenation would be possibly attributed to the sterical hindrance originated from the substituent side of 2-phenylpyridine linker during the formation of cyclometalated intermediate within MOF lattices, thereby avoiding the generation of the di-halogenated products.

Owing to the excellent reactive nature of UiO-67-dcppy in C-H halogenation, we then tested the C-H oxidative functionalization of UiO-67-dcppy. Initially, UiO-67-dcppy was treated with Pd(OAc)$_2$ (20 mol%) and PhI(OAc)$_2$ (5 equiv.) in DMF. It was found that the reaction could proceed, and a small amount of desired di-acetoxlated product was obtained (15%). After optimizing the reaction conditions, the yield of the desired product via C-H oxidative PSM protocol could be improved by using DCE in place of DMF as solvent, affording 2,6-diOAc-UiO-67-dcppy in a good yield (75%, Table 1, entry 6 and Fig. 2). Additionally, the IR spectra of 2,6-diOAc-UiO-67-dcppy with C-H stretching vibrations (2800~3000 cm^{-1}) and the characteristic C=O stretching vibrations (~1770 cm^{-1}) clearly demonstrated the efficient introduction of acetoxyl group (CH_3CO) via the current PSM approach (Fig. S2†). The negative ion mass spectrum of digested 2,6-diOAc-UiO-67-dcppy gave a value of *m/z* 358, which is consistent with the presence of molecular ion peak of [Hdcppy-diOAc]$^-$. Furthermore, it is of interest to note that chelation-directed C-H activation could be extended to C-C bond-forming PSM of UiO-67-dcppy with slightly modification of the reaction conditions. Our preliminary results showed that, the reaction of UiO-67-dcppy with phenylboronic acid (3 equiv.) in the presence of Pd(OAc)$_2$ (30 mol%) and 1,4-benzoquinone (3 equiv) in DMF, gave desired coupling product 2-Ph-UiO-67-dcppy with relatively low yield (20%, Table 1, entry 7 and Fig. 2), which is currently under further optimization in our laboratory.

The resultant functionalized MOFs after PSM were shown to possess the same structure and comparable thermal stability as that of parent UiO-67-dcppy as evidenced by PXRD (Fig. 3), Brunauer–Emmett–Teller (BET) surface area analysis (Table S4†), thermogravimetric analysis (TGA, Fig. S4†), scanning electron microscopy (SEM) images (Fig. S5†). It is demonstrated that the crystallinity of the functionalized UiO-67-dcppy materials remain reserved, although the decreased crystallinity of UiO-67-dcppy-OAc was observed, which was confirmed by drastic BET surface decrease from 2281 to 380 cm^2/g (Table S4†) possibly owing to a bit harsh condition using acetic acid and higher temperature (80 °C). The chemical stability of these functionalized UiO-67-dcppy derivatives was also found to be quite similar to UiO-67-dcppy, with good tolerance to polar solvents including methanol, ethanol, acetone and DMF. Comparing with that of parent Uio-67-dcppy materials, the C-H functionalized Uio-67-dcppys showed a significantly decrease of the BET surface area. The larger molecular volume of the acetoxy group as compared with chloro group led to decreased more BET surface area for 2,6-diOAc-Uio-67-dcppy than that of 2,6-diCl-Uio-67-dcppy (Table S4†; BET surface areas of 380 vs. 930 m^2g^{-1}). However, inductively coupled plasma-mass spectrometry (ICP-MS) analysis of the obtained UiO-67-dcppy-Br showed the presence of a little amount of palladium residue (2.8 wt%), which will further require much efforts to overcome this problem. Overall, all of the functionalized MOFs are still highly porous and crystalline even after post-synthetic modification, indicating that all of them would provide a useful platform for the further development of their potential applications in the field of materials.

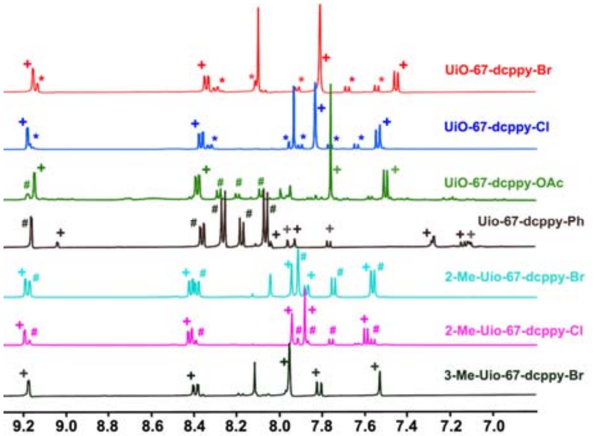


Fig. 2 ^{1}H-NMR data of organic linker of the digested post-modified UiO-67-dcppy materials; di-substituted product (+), mono-substituted product (*) and the remaining starting material (#).

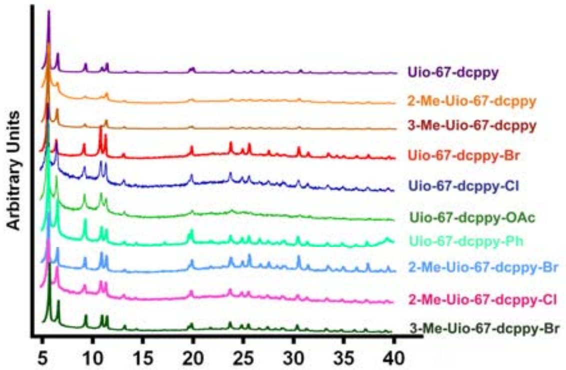


Fig. 3 PXRD patterns for the parent and C-H functionalized UiO-67-dcppy materials.

Considering the fact that pyridine-based polymers can be served as good adsorbents for phenolic compounds,[16] which are considered as one of the most important set of organic contaminants,[17] the obtained functionalized UiO-67 materials were also evaluated for their adsorbent ability in removing phenolic compounds from water (Fig. S6A†). Owing to the electronically distinct effect of different functionalized groups incorporated onto the wall of UiO-67-dcppy, these MOFs showed different adsorbent capacity of phenol, and UiO-67-dcppy-Br was the best one with an adsorption capacity of 45 mg/g. More significantly, the adsorption capacities of UiO-67-dcppy-Br for phenol derivatives bearing electron-withdrawing groups were dramatically increased to 112, 205 and 361 mg/g (Fig. S6B†) for 4-Cl-phenol, 4-nitro-phenol and 2-nitro-phenol, respectively, possibly owing to the enhanced acidity of hydroxyl group of phenols. Furthermore, the treatment of 2-nitro-phenol solution (50 mg/L, 10 mL) with UiO-67-dcppy-Br (100 mg) for 3 hours, resulted in excellent removal efficiency (96.2%) (Fig. S6C†), demonstrating the potential practical application of UiO-67-dcppy-Br for cleaning hazardous materials from contaminated water.

We have presented here the first example of a convenient PSM protocol for Pd-catalysed C-H functionalization within MOF lattices via a cyclopalladation strategy, leading to direct installation of C-X (*i.e.* chloro and bromo), C-O and C-C bond onto the linker of MOFs. The superior catalytic C-H bromination performance and reactivity of UiO-67-dcppy were observed, suggesting that C-H functionalization of MOFs would be an intriguing late-stage functionalization approach as advantageous alternative to traditional interconversions of functional groups in PSM of MOFs. More significantly, the resulting UiO-67-dcppy-Br has shown remarkable adsorbent ability of the phenol derivatives bearing electron-withdrawing groups from contaminated water. Further studies on wider applications of these functionalized MOFs are currently in progress in our laboratory.

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Notes and references

[a] *ZJU-ENS Joint Laboratory of Medicinal Chemistry, College of Pharmaceutical Sciences, Zhejiang University, Hangzhou, 310058, P. R. China. E-mail: dongxw@zju.edu.cn*
[b] *Department of Chemistry, South University of Science and Technology of China, Shenzhen, 518055, P. R. China. E-mail: liuxy3@sustc.edu.cn*
[c] *Department of Chemistry, State Key Laboratory of Synthetic Chemistry, The University of Hong Kong, Pokfulam Road, Hong Kong, P. R. China. E-mail: cmche@hku.hk*
[d] *HKU Shenzhen Institute of Research and Innovation, Shenzhen, 518053, P. R. China*
[+] T. Liu and D.-Q. Li contributed equally to this work

† Electronic Supplementary Information (ESI) available: Experimental procedures, characterizations of synthesized compounds and MOFs, Table S1–S4 and Fig. S1–S6. See DOI: 10.1039/c000000x/

1. a) M. P. Suh, H. J. Park, T. K. Prasad and D. W. Lim, *Chem. Rev.*, 2012, **112**, 782; b) K. Sumida, D. L. Rogow, J. A. Mason, T. M. McDonald, E. D. Bloch, Z. R. Herm, T. H. Bae and J. R. Long, *Chem. Rev.*, 2012, **112**, 724; c) J. R. Li, J. Sculley and H. C. Zhou, *Chem. Rev.*, 2012, **112**, 869; d) P. Horcajada, R. Gref, T. Baati, P. K. Allan, G. Maurin, P. Couvreur, G. Ferey, R. E. Morris and C. Serre, *Chem. Rev.*, 2012, **112**, 1232; e) J. Lee, O. K. Farha, J. Roberts, K. A. Scheidt, S. T. Nguyen and J. T. Hupp, *Chem. Soc. Rev.*, 2009, **38**, 1450; f) L. E. Kreno, K. Leong, O. K. Farha, M. Allendorf, R. P. Van Duyne and J. T. Hupp, *Chem. Rev.*, 2012, **112**, 1105; g) C. Y. Lee, O.

K. Farha, B. J. Hong, A. A. Sarjeant, S. T. Nguyen and J. T. Hupp, *J. Am. Chem. Soc.*, 2011, **133**, 15858.

2. a) H. Furukawa, K.E. Cordova, M. O'Keeffe, O.M. Yaghi, *Science*, **2013**, 1230444; b) F. A. Paz, J. Klinowski, S. M. Vilela, J. P. Tome, J. A. Cavaleiro and J. Rocha, *Chem. Soc. Rev.*, 2012, **41**, 1088.
3. S. M. Cohen, *Chem. Rev.*, 2012, **112**, 970.
4. a) K. K. Tanabe and S. M. Cohen, *Angew. Chem. Int. Ed.*, 2009, **48**, 7424; b) C. D. Wu and W. Lin, *Angew. Chem. Int. Ed.*, 2007, **46**, 1075.
5. R. B. Getman, Y. S. Bae, C. E. Wilmer and R. Q. Snurr, *Chem Rev*, 2012, **112**, 703.
6. a) C. Volkringer and S. M. Cohen, *Angew. Chem. Int. Ed.*, 2010, **49**, 4644; b) L. Gao, C. Y. Li, H. Yung and K. Y. Chan, *Chem. Commun.*, 2013, **49**, 10629; c) L. Ma, J. M. Falkowski, C. Abney and W. Lin, *Nat. Chem.*, 2010, **2**, 838; d) C. Liu, T. Li and N. L. Rosi, *J. Am. Chem. Soc.*, 2012, **134**, 18886; e) A. Huang, W. Dou and J. Caro, *J. Am. Chem. Soc.*, 2010, **132**, 15562.

7 a) E. D. Bloch, D. Britt, C. Lee, C. J. Doonan, F. J. Uribe-Romo, H. Furukawa, J. R. Long and O. M. Yaghi, *J. Am. Chem. Soc.*, 2010, **132**, 14382; b) K. Manna, T. Zhang, W. Lin, *J. Am. Chem. Soc.*, 2014, **136**, 6566; c) M. J. Ingleson, J. P. Barrio, J.-B. Guilbaud, Y. Z. Khimyak and M. J. Rosseinsky, *Chem. Commun.*, 2008, 2680; d) X. Zhang, F. X. Llabrés i Xamena, A. Corma, *J. catal.* 2009, **265**, 155; e) H. Feia, S. M. Cohen, *Chem. Comm.* 2014, **50**, 4810; f) L. Li, S. Tang, C. Wang, X. Lv, M. Jiang, H. Wu and X. Zhao, *Chem. Commun.*, 2014, **50**, 2304.

8. a) P. V. Dau, M. Kim and S. M. Cohen, *Chem. Sci.*, 2013, **4**, 601; b) C. Wang, Z. Xie, K. E. deKrafft and W. Lin, *J. Am. Chem. Soc.*, 2011, **133**, 13445.
9. a) J. Wencel-Delord and F. Glorius, *Nat Chem*, 2013, **5**, 369-375; b) T. Droge, A. Notzon, R. Frohlich and F. Glorius, *Chem. Eur. J.*, 2011, 17, 11974.

10 a) T. W. Lyons and M. S. Sanford, *Chem. Rev.*, 2010, **110**, 1147; b) R. Giri, B. F. Shi, K. M. Engle, N. Maugel and J. Q. Yu, *Chem. Soc. Rev.*, 2009, **38**, 3242.

11. M. J. Katz, Z. J. Brown, Y. J. Colon, P. W. Siu, K. A. Scheidt, R. Q. Snurr, J. T. Hupp and O. K. Farha, *Chem. Commun.*, 2013, **49**, 9449.
12. a) J. H. Cavka, S. Jakobsen, U. Olsbye, N. Guillou, C. Lamberti, S. Bordiga and K. P. Lillerud, *J. Am. Chem. Soc.*, 2008, **130**, 13850; b) V. Guillerm, F. Ragon, M. Dan-Hardi, T. Devic, M. Vishnuvarthan, B. Campo, A. Vimont, G. Clet, Q. Yang, G. Maurin, G. Ferey, A. Vittadini, S. Gross and C. Serre, *Angew. Chem. Int. Ed.*, 2012, **51**, 9267;
13. a) P. L. Arnold, M. S. Sanford, S. M. Pearson, *J. Am. Chem. Soc.* 2009, **131**, 13912; b) D. Kalyani, A. R. Dick, W. Q. Anani, M. S. Sanford, *Org. Lett.* 2006, **8**, 2523.
14. Such non-porous amorphous Zr-based powder was obtained via solvothermal method without usage of con. HCl as additive.
15. T. Murase, Y. Nishijima, M. Fujita, *J. Am. Chem. Soc.*, 2012, **134**, 162.
16. a) N. Sahiner, O. Ozay, N. Aktas, *Chemosphere* 2011, **85**, 832; b) N. Kawabata, K. Ohira, *Environ. Sci. Technot.* 1979, **13**, 1396.
17. a) A. Kumar, S. Kumar, S. Kumar, D. V. Gupta, *J. Hazard. Mater.* 2007, **147**, 155; b) M. C. Burleigh, M. A. Markowitz, M. S. Spector, B. P.Gaber, *Environ. Sci. Technol.* 2002, **36**, 2515.