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Green Synthesis of 1,4-Dihydropyridine using MIL-101 (Cr) MOF as catalyst

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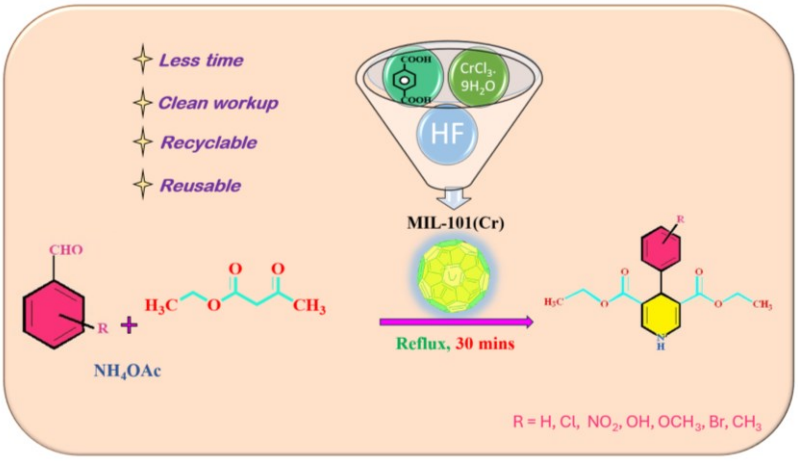
Abstract

The synthesis of 1,4-dihydropyridine through Hantzsch's multicomponent reaction was carried out using MIL-101(Cr) metal organic framework (MOF) as a catalyst. The catalyst MIL-101(Cr) was synthesised by the hydrothermal method and characterized using various spectroscopic techniques like FT-IR, XRD, and UV-Vis spectroscopy. The involvement of MIL-101(Cr) MOF as a heterogeneous catalyst has shown great catalytic activity and enhanced efficiency even with small catalyst loading, less reaction time, higher yield, clean workup process, less waste generation, recyclable and reusable properties. The synthesised 1,4-dihydropyridine derivatives were characterized by ^{1}H and ^{13}C NMR spectroscopy.



Keywords: Metal organic framework, 1,4-dihydropyridine, Hantzsch reaction, Multicomponent reaction.

Introduction

Metal organic framework (MOF) is a type of crystalline, porous material resulting from a coordination bond between metal ions and organic bridging ligands. Metal-organic frameworks (MOFs) are also recognized as porous coordination polymers (PCPs).[1] MOFs have potential applications in various fields, including separation, gas storage[2], sensor technology[3], catalysis[4], ion exchange[5], drug delivery[6], and luminescence[7] because of their specific porous structure. MOFs are often employed in synthetic organic reactions as catalysts because of their porous crystalline nature, high stability, high surface area, tunable pore size, and tunable functionalities.

Mainly, MOF's ability to act as a heterogeneous catalyst in synthetic chemical reactions is gaining much attention among researchers, so MOFs have been used in many catalytic reactions like organic catalysis, asymmetric catalysis, and photocatalysis.[1] As the pores and pore windows of MOFs have a high volume, a large amount of large reactant molecules can diffuse into the pores, and at the same time, the same amount of large product molecules can move out of the framework easily.[8] The catalytic activities of MOFs are due to the presence of catalytically active sites like metal atoms located at the nodes, which act as Lewis acids, and exposed terminal ligands that usually act as Lewis bases.[9] For solid catalysts like MOFs, the accessibility of catalytic sites is more important. MOFs are mainly used as catalysts for different organic transformations, including Knoevenagel condensation, Aldol condensation, Michael addition, Henry reaction, cycloaddition reaction, and one-pot cascade reactions[10]

Even though various MOFs are being synthesised, MIL-101(Cr) plays an important role in catalysis as it has a high specific surface area, chemical, and thermal stability, it was first synthesised by Ferey and co-workers in 2005.[11] MIL-101(Cr) was made up of chromium(III) trimeric octahedral clusters and carboxylate moieties and has the chemical composition of $\{Cr_3F(H_2O)_2O(BDC)_3.nH_2O\}$(1,4-benzenedicarboxylate (BDC)). It can withstand high temperatures up to 300℃, and it is insoluble in water and organic solvents such as DMF, DMSO, acetonitrile, ethanol, and acetone. MIL-101(Cr) was used as a catalyst in the oxidation of aryl sulfide, epoxidation, cyanosilylation, and desulfurization reactions.[12] MIL-101(Cr) showed a good site selectivity and reasonably high conversions in organic synthesis. MIL-101(Cr) can be synthesised using various synthesis methods like the hydrothermal, microwave-assisted, and dry gel conversion methods.[13]

The application of reusable metal-organic frameworks as a heterogeneous catalyst for the selective construction of biologically important organic motifs has been identified as a great alternative to the conventional acid catalyst.[14] Specially, MIL-101(Cr) catalyst has been efficiently utilized to synthesize various biologically important heterocyclic compounds. Recently, MIL-101(Cr) was used to catalyse the one-pot, three-component reaction of benzil, 4-chlorobenzaldehyde, and ammonium acetate, giving 2,4,5-trisubstituted imidazole under solvent-free conditions. The Lewis acidic property of the metal centre present in the catalyst activates the carbonyl group to form imine intermediates, which further leads to the formation of imidazole. The heterogeneous MIL-101(Cr) catalyst showed high catalytic activity and high efficiency; it was reused up to 5 times without major loss in its efficiency. The reaction was completed within 10 minutes to give a higher yield using only a small amount (5 mg) of catalyst to achieve the desired product.[15]

By utilizing the exceptional catalytic potential of MIL-101(Cr), biologically important, valuable benzoxazoles were reported by the condensation reaction of 2-aminophenols/2-aminothiophenol/o-phenylenediamine with various aldehydes in the presence ethanol/xylene as a solvent and 10 mg of MIL-101(Cr) was used as a heterogeneous catalyst under gentle reaction conditions gave a larger yield. The formation of benzoxazoles proceeds through the coordination of aldehydes to the Lewis acidic site (catalytic site) in MOF, which was formed from chromium(III), followed by the formation of an imine intermediate, and lastly the intramolecular addition of XH group (X= N, O, S). This novel method of synthesis employed MIL-

101(Cr) as a catalyst, showed strong functional group tolerance, broad substrate scope, and a clean synthesis process, making it applicable in the industrial synthesis of benzoazoles.[16] Similarly, MIL-101(Cr) was used to carry out the Ullmann reaction to synthesize pharmaceutically active biphenyl and biphenyl diols. [17] The main advantages of using MIL-101(Cr) catalyst, it requires a very short reaction time, very clean synthesis, low solvent usage, mild reaction conditions, and higher yield when compared with other MOF catalysts.

MIL-101(Cr) was used for the reduction of imines, to give corresponding amines in a good yield. MIL-101(Cr), along with trichlorosilane as a hydrogen source, reduces the imine (-C═NH) bonds to give respective amines. The reaction showed enhanced site selectivity because of its tunable pore size and surface area. Further, the mechanistic studies, such as FT-IR and DRIFT spectroscopy, revealed that the porous structure of the MIL-101(Cr) was responsible for the enhanced catalytic activity of the interaction between substrate and catalyst.[18]

1,4-dihydropyridine is a pyridine-based, important class of heterocyclic compounds that shows excellent pharmacological activities such as anticancer[19], antiviral, antimicrobial, anti-inflammatory[20,] antihypertensive[21], and anti-anginal. The traditional synthesis method of 1,4-dihydropyridine was the Hantzsch reaction.[22] Over the period, various synthetic preparation methods have been developed and used to prepare 1,4-dihydropyridines with specific substitutions and functionalities. However, those methods have some drawbacks, like extended reaction time, expensive catalysts, higher temperature, and complicated workup procedures.[15] Nowadays, the application of MOF as a heterogeneous catalyst in the synthesis of 1,4-dihydropyridine has been gaining lots of attention because of its increased efficiency, selectivity, and sustainability.

Due to its increased stability and high catalytic activity, sulfonic acid functionalized MIL-101-SO3H, MOF has been used to synthesize 1,4-dihydropyridine via the Hantzsch reaction. The optimum temperature and time required for the full conversion were 60℃ and 8h, respectively. The catalyst was recovered and reused for 8 cycles without a major decrease in its catalytic activity, which was confirmed by FTIR, Powder XRD, and SEM analysis. The reaction was initiated by the sulfonic group present in the catalyst; only a smaller amount of the catalyst was required for the reaction. The catalyst showed good stability and functional group tolerance.[23] Recently, a new 3D interpenetrated MOF, IITKGP-51, was developed and used as a heterogeneous catalyst in one-pot Hantzsch condensation reaction. The reaction mixture was stirred at 60℃ in ethanol solvent medium for 4h to get the desired product, and the catalyst showed good functional group tolerance.[24]

By considering this fact herein, we report the synthesis of 1,4-dihydropyridine using MIL-101(Cr) as a catalyst without any anchoring group introduced into the MOF, such as functional groups. The involvement of metal-organic frameworks as a green and heterogeneous catalyst in the synthesis of 1,4-dihydropyridine was very suitable due to their large surface area, tunable porosity, and high efficiency. The MIL-101(Cr) alone showed great catalytic activity, compared to the pre-/post-functionalized MOFs in the same Hantzsch reaction. Even with low catalytic loading of MOF exhibited good catalytic activity in a one-pot, three-component reaction of 1,4-dihydropyridine, and the separation of the catalyst from the reaction mixture was very easily achievable. The MIL-101(Cr) is a recoverable and reusable catalyst that also reduces reaction time to give a good yield. It can be synthesised using easily available starting materials.

Results and Discussion

Characterization of MIL-101(Cr) catalyst

The preparation of the catalyst was achieved from chromium chloride ($CrCl_3$ .9 H_2O), terephthalic acid (BDC), and hydrofluoric acid (HF) using the reported procedure.[11] It was characterized using UV, FTIR, and X-ray

analyses.

UV–Vis absorption spectroscopy

Figure 1 shows the UV-Vis spectrum of synthesised MIL-101(Cr). Three electronic transitions can be observed at 240, 440, and 594 nm. The peak observed in the UV region (240 nm) was due to the chromium(III) compounds. The peak at 440 nm corresponds to π–π* transition, which is due to the presence of an aromatic compound. These electronic transitions match with previously reported.[25]

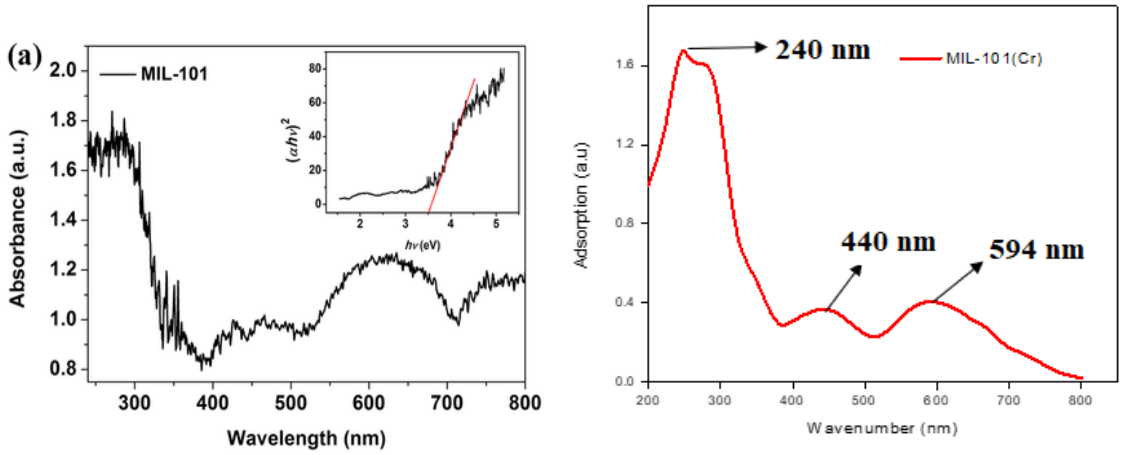


Figure 1. a) UV spectra of reported MIL-101(Cr), **b)** UV spectra of synthesized MIL-101(Cr).

FT-IR spectroscopy

The functional groups of MIL-101(Cr) were analysed using Fourier transform infrared (FTIR) spectroscopy, as Figure 2 illustrates. The broad band at 3391 cm^{-1} is attributed to stretching vibrations. The band at 1623 cm^{-1} corresponds to bending vibrations. The O-C-O symmetrical stretching vibration band at 1397 cm^{-1} confirms the presence of BDC (benzenedicarboxylate) within the MIL-101(Cr) structure.[26] The presence of the benzene ring was confirmed by the additional bands between 600 and 1600 cm^{-1}, which include the C=C stretching vibration at 1509 cm^{-1} and the C-H deformation vibrations at 747, 883, 1018, and 1105 cm^{-1}, respectively. Peaks connected to oxygen stretching vibrations with metals were typically seen in the 400–800 cm^{-1} range, and in this spectrum, the peak at 662 cm^{-1} is connected to the Cr-O vibration. The FTIR spectrum of the synthetic MIL-101(Cr) shows good agreement with previously published ones.

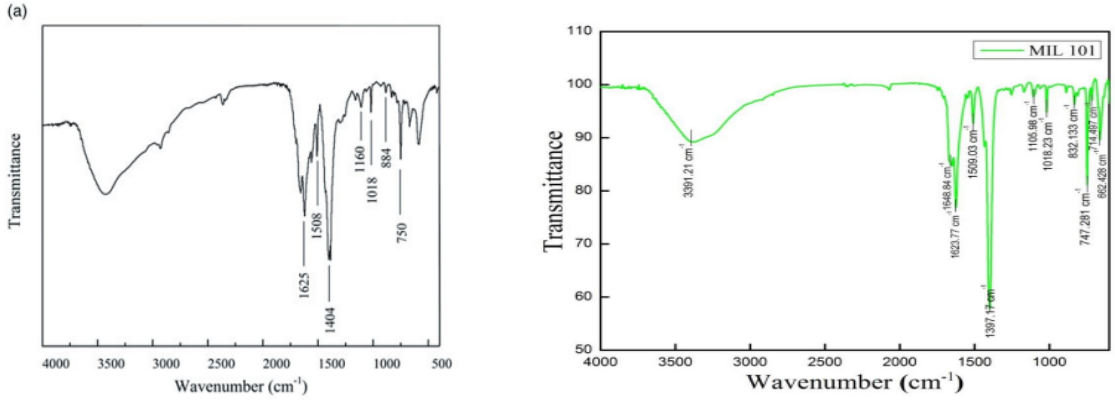


Figure. 2. a) FTIR spectra of Reported MIL-101(Cr), **b)** FTIR spectra of synthesized MIL-101(Cr).

X-ray diffraction analysis

MIL-101(Cr) phase identification was evaluated using XRD, as Figure 3 illustrates. Since only desired peaks were seen in the XRD pattern and undesired peaks were absent, it was confirmed that MIL-101(Cr) was pure and crystalline. Six major peaks that may be seen at 2^{θ} 14 1.64, 2.7, 3.2, 3.88, 5.04, and 8.94. The one produced here and the stated XRD pattern for MIL-101(Cr) show good agreement with previous reported

papers.[27] MIL-101(Cr) was synthesized, it may be claimed, and a highly crystalline structure was obtained. The XRD pattern's intense peaks at tiny angles (2^{θ}) show that this porous material has a lot of pores in its structure.

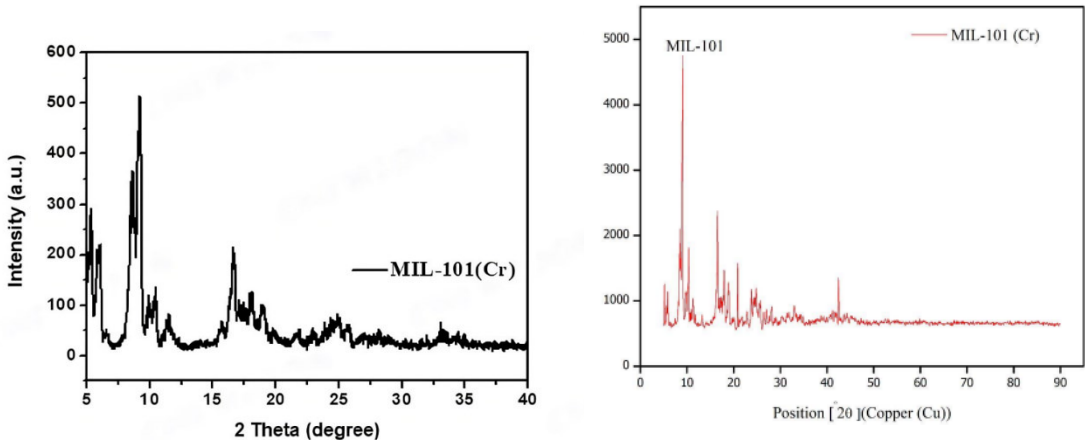
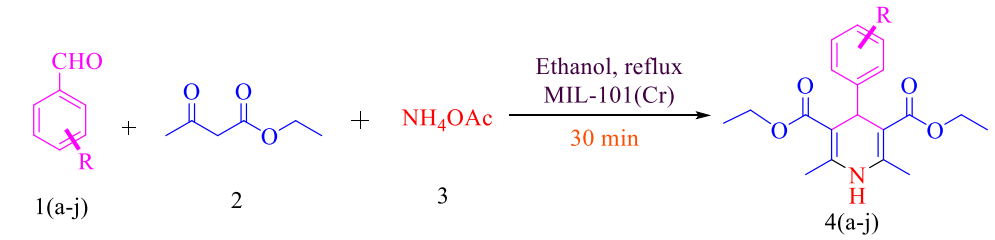


Figure 3. (a) XRD pattern of reported MIL-1(Cr) **(b)** XRD pattern of synthesized MIL-1(Cr)

Catalytic activity of MIL-101(Cr)

Synthesis of diethyl 4-(4-chlorophenyl)-2,6-dimethyl-1,4-dihydropyridine-3,5-dicarboxylate 4b

In a round-bottom flask, 4-chlorobenzaldehyde (1b; 0.1 mmol), 20 mg of MIL-101(Cr), ethyl acetoacetate (2; 0.23 mmol), and ammonium acetate (3; 0.29 mmol) in ethanol were added, and the mixture was refluxed for 30 min. After completion of the reaction, as evidenced by TLC, the spin was centrifuged to remove the catalyst, and the supernatant solution was added to the crushed ice to obtain the precipitation. The crude product was filtered and recrystallized using ethanol. The catalytic activity of MIL-101(Cr) was studied by repeating the same reaction conditions. The reaction gave a 95% yield in 30 minutes.



1a: R = H
1b: R = 4-Cl
1c: R = 2-Cl
1d: R = 4-Br
1e: R = 4-NO_2
1f : R = 3-NO_2
1g: R = 4-OH
1h: R = 4-OCH_3
1i: R = 2-OCH_3
1j: R = 4-CH_3

4a: R = H
4b: R = 4-Cl
4c: R = 2-Cl
4d: R = 4-Br
4e: R = 4-NO_2
4f : R = 3-NO_2
4g: R = 4-OH
4h: R = 4-OCH_3
4i: R = 2-OCH_3
4j: R = 4-CH_3

Scheme 1. Synthesis of 1,4-dihydropyridine using MIL-101(Cr) catalyst.

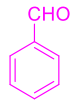
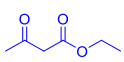
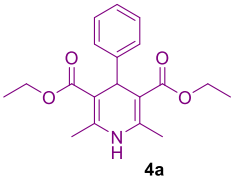
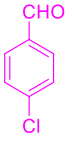
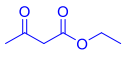
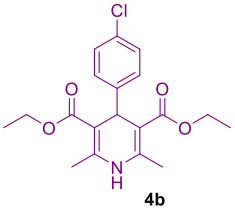
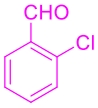
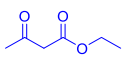
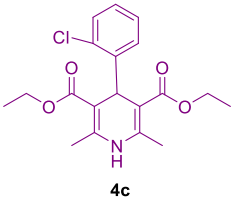
Table1. Optimization of reaction conditions catalyzed by MIL-101(Cr)

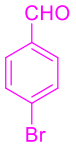
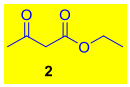
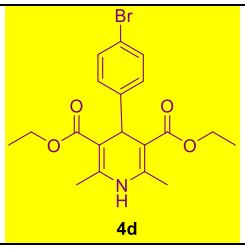
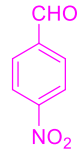
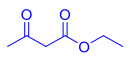
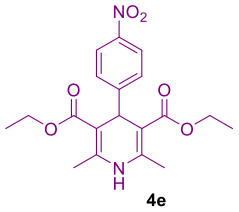
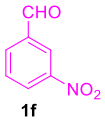
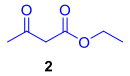
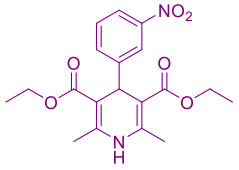
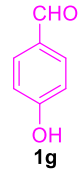
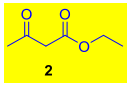
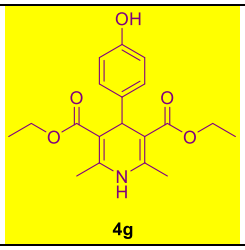
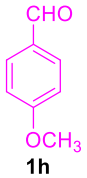
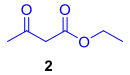
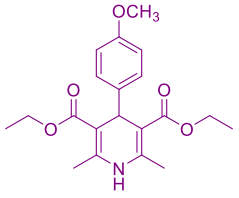
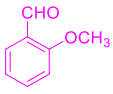
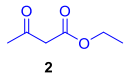
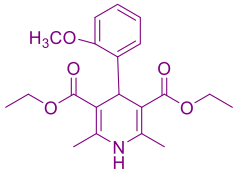
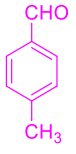
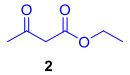
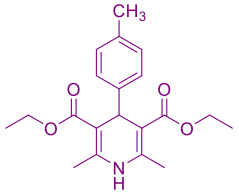
Entry	Catalyst weight (mg)	Solvent	Temperature (°C)	Time (min)	Yield (%)
1	-	Ethanol	Reflux	120	0
2	-	Ethanol	RT	120	trace
3	5	THF	Reflux	120	47

4	5	H_2O	Reflux	120	48
5	5	Ethanol	Reflux	60	81
6	10	Ethanol	Reflux	30	83
7	15	Ethanol	Reflux	30	87
8	**20**	**Ethanol**	**Reflux**	**30**	**95**
9	25	Ethanol	Reflux	30	82
10	20	Methanol	Reflux	30	86
11	20	CH_3CN	Reflux	30	79
Reaction conditions: **1b** (0.1 mmol), **2** (0.23 mmol), and solvent (5mL).					

Experimental investigations have been conducted on the preparation of 1,4-dihydropyridine derivatives, demonstrating that parameters such as solvent, temperature, time, and the amount of catalyst used are crucial factors that influence the reaction rate and yield. To determine suitable reaction conditions, the reaction was initially carried out under reflux conditions in different solvents, it was found that ethanol was the most efficient solvent. Next, the experiment was conducted at room temperature, without any catalyst, and the reaction yield was found to be very low. With a catalyst, the reaction gave a moderate to good yield under reflux conditions. To evaluate the appropriate amount of catalyst needed, the model reaction was carried out using different amounts of catalyst (20, 15, 10, and 5 mg). It was found that the most effective amount of catalyst was 20 mg, and larger amounts decreased the yield. Furthermore, the reaction time was also optimized, the use of the catalyst reduced the reaction time significantly. (Table 1). All the 1,4-dihydropyridine derivatives are synthesized and their yield and melting points, along with reported compounds, are given in Table 2.

Table 2. Synthesis of 1,4-dihydropyridine derivatives

S. No	Aldehyde	Ethyl acetoacetate	Nitrogen donor	1,4 dihydropyridine Derivative	Yield (%)	Reported Yield (%)	Melting point (°C)	Reported Melting point (°C)
1	 1a	 2	NH_4OAc 3	 4a	92	90	157-159	156-158[28]
2	 1b	 2	NH_4OAc 3	 4b	95	82	146-148	144-146[28]
3	 1c	 2	NH_4OAc 3	 4c	92	90	132-134	130-132[29]

4	 **1d**	 **2**	NH_4OAc **3**	 **4d**	94	93	158-160	160-162[28]
5	 **1e**	 **2**	NH_4OAc **3**	 **4e**	93	92	135-137	130-132[28]
6	 **1f**	 **2**	NH_4OAc **3**	 **4f**	92	91	160-162	164-166[28]
7	 **1g**	 **2**	NH_4OAc **3**	 **4g**	84	81	233-235	230-232[28]
8	 **1h**	 **2**	NH_4OAc **3**	 **4h**	83	82	153-155	157-159[28]
9	 **1i**	 **2**	NH_4OAc **3**	 **4i**	88	87	137-139	139-141[29]
10	 **1j**	 **2**	NH_4OAc **3**	 **4j**	86	85	141-143	144-146[28]
Reaction time = 30 min (for all the reactions)								

Reusability of the catalyst

One of the interesting features of MIL-101(Cr) was its recyclability. The catalyst can be recovered and reused up to 5 cycles, without a major decrease in its efficiency, as shown in Figure 4. In this study, 4-

chlorobenzaldehyde (1b; 0.1 mmol), ethyl acetoacetate (2; 0.23 mmol), and ammonium acetate (3; 0.29 mmol) were refluxed under the same reaction conditions. The catalyst was separated after each cycle by centrifuging the reaction mixture and thoroughly rinsing with distilled water, followed by ethanol. The catalyst was then dried in the oven for 3 hrs at 120 ◦C. In the first, second, third, fourth, and fifth cycles, the catalyst produced 95%, 92%, 89%, 85%, and 82% product, respectively.

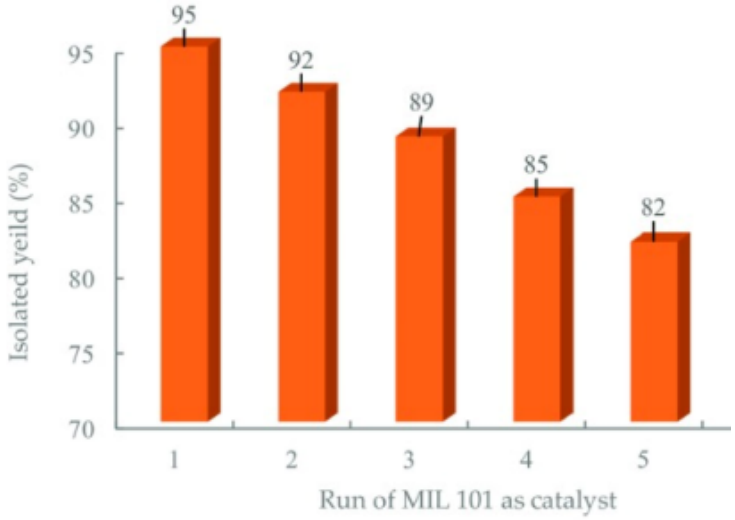


Figure 4. Reusability of the MIL-101(Cr) catalyst for five cycles.

Conclusions

In conclusion, MIL-101(Cr) was synthesised and used as a catalyst in the Hantzsch reaction to synthesize 1,4-dihydropyridine derivatives. The reaction was carried out under mild reaction conditions, and only a small amount of catalyst was used. MIL-101(Cr) was a great choice of catalyst as it produced a good yield of product, 95% yield, under lower temperatures and short reaction times. The reaction gave almost pure products, evidenced by TLC, making it an easier process to get pure 1,4-dihydropyridine derivatives. The catalyst's recyclability and reusability were also explored by simply removing it from the reaction mixture by filtration and reusing it. The catalyst was active up to 5 cycles under ideal conditions and showed good efficiency.

Experimental Section

General. Chromium chloride ($CrCl_3.9H_2O$), terephthalic acid (BDC), hydrofluoric acid (HF), *N,N*-dimethyl formamide (DMF), substituted benzaldehyde, ethyl acetoacetate, ammonium acetate, and ethanol were acquired from Merck and were utilized without any further purification. XRD spectra were analysed using an Empyrean series III diffractometer with an energy resolution of 450 eV. FT-IR spectra (4000- 400 cm^{-1}) were recorded using KBr disks on an infrared spectrometer. ^{1}H and ^{13}C NMR spectra were recorded on a Bruker Multiprobe Nuclear Magnetic Resonance Spectrometer - 400 MHz, and chemical shift values are reported in ppm (parts per million) using TMS as the internal reference.

Synthesis of MIL-101(Cr). MIL-101(Cr) MOF was synthesised hydrothermally by dissolving $CrCl_3.9H_2O$ (1 mmol) and BDC (1.5 mmol) in deionized water (DI, 20 mL) and followed by the addition of HF (20 µL). Then the mixed

suspension was vigorously stirred for 20 min and transferred to a teflon-lined stainless-steel autoclave. After that, the autoclave was kept under autogenic pressure at 180°C for 8h. The resulting green solid was separated from the mixture via centrifuge (5 min) and thoroughly washed with deionized water and DMF many times. The solid product was post-treated in water (20 mL) at 80 °C for 1h and ethanol (20 mL) at 70 °C for 3h, respectively. After centrifugation, the obtained solid was dried at 120 °C under vacuum overnight for further use.

General procedure for the synthesis of 1,4-dihydropyridine. MIL-101(Cr) was used as a catalyst in one-pot three-component synthesis of 1,4-dihydropyridine derivatives. benzaldehyde, ethyl acetoacetate, and ammonium acetate were refluxed in the presence of MIL-101(Cr) as a catalyst. The progress of the reaction was monitored by TLC using hexane/DCM as eluting mixture. After completion of the reaction, the reaction mixture was extracted by using DCM and water (3 × 100 mL). Then the organic layer was collected and dried over anhydrous sodium sulphate, filtered, and the solvent was removed under vacuum to afford 1,4-dihydropyridine.

Dimethyl 2,6-dimethyl-4-phenyl-1,4-dihydropyridine-3,5-dicarboxylate (4a).[28] Pale yellow colour; yield: 92%; MP: 156-158 °C; ^{1}H NMR ($CDCl_3$, 400 MHz) δ ppm: 1.21 (t, *J* 6.8 Hz, 6H, $2CH_3$), 2.34 (s, 6H, $2CH_3$), 4.08 (q, *J* 6.8 Hz, 4H, $2CH_2$), 4.99 (s, 1H, CH), 5.54 (s, 1H, NH), 7.10-7.14 (m, 1H, ArH), 7.18–7.22 (m, 2H, ArH), 7.28–7.29 (m, 2H, ArH). ^{13}C NMR (100 MHz, $CDCl_3$): δ 14.3, 19.6, 39.6, 59.7, 104.23, 126.1, 127.8, 128.0, 143.8, 147.8, 167.6.

Dimethyl 4-(4-chlorophenyl)-2,6-dimethyl-1,4-dihydropyridine-3,5-dicarboxylate (4b).[28] Yellow colour; yield: 95%; MP: 146-148 °C; ^{1}H NMR ($CDCl_3$, 400 MHz) δ ppm: 1.25 (t, *J* 7.1 Hz, 6H, $2CH_3$), 2.38 (s, 6H, $2CH_3$), 4.18 (q, *J* 7.1 Hz, 4H, $2CH_2$), 5.12 (s, 1H, CH), 5.89 (br, 1H, NH), 7.16–7.21 (m, 4H, ArH). ^{13}C NMR (100 MHz, $CDCl_3$): δ 14.6, 19.9, 42.6, 59.9, 104.23, 126.1, 127.5, 129.1, 143.9, 148.8, 167.8.

4-(-2-Chlorophenyl)-1,4-dihydro-2,6-diethyl-4-phenylpyridine-3,5-dicarboxylate (4c).[29] Pale yellow colour; yield: 92%; MP: 132-134 °C; ^{1}H NMR ($CDCl_3$, 400 MHz) δ ppm: 1.31 (t, *J* 7.2 Hz, 6H, $2CH_3$), 2.29 (s, 6H, $2CH_3$), 4.18 (q, *J* 7.2 Hz, 4H, $2CH_2$), 5.42 (s, 1H, CH), 5.88 (s, 1H, NH), 7.06 (dt, 1H, ArH *J* 1.5, 7.6 Hz), 7.12 (dt, 1H, ArH *J* 1.2, 7.6 Hz), 7.23–7.25 (m, 2H, ArH). ^{13}C NMR (100 MHz, $CDCl_3$): δ 14.4, 19.5, 39.7, 59.8, 104.13, 126.5, 126.8, 127.8, 128.1, 131.4, 143.7, 148.8, 167.5.

Dimethyl 4-(4-bromophenyl)-2,6-dimethyl-1,4-dihydropyridine-3,5-dicarboxylate (4d).[28] Light brown colour; yield: 94%; M.P = 160–162 °C, ^{1}H NMR (400 MHz, $CDCl_3$) δ: 1.23 (t, *J* 7.1 Hz, 6 H, $2CH_3$), 2.35 (s, 6 H, $2CH_3$), 4.11 (q, *J* 7.1 Hz, 4 H, $2CH_2$), 5.33 (s, 1H, CH), 5.73 (s, 1H, NH), 7.12–7.31 (m, 4H, ArH). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 14.2, 19.3, 39.3, 59.9, 104.0, 128.1, 131.0, 130.2, 142.3, 148.3, 167.7.

4-(-4-Nitrophenyl)-1,4-dihydro-2,6-diethyl-4-phenylpyridine-3,5-dicarboxylate (4e).[28] Dark yellow colour; yield: 93%; MP: 160-162 °C; ^{1}H NMR ($CDCl_3$, 400 MHz) δ ppm: 1.27 (t, *J* 7.2 Hz, 6H, $2CH_3$), 2.39 (s, 6H, $2CH_3$), 4.19 (q, *J* 7.2 Hz, 4H, $2CH_2$), 5.15 (s, 1H, CH), 5.87 (br, 1H, NH), 7.75 (d, *J* 8.7 Hz, 2H, ArH), 8.06 (d, *J* 8.7 Hz, 2H, ArH). ^{13}C NMR (100 MHz, $CDCl_3$): δ 14.7, 19.8, 42.7, 59.8, 104.13, 126.3, 127.7, 129.3, 143.8, 148.9, 167.7.

Dimethyl 2,6-dimethyl-4-(3-nitrophenyl)-1,4-dihydropyridine-3,5-dicarboxylate (4f).[28] Yellow colour; yield: 92%; M.P = 132–134 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 1.23 (t, *J* 7.1 Hz, 6H, $2CH_3$) 2.24 (s, 6H, $2CH_3$), 4.10 (q, *J* 7.1 Hz, 4H, $2CH_2$), 5.07 (s, 1H, CH), 5.71 (br, 1H, NH), 8.01–7.35 (m, 4H, ArH). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 14.2, 19.3, 38.7, 59.9, 103.6, 121.6, 122.5, 123.3, 136.2, 145.0, 146.7, 150.3, 168.1.

4-(-4-Hydroxyphenyl)-1,4-dihydro-2,6-diethyl-4-phenylpyridine-3,5-dicarboxylate (4g).[28] Pale yellow colour; yield: 84%; MP: 233-235 °C; ^{1}H NMR ($CDCl_3$, 400 MHz) δ ppm: 1.17 (t, *J* 6.9 Hz, 6H, $2CH_3$), 2.37 (s, 6H, $2CH_3$), 4.16 (q, *J* 6.9 Hz, 4H, $2CH_2$), 5.14 (s, 1H, CH), 5.93 (br, 1H, NH), 7.85 (d, *J* 8.8 Hz, 2H, ArH), 8.16 (d, *J* 8.8 Hz, 2H, ArH), 9.09 (bs, 1H, OH). ^{13}C NMR (100 MHz, $CDCl_3$): δ 14.8, 19.9, 42.8, 59.9, 104.6, 126.7, 127.9, 129.5, 143.9, 148.6, 167.8.

Dimethyl 4-(4-methoxyphenyl)-2,6-dimethyl-1,4-dihydropyridine-3,5-dicarboxylate (4h).[28] Pale yellow colour; yield: 83%; M.P = 153–155 °C, ^{1}H NMR (400 MHz, $CDCl_3$) δ: 1.22 (t, *J* 7.1 Hz, 6H, $2CH_3$), 2.32 (s, 6H, $2CH_3$), 3.75 (s, 3H, CH_3), 4.09 (q, *J* 7.1 Hz, 4H, $2CH_2$), 5.05 (s, 1H, CH), 5.72 (s, 1H, NH), 7.18–6.81(m, 4H, ArH). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 14.3, 19.2, 39.3, 53.7, 59.8, 103.5, 113.6, 131.1, 136.3, 146.5, 158.0, 167.8.
Dimethyl 4-(2-methoxyphenyl)-2,6-dimethyl-1,4-dihydropyridine-3,5-dicarboxylate (4i).[29] Pale yellow colour; yield: 88%; M.P = 137–139 °C, ^{1}H NMR (400 MHz, $CDCl_3$) δ: 1.24 (t, *J* 7.1 Hz, 6H, $2CH_3$), 2.34 (s, 6H, $2CH_3$), 3.90 (s, 3H, CH_3), 4.07 (q, *J* 7.1 Hz, 4H, $2CH_2$), 5.11 (s, 1H, CH), 5.73 (s, 1H, NH), 7.40–6.80 (m, 4H, ArH). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 14.1, 19.3, 32.6, 54.3, 59.8, 103.9, 112.7, 121.7, 122.1, 127.9, 131.2, 146.5, 158.3, 167.7.
Dimethyl 2,6-dimethyl-4-(*p*-tolyl)-1,4-dihydropyridine-3,5-dicarboxylate (4j).[28] Pale yellow colour; yield: 86%; M.P = 135–137 °C, ^{1}H NMR (400 MHz, $CDCl_3$) δ: 1.21 (t, *J* 7.1 Hz, 6H, $2CH_3$), 2.22 (s, 3H, CH_3), 2.32 (s, 6H, $2CH_3$), 4.07 (q, *J* 7.1 Hz, 4H, $2CH_2$), 5.02 (s, 1H, CH), 5.73 (s, 1H, NH), 7.19–7.02 (m, 4H, ArH). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 14.2, 19.5, 21.3, 39.4, 59.7, 104.1, 127.7, 128.3, 135.4, 143.9, 146.3, 168.1.

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Supplementary Material

Supplementary data associated with this article are available in the Electronic Supplementary Material (ESI).

References

1. Yuan-Biao, H.; Jun, L.; Xu-Sheng, W.; Rong, C. *Chem. Soc. Rev.* **2017**, *46*, 126-157. https://doi.org/10.1039/C6CS00250A
2. Jiewei, L.; Lianfen, C.; Hao, C.; Jianyong, Z.; Li Z.; Cheng-Yong, S. *Chem. Soc. Rev.* **2014**, *43*, 6011-6061. https://doi.org/10.1039/C4CS00094C
3. Won-Tae, K.; Ji-Soo, J.; Il-Doo, K. *Chem.* **2019**, *5*, 1938−1963. https://doi.org/10.1016/j.chempr.2019.04.013
4. Anastasiya, B.; Nikita, K.; Il Son, K.; Jeremy, A. B.; Adrian, R.; Jorge, G. *Chem. Rev.* **2020**, *120*, 8468−8535. https://doi.org/10.1021/acs.chemrev.9b00685
5. Maria-Magdalena, T.; Petra Ágota, S. *Mater. Adv.* **2022**, *3,* 8815-8829. https://doi.org/10.1039/D2MA00880G
6. Kaiyuan, N.; Taokun, L.; Geoffrey, T. N.; Wenbin, L. *Acc. Chem. Res.* **2020**, *53*, 1739−1748. https://doi.org/10.1021/acs.accounts.0c00313
7. Yuanjing, C.; Fengliang, Z.; Banglin, C.; Guodong, Q. *Chem. Commun.* **2015**, *51*, 7420-7431. https://doi.org/10.1039/C5CC00718F
8. Antje, H.; Kristina, G.; Ralph, K.; Stefan, K. *Chem. Commun.* **2008**, 4192-4194. https://doi.org/10.1039/B718371B

9. Sandip, S.; Jian, Z.; Rama, S V.; Xiao-Ying, Y.; B Peter, M.; Radha Kishan, M. *Synth. Catal*. **2016**, *1*, 1–8. http://dx.doi.org/10.4172/2574-0431.100005
10. Li, Z.; Xiao-Qin, L.; Hai-Long, J.; Lin-Bing, S. Chem. Rev. **2017**, *117*, 8129−8176. https://doi.org/10.1021/acs.chemrev.7b00091
11. Férey, G.; Mellot Draznieks, C.; Serre, C.; Millange, F.; Dutour, J.; Surblé, S.; Margiolaki, I. *Science*, **2005**, *309*, 2040. https://doi.org/10.1126/science.1116275
12. Tian, Z.; Felix, J.; Ishtvan, B.; Binh, N.; Stefan, K. H.; Christoph, J. *Dalton Trans*. **2015**, *44*, 16791-16801. https://doi.org/10.1039/C5DT02625C
13. Samiran, B.; Chao, C.; Wha-Seung, A. *RSC Adv.* **2014**, *4*, 52500-52525. https://doi.org/10.1039/C4RA11259H
14. Changlei, X.; Jiamin, W.; Seyed Ali, D.; Abbas, S. N.; Yan, Y.; Quyet, V. L.; Dokyoon, K.; Rajender, S. V.; Ali, T-R.; Ho Won, J.; Mohammadreza, S. *Mol. Catal.* **2023**, *546*, 113217. http://dx.doi.org/10.1016/j.mcat.2023.113217
15. Faranak, M.; Fatemeh, Z.; Owen, J. G.; Zari, T. *Nanomaterials,* **2021**, *11(4)*, 845. https://doi.org/10.3390/nano11040845
16. Esmaeil, N.; Farhad, P.; Fatemeh, D.; Foroogh, B.; Ali, K. N. *ACS Omega*, **2018**, *3(12)*, 17135−17144. https://doi.org/10.1021/acsomega.8b02309
17. Jenis, T.; Manisha, G.; Anshul, Y.; Krishnakant, W.; Paresh, M. *Res. Chem. Intermed*. **2024,** *50*, 1645–1660. https://doi.org/10.1007/s11164-024-05240-6
18. Jingwen, C.; Xiaoling, C.; Zhiguo, Z.; Zongbi, B.; Huabin, X.; Qiwei, Y.; Qilong, R. *Mol. Catal*. **2015***, 445*, 163-169. https://doi.org/10.1016/j.mcat.2017.11.012
19. Ann Riya, N.; Ritchu, B.; Sonia, D.; Thakur Gurjeet, S.; Kirandeep, K.; Vanshika, D. *Biointerface Res. Appl. Chem.* **2022**, *12*, 3117-3134. https://doi.org/10.33263/BRIAC123.31173134
20. Vivek, K. S.; Sunil, K. S. *RSC Adv.* **2017**, *7*, 2682 - 2732. https://doi.org/10.1039/C6RA24823C
21. Michele, D. L.; Giuseppina, I.; Gaetano, R. *Pharmaceutics,* **2019**, *11(2)*, 85. https://doi.org/10.3390/pharmaceutics11020085
22. Parthiban, A.; Parameshwar, M.; *RCS Adv*. **2022**, *12*, 29253-29290. https://doi.org/10.1039/D2RA04589C
23. Devarajan, N.; Suresh, P. *New J. Chem.* **2019**, *43*, 6806-6814. https://doi.org/10.1039/C9NJ00990F
24. Santha Kumari, M.; Krishnan, V. B. R. K.; Ravi Kumar, K.; Siddique Akber, A.; Irfan Aamer, A.; Hari Babu B. *Chemistry and Biodiversity*, **2024**, *20*, e202201158. https://doi.org/10.1002/cbdv.202201158
25. Zhiguo, S.; Menglu, W.; Jiaming, F.; Run, F.; Yue, Z.; Li, Z. *Adv. Compos. Hybrid Mater.* **2021***, 4,* 1322–1329. https://doi.org/10.1007/s42114-021-00337-7
26. (a) Sibnath, K.; Baichuan, S.; Anutosh, C. *Energy,* **2015**, *91,* 772-781. https://doi.org/10.1016/j.energy.2015.08.096
(b) Zhijuan, Z.; Sisi, H.; Shikai, X.; Hongxia, X.; Zhong, L. *Energy & Fuels*, **2011,** *25,* 835-842. https://doi.org/10.1021/ef101548g
27. Shadmehr, J.; Zeinali, S.; Tohidi, M. *J. Dispers. Sci. Technol.* **2019,** *40(10)*, 1423–1440. https://doi.org/10.1080/01932691.2018.1516149
28. Abdelmadjid, D.; Raouf, B.; Ali, B.; Salah, R.; Bertrand, C. *Synlett,* **2008,** *4,* 509-512. https://doi.org/10.1055/s-2008-1032093

29. El-Remaily, M. A. A. A.; Hamad, H. A.; Soliman, M. M. A.; Elhady, O. M. *Appl. Organomet. Chem.* **2021**, *35*, e6238.
http://dx.doi.org/10.1002/aoc.6238