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MIL-101(Fe) as an active heterogeneous solid acid catalyst for the regioselective ring opening of epoxides by indoles

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ABSTRACT

Ring opening of an epoxide by a nucleophile is considered as one of the viable strategies to prepare biologically active molecules using homogeneous or heterogeneous Lewis acid catalysts. Very often, the ring opening of epoxide was performed with oxygen, sulfur and nitrogen based nucleophiles. Recently, metal organic frameworks (MOFs) were identified as one of the promising solid heterogeneous catalysts for ring opening of epoxide with oxygen and nitrogen based nucleophiles, but however, use of carbon nucleophile like indole is limited. Hence, the present work reports the catalytic performance of MIL-101(Fe) as a highly active regioselective heterogeneous solid Lewis acid catalyst in promoting the ring opening of styrene oxide by indole. Among the various catalysts employed for this reaction, MIL-101(Fe) exhibited the highest catalytic activity. A series of control experiments indicated the pivotal role played by Lewis acids within the frameworks of MIL-101(Fe) and further, the catalytic reaction was found to be heterogeneous in active as evidenced by leaching test. Further, MIL-101(Fe) was reused four cycles with no decay in its activity. Also, MIL-101(Fe) exhibited wide substrate scope in providing series of heterocyclic compounds in moderate to higher yields. A suitable mechanism was also proposed considering the present results and the knowledge from the literature.

1. Introduction

Many natural products including alkaloids [1,2] consist core heterocyclic moieties like indole, pyrrole and imidazole moieties or their derivatives and have been widely used as biologically active compounds [3], pharmaceutical agents, agrochemicals [4,5] and as receptors [6,7]. Furthermore, alkylated indoles and pyrroles have also been considered as important molecules due to their antibiotic, anticancer activities [8] and development of functional organic materials [9]. Scheme 1 provides some of the biologically relevant active compounds possessing indole moiety showing multifunctional properties like protein farnesyl transferase inhibitors that exhibit anticancer properties. Considering these interesting properties of alkylated indoles, chemists are motivated to develop catalytic methods that can provide heterocyclic compounds having these core moieties in high yield under mild reaction conditions. On the other hand, epoxides are often used as versatile intermediates in organic synthesis due to electrophilic nature of carbon which can undergo ring opening reactions with series of nucleophiles to afford synthetically important products [10,11].

Besides the use of enzymes and hydrogen bond catalysts for the ring opening of epoxides to biologically important monomers [12–14], ring opening reaction of epoxides with nitrogen/oxygen nucleophiles has also

been studied either with acidic or basic catalysts which include nano TiO₂ [15], activated silica [16], SbCl₃/K-10 [17], HBF₄-SiO₂ [18], nano MgO [19], magnetic nano Fe₃O₄ and CuFe₂O₄ [20], sulfated zirconia [21], MCM-41 [22], cucurbituril [23], RuCl₃.nH₂O [24], Bi(OTf)₃ [25], InBr₃ [26], and Cr-salen complexes [27], organocatalysts [28] and high-pressure conditions [29]. Although the ring opening reaction of epoxides with indoles was studied with wide range of catalysts, these methods show some drawbacks like long reaction time, low yield, formation of polymerized products, need of toxic solvents and expensive nature of catalysts. According to green chemistry principles and regulations, environmental and economic considerations have recently created strong interests in redesigning catalysts processes to eliminate or minimize the use of harmful substances and the generation of hazardous waste by-products. In this aspect, the development of heterogeneous catalytic processes is more advantageous compared to their homogeneous counterparts in the production of fine chemicals due to their ease of handling, simple workup procedures and most importantly their ability to reuse in many cycles [30].

MOFs are porous crystalline materials whose framework is assembled between the coordination of metal ions and polytopic organic linkers leading to one, two and three dimensional networks [31,32] with ultrahigh porosity and surface areas extending up to $5000 \text{ m}^2/\text{g}$ [33,34]. These unique and remarkable features of MOFs have been reflected in

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Soraphinol A

Actinopolymorphole B



N_1 -arylsulfonyltryptamine



various fields like heterogeneous catalysis [35–38], gas separation [39], gas storage [40], drug release [41], chemical sensing [42], proton conduction [43] and others. Although MOFs have been employed as heterogeneous catalysts for the ring opening of epoxides, most of these MOFs were employed as catalysts with alcohols [44–50] and amines [51,52] as nucleophiles while the ring opening of epoxide by carbon nucleophile using MOF as catalysts is rarely explored [53,54].

Discovery of MIL-100 or MIL-101 (MIL: Materials Institute Lavoisier) families of MOFs by Ferey and coworkers is one of the major breakthroughs in MOF chemistry due to their high stability [55]. In brief, the crystal structure of MIL-101(Fe) was constructed by the coordination of inorganic trimeric iron building units connected with 1,4-benzenedicarboxylate (BDC) linkers leading to porous three-dimensional network with microporous channels (1.2 and 1.45 nm) and two different mesoporous cages of *ca.* 2.9 nm and 3.4 nm. Although MIL-101(Fe) [56–59] and MIL-based catalysts [60–62] have been employed as heterogeneous catalysts for broad range of organic reactions but no effort has been made to prepare alkylindoles.

Hence, the present work reports the synthesis of MIL-101(Fe) and investigate its catalytic activity as solid Lewis acid catalyst for the ring opening of epoxides using indoles as the carbon nucleophiles under solvent-free conditions. Further, some of the objectives of this work are to develop environmentally benign, robust catalyst for ring opening of epoxide by carbon nucleophiles to obtain broad range of heterocycles, to study catalyst stability by reusability, leaching tests and the feasibility of this method to other substrates. This catalyst offers a direct method to achieve biologically relevant products in high yields and it can also be considered as a probe reaction to test solid Lewis acidity of a catalyst.

2. Experimental procedure

2.1. Materials

Cu₃(BTC)₂ and Fe(BTC) are commercially known as Basolite C300 and Basolite F300 MOFs, respectively, were purchased from Sigma Aldrich. Similarly, FeCl₃.6H₂O, Cr(NO₃)₃.9H₂O, Co(NO₃)₂.6H₂O, Zn(NO₃)₂.6H₂O, terephthalic acid, 2-methylimidazole, indole derivatives, imidazole, benzimidazole, pyrrole and styrene oxide were purchased from Sigma Aldrich and used as received. Solvents were also received from Sigma Aldrich and used as received without any further purification.

2.2. Instrumentation

Powder XRD diffraction patterns for these samples were measured using Philips X'Pert diffractometer with the CuK_{α} radiation ($\lambda = 1.5417$ Å) in the refraction mode. FT-IR spectra were recorded in the region of 400-4000 cm⁻¹ with 2 cm⁻¹ resolution with a Bruker tensor 27 series FT-IR spectrometer. SEM images were collected from Hitachi S-3000H scanning electron microscope. Nitrogen adsorption isotherms were measured at 77 K on a Micromeritics ASAP 2000 volumetric adsorption analyser. The samples were degassed at 423 K for 2 h prior to the measurements. The specific surface area was calculated by

applying the BET model to the nitrogen adsorption data. Gas chromatography was employed to determine conversion and selectivity with Agilent 7820 A model using nitrogen as carrier gas. Also, GC–MS was used to confirm the products using 5890 B instrument. IR spectra of adsorbed CO were recorded at low temperature (-176 °C) with a Nexus 8700 FT-IR spectrometer using a DTGS detector and acquiring at 4 cm⁻¹ resolution. An IR cell allowing in situ treatments in controlled atmospheres and temperatures from -176 °C to 500 °C has been connected to a vacuum system with gas dosing facility. For IR studies the samples were pressed into self-supported wafers and treated at 150 °C in vacuum (10⁻⁵ mbar) for 1.5 h. After activation the samples were cooled down to -176 °C under dynamic vacuum conditions followed by CO dosing at increasing pressure (0.05–4 mbar). IR spectra were recorded after each dosage.

2.3. Synthesis of MIL-101(Fe)

MIL-101(Fe) solids were prepared by following an earlier procedure reported in the literature [63,64]. Briefly, FeCl₃.6H₂O (0.675 g, 2.5 mmol) and BDC (0.206 g, 1.25 mmol) were dissolved in DMF (15 mL) under vigorous stirring to obtain a clear solution. Then, the resulting solution was transferred into a Teflon-lined stainless-steel autoclave and heated at 120 °C for 24 h. After this time, the system was cooled to room temperature and the resulting precipitate was filtered and washed several times with DMF (3 × 30 mL) and methanol (3 × 30 mL) to remove unreacted organic species trapped within the pores and finally dried at 80 °C for 8 h.

2.4. Synthesis of MIL-101(Cr)

MIL-101(Cr) was also prepared by adopting an earlier procedure described in the literature [63]. Initially, Cr(NO₃)₃·9H₂O (0.4 g, 1 mmol) and BDC (0.25 g, 1.5 mmol) were added to a Teflon-lined autoclave containing 8 mL of demineralized water and 10 μ L of HF. Then, the autoclave was heated at 200 °C for 8 h. After this time, the system was cooled to room temperature, the resulting precipitate was washed with DMF (3 \times 30 mL) and finally dried at 80 °C for 8 h.

2.5. Synthesis of Co-ZIF-67

ZIF-67 was synthesized according to a slightly modified literature procedure [65]. In brief, cobalt nitrate hexahydrate (2.910 g, 10 mmol) was dissolved in methanol (50 mL) followed by the addition of a solution of 2-methylimidazole (3.284 g, 40 mmol) in methanol (50 mL). This mixture was stirred at room temperature for 1 h and then kept for 24 h at room temperature. The resulting purple precipitate was collected by centrifugation, washed with methanol for three times (3 × 30 mL) and finally dried under vacuum at 80 °C for 8 h.

2.6. Synthesis of Zn-ZIF-8

A solution of zinc nitrate hexahydrate (2.970 g, 10 mmol) dissolved in 50 mL of methanol and a solution of 2-methylimidazole (3.284 g, 40 mmol) in methanol (50 mL) was mixed. Later, this solution was

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stirred at room temperature for 1 h and then kept for 24 h at room temperature. The resulting white precipitate was collected by centrifugation, washed with methanol for three times (3×30 mL) and finally dried under vacuum at 80 °C for 8 h.

2.7. General procedure for the ring opening of styrene oxide by indole with and without solvent

In a typical catalytic ring opening reaction, the reaction flask was charged with 15 mg of catalyst followed by the addition of indole



Fig. 1. Powder XRD of (a) fresh and (b) four times reused MIL-101(Fe).



Fig. 2. N2 absorption-desorption isotherms of MIL-101(Fe).

(0.25 mmol), styrene oxide (0.3 mmol). To this mixture, 1 mL of solvent was added and then this reaction mixture was placed on a preheated oil bath maintained at 60 °C. This heterogeneous mixture was stirred for the required time as shown in Table 1. A known aliquot of sample was periodically taken from the reaction mixture, diluted with acetonitrile and filtered with a syringe filter. This aliquot was analyzed by gas chromatography to determine conversion and selectivity using internal standard. After the required time, the reaction was stopped and the reaction flask was allowed to cool to room temperature. Later, the mixture was diluted with acetonitrile and filtered. This sample was analyzed by gas chromatography to determine the final conversion and selectivity as mentioned above. The products were confirmed by GC–MS and ¹H-NMR analyses. A similar procedure was followed without the addition of 1 mL solvent for reactions under solvent-free conditions.

Reusability experiments were performed identically as shown above except the use of recovered catalyst obtained by filtration after the reaction, washed three times with fresh acetonitrile (3 mL) and dried at 100 $^\circ$ C for 3 h.

3. Results and discussion

MIL-101(Fe) was synthesized [63] and characterized by powder XRD, FT-IR, BET surface area and SEM analysis to reveal the formation of porous MOFs and to understand its morphology. Fig. 1 shows the powder XRD pattern of MIL-101(Fe), the crystalline nature and the peak positions coincide with the previously reported diffraction patterns [64,66,67], thus confirming the existence of MIL-101(Fe). FT-IR of MIL-101(Fe) is shown in Figure S7 and it agrees with the earlier report [68]. The specific BET surface area and porosity of MIL-101(Fe) [63] was measured by gas adsorption-desorption experiments and the results are presented in Fig. 2. The BET surface area and pore volume of MIL-101(Fe) were 2293 m²/g and 1.12 cm³/g, respectively. The pore size of MIL-101 mainly ranges between 8.1-25 Å and the as-synthesized sample pore size was 22 Å. This value is in agreement with the reported data of MIL-101(Fe). Furthermore, SEM images were measured to reveal the morphology of MIL-101(Fe) sample and exhibit an octahedral shape (Fig. 3) [67,69]. In a similar way, the synthesis of MIL-101(Cr) was confirmed by characterizing with powder XRD [70], FT-IR [68] techniques (Figures S1, S2) and the observed results are in agreement with the previous studies. Also, structural and morphological studies of Co-ZIF-67 and Zn-ZIF-8 were also confirmed by powder XRD, SEM (Figures S3, S4, S5 and S6) [71]. In particular, powder XRD clearly indicated the characteristic diffraction patterns of ZIF-67 and ZIF-8. Furthermore, SEM analysis revealed that the particles are like microcrystals with polyhedral shape.



Fig. 3. SEM images of (a) before and (b) four times reused MIL-101(Fe).

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After ascertaining the structural formation of MIL-101(Fe), the studies were performed to evaluate the catalytic performance of MIL-101(Fe) in the ring opening reaction by choosing styrene oxide and indole as starting materials. Further, the activity of MIL-101(Fe) was also compared with other analogous MOF catalysts namely, MIL-101(Cr), Fe(BTC), Cu₃(BTC)₂, Co-ZIF-67 and Zn-ZIF-8 under identical conditions. A blank control experiment in the absence of catalyst under solvent free conditions afforded 3% yield at 60 °C. The catalytic performance of MIL-101(Fe) was tested in various solvents at 60 °C and the results are shown in Table 1. The yield of the desired product was 18, 17. 81 and 71% in toluene, acetonitrile, chloroform and dichloroethane as solvents, respectively. In contrast, the activity of MIL-101(Fe) was negligible in DMF while 9% vield was observed at 60 °C in ethanol under identical conditions. The negligible activity of MIL-101(Fe) in DMF may be due to its ability to coordinate with the Lewis acid sites in MIL-101(Fe) and in fact, removal of DMF by thermal activation affords higher activity in many Lewis acid MOFs catalyzed reactions [72]. On the other hand, the lower activity of MIL-101(Fe) in ethanol is due to competitive reactivity between carbon and oxygen nucleophiles, namely indole and ethanol, respectively. Further, blank control experiments in the absence of catalyst in these solvents showed no product formation and these data are given in Table 1. Considering low to moderate activity of MIL-101(Fe) in the ring opening of styrene oxide by indole in various solvents, an attempt was made to increase the yield of the desired product by performing the same reaction under solventfree conditions. Interestingly, the ring opening of styrene oxide by

Table 1

Optimization of reaction conditions for the ring opening of styrene oxide by indole under various reaction conditions.^a

| | + | Catalyst | | он |
|-----------------|------------------------------------|-----------|-------------------|---------------------------|
| Entry | Catalyst | T (°C) | Solvent | Yield ^b (%) |
| 1 | _ | 60 | _ | 3 |
| 2 | MIL-101(Fe) | 60 | Toluene | 18 (0) |
| 3 | MIL-101(Fe) | 60 | ACN | 17 (0) |
| 4 | MIL-101(Fe) | 60 | CHCl ₃ | 81 (0) |
| 5 | MIL-101(Fe) | 60 | DCE | 71 (1) |
| 6 | MIL-101(Fe) | 60 | DMF | 0 (0) |
| 7 | MIL-101(Fe) | 60 | Ethanol | 9 (0) |
| 8 | MIL-101(Fe) | 40 | - | 46 |
| 9 | MIL-101(Fe) | 50 | - | 74 |
| 10 | MIL-101(Fe) | 60 | - | 92 |
| 11 ^c | MIL-101(Fe) | 60 | - | 48 |
| 12^{d} | MIL-101(Fe) | 60 | - | 91 |
| 13 ^e | MIL-101(Fe) | 60 | - | 65 |
| 14 ^f | MIL-101(Fe) | 60 | - | 85 |
| 15 ⁸ | MIL-101(Fe) | 60 | - | - |
| 16 ^h | MIL-101(Cr) | 60 | - | 76 |
| 17 ^h | Fe(BTC) | 60 | - | 40 |
| 18 ^h | Cu ₃ (BTC) ₂ | 60 | - | 33 |
| 19 ^h | Co-ZIF-67 | 60 | - | 14 |
| $20^{\rm h}$ | Zn-ZIF-8 | 60 | - | 4 |

^a **Reactions conditions**: indole (0.25 mmol), styrene oxide (0.3 mmol), catalyst (15 mg), solvent (1 mL), 60 °C, 12 h.

^b Yield was determined by GC. Values in parentheses indicate the yield obtained in the absence of catalyst.

- ^c MIL-101(Fe) (5 mg).
- ^d MIL-101(Fe) (25 mg).

 $^{\rm e}\,$ indole (1 mmol), styrene oxide (1 mmol), catalyst (15 mg), neat, 60 °C, 12 h.

^f after fourth reuse.

 $^{\rm g}\,$ in presence of pyridine (0.25 mmol).

h 15 mg of catalyst.

indole using MIL-101(Fe) exhibited 46% yield under solvent-free conditions at 40 $^{\circ}$ C while the yield gradually enhanced to 74% at 50 $^{\circ}$ C and to 92% at 60 $^{\circ}$ C under identical conditions.

Fig. 4 shows the effect of temperature in the ring opening of styrene oxide by indole using MIL-101(Fe) as a heterogeneous catalyst. The yield of the product increases as a function of time at all temperatures up to 12 h and no further increase in the yield is noticed in all cases. This may be due to inability of reactants to reach the active site due to steric hindrance imposed by high population of products. The recovered MIL-101(Fe) catalyst after the reaction indicated no noticeable differences in the crystallinity, structural morphology and stretching frequency than that of fresh solid by powder XRD, SEM and FT-IR respectively. These results confirm that the physical, mechanical and chemical state of MIL-101(Fe) is retained during the course of the reaction. Further, iron content between the fresh and the recovered MIL-101(Fe) after the reaction remains unchanged.

The activity of MIL-101(Fe) was significantly decreased to 48% yield upon lowering the catalyst loading from 15 to 5 mg under identical conditions while the increase of catalyst from 15 to 25 mg showed almost similar yield of the product (entries 10 and 12, Table 1), thus suggesting the optimum loading of the catalyst as 15 mg. In all cases, no significant increase in the yield was observed after 12 h. Fig. 5 shows the effect of catalyst loading on the formation of the desired product in the ring opening of styrene oxide by indole.

MIL-101(Cr) was demonstrated as a solid Lewis acid catalyst mainly



Fig. 4. The ring opening of styrene oxide by indole using MIL-101(Fe) as a solid catalyst at (a) 40, (b) 50 and (c) 60 °C.



Fig. 5. Time conversion plot for the ring opening of styrene oxide by indole using (a) 5 (black line), (b) 15 (red line) and (c) 25 mg (blue line) (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article).

due to the existence of coordinately unsaturated position around Cr^{3+} within the crystal structure [73–75]. In this context, the catalytic activity of MIL-101(Cr) was also studied in the ring opening of styrene oxide by indole under solvent-free conditions at 60 °C and observing 76% yield. This activity data of MIL-101(Cr) was comparatively lower than with MIL-101(Fe). Under identical conditions, Fe(BTC) resulted 40% yield which is two-fold decrease in the activity of MIL-101(Fe). This lower activity of Fe(BTC) may be explained due to its lower surface area (860 m²/g) and pore volume (0.462 cm³/g) compared to MIL-101(Fe). Further, Cu₃(BTC)₂ solid gave 33% yield under identical conditions. In contrast, the activity of Co-ZIF-67 and Zn-ZIF-8 was significantly low under identical reactions conditions (Fig. 6). The activity was not enhanced further for all these catalysts after 12 h.

A control experiment was performed with pyridine as a catalyst poison to provide some insights on the nature of active sites in MIL-101(Fe). Interestingly, the ring opening of styrene oxide by indole using MIL-101(Fe) as catalyst afforded no product in the presence of pyridine. This result indicates that pyridine is acting as a catalyst poison by strongly coordinating with the Lewis acid site, namely Fe^{3+} and inhibiting the interaction of styrene oxide. In another experiment, the ring opening of styrene oxide by indole was performed with Fe (NO₃)₃.9H₂O as homogeneous catalyst with similar iron loading and observed 50% yield. This result further confirms the active participation of Fe³⁺ as Lewis acid sites as active sites to promote this reaction.

Hot-filtration or leaching test is one of the ways to ascertain the stability of heterogeneous catalysts. The ring opening of styrene oxide by indole was started with MIL-101(Fe) in chloroform as shown in Table 1 and the solid was removed by filtration under the reaction temperature after 15 min. Then, the resulting reaction mixture without MIL-101(Fe) was continued for the remaining time (12 h). The catalytic performance was significantly inhibited upon removal of MIL-101(Fe) (Fig. 7). These data clearly infer the absence of Fe³⁺ in the solution thus emphasizing the leaching of iron and high stability of MIL-101(Fe) under the present experimental conditions. Furthermore, the iron content of the fresh and the recovered MIL-101(Fe) was analyzed by ICP-OES and confirmed the absence of Fe leaching.

Reusability experiments are performed in heterogeneous catalysis to ascertain the stability of solid catalyst under the optimized reaction conditions. In this context, MIL-101(Fe) was separated from the reaction mixture and repeatedly washed with acetonitrile, dried at 100 °C. The recovered solid was reused four cycles with a minimal decrease in the yield (Fig. 8). These data clearly proved that MIL-101(Fe) is a robust solid catalyst which can promote ring opening of styrene oxide by indole without a significant drop in its activity. Furthermore, four times reused MIL-101(Fe) was characterized by powder XRD, FT-IR and SEM



Fig. 6. Time versus yield plot for the ring opening of styrene oxide by indole using (a) Zn-ZIF-8 (b) Co-ZIF-67 (c) $Cu_3(BTC)_2$ (d) Fe(BTC) (e) MIL-101(Cr) and (f) MIL-101(Fe) as heterogeneous solid catalysts.



Fig. 7. Time versus yield plot for the ring opening of styrene oxide by indole (a) in the presence of MIL-101(Fe) and (b) upon filtration of MIL-101(Fe) solid after 15 min and the reaction mixture stirred without catalyst under identical conditions. **Reaction conditions:** indole (0.25 mmol), styrene oxide (0.3 mmol), MIL-101(Fe) (15 mg), CHCl₃ (1 mL), 60 °C.



Fig. 8. Reusability data for the ring opening of styrene oxide with indole using MIL-101(Fe) as a heterogeneous solid catalyst.

techniques. The identical structural integrity between the fresh and four times reused MIL-101(Fe) in powder XRD indicated that the crystalline nature is retained during the consecutive reuses (Fig. 1). Similarly, no significant differences in the stretching frequencies by FT-IR spectra were seen between the fresh and four times reused MIL-101(Fe) (Figure S7), thus indicating the absence of metal linker cleavage. On the other hand, SEM images of the fresh and four times reused MIL-101(Fe) showed almost similar morphology with clear octahedral crystals (Fig. 3). All these characterization results of the reused solid confirm that the structural integrity and morphology of MIL-101(Fe) is preserved during the repeated uses.

These encouraging catalytic results and high stability of MIL-101(Fe) prompted us to screen the scope of this solid with other derivatives. The observed catalytic data are given in Table 2. The ring opening of styrene oxide with N-methylindole in the presence of MIL-101(Fe) exhibited 87% yield after 12 h at 60 °C. Similarly, the reaction of 2-methylindole with styrene oxide also afforded 90% yield under identical conditions. Further, the ring opening reaction of styrene oxide by 5-methoxyindole with MIL-101(Fe) exhibited 86% yield. Interestingly, a bulky substrate like 5-bromoindole and styrene oxide afforded 88% yield. These results clearly suggest that the reaction occurs within the pores of MIL-101(Fe) due to its higher surface area and pore volume compared to Fe(BTC). Although the reaction of 5-chloroindole and

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Table 2

Ring opening of styrene oxide with different nucleophiles using MIL-101(Fe) as a heterogeneous solid Lewis acid catalyst.^a



^a**Reaction conditions:** Nucleophile (0.25 mmol), electrophile (0.3 mmol), MIL-101(Fe) (15 mg), 60 °C, 12 h.

^bYield was **determined** by GC.

styrene oxide resulted in 89% yield, but however, the ring opening reaction between 5-nitroindole and styrene oxide did not provide any product under identical conditions. The ring opening of styrene oxide was also efficient with other heterocyclic nucleophiles like pyrrole, imidazole and benzimidazole showing 74, 81 and 68% yields, respectively under identical conditions. Moderate yields with these carbon nucleophiles may be due to electronic influences of the heteratoms in these heterocycles, but, however, further studies are required to confirm this hypothesis.

Considering the results observed in the present work and previous reports, a suitable reaction mechanism is proposed for the ring opening of styrene oxide by indole using MIL-101(Fe) as catalyst as shown in Scheme 2. Styrene oxide interacts with the coordinatively unsaturated sites available in MIL-101(Fe) catalyst through oxygen, thus making electron deficient carbon centers [44,53]. Subsequently, carbon nucleophile attacks styrene oxide to a carbon with more electron deficiency to give the desired product.



Scheme 2. Proposed mechanism for the ring opening of styrene oxide by indole in the presence of MIL-101(Fe) as a solid heterogeneous catalyst.

CO adsorption experiments were performed to prove the existence of Lewis acid sites in the as-synthesised MIL-101(Fe) sample. Further, CO adsorption was carried out by introducing calibrated doses of CO on



Fig. 9. IR spectra of outgassed MIL-101(Fe) during CO adsorption.

the activated MIL-101(Fe) sample at 150 °C. IR spectra of CO adsorption at -176 °C (Fig. 9) over activated MIL-101(Fe) show the presence of IR bands at 2179 and 2166 cm⁻¹ associated to Lewis acid sites arising from Fe³⁺ and Fe²⁺ sites, respectively [76,77] in addition to a band at 2134 cm⁻¹ due to physisorbed CO. Further, the presence of Fe²⁺ in the IR spectra is believed due to the partial reduction of Fe³⁺ to Fe²⁺ site upon adsorption of CO [78].

4. Conclusions

In the present work, MIL-101(Fe) was shown to be an efficient heterogeneous solid Lewis acid catalyst among other analogous catalysts like MIL-101(Cr), Fe(BTC), Cu₃(BTC)₂, ZIF-8 and ZIF-67 in the ring opening of styrene oxide by indole with very high yield and regioselectivity under mild reaction conditions. The high activity of MIL-101(Fe) compared to other solids was due to the high population of Lewis acid sites, high surface area and pore volume than other catalysts. Further, leaching test indicated the heterogeneity of the reaction and MIL-101(Fe) was reused four cycles without any significant loss in its activity. In addition, four times reused MIL-101(Fe) was characterized by powder XRD, FT-IR, SEM analyses and observing that the structural integrity and morphology of the reused sample are almost identical in respect to fresh solid. Also, MIL-101(Fe) exhibited wide substrate scope by showing high product yields and regioselectivity in the ring opening of styrene oxides with other indole derivatives.

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Appendix A. Supplementary data

Supplementary material related to this article can be found, in the online version, at doi:https://doi.org/10.1016/j.mcat.2019.110628.

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