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# Metal-organic framework MIL-53(Al): synthesis, catalytic performance for the Friedel-Crafts acylation, and reaction mechanism

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Metal-organic framework MIL-53(Al) was synthesized by a solvothermal method using aluminum nitrate as the aluminium source and 1,4-benzenedicarboxylic acid (H<sub>2</sub>BDC) as the organic ligand. The structure of samples was characterized by X-ray diffraction (XRD) and Fourier transform infrared spectroscopy (FT-IR). The catalytic activity and recyclability of MIL-53(Al) catalyst for the Friedel-Crafts acylation reaction of indole with benzoyl chloride were evaluated. The reaction conditions were optimized and a reaction mechanism was suggested. The results showed that the MIL-53(Al) catalyst exhibited good catalytic activity and recyclability for the Friedel-Crafts acylation reaction. When the molar ratio of indole and MIL-53(Al) catalyst was 1:0.06 ( $n_1:n_{catalyst}$ ), the molar ratio of indole and benzoyl chloride was 1:3, and the solvent was dichloromethane, the conversion of indole could reach 97.1% and the selectivity of 3-acylindole could reach 81.1% at 25 °C after 8 h. The catalyst can be reused without significant degradation in catalytic activity. After the catalyst was reused five times, the conversion of indole was 87.6% and the selectivity of 3-acylindole was 79.5%.

MIL-53(Al), catalyst, Friedel-Crafts, acylation, indole, 3-acylindoles

## 1 Introduction

Friedel-Crafts acylation reactions are important C–C bondforming processes [1]. They are the most powerful method of preparing aromatic ketones, which have advantages of simplicity and high selectivity. Heterocyclic aromatic ketones are important organic intermediates in the synthesis of fine chemicals, which are mainly used as medicines and in prepared spices and agricultural chemicals. Some of these chemicals also have biological activity [2]. Indole and indole derivatives are the most heterocyclic aromatic compounds found in nature. Specifically, carbonyl groups of 3-acylindoles, synthesized by the Friedel-Crafts acylations of indole with benzoyl chloride, can readily undergo a variety of transformations such as C–C and C–N coupling reactions. Thus, the synthesis of 3-acylindoles has gained considerable attention among heterocyclic organic chemists [3]. Traditionally, a wide variety of 3-acylindoles have been prepared by several well-known methods such as Vilsmeier-Haack type reaction [4], Grignard reactions [5], and Friedel-Crafts acylations. The Vilsmeier-Haack type reaction is simple and can achieve high yields, but its application ranges are restricted and are only suitable for active substrate. This method uses unacceptable amounts of environmentally unfriendly POCl<sub>3</sub> which acts as a chlorinating agent in the reaction. Although Grignard reactions can improve the selectivity of 3-acylindole, they also increase the complexity of the synthesis process and lower the overall yields. Friedel-Crafts acylations are environmentally friendly and easy to carry out. This method requires Lewis acids as catalysts, such as AlCl<sub>3</sub> [6] and InCl<sub>3</sub> [7]. However, the required amounts of these catalysts generate a great deal of waste. In order to reduce pressure on the environment,

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porous material-loaded metal or metal oxide, microporous, and mesoporous molecular sieves are widely synthesized; these include metal triflate-loaded SBA-15 [8], sulfurized zirconia-loaded MCM-41 [9], HPA/SiO<sub>2</sub> [10], and mesoporous HZMS-5 [11]. However, their catalytic performances need to be improved.

Metal-organic frameworks (MOFs) are formed by selfassembly of polydentate organic ligands and metal ions, for which they construct 3D porous network structures. In recent years, because of their unique properties such as unsaturated metal active sites, easy functionalization, and large surface area, they are widely used in the field of catalysis [12,13]. Nguyen et al. [14] used the metal active site of Zn in IRMOF-8 to catalyze a Friedel-Crafts acylation reaction of toluene and benzoyl chloride. After 6 h of reaction, the conversion of toluene reached 95.0% and the IRMOF-8 catalyst could be reused without significant degradation of its catalytic activity. Li et al. [15] used Zn-BTC@SiO<sub>2</sub>@Fe<sub>3</sub>O<sub>4</sub> as catalyst to catalyze Friedel-Crafts acylation of toluene with toluoyl chloride. When the amount of the Zn-BTC catalyst was 3.7% (mass fraction), the conversion of toluene was 78.8% at 120 °C for 4.5 h and showed high catalytic activity. The catalyst also had a good superparamagnetism that could facilitate recycling.

The metal-organic framework (MIL-53(Al)), which is built up by the interconnection of infinite trans chains of corner-sharing (via OH groups) AlO<sub>4</sub>(OH)<sub>2</sub> octahedra with BDC ligands, has a 3D skeleton structure composed of 1D rhombus channels. MIL-53(Al) has Lewis acid sites  $(Al^{3+})$ of uniform distribution, specific surface area [16], and remarkable thermal and chemical stability [17] and has been used as heterogeneous catalyst. Garibay et al. [18] catalyzed alcoholysis of epoxides reaction in presence of epoxides maleic acid-functionalized MIL-53(Al)-AMMal. In that work, the conversion of ethylene oxide could reach 100% and the MIL-53(Al)-AMMal catalyst could be reused with consistent catalytic activity over three runs. Ishida et al. [19] used Au/MIL-53(Al) to catalyze oxidation of benzyl alcohol reaction. Compared to Au/CPL-1 catalyst, Au/MIL-53(Al) could effectively improve the conversion of reaction and selectivity of the main product, methyl benzoate. Huang et al. [20] reported that Pd@MIL-53(Al) and Pd@MIL-53(Al)-NH<sub>3</sub> catalyzed a Heck reaction of bromobenzene with styrene. Due to the increase of their surface area, these catalysts exhibited efficient catalytic activity for Heck reaction and could be easily recovered and reused. However, it has not been reported that the Friedel-Crafts acylation of indole with benzoyl chloride is catalyzed by MIL-53(Al) to produce 3-acylindole.

In this work, the MIL-53(Al) catalyst was synthesized and characterized by XRD, FT-IR. The catalytic performance of MIL-53(Al) was evaluated for Friedel-Crafts acylation reaction of indole and benzoyl chloride. The effects of temperature, time, catalyst contents, molar ratio of the reactants, solvent, substituents, and reusability of catalyst on the reaction were all studied in this work.

## 2 Experimental

#### 2.1 Synthesis of MIL-53(Al)

MIL-53(Al) was synthesized by a solvothermal method following literature procedures [21,22]. First, 13 g (35 mmol) aliquot of aluminum nitrate (Al(NO<sub>3</sub>)<sub>3</sub>·9H<sub>2</sub>O) and 2.88 g (17.5 mmol) 1,4-benzenedicarboxylic acid ( $H_2BDC$ ) were mixed with 50 mL deionized water in a 100 mL Teflon-lined stainless steel autoclave, then placed in an oven at 220 °C for 72 h. After completion of the reaction, the autoclave was cooled down to room temperature. The product was filtered, and washed four times with deionized water. It was then purified by a solvent extraction method using N,N'-dimethylformamide (DMF) to remove uncoordinated H<sub>2</sub>BDC. The resultant white powder was washed with methanol three times to remove the DMF molecules trapped inside its cavities. Finally, the powder was dried in vacuum at 80 °C for 2 h. MIL-53(Al) was obtained in a yield of 82.4%. The elemental C and H analysis was carried out using the CARLO ERBA 1106. The respective percentages of C and H were 45.23% and 2.56 (Calculated C: 46.15, H: 2.40).

## 2.2 Catalytic reaction

Friedel-Crafts acylation of indole with benzoyl chloride using MIL-53(Al) catalyst was carried out in a flask reactor with a reflux condenser and continuous stirring. In a typical catalytic reaction, solvent dichloromethane (CH<sub>2</sub>Cl<sub>2</sub>, 3 mL) was first put into the reactor, then indole (0.468 g, 4 mmol), benzoyl chloride (1.680 g, 12 mmol), and n-dodecane (0.136 g, 0.8 mmol) as an internal standard were added successively to a 50 mL reactor containing the MIL-53(Al) (counted on the basis of the molar ratio with the reactant indole,  $n_1:n_{\text{catalyst}}$ , 1:0.05–1:0.07). Then the mixture was stirred at a certain temperature (15-40 °C) for several hours. After the reaction, the catalyst was separated from the solvent by simple centrifugation and the liquid layer was analyzed with reference to n-dodecane by a gas chromatography-flame ionization detector (GC-FID) (Beijing Beifen-Ruili Analytical Instrument Co., Ltd., SP-2100, China). The GC instrument was equipped with a capillary column (HJ. PONA, 50 m×0.2 mm×0.50 µm). The conversion of indole (X), selectivity of 3-acylindole  $(S_3)$ , yield of 3-acylindole  $(Y_3)$ , selectivity of N-acylindole  $(S_4)$ , yield of N-acylindole  $(Y_4)$ , and recovery of catalyst (R) were also calculated. After the first run of the Friedel-Crafts acylation reaction, the catalyst was separated from the reaction mixture, washed with CH<sub>2</sub>Cl<sub>2</sub> (4×10 mL), dried under vacuum at 80 °C for 12 h, and reused for the next run. Catalyst recycling performance was evaluated according to the above reaction procedure.

## 2.3 Characterizations

The X-ray diffraction (XRD) pattern was collected on a D/Max 2500 VB 2+/PC diffractometer (Rigaku, Japan) with Cu-K $\alpha$  irradiation ( $\lambda$ =1.5418 Å, 40 kV, 200 mA) in the 2 $\theta$  range of 5° to 50°. Fourier transform infrared spectroscopy (FT-IR) was recorded on a Bruker model Tensor-27 (Germany) in the KBr/MIL-53(Al) pellets. The spectra were collected after accumulation of 64 scans with a resolution of 1 cm<sup>-1</sup>, at a scan range of 400–4000 cm<sup>-1</sup>.

## 3 Results and discussion

## 3.1 MIL-53(Al) structure

The XRD patterns of the MIL-53(Al) before and after the reaction, and those of the simulated MIL-53(Al), are shown in Figure 1. The XRD pattern of the experimentally synthesized MIL-53(Al) shows main diffraction peaks at  $2\theta$ = 9.30°, 12.58°, 17.76°, 23.24°, 25.10°, 27.16°. Similarly, the characteristic diffraction peaks of the simulated MIL-53(Al) were found at  $2\theta = 9.34^{\circ}$ ,  $12.54^{\circ}$ ,  $17.88^{\circ}$ ,  $23.36^{\circ}$ ,  $25.20^{\circ}$ , 27.26° [23]. Overall characteristic peaks of the synthesized MIL-53(Al) were consistent with the simulated patterns. Comparison of the experimental and the simulated XRD patterns illustrated that crystalline structure of MIL-53(Al) was obtained under the applied synthesis conditions and that the catalyst exhibited a good crystal structure. The XRD patterns of the MIL-53(Al) before and after the reaction show the same characteristic diffraction peaks, at a slightly lower intensity. This result shows that MIL-53(Al) exhibits remarkable stability after catalytic reactions.

The FT-IR spectra of the (MIL-53(Al) and BDC) materials at room temperature in the skeletal region of 400–4000  $\text{cm}^{-1}$  are shown in Figure 2. Two absorption bands of MIL-53(Al) material, located at 1606.4 and 1508.8  $\text{cm}^{-1}$ , could



Figure 1 XRD patterns for the MIL-53(Al) after and before the reaction, and the pattern for the simulated MIL-53(Al).



Figure 2 FI-IR spectra for the synthesized MIL-53(Al) (a), H<sub>2</sub>BDC (b).

be assigned to -C=O asymmetric stretching; the bands at 1446.4 and 1416.0  $\text{cm}^{-1}$  could be assigned to -C=O symmetric stretching [24]. These values were consistent with the presence of -C=O coordinated to aluminum. There was no absorption peak in the 1700.0 cm<sup>-1</sup> region, which shows that BDC had been completely removed from the pores of the structure. However, because MIL-53(Al) absorbed moisture from the air, the vibrational bands at 1632.0 cm<sup>-1</sup> and in the 3600-3500 cm<sup>-1</sup> region respectively correspond to the bending and stretching modes of water. For the BDC material, a strong absorption peak was observed at 1700 cm<sup>-1</sup>; this could be attributed to stretching vibration of -COOH. When we compared the two FT-IR spectra, we found that the stretching vibrations of -COOH of the synthetic MIL-53(Al) shifted to a lower wave number. In addition, the asymmetric stretching and symmetric stretching of -COOH showed different wavelengths, which illustrated the coordination between -COOH and Al. In summary, the synthesized samples showed similar structures to the samples of standard MIL-53(Al).

#### 3.2 Catalytic performance of MIL-53(Al)

Based on the above characterization and analysis, MIL-53 (Al) catalyst was used in a Friedel-Crafts acylation reaction of indole with benzoyl chloride. Different reaction temperatures, times, and catalyst contents were measured, as well as catalyst recycling ability. The reaction equation of indole with benzoyl chloride is shown in Scheme 1.

## 3.2.1 Effect of different temperatures

Table 1 shows the effect of temperature on the conversion of indole, product selectivity, and yield for Friedel-Crafts



**Scheme 1** The Friedel-Crafts acylation reaction of indole with benzoyl chloride.

Table 1 Conversion, selectivity, and yield at different temperatures over MIL-53(Al) catalyst  $^{\rm a)}$ 

Entry	<i>t</i> (°C)	X(%)	$S_{3}$ (%)	$Y_3$ (%)	$S_4$ (%)	$Y_4$ (%)
1	15	97.1	68.1	78.8	31.9	21.2
2	20	97.1	77.4	89.6	22.6	10.4
3	25	97.1	81.1	93.9	18.9	6.1
4	30	89.2	81.0	86.2	19.0	13.8
5	40	81.3	80.9	78.4	19.1	21.6
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a) Reaction conditions:  $n_1:n_{\text{catalyst}}=1:0.06$ , indole (4 mmol), benzoyl chloride (12 mmol), CH<sub>2</sub>Cl<sub>2</sub> (3 ml); reaction time 8 h.

acylation. When the temperature was 15 °C, the conversion of indole was 97.1%; the selectivity of 3-acylindole was 68.1%; the yield of 3-acylindole reached 78.8%; and the selectivity of N-acylindole was 31.9%. When the temperature was increased from 15 to 25 °C, the conversion of indole decreased but the selectivity of 3-acylindole showed an increasing trend; accordingly, the selectivity of Nacylindole showed a decreasing trend. When the temperature was increased from 25 to 40 °C, the conversion of indole dropped to 81.3% and the selectivity of the two products remained almost constant. With the increasing of temperature, the yield of 3-acylindole increased first and then dropped; its maximum yield reached 93.9% at 25 °C. These results were consistent with [25], which used Et<sub>2</sub>AlCl to catalyze the Friedel-Crafts acylation of indole with benzoyl chloride. Wynne et al. [25] found the same trends of the conversion of indole and the selectivity of 3-acylindole. The reason for these results might be that the active Al<sup>3+</sup> sites of MIL-53(Al) were more conducive to reacting with electrophile benzoyl chloride and forming acylium ion at low temperature, which could further induce electrophilic substitution [26].

The results in Table 1 show that the conversion of indole and the selectivity of 3-acylindole were higher when the reaction temperature was 25 °C. When MIL-53(Al) exhibited high catalytic activity, the conversion of indole achieved 97.1% and the selectivity of 3-acylindole reached 81.1%. These results were consistent with [1], in which a traditional Lewis acid catalyst, ZnCl<sub>2</sub>, was used for a Friedel-Crafts acylation reaction. In conclusion, the reaction occurred under milder reaction conditions when a Friedel-Crafts acylation of indole with benzoyl chloride was catalyzed by MIL-53(Al).

## 3.2.2 Effect of different reaction times

Figure 3 shows the effect of reaction time on the conversion of indole and products selectivity. As we may see, after 2 h of reaction time, the conversion of indole rose to 80.4%; the selectivity of 3-acylindole reached 67.4%; and the selectivity of *N*-acylindole was 32.6%. With the extension of reaction time, the conversion of indole and the selectivity of 3-acylindole increased and the selectivity of *N*-acylindole decreased. When the reaction time was extended to 12 h, the conversion of indole increased to 98.1%; the selectivity of



**Figure 3** Effect of the MIL-53(Al) catalyst on the Friedel-Crafts acylation reaction at different times. Reaction conditions:  $n_1:n_{\text{catalyst}}=1:0.06$ , 25 °C, indole (4 mmol), benzoyl chloride (12 mmol), CH<sub>2</sub>Cl<sub>2</sub> (3 mL).

3-acylindole increased to 81.1%; and the selectivity of *N*-acylindole dropped to 18.9%. Before the reaction time reached 8 h, the conversion of indole obviously increased as the reaction time increased. This result indicated that the reaction rate between the indole and benzoyl chloride was faster during this period of time. After the reaction time reached 8 h, the conversion of indole and the selectivity of 3-acylindole did not show obvious changes with the extension of reaction time.

These time-linked changes of reaction conversion and selectivity were consistent Phan *et al.* [27], who catalyzed a Friedel-Crafts acylation reaction in the presence of MOF-5 catalyst. This catalytic activity of MIL-53(Al) can be explained by the fact that its active sites were abundant before 8 h, during which time the reactants could come into full contact with catalyst. Therefore, with the increasing of reaction time, both the conversion and selectivity of the reaction increased rapidly. During the prolonged reaction time, however, some parts of the active sites became covered with solvent or product molecules. Conversion and selectivity of the reaction time, due to a deactivation of active sites or a decrease in the effective concentration of reactants [28].

The results in Figure 3 show that the optimal reaction time was 8 h, during which MIL-53(Al) exhibited high catalytic activity; the conversion of indole achieved 97.1%; and the selectivity of 3-acylindole reached 81.1%. Compared with [29], MIL-53(Al) showed better catalytic activity than the AlCl<sub>3</sub> used as catalyst for the Friedel-Crafts acylation reaction of indole. This behavior could be explained by the fact that –COOH groups would provide more Lewis acid catalytic sites, which could enhance the catalytic activity of MIL-53(Al). Most importantly, the Friedel-Crafts acylation reaction between indole and benzoyl chloride over MIL-53(Al) catalyst could yield a higher conversion of indole and a higher selectivity of 3-acylindole after a short

reaction time at room temperature.

## 3.2.3 Effect of mole ratio of the reactants

Table 2 shows the effect of the molar ratio of reactants indole with benzoyl chloride on the conversion of indole and on the selectivity and yield of two products. The reagent molar ratio is also a main factor that must be taken into consideration during the reaction. When the molar ratio of the indole and benzoyl chloride was 1:1, the conversion of indole was 89.2%; the selectivity of 3-acylindole was 66.7%; and the yield of 3-acylindole was 66.4%. With the increasing of the molar ratio of indole and benzoyl chloride, the conversion of indole and the yield of 3-acylindole increased first and then dropped, whereas the selectivity of 3-acylindole increased first and then remained almost constant. When the ratio was increased to a certain level (1:3), it exhibited the optimal catalytic activity: the conversion of indole reached 97.1%; the selectivity of 3-acylindole was 81.1%; and the yield was 93.9%.

From Table 2, we may see that both the conversion and the selectivity of 3-acylindole increased gradually, and then remained almost constant when the molar ratio increased to a certain value with the increasing of the molar ratio of the reactants. The reason might be that when the molar ratio between indole and benzoyl chloride was small, sufficient contact could not be obtained between the catalyst and the reactants. At this time, the conversion and the selectivity of 3-acylindole would increase with the increasing of molar ratio. In a heterogeneous reaction, mass-transfer limitation might have a significant effect on the reaction rate in the reaction system [14]. However, when the molar ratio between indole and benzoyl chloride rose to a certain value (1:3), because of the presence of a large amount of benzoyl chloride, the benzoyl chloride would have a solvent effect and change the distribution of indole between catalyst surface and liquid phase [27]. Thus, the conversion and selectivity of 3-acylindole remained almost constant. In summary, when MIL-53(Al) was used as catalyst for a Friedel-Crafts acylation reaction of indole and benzoyl chloride, the optimal mole ratio was 1:3.

#### 3.2.4 Effect of different catalyst contents and solvent

Table 3 shows the effect of different catalyst contents and solvents on the conversion, selectivity, and yield of the

**Table 2** Conversion, selectivity, and yield at different molar ratios of thereactants over MIL-53(Al) catalyst  $a^{ij}$ 

Entry	Molar ratio	X(%)	$S_{3}$ (%)	$Y_3$ (%)	$S_4$ (%)	$Y_4$ (%)
1	1:1	89.2	66.7	66.4	33.3	33.6
2	1:2	91.1	70.1	71.5	29.9	28.5
3	1:2.5	94.2	76.3	86.9	23.7	13.1
4	1:3	97.1	81.1	93.9	18.9	6.1
5	1:4	94.8	80.0	91.6	20.0	9.4

a) Reaction conditions:  $n_1:n_{\text{catalyst}}=1:0.06, 25 \text{ °C}, \text{ CH}_2\text{Cl}_2 (3 \text{ mL}); \text{ reaction time 8 h.}$ 

reaction. The effect of catalyst content on the reaction was observed first. When the catalyst content was 1:0.05, the conversion of indole was 90.3%; the selectivity of 3-acylindole was 75.5%; and the yield of 3-acylindole was 81.8%. With the increasing of MIL-53(Al) content, the conversion of indole, the selectivity of 3-acylindole, and the yield of 3-acylindole first increased quickly and then remained almost constant.

When catalyst content was increased to 1:0.07, the conversion of indole rose to 97.2%; the selectivity of 3acylindole rose to 81.0%; and the yield of 3-acylindole rose to 93.8%. This result might be due to an effective absorptive properties effect of MIL-53(Al) [30] in which the excess of catalyst content contributes to the absorption of reactants and thus decelerates the speed of the reaction. In comparison with [26], which reported the use SnCl<sub>4</sub> as catalyst for Friedel-Crafts acylation reaction of indole, our yield was 95.0% when catalyst content was 1.20 mmol (1:1.2). However, we used only 0.06 mmol (1:0.06) MIL-53(Al) to catalyze the reaction but obtained a yield of 93.9%, which showed that MIL-53(Al) has higher catalytic activity than traditional Lewis acid catalysts. Clearly, MIL-53(Al) showed high catalytic activity for Friedel-Crafts acylation reaction: the optimal content of catalyst was 1:0.06; the conversion of indole was 97.1%; the selectivity of 3-acylindole was 81.1%; and the yield was 93.9%.

The effect of different solvents on the reaction performance is also list in Table 3. The content of catalyst was fixed at 1:0.06. When dichloromethane and trichloromethane were used as solvents, the respective conversions of indole were 97.1% and 96.2%; the respective selectivities of 3-acylin-dole were 81.1% and 80.3%; and the respective yields of 3-acylindole were 93.9% and 92.5%. However, when the nonpolar cyclohexane was used as solvent, the conversion of indole was only 89.6%; the selectivity of 3-acylindole dropped to 79.5%; and the yield of 3-acylindole decreased to 86.2%. These results were consistent with previous literature [31] in that polar solvents were more beneficial to a Friedel-Crafts acylation of indole with benzoyl chloride (because indole and benzoyl chloride are both polar materials). According to the theory of similar compatibility, it is easy to dissolve reactants in polar solventsa situation that favors full contact between two reactants

 
 Table 3
 Conversion, selectivity, and yield at different catalyst contents and solvents over MIL-53(Al) catalyst <sup>a)</sup>

Entry	n1: n <sub>catalyst</sub>	Solvent	X(%)	$S_3$ (%)	$Y_{3}(\%)$	$S_4$ (%)	$Y_4$ (%)
1	1:0.05	$CH_2Cl_2$	90.3	75.5	81.8	24.5	18.2
2	1:0.06	$CH_2Cl_2$	97.1	81.1	93.9	18.9	6.1
3	1:0.07	$CH_2Cl_2$	97.2	81.0	93.8	19.0	6.2
3	1:0.06	CHCl <sub>3</sub>	96.2	80.3	92.5	19.7	7.5
4	1:0.06	cyclohexane	89.6	79.5	86.2	20.5	13.8
5	1:0.06	nitrobenzene	84.4	73.4	74.8	26.6	25.2

a) Reaction conditions: 25 °C, indole (4 mmol), benzoyl chloride (12 mmol); reaction time 8 h.

and thus improves conversion. When nitrobenzene was used as solvent, the conversion of indole was only 84.4% and the selectivity of 3-acylindole sharply dropped to 73.4%. The reason could be a possible reaction of weak nucleophilic nitrobenzene with electrophilic benzoyl chloride [32], which would have caused the decline in both the conversion of indole and the selectivity of 3-acylindole. In summary, the experimental results of Friedel-Crafts acylation of indole and benzoyl chloride over MIL-53(Al) catalyst demonstrated that the optimal solvent was dichloromethane with the highest conversion of indole (97.1%), the highest selectivity of 3-acylindole (81.1%), and the highest yield (93.9%).

## 3.2.5 Effect of different substrates

The efficiency of this catalyst was studied in Friedel-Crafts acylations of various indole derivatives with benzoyl chloride under the optimized reaction conditions. The results are summarized in Table 4, where we may see that the reaction conversion was higher when the indole had electrondonating groups such as H, CH<sub>3</sub>, and OCH<sub>3</sub>. When these groups reacted with benzoyl chloride, the respective conversions of indole were 97.1%, 98.4%, and 99.0. At the same time, the electron-drawing group NO<sub>2</sub> decreased the conversion to 79.6%. But the differences between reactants did not have obvious influence upon the selectivity of 3acylindole, which was nearly 81.0%. These results were in accordance with the mechanism of acylation reaction that stipulates an electron-donating group within idole improves its nucleophilic property [33]. Conversely, a strong electrophilic group can decrease the nucleophilic properties of indole and hinder a Friedel-Crafts acylation reaction of the indole with carbonyl-positive ions of benzoyl chloride. When MIL-53(Al) was used as catalyst, electron-donating groups on the indole were beneficial to the Friedel-Crafts acylation reaction and electron-drawing groups hindered reaction, which showed that the catalyst conformed to the reaction mechanism of classic Friedel-Crafts acylation reaction.

# 3.2.6 Catalyst recovery and recycling

Figure 4 shows the results of MIL-53(Al) catalyst recovery and recycling in a Friedel-Crafts acylation over five successive runs. The conversion of indole, the selectivity of 3-

Table 4 Conversion, selectivity, and yield of different substrates over MIL-53(Al) catalyst  $^{\rm a)}$ 

Entry	Substrates	R	X(%)	$S_3(\%)$	$Y_3(\%)$	$S_4(\%)$	$Y_4(\%)$
1	<b>1</b> a	Н	97.1	81.1	93.9	18.9	6.1
2	1b	2-CH <sub>3</sub>	98.4	80.9	95.4	19.1	4.6
3	1c	5-OCH <sub>3</sub>	99.0	81.0	96.0	19.0	4.0
3	1d	6-NO <sub>2</sub>	79.6	80.8	77.5	19.2	22.5

a) Reaction conditions: 25 °C,  $n_1:n_{\text{catalyst}}=1:0.06$ , CH<sub>2</sub>Cl<sub>2</sub> (3 mL); reaction time 8 h.



**Figure 4** Recycling of the MIL-53(Al) catalyst in a Friedel-Crafts acylation of benzene with benzoyl chloride. Reaction conditions: 25 °C, indole (4 mmol), benzoyl chloride (12 mmol), CH<sub>2</sub>Cl<sub>2</sub> (3 mL); reaction time 8 h.

acylindole, the yield, and the recycle rate of the catalyst were considered. Generally, catalyst recycling is an important issue in industry.

Figure 4 shows that after the fifth run, the conversion of indole, the selectivity of 3-acylindole, and the yield of 3acylindole respectively fell to 87.6%, 79.5%, and 84.2%. In parallel, the recycling rate of MIL-53(Al) catalyst fell from 99.1% to 87.5%. This indicated that MIL-53(Al) could be reused without significant degradation in catalytic activity, and shows that MIL-53(Al) catalyst has excellent chemical stability. Additional investigations were undertaken to analyze the MIL-53(Al) catalyst deactivation in the Friedel-Crafts acylation reaction. The catalytic activity had been lost over repeated uses, and the recovery dropped fell below 100%. Reduction of the catalyst caused the decrease in the conversion of indole and the selectivity of 3-acylindole. Most importantly, MIL-53(Al) maintained high catalytic activity after the fifth run, which shows it has stable catalytic performance and great recycling ability for the Friedel-Crafts acylation reaction of indole with benzoyl chloride.

#### 3.3 Reaction mechanism

The Friedel-Crafts acylation reactions use Lewis acids as catalysts to form organic compounds of carbon-carbon bonds. Friedel-Crafts acylation reactions mostly use homogeneous catalysts such as AlCl<sub>3</sub> [34] and ZrCl<sub>4</sub> [31]. The Lewis acid sites of the catalysts are catalytic-active centers, as when AlCl<sub>3</sub> was used as a Lewis acid catalyst for Friedel-Crafts acylation and the Lewis acid Catalyst for Friedel-Crafts acylation and the Lewis acid Catalyst for Friedel-Crafts first react with benzoyl chloride to form an activated complex; this transient complex then produces the acylium ion. The nucleophilic aromatic benzene then attacks the acylium ion to form the products, and the removed hydrogen interacts with halogen to form hydrogen halide.

Although the traditional homogeneous Lewis acid catalysts exhibit high activity for this reaction, they suffer from difficult recovery, high usage amounts, and high economic cost, all of which limit their applications in industry.

To solve the problem of catalyst recovery, various loaded Lewis acid catalysts are desirable for Friedel-Crafts acylation reactions. Selvakumar et al. [8] used the Zn-triflate molecule-loaded SBA-15 silicate to catalyze a Friedel-Crafts acylation of naphthalene with *p*-toluoyl chloride. During the reaction, the Lewis acid sites  $Zn^{2+}$  of the triflate molecules were the catalytic active centers, and the hydroxyl groups of SBA-15 structure increased the acid sites of the catalyst. The reaction mechanism can be expressed by two reaction steps. The first step is that toluoyl chloride interacts with the metal triflate  $(Zn^{2+})$  to form an acyl cation-zinc triflate-activated complex. This transient complex promotes the formation of acylium ion, which is a highly active species. In the second step, the acylium ion reacts with the nucleophilic naphthalene, which gives rise to the formation of 2-acylnaphthalene and eventual regeneration of the catalyst.

However, the catalytic performances of the loaded catalysts are not satisfactory. MOFs have a regular pore structure and a large specific surface area. Metal ions of some MOFs have highly dispersed Lewis acid sites, which exhibit excellent catalytic performance for Friedel-Crafts acylation reactions.

The structure unit of MIL-53(Al) is shown in Figure 5. Based on the characteristics of MIL-53(Al) with Lewis acid  $(Al^{3+})$  catalytic active centers of uniform distribution, a study of the Friedel-Crafts acylation reaction between indole and benzoyl chloride was initiated.

Table 5 shows a comparison of catalytic performance for the Friedel-Crafts acylation reactions of indole with benzoyl chloride using the traditional Lewis acid catalysts AlCl<sub>3</sub> [6], Et<sub>2</sub>AlCl [35], ZrCl<sub>4</sub> [31], and the MIL-53(Al) produced in this work.

From Table 5, it can be seen that, compared with the traditional Lewis acid catalysts, the MIL-53(Al) catalyst has a higher TOF. This shows that when MIL-53(Al) was used for the Friedel-Crafts acylation reaction of indole with benzoyl chloride, the Lewis acid (Al<sup>3+</sup>) catalytic-active centers in MIL-53(Al) showed higher activity. The proposed reaction mechanism is shown in Scheme 2. During the reaction, the metal cations Al<sup>3+</sup> of MIL-53(Al) are the catalytic active centers, and ligands BDC that surround Al<sup>3+</sup> promote the



Figure 5 Structure model of MIL-Al<sup>3+</sup>.

Table 5 Catalytic performance of different Lewis acids

Lewis acids <sup>a)</sup>	$n_1:n_{\text{catalyst}}^{\text{b}}$	$T(\mathbf{h})^{\mathbf{c})}$	Yield (%) d)	TOF $(h^{-1})^{e}$	Ref.
AlCl <sub>3</sub>	1:6	2	88.0	0.07	[6]
Et <sub>2</sub> AlCl	1:1.5	2	80.0	0.27	[35]
$ZrCl_4$	1:1.2	4	71.0	0.15	[31]
MIL 52(AI)	1.0.06	2	80.4	6.70	This work
WIIL-55(AI)	1.0.06	4	90.3	3.77	This work

a) Reaction conditions: AlCl<sub>3</sub>: 25 °C, solvent CH<sub>2</sub>Cl<sub>2</sub>; Et<sub>2</sub>AlCl: 0 °C, solvent CH<sub>2</sub>Cl<sub>2</sub>; ZrCl<sub>4</sub>: 30 °C, solvent anhyd DCE; MIL-53(Al): 25 °C, solvent CH<sub>2</sub>Cl<sub>2</sub>; b) catalyst contents, counted on the basis of the molar ratio with the reactant indole; c) reaction time; d) yield of isolated product; e) turn over frequency by the amount of reactants converted per atom per hour.

reaction. At first, the  $Al^{3+}$  of MIL-53(Al) participates in the direct bonding of the benzoyl chloride (1) to form activated complex (2), after which this unstable complex converts to an acylium ion (3). Next, a nucleophile indole (4) attacks the acyl ion (3) and an electrophilic substitution reaction occurs to generate the indole intermediate (5). After the charge transfer to the chlorine ion occurs, the HCl and product 3-acylindole (7) is formed. The MIL-53(Al) catalyst can be regenerated and reused for catalytic reactions.

## 4 Conclusions

MIL-53(Al) catalyst was synthesized by a solvothermal method and characterized by XRD and FT-IR. The catalytic activity of MIL-53(Al) was evaluated for a Friedel-Crafts acylation reaction between indole and benzoyl chloride. The results showed that the synthesized catalyst was MIL-53(Al). The optimal reaction conditions included a 1:3 molar ratio of indole and benzoyl chloride, a 1:0.06 catalyst content, dichloromethane as solvent, 25 °C reaction temperature, and 8 h reaction time. Under these conditions, MIL-53(Al) exhibited better catalytic activity with its highest conversion at 97.1% as well as an 81.1% selectivity of 3-acylindole and a 93.9% yield of 3-acylindole. Electron-donating groups on the indole were beneficial to the Friedel-Crafts acylation reaction and electron-drawing groups



Scheme 2 Proposed reaction mechanism for Friedel-Crafts acylation of indole with benzoyl chloride.

hindered the reaction; these results were consistent with the mechanism of the classic Friedel-Crafts acylation reactions. In addition, MIL-53(Al) could be separated from the reaction system by centrifugation and kept at high catalytic activity after being reused five times. MIL-53(Al) resolved the problems with traditional Lewis acid catalysts (AlCl<sub>3</sub>, FeCl<sub>3</sub>, and SnCl<sub>4</sub>) such as difficult recycling, poor reusability, and environmental pollution potential. This kind of catalyst thus provides good prospects for future industrial applications of Friedel-Crafts acylation reactions.

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