Accepted Manuscript

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PII:	S0926-860X(15)30123-X
DOI:	http://dx.doi.org/doi:10.1016/j.apcata.2015.08.028
Reference:	APCATA 15522
To appear in:	Applied Catalysis A: General
Received date:	12-6-2015
Revised date:	19-8-2015
Accepted date:	22-8-2015
Received date: Revised date: Accepted date:	12-6-2015 19-8-2015 22-8-2015

Please cite this article as: Ubed S.F.Arrozi, Husni W.Wijaya, Aep Patah, Yessi Permana, Efficient Acetalization of Benzaldehydes using UiO-66 and UiO-67: Substrates Accessibility or Lewis Acidity of Zirconium, Applied Catalysis A, General http://dx.doi.org/10.1016/j.apcata.2015.08.028

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Efficient Acetalization of Benzaldehydes using UiO-66 & UiO-67:

SubstratesAccessibilityor Lewis Acidity of Zirconium

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Graphical abstract

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Highlights

- UiO-66 and UiO-67 were studied in acetalization of benzaldehydes with alcohols.
- Effect of nature of linker ligands on Lewis acidity and catalytic properties was studied.
- Relative Lewis acidity of Zr in UiO-67 is higher than that in UiO-66.
- Reaction rate of acetalizations catalyzed by UiO-66 is faster than that by UiO-67.

Abstract: Porous metal-organic frameworks of $Zr_6O_4(OH)_4(CO_2)_{12}$ clusters connected by organic linkers of 1,4-benzenedicarboxylate (UiO-66) and biphenyl-4,4'-dicarboxylate (UiO-67) were prepared using a solvothermal method and used as efficient catalysts for acetalization of benzaldehydes with alcohols. UiO-66 showed better catalytic activity than UiO-67, (i.e. 91% vs 86%)when the catalyst was employed in the benzaldehyde acetalization in methanol for an hour at r.t. (28 °C). UiO-66 was further explored as the catalyst to observe effects of catalyst concentrations, alcohols, bulkierbenzaldehydes, and recyclability. The performance of other catalysts, including the MOF precursor, was also examined to compare the activity and to explain the importance of a MOF structure.RelativeLewis acidity of Zr in UiO-66 and UiO-67 was achieved by natural bond orbital (NBO) analysis using DFT/B3LYP method. It was found that accessibility of substrates to internal active sites might play a dominant role than the Lewis acidity ofZr-MOFs.

Keywords: UiO-66, UiO-67, acetalization, catalytic properties, Lewis acidity, NBO analysis.

1. Introduction

Acetalization is one of widely used synthetic strategies for protecting carbonyl group of ketones and aldehydes [1,2]. Acetalsareimportant reactants for synthesizing functional compounds including steroids, pharmaceuticals, and fragrances[3]. Such a reactionwasgenerally carried out by reacting a carbonyl compound with an alcohol (Scheme 1) and/or corresponding trimethyl orthoformate[4]. Reported catalysts employed in such reactions include CoCl₂[4], LaCl₃[5], NCS/thiourea[6], 1,4-dimethyl-1H-1,2,4-triazol-4-ium iodide[7], ruthenium(III)-polyvinyl pyridine complex[8], indium(III) fluoride[9], 3-methyl-1- (methoxycarbonylmethyl)imidazolium tetrafluoro-borate[10], hydroxylamine hydrochloride; lithium carbonate[11], and ruthenium trichloride/trimethyl orthoformate adduct[12]. However, numerous attempts to improve the atom efficiency have become a great demand. This includes elimination of dehydrating agents and the use of recyclable catalysts. The utilization of heterogeneous catalysts offers easy catalyst recovery and recycling, as well as product separations[13]. Indeed, several heterogeneous catalysts have been reported in acetalization reactions, such as mesoporous aluminosilicates[14], MCM-41, JRC-SiO-4, and silica gel[15].However, factors affecting their catalytic activities, such as Lewis acidity and substrateaccessibility into active sites,need to be elaborated.

Metal-organic frameworks (MOFs) have received much attention in recent years due to their wide potential applications such as gas storages, gas separations, sensors, luminescence, drug deliveries, and catalyses[16-20]. Their unique properties contribute widely to their applications, i.e. high surface area, tunable pore size, ease of processability, structural diversity, and geometrical control[21]. In the field of catalyses, MOFs are able to serve as catalysts or as catalyst-supports for several organic transformations[22], such as Friedel-Crafts acylations[23], Pall-Knorr reactions[24], Knoevenagel reactions[25], cyanosilylation[26,27], ring-opening of epoxides[28], aerobic oxidations[29], hydrogenations[30], Suzuki-Miyaura cross-coupling[31], and transesterifications[32]. Among more than 20,000 known MOFs, there are several transition metal-based MOFs that have shown stability under liquid-phase reaction conditions[33,34], including porous zirconium-based MOFs which consist of zirconium clusters ($Zr_6O_4(OH)_4$) as building units [35] and organic linkers of 1,4-benzenedicarboxylate (UiO-66, UiO = University of Oslo) or biphenyl-4,4'-dicarboxylate (UiO-67). Both materials were reported to demonstrate good stability at high temperature (up to 540 °C) and high mechanical pressure (up to 10,000 kg/cm²)[35a]. These MOFs are also stable in water and common organic solvents[35a].

UiO-66 was reported to have high activity in various organic reactions, such as epoxidation of cyclooctene[36], CO₂ cycloaddition of styrene oxide[37], and cyclization of citronellal[38]. Timofeeva et al.[39] has also reported the effect of $-NH_2$ or $-NO_2$ group functionalized 1,4-benzenedicarboxylate linker in the UiO-66 structure and observed its catalytic activity on acetalization of benzaldehyde with methanol. The results showed that functionalization of an organic linker with an electron withdrawing group (O₂N-H₂BDC) increased the catalytic activity, while employment of $-NH_2$ moiety as an electron donating group gave lower catalytic activity. Employment of MOFs with identical organic linkers yet different metal centers, namely $Cu_3(BTC)_2$ (BTC =1,3,5-benzenetricarboxylate), Fe(BTC), and Al₂(BDC)₃ (BDC = 1,4-benzenedicarboxylate), in the same benzaldehyde acetalization showed different catalytic activity, i.e., catalytic

activity of Cu-based MOF washigher than FeandAlones, with benzaldehyde conversion of 88%, 71% and 66%, respectively[40]. Differences affected by metals and organic linkers suggested the need of a thorough investigation in this field.

In this work, we report the exploration of UiO-66 and UiO-67 on acetalization of benzaldehydes with alcohols, including the effect of a Zr-MOF structure compared to its precursors (organic linker and ZrCl₄), the effect of pore sizes, and the effect of relative Lewis acidity of Zrat UiO-66 and UiO-67. Relative Lewis acidity were achieved using a natural bond orbital (NBO) analysis, calculated by Density Functional Theory (DFT) method. The effect of substrates accessibility was studied from catalytic results and pore sizes of the MOFs.

2. Experimental

2.1 Material and Instrumentation

1,4-Benzenedicarboxylic acid(H₂BDC), biphenyl-4,4'-dicarboxylic acid(H₂BPDC) and 3,5-di-tert-butyl-2hydroxybenzaldehyde were purchased from Sigma-Aldrich. *N,N'*-dimethylformamide (DMF), zirconium(IV) chloride, benzaldehyde, 2-hydroxybenzaldehyde, methanol, ethanol, CoCl₂, naphthalene, and chloroform were commercially obtained from Merck. All reagents and starting materials were used as received without any further purification.

X-ray powder diffraction (XRD) patterns were recorded using CuKα radiation source on a Bruker D8 Advance XRD. Nitrogen physisorption measurements were conducted bya Quantachrome Autosorb iQ-AG system with samples pretreated by heating under vacuum at 200 °C for 6 hours and measurement temperature

of -196°C. Thermogravimetric measurements were conducted by a thermal analyzer NetzschSTA 449 F1 Jupiter with heating rate of 40 K/min in argon atmosphere. A Bruker Alpha instrumentwas used to collect Fourier transform infrared (FTIR) spectra with samples being dispersed on potassium bromide pellets. The spectrum was generated in resolution of 2 cm⁻¹, collected 16 times, and corrected for a background noise. Scanning electron microscope (SEM) analysis was carried out by JEOL-JSM-6510LV. Gas chromatography (GC) analyses were performed using a Techcomp GC-7900 with a flame ionization detector (FID) and a Kromat KB-1 (100% polydimethylsiloxane)capillary column (length = 15m, inner diameter = 0.25mm, and film thickness = 0.25µm). Temperature program for GC analyses was set at 100°C for 1 min and raised to 190 °C at rate of 30 °C/min and from 190 °C to 210 °C at rate of 10 °C/min. The temperature was finally kept for 5 min at 210 °C. Naphthalene (0.078 mmol) was used as an internal standard to calculate reaction conversions. ¹HNMR spectra were recorded on a JEOL JNM ECA 500 spectrometer.

2.2 Synthesis of UiO-66 and UiO-67

UiO-66 was synthesized by a solvothermal method according toreported procedures[35] with some changes in molar ratio of ZrCl₄: H₂BDC: DMF. In our typical preparation, ZrCl₄ (0.208 g, 0.893 mmol) was dissolved in 20 ml of DMF, then the mixture was added by 0.148 g of H₂BDC(0.893 mmol) under nitrogen atmosphere at r.t. (28 °C). The obtained mixture was sealed in a solvothermal autoclave and placed in a pre-heated oven at 120 °C for 24 hours. Crystallization was allowed in a static condition. After cooling to r.t., the mixture was filtered and washed three times with 5 ml of DMF at r.t. and filtered to give white solid precipitates. The precipitates wereimmersed in 10 mL of chloroform at r.t. and replaced daily for 3 times. The materials weredried in vacuo at 140 °C for 8 hours, yielding white powder crystals. UiO-67 was synthesized with the same procedure as above by replacing H₂BDC to H₂BPDC as the organic linker. Formations of UiO-66 and UiO-67 were confirmed from their XRD patterns (supplementary material; Fig. S2) as reported in the literature [35, 41].

2.3 Catalytic studies

Prepared Zr-MOF catalysts were activated prior to catalytic test by drying the catalyst in vacuo at 140 °C for 8 hours. A 50 ml Schlenk tube was charged with 50 mg of the catalyst, 3 mL of methanol(74 mmol), 0.98 mmol of substrate (benzaldehydes), and 0.078 mmol of naphthalene as an internal standard. The reaction

mixture was then stirred at 500 rpm atr.t.(28 °C) and for a required time. Reaction conversions were monitored by taking aliquots from the reaction mixture at different time intervals and analyzed by GC with naphthalene as an internal standard. The product was also confirmed by ¹H NMR (analyses of the product by GC and ¹H NMR are available in the supplementary material; Fig. S8 and S9). The catalyst wasseparated by centrifugation and dried in vacuo at 140 °C for 3 hours and reemployedfor recyclability tests.

2.4 Computational Details

The calculation of geometry optimizations and NBO analyses were performed on High Performance Computing (HPC) system of Institut Teknologi Bandung (ITB). All calculations in this work were performed using Gaussian 09 software package. Becke three-parameter hybrid method combined with the LYP correlation function (B3LYP) was used for the DFT calculations [42]. The LANL2DZ basis set was used for Zr atom [43], while 6-31G(d) basis set was used for C, H, and O atoms. The NBO (natural bond orbital) 3.1 program included in the Gaussian 09 package was used to analyze the Lewis acidity of Zr-MOFs.

3. Results and discussion

3.1 Preparation of UiO-66 and UiO-67

UiO-66 and UiO-67 were initially reported by the Lillerud group from University of Osloto havea cubic close packed (CCP) structure, of which the cluster wasa 12-coordinated complex, resulting in nanosized porematerials [35]. The utilization of MOFs in many applications, particularly as catalysts such as the one in our work, requires evacuation of guest molecules especially trapped-solventsderived from the synthesis process. This activation becomes an important point not only to avoid pore blockage [44], but also to expose more active sites in the frameworks. For that reasons, solvent-exchange inas-synthesized UiO-66 and UiO-67 was carried out by replacing DMF (bp = 152 °C) with excessive chloroform (bp = 61 °C). Immersing the Zr-MOFs in chloroform and heating them under reduced pressure allowed the removal of DMF[13].

The obtained powder was characterized by FTIR, XRD, TGA, SEM, and N₂ physisorption (provided in the supplementary material). The high crystalline phase of synthesized Zr-MOFs were confirmed by powder XRD analysis to be UiO-66 and UiO-67 as indicated from characteristic diffractions at 2θ of 7.4 and 8.5 degrees for UiO-66 and 5.7 and 6.5 degrees for UiO-67 (supplementary material; Fig. S2). Lower angle-shifts of d_{111} and d_{200} reflections in UiO-67compared to ones in UiO-66were indicated the employment of longer

linker of BPDC between the building unit of $Zr_6O_4(OH)_4$ in UiO-67. These results were ingood agreement with previously reported UiO-66 & 67 by the group of Lillerud [35,45].FTIR spectra showed that the carbonyl vibration at free ligands has shifted to weaker wavenumbers at Zr-MOFs and vibrations of hydroxyl moety at free ligand were no longer presence at Zr-MOFs (supplementary material; Fig. S1). The spectra also showed the presence of Zr-O vibrations[35b]in UiO-66 (668 cm⁻¹) and UiO-67 (663 cm⁻¹).

Thermal gravimetric analysis (TGA) profiles of these MOFs also showed thermal resistance up to 600°C which was in good agreement with reportedliteratures[35,45]. The SEM images of UiO-66 & 67 showed that those materials were in the form of agglomerates as seen in the previously reported morphology [35,45,46]. Surface area measurement is a significant parameter in MOFs. Therefore, the MOFs were tested by N₂ physisorption. The BET (Brunauer-Emmett-Teller) surface areas of synthesized UiO-66 and UiO-67 were 901 and 490 m²/g, respectively, while pore size (BJH method)of these MOFs were 3.17 nm (UiO-66) and 3.01 nm (UiO-67). Here, the synthesized UiO-66 was higher in surface area and pore size than the reported literature by Ebrahim *et al*[46], while the synthesized UiO-67 showed a reverse result [45, 46]. Heating the assynthesized UiO-67 for additional 4 days only increased the surface area to 490 m²/g. Thus, no further attempt was conducted to increase the surface area of the synthesized UiO-67 by such a method. The lower surface area and pore size of synthesized UiO-67 was likely caused by trapped-DMF molecules inside the UiO-67 structure or coordination of the solvent to Zr vacant sites. We then employed these MOFs as catalysts in acetalization reactions of several aldehydes and alcohols with various parameters affecting the catalytic activity.

3.2 Catalytic activities of UiO-66 and UiO-67

Initial study was conducted by comparing catalytic activities of UiO-67 and its precursors (a mixture of ZrCl₄ and H₂BPDC)(Fig. 1). This study addressed the importance of MOF structure as a catalyst in acetalization reactions. Benzaldehyde and methanol were used as a model reaction. Reaction conditions (r.t. of 28 °C, 0.98 mmol benzaldehyde, 74 mmol methanol)and concentrations of MOF precursors were set to be the same asconcentration of UiO-67 catalyst (a mixture of 0.09 mmol ZrCl₄ and 1.7 mol eq. of H₂BPDC,that was equivalent to the preparation of 50 mg UiO-67). Figure 1 shows that in the absence of a catalyst, the reaction

at 28 °C for 1 hour gave 19% benzaldehyde conversion (Fig 1, f). Such a reaction was probably catalyzed by a proton in the reaction mixture. The acidity of the mixture (pH = 5) confirmed this phenomenon.

Catalytic tests were further investigated using $ZrCl_4$ as zirconium precursor for Zr-MOFs. Methanolysis of benzaldehyde by 30 mg of $ZrCl_4(0.13 \text{ mmol})$ in fact gave higher conversion than the reaction without catalyst (Fig. 1; c vs f). The conversion was even higher with the increase of $ZrCl_4$ concentration (Fig. 1; b vs c). However, an increase of $ZrCl_4$ concentration up to 70 mg (0.30 mmol; 30.6 mol% based on benzaldehyde) was still lower than the employment of 50 mg of UiO-67, which was prepared from $ZrCl_4$ of 0.09 mmol(Fig. 1; b vs a). To observe a contributed effect of free ligand, the reaction was also tested using H₂BPDC as a catalyst. The result showed that in an hour, 12mol% H₂BPDC was able to convert 43% of benzaldehyde into benzaldehydedimethylacetal. This can be rationalized by the presence of Bronsted protons at H₂BPDC. In fact, the pH of this free ligand in wet methanol was 4.

Employment of UiO-67 precursors, i.e. a mixture of ZrCl₄ and H₂BPDC, in equivalent amounts of those required to generate 50 mg of UiO-67, was also performed (Fig. 1, e). Such a mixture gave benzaldehyde conversion of only 35%, lower than that of UiO-67 (85%; Fig. 1; e vs a). Thus, the highest conversion was achieved when the structure of a catalyst was as a framework of UiO-67 rather than as its precursor. Such a fact was possibly attributed by electron withdrawing character of H₂BPDC linker which therefore reduced electron density at Zr cluster in comparison to ZrCl₄. The electron density reduction at Zr is ascribed to the increase of Lewis acidity of UiO-67 as a whole. Possible active sites at UiO-67 are exchangeable coordination positions around the Zr ion clusters [47] and unsaturated site at Zr ion clusters. In fact, in the structure of UiO-66, not all of Zr ions were reported to be fully coordinated[35b]. This results in unsaturated sites of Zr ions which act as vacant sites.

The kinetic and reaction mechanism of acetalization catalyzed by heterogeneous catalysts with Lewis acidicactive sites have been studied, for examples, with the employment of zeolites and MIL-101/PTA [48,49]. In this work, we attempted to observe kinetic profile of the catalyst during the reaction by taking aliquots from the mother liquor at different time intervals and analyzed them by GC. Conversion profiles and kinetic profiles of UiO-66 and UiO-67 in benzaldehydes acetalization with alcoholsare provided in Fig. 2 and

Slow induction period of UiO-67 (16% conversion within 15 min) in comparison to UiO-66 (86% conversion within 15 min) showed a diffusion limitation of substrates into active sites likely because of pore blockages in UiO-67. Prolonged reaction up to 24 hours gave lower benzaldehyde conversion than that of an hour reaction (Fig. 2), indicating a reverse hydrolysis of the acetal product. To avoid such a reverse reaction, we monitored reactions within an hour. In contrast to the finding by Timofeeva and co-workersthatreported a much lower UiO-66 activity on benzaldehyde acetalization within 1 hour (conversion of ca. 13%) [39], we observed that UiO-66 was very active in the same reactioncondition (conversion of 91% within an hour). This was probablybecause of the presence of nitrobenzene as an internal standard in the Timofeeva's reaction. Initial experiments employing naphthalene in the absence of catalysts showed no effect of naphthalene as an internal standard to our reactions (supplementary material; Table S2).

The presence of Lewis acidic sites was confirmed by addition of pyridine in equimolar amount to benzaldehyde in the reaction mixture. As pyridine may strongly coordinate to Lewis acidic metals, thus the active site is likely to be at Zr atoms when Lewis acidity attributed by Zr was poisoned[40,52]. Here, poisoning of UiO-66 by pyridine indeed decreased the activity of the MOF drastically to 21% for an hour reaction (Fig. 2-c).

Figure 3 describes the reaction to be second order to benzaldehyde, and thus it gives straight lines in the plot of $1/[benzaldehyde] (M^{-1}) vs t$ (minutes). On the other hand, assuming the reaction was first order to benzaldehyde and approaching it as a pseudo-first order rate, we obtained non-linear lines from the graphic of $\ln \frac{[benzaldehyde]_t}{[benzaldehyde]_o}vs t$ (minutes) (supplementary material, Fig. S6).

Rate constants (k_{obs})thus can be calculated by a slope resulted from each line in Fig. 3, i.e., 1.05 M⁻¹·min⁻¹ for reaction catalyzed by UiO-66 and 0.05 M⁻¹·min⁻¹ for UiO-67. These rate constants can be used further to determine turnover number (TON) by using expression of TON = $\frac{[benzaldehyde]_0 \cdot \%conversion}{[catalyst]}$ measured at 1 hour.[49] Approximating Zr content in UiO-66 and UiO-67 are equally 30% [50], TON of benzaldehyde acetalization with methanol catalyzed by UiO-66 and UiO-67 are 556 and 523, respectively.

This result indicates that although Zr at UiO-67 has a relativelybetter Lewis acidity, UiO-66 showed better catalytic activity in the first hour of reaction. This is probably caused by a poor accessibility of substrates into active sites of UiO-67 than into UiO-66. It is noteworthy to mention that although the BET surface area of UiO-67 (491 m²/g) was measured to be lower than that of UiO-66 (901 m²/g), the high crystalline of the two MOFs and lower-angle shifts of characteristic d_{111} and d_{200} reflections in UiO-67 XRD patterns(which described the lengthening of *d* spacing, supplementary material; Fig. S2)explained that the drop in surface area was suggested due to a pore blockage likely by trapped- or coordinated-DMF solvent instead of a significant drop in number of Zr clusters per identical mass. This, therefore, suggested that the employment of the same mass of 50 mg Zr-MOFs in the catalytic test –by which the surface area of UiO-67 is about half of UiO-66 –does not directly describe a drop ofZr content in UiO-67.

3.3 Relative Lewis acidity of Zr and substrate accessibilityin UiO-66 and UiO-67

A comparison of two MOFs with the same metal, yet with different length of linkers has also been studied by Nguyen L. T. L., et al.[23] They compared Zn-based MOFs containing 1,4-benzenedicarboxylate (MOF-5) with 2,6-naphthalenedicarboxylate organic linker (IRMOF-8) for a Friedel-Crafts acylation of toluene, of which the surface area of MOF-5 was reported to be higher than that of IRMOF-8, while the pore size of MOF-5 was in reverse [23]. The result showed that IRMOF-8 gave higher conversion than MOF-5 in the same reaction condition. This described that accessibility of substrate to active sites was more pronounced than surface areas. However, limited knowledge is available on the effect of those different ligands with Lewis acidity.

Herein we attempted to distinguish the Lewis acidity of Zr in UiO-66 and UiO-67by means of a computational approach. TheseMOFshave the same metal and a similar structure. They only differ in linkers. Computational study to examine Lewis acidities MOFs containing copper and 2 different linkers (5-methylisophtalate and 1,3,5-benzenetricarboxylate)were reported by the group of Zhong [42]. The structure of perfect Zr-MOFs contain 12-coordinated ligands for each clusters of $Zr_6O_4(OH)_4$.[35b] In fact, the group of Lillerud observed that as-synthesized UiO-66 showed a weaker thermal strength compared to a modeled UiO-66 of perfect 12-coordinated MOF, which indicated a defect structure of UiO-66 [35b]. Therein they proposed 11 ligands were coordinated in the zirconium framework. Here we calculated the Lewis acidity of UiO-66 and UiO-67with structures of 11-coordinated ligands in each cluster and lefta vacant site at Zr atom. Geometry

optimizations of these Zr-MOFs were performed by considering cationic structure of +1 charge and multiplicity of singlet for all models. After acquiring optimized geometry of these models using B3LYP methodwith basis sets of LANL2DZ for Zr and 6-31G(d) for C, H, and O atoms(Fig. 4), analysis of Lewis acidity of such MOFs were further performed using natural bond orbital (NBO) analysis. Different ligands mayprovide different electron density at each metal centers. Higher electron withdrawing character of a ligand may lowerelectron density atZr, and thus increase Lewis acidity of aZr-MOF. We found that thenatural charge of Zr in11-coordinated UiO-66 was higher than that in UiO-67 (Table 1). Thus, relative Lewis acidity of Zr in UiO-67 is higher than that inUiO-66, by which theoretical activities of such Zr-MOFs were inreverse to experiments. As UiO-66 experimentally gavehigher catalytic activity and pore size distribution than UiO-67, the reverse result between experimental activitiesandcalculated Lewis acidityindicated a dominant factor of substrate accessibilitiesintoactive sitesoverthe Lewis acidity of the catalyst.

As catalyst concentration plays an important role towardshigh yield of products, we also studied the effect of UiO-66 quantity in the benzaldehyde acetalization. Employment of 5, 10, and 50 mg of UiO-66 to the reaction showed that the smallest concentration gave the lowest conversion (Fig.5c). Increasing the quantity of the catalyst indeed enhanced the conversion (Fig. 5b). However, a further increase of the catalyst did not further increase significantly the catalytic conversion(Fig. 5; b vs a). Thus, herein we employed UiO-66 of 10 mg to further investigate other parameters affecting catalytic reaction.

We were also interested in investigating the effect of ethanol as anothertype of alcohol in this reaction. Ethanol was used in equimolarin the reaction, carried out with UiO-66. Significant decrease of conversion was observed when ethanol was used as an alcohol source (13%),in comparison to that of methanol (93%) (Fig. 6, a vs d). Such results indicated that the longer alkyl carbon of ethanol likely reduced its diffusion into internal surface of UiO-66 at which the reaction likely took place predominantly, and hence the reaction rate and benzaldehyde conversion decreased significantly [13,40]. The fact also implies that the entrance of substrates to active sites plays a dominant role in determining the overall rate.

Anhydrous cobalt chloride has been reported to be active in benzaldehyde acetalization [4]. To provide a comprehensive understanding a reaction site at UiO-66, we then conducted analog reactions with anhydrous CoCl₂ either for benzaldehyde methanolysis or benzaldehyde ethanolysis (Fig. 6b and c). The catalytic activity of UiO-66 clearly showed a great superiority than CoCl₂ for benzaldehyde methanolysis(Fig. 6a vs b).

However, a homogeneous phase of CoCl₂gave better conversion than UiO-66 when longer chain of ethanol was selected as the substrate(Fig. 6c and d; conversion of 37% and 25%, respectively). As the size of catalystpores and the size of substrates gave a significant influence to the reactivity, this result implies that the reaction catalyzed by UiO-66 was taken place at internal surfaces.

We also assessed how the size of benzaldehydesaffectedto the reactivity. Herein, we examined otherbenzaldehyde derivatives, i.e. 2-hydroxybenzaldehydeand 3,5-di-tert-butyl-2-hydroxybenzaldehyde. Reactions were carried out using 10 mg of UiO-66 in methanol for an hour. As shown in Fig. 7, the smallest benzaldehyde gave the highest conversion(Fig. 7-a), while 2-hydroxybenzaldehyde resulted in lower conversion (53%; Fig. 7-b). In addition, larger size of 3,5-di-tert-butyl-2-hydroxybenzaldehyde only gave1% of conversion(Fig. 7-e). This explains that bulkier substrates hardly diffuse to internal active sites of UiO-66. To further support our conclusion, we examined the same reaction usingCoCl₂, a complex that has been reported to be active in acetalization of benzaldehydes[4]. Graphic b and c in Fig. 7gave comparison of 2-hydroxybenzaldehyde acetalization with methanol using UiO-66 and CoCl₂. Here we still observed a superiority of UiO-66 in comparison to homogeneous phase of CoCl₂. However, acetalization of a larger benzaldehyde of 3,5-di-tert-butyl-2-hydroxybenzaldehyde using UiO-66 gave lower catalytic activity than CoCl₂(Fig. 7e). This supports our previous conclusion that the reaction site was at internal surface of UiO-66 and not at external surface.

To consider UiO-66 as an efficient catalyst, we compared it to other homogenous and heterogeneous catalysts. The experiments were adjusted to have similar reaction conditions with UiO-66 (Table 2). At first, conventional Lewis acid such as ZnCl₂ and CoCl₂ in the same phase with the reaction mixture were employed for this acetalization of benzaldehyde and methanol. These catalysts gave lower activities than UiO-66 with conversion of 40% and 34%, respectively. A reaction catalyzed by ZnCl₂ for 24 hours gave lower conversion (39%). Compared to other reported MOFs as heterogeneous catalysts, UiO-66 also shows higher catalytic efficacy than Cu₃(BTC)₂, Fe(BTC), Al₂(BDC)₃,[38] InF₃,[9] and mesoporous aluminosilicate[14] in 1 hour of reactions. To further enhance the catalytic activity of UiO-66, functionalization of the organic linker with electron withdrawing group, [39,52] and the addition of dehydrating agent such as trialkyl orthoformate[53] become alternative routes to be studied.

In the field of heterogeneous catalyst, a metal leaching during the reaction is considered as an important issue. In this respect, Timofeeva and co-workers[39] has confirmed the absence of a leaching process in UiO-66,by which a catalytic reaction using UiO-66 resulted no change of conversion when the catalyst was separated from the solution and the reaction was continued to longer reaction time.

3.4 Recyclability of UiO-66 and UiO-67

One of the advantageous of heterogeneous catalyst is the ease of separation and its recyclability. A test of recyclability of UiO-66 in the acetalization of benzaldehyde and methanol was performed up to 4 runs. After the initial run, UiO-66 was separated bycentrifugation and dried under vacuum in 140 °C for 6 hours. The recycled UiO-66 was then reused in the same reaction and monitored by GC for an hour. Here UiO-66 was observed to demonstrate no significant loss in activitywhen it was recycled up to 4 runs(Fig 8), which was identical with a work by Timofeeva[39].

To observe a possibility of structural deformation and its effect on catalytic activity, the recycled UiO-66was characterized by FT-IR and PXRD. FT-IR analysisshowed no change of characteristic vibrationsbefore and after being employed in the reaction(Fig. 9). However broaden peaks around 500–1000 cm⁻¹ and 1500–1750 cm⁻¹ indicated the presence of remained organic compounds from the reaction which might blockage the pore and explained a slight reduction in activity of the following runs. The PXRD analysisalso demonstrated a drop of structural crystallinity in the second run ofUiO-66 (41%) compared to the fresh one (71%)(Fig. 10). This significant structural deformation however gave no dramatic effect to its catalytic activity, of which the second run catalyst still achieved 91% conversion in the reaction. This phenomenon thus reflects no significant influence of substrate diffusion into deformed catalyst.

4. Conclusions

UiO-66 and UiO-67 were preparedusing a solvothemal method with a slight modificationon molar ratio of ZrCl₄:H₂BDC/H₂BPDC:DMF. The MOFs were characterized by FT-IR, PXRD, TGA, and N₂ physisorption and employed in acetalization reactions of benzaldehydes with alcohols. Active sites of the MOF were

identified by a pyridine test, by which pyridine likely poisoned the exisiting Lewis acidic site of zirconium.UiO-67 gavehigher catalytic activity compared to its precursors (ZrCl₄ and H₂BPDC), showing the importance of MOF structure formation in catalysis. Yet,UiO-67has a lower catalytic activity compared to UiO-66. An NBO analysis using DFT/B3LYP method gave information on relative Lewis acidities of Zr in UiO-66 and UiO-67. The relative Lewis acidity order was observed to be UiO-67 > UiO-66. Although Zr in UiO-67 was observed to have higher Lewis acidity than that in UiO-66, we observed that accessibility of substrates into active sites was likely more dominant than the Lewis acidity in this catalytic reaction. Further studies using UiO-66 as the catalyst showed that the reaction took place predominantly inside the pore, and therefore bulkier substrates was catalyzed slower. Recyclability studies of UiO-66 also shows that UiO-66 may act as a Lewis acid catalyst up to 4 runswith no significant loss in activity.

Acknowledgement

USFAthanks to BU-DIKTIscholarship for Master Program at Chemistry Department of ITB.AP and YP acknowledge Hibah IA-ITB 2011 and Hibah Desentralisasi Dikti 2015 for financial support on Zr-MOFs research and also for Hibah Kerma-LN DIKTI 2012 for partial support on catalysis research using organic/inorganic hybrid materials. Authors acknowledge HPC (High Performance Computing) facilities at ITB and thank to Dr. Muhamad Abdulkadir Martoprawiro,Dr. Muhammad Yusuf, Mr. Raden Aditya Wibawafor fruitful discussion on DFT-NBO calculations.

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Scheme 1. Acetalization of benzaldehyde in methanol solvent.

Figure 1. Conversion profiles for benzaldehyde acetalization in an hour, catalyzed by (a) 50 mg UiO-67; (b) 70 mg ZrCl₄ (0.30 mmol); (c) 30 mg ZrCl₄(0.13 mmol); (d) 30 mg H₂BPDC (0.12 mmol); (e) a mixture of ZrCl₄ (21 mg, 0.09 mmol) and H₂BPDC (28 mg, 0.16 mmol) (equivalent to the preparation of 50 mg UiO-67); and (f) blank (no catalyst). Reaction condition: benzaldehyde (0.98 mmol), methanol 3 mL (74 mmol), r.t. of 28 °C.

Figure 2. Conversion profiles of benzaldehyde acetalization within an hour, catalyzed by (a) UiO-66; (b) UiO-67; and (c) pyridine/UiO-66. Conversion by UiO-66 and UiO-67 after 24 hours were also taken (a and b).Reaction condition: benzaldehyde (0.98 mmol), methanol 3 mL (74 mmol), r.t. of 28 °C.

Figure 3. Initial reaction rate of benzaldehyde acetalization with methanol catalyzed by(a) UiO-66 and (b) UiO-67.

Figure4. (a) Modeled structures of (a) UiO-66 and (b) UiO-67 optimized by DFT/B3LYP method.

Figure5. Effect of catalyst concentrationonacetalization of benzaldehyde, catalyzed by UiO-66, (a) 50 mg, (b) 10 mg, and (c) 5 mg. Reaction condition: r.t., benzaldehyde (0.98 mmol), alcohols (74 mmol). Figure6. Plot of conversion within 60 minute reactionfor the acetalization of benzaldehyde with (a, b) methanol; (c, d) ethanol. Reaction condition: benzaldehyde (0.98 mmol), alcohols (74 mmol), CoCl₂50 mg (0.39 mmol), UiO-66 10 mg, r.t.(28 °C).

Figure7. Effect of molecular sizes of benzaldehydes on catalytic activities by UiO-66 and CoCl₂. (a) Benzaldehyde;(b, c) 2-Hydoxybenzaldehyde; and (d, e) 3,5-Di-tert-butyl-2-hydroxybenzaldehyde. Reaction condition: benzaldehyde (0.98 mmol), methanol (74 mmol), CoCl₂ 50 mg (0.39 mmol), UiO-66 10 mg, r.t. (28 °C).

Figure8. Recycling studies of the catalyst (a) monitored per 10 minutes and compared with the fresh one, (b)

examined up to 4 runs for 1 h each.

Figure9. FT-IR spectra of fresh UiO-66 and recycled UiO-66.

Figure 10. PXRD of fresh UiO-66 and recycled UiO-66.

Table 1. The NBO natural charge of UiO-66 and UiO-67

No	Zr-MOF	Ligand	Natural Charge e	
			Zr (0)	Zr (3)
1	UiO-66	H ₂ BDC	0.86189	0.86282
2	UiO-67	H ₂ BPDC	0.85691	0.85769

Table 2. Comparison of UiO-66 with other catalysts in acetalization of benzaldehyde with methanol^a

Entry	Catalyst	Time (h)	Conversion ^b (%)	Remark
1	UiO-66	1;24	91; 83	This work
2	ZnCl ₂	1;24	40; 39	This work
3	LiTN ^c	1;24	11; 9	This work
4	CoCl ₂	1	34	This work
5	Cu ₃ (BTC) ₂	2;24	63; 88	Ref [38]
6	Fe(BTC)	2;24	49; 71	Ref [38]
7	$Al_2(BDC)_3$	24	66	Ref [38]

^aReaction conditions: r.t. (28 °C), benzaldehyde (0.98 mmol), methanol 3 mL (74 mmol), catalysts (50 mg).
^bDetermined by GC using naphthalene as an internal standard, except for entries 5–7 (taken from ref. 38).
^cLiTN: Anionic interlayer structures of Taeniolite with host cation of Li⁺ (ref. 54).