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A Mesoporous Indium Metal–Organic Framework: Remarkable Advances in Catalytic Activity for Strecker Reaction of Ketones

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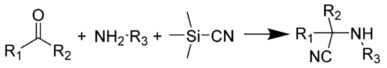
Supporting Information

ABSTRACT: With the aim of developing new highly porous, heterogeneous Lewis acid catalysts for multicomponent reactions, a new mesoporous metal–organic framework, InPF-110 ($[In_3O(btb)_2(HCOO)(L)]$, (H_3btb = 1,3,5-tris(4-carboxyphenyl)benzene acid, L = methanol, water, or ethanol), has been prepared with indium as the metal center. It exhibits a Langmuir surface area of 1470 $m^2\ g^{-1}$, and its structure consists of hexagonal pores with a 2.8 nm aperture, which allows the diffusion of multiple substrates. This material presents a large density of active metal sites resulting in outstanding catalytic activity in the formation of substituted α-aminonitriles through the one-pot Strecker reaction of ketones. In this respect, InPF-110 stands out compared to other catalysts for this reaction due to the small catalyst loadings required, and without the need for heat or solvents. Furthermore, X-ray single crystal diffraction studies clearly show the framework–substrate interaction through coordination to the accessible indium sites.

The development of new heterogeneous Lewis acid catalysts is important because a large number of organic transformations of interest require the use of such species.[1] Heterogeneous catalysts offer clear advantages regarding their reuse and recyclability. However, they typically display lower activity than their homogeneous counterparts.[2] Porous solids are used to enhance the number of active sites accessible to the substrates. This is the case of metal–organic frameworks, MOFs, a class of materials constructed by the joining of metal clusters, denoted secondary building units (SBUs), through organic linkers, to produce crystalline solids with potential porosity.[3] MOFs have been synthesized with a plethora of metal elements. This fact, along with the high surface area values that they might exhibit, makes MOFs very promising heterogeneous Lewis acid catalysts. In particular, MOFs constructed with group 13 elements have been proven to be very efficient Lewis acid catalysts in various organic transformations.[4] Recently, we reported the catalytic activity of a series of isostructural MOFs in the Strecker multicomponent reaction (MCR), which was carried out in one pot, finding that the solids' activity can be tuned to address the different steps involved in the reaction and, therefore, to obtain the desired product.[5] Thus, although one-pot MCRs offer advantages in atom economy, process simplification, purification steps, and waste reduction, they require the use of highly active and selective catalysts to avoid the formation of byproducts as a result of side reactions. Furthermore, the presence of sufficiently large pore and aperture dimensions to allow the diffusion of the involved molecules is a main goal in the design of a new catalyst.

The Strecker[6] reaction is used to prepare α-aminonitriles with the combination of a carbonyl, an amine, and a cyano derivative (Scheme 1).

Scheme 1. 3C Strecker Type Reaction



This approach offers high atom economy, and the possibility of incorporating additional functional groups through the choice of the corresponding carbonyl precursor.[7] However, poor conversions are typically obtained when ketones are employed, limiting their use in this reaction. Thus, new active catalysts are required to allow the use of substituted ketones.

Herein we report the synthesis, crystal structure, gas sorption characterization, and catalytic activity in the one-pot three-component Strecker reaction of a new mesoporous MOF, $[In_3O(btb)_2(HCOO)(L)]$, (H_3btb = 1,3,5-tris(4-carboxyphenyl)benzene acid, L = methanol, water, or ethanol), constructed with indium as the metal center (Figure 1). This new material, denoted InPF-110 (InPF = indium polymeric framework), has a structure with hexagonal channels of ca. 3 nm aperture, and it shows remarkable catalytic activity in the Strecker reaction with the use of ketones. The activity of InPF-110 is wide in the scope of this reaction, showing good to excellent activity when used with up to eight different ketones and six different amines.

Reaction of $In(NO_3)_3$ with H_3btb in DMF in the presence of nitric acid at 150 °C affords crystals of InPF-110 (see section 1 of Supporting Information (SI) for detailed conditions; CCDC number 1483220). Single crystal X-ray diffraction analysis indicates that the compound crystallizes in the hexagonal system, space group $P\overline{6}2c$, with lattice parameters $a = 31.8903(7)$ Å and $c = 17.1915(5)$ Å. The inorganic SBUs are formed by three indium atoms in an octahedral coordination environment, sharing a central oxygen atom, and coordinated to six carboxylate groups from the linkers (Figure 1). This type of SBU is commonly found

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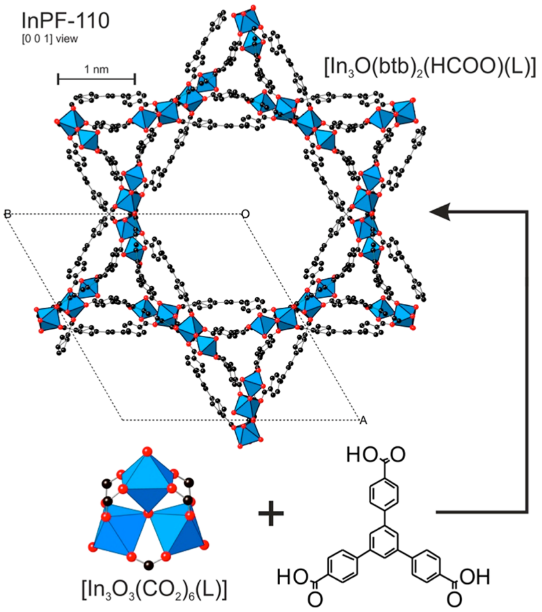


Figure 1. H_3btb linker is combined with a trimeric In-SBU to produce InPF-110. C is black, O is red, and In atoms are blue polyhedra. L = solvent ligand (water, methanol, ethanol).

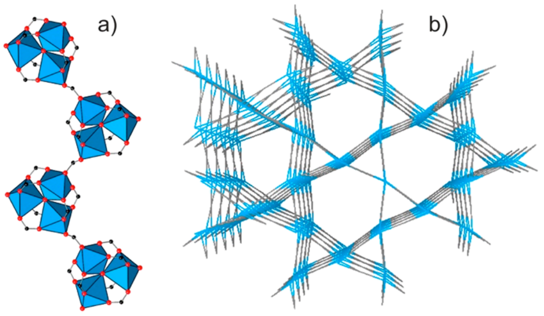


Figure 2. (a) The trimeric inorganic SBUs in InPF-110 are disposed forming chains by the direct linkage through formate anions. (b) Consideration of the chain as a rod-shaped SBU results in a topologically simplified **npo-e** network.

in other trivalent-metal based MOFs.[8] The coordination of the SBU is completed by a solvent ligand, and by two formate anions, which connect to two adjacent SBUs (Figure 2a). Since no formic acid was added in the synthesis, these formate anions are likely produced by decomposition of DMF molecules during the MOF formation reaction. Each SBU is connected to six btb^{3-} linkers. If we do not consider the direct connection of the SBUs through the formate linkers, the structure of InPF-110 presents a binodal topology denoted **3,6T60**,[9] with the presence of 3 and 6 coordinated nodes. This structure type has been previously described for a related scandium MOF, with a cationic structure wherein the trimers are not directly connected.[10] In the case of InPF-110, if we consider the direct linkage among inorganic SBUs through the formate anions, a different topological simplification can be made consisting of a rod-shaped SBU with a node at the position of the formates, and another node at the middle point between two btb^{3-} linkers that are crystallographically independent. This simplification results in a binodal 4- and 6-connected network with an **npo-e** topology, which resembles a kagomé net (Figure 2b).[11] The InPF-110 structure possesses two types of interconnected pores, with 55.8% of accessible void space, according to PLATON.[12] Hexagonal channels run along the *c* axis, with a maximum dimension of 2.8 nm. Perpendicularly are located microporous cavities with a diameter of 3.6 Å that can be reached from the main pore and offer access to the active indium centers. The permanent porosity of InPF-110 was proven by N_2 adsorption isotherms performed at 77 K. Prior to sorption analysis, the material was activated by solvent exchange with methanol (3 times) followed by heating at 200 °C under dynamic vacuum. The isotherm profile (Figure 3a) shows a clear step at $P/P_0 = 0.11$, indicative of the presence of mesopores. The calculated Brunauer−Emmett−Teller surface area is 1125 m^2 g^{-1} (1470 m^2 g^{-1} Langmuir).

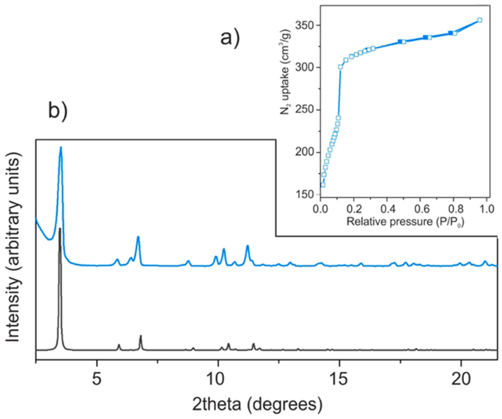


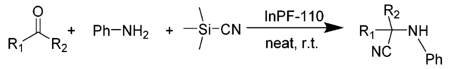
Figure 3. (a) N_2 adsorption isotherm of InPF-110. Empty and filled symbols represent adsorption and desorption points, respectively. (b) Calculated and experimental PXRD patterns for InPF-110 calcd (gray), InPF-110 expt (blue).

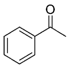
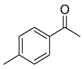
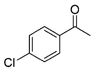
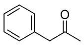
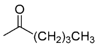
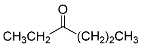
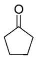
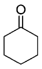
During the optimization of the reaction conditions we frequently noticed the presence of crystals belonging to a different phase, which we denote InPF-50 (section 4 of SI; CCDC number 1483221). Pure InPF-110 was obtained from a mixture of 0.33 mmol of In(NO$_3$)$_3$, 0.15 mmol of H_3btb, 2.5 mL of DMF, and 0.8 mL of nitric acid, heated at 150 °C for 4 h. Use of a higher temperature results in the formation of In(OH)$_3$, while reducing the temperature (130 °C) promotes the appearance of InPF-50. Furthermore, to ensure reproducibility it was necessary to dry the commercial indium nitrate by heating it at 105 °C for an overnight period, after observing that the amount of water influences the appearance of indium hydroxide. Phase purity was determined by PXRD comparison with the calculated pattern (Figure 3b).[13]

The catalytic activity of InPF-110 was studied with a three-component Strecker reaction among acetophenone, aniline, and trimethylsilyl cyanide (TMSCN) (see section 6 of SI for details). The selected standard conditions allow comparison with previously reported data, regarding the catalytic activity of indium MOFs synthesized by our group.[5] Other catalysts previously used in this same reaction include In-MOF 1 and In-MOF 2,[14] which were used with a 10 times higher catalyst loading (see Tables S5.1 and S5.2). In other cases, the use of solvents as dichloromethane, toluene or chloroform, and temperatures higher than rt was required. Similarly, soluble catalysts,[15] such as *o*-benzenedisulfonimide, and sulfonic acid based nanoreactors[16] have also been employed in larger catalyst loadings. InPF-110, even without any solvent, also outperforms previously reported MOFs tested in the same reaction, as shown in SI Table 5.2.

Table 1 (entry 1) shows that the product is obtained with a 99% yield in 4 h, using a catalyst loading of 0.5 mol % (other catalyst loadings were also tested; see Table S6 of the SI). When the InPF-110 catalyst was washed with ethanol instead of methanol, longer reaction times (10 h) were required to reach the same yield, while the reaction time was similar in the case of washing with water compared to methanol (Table 1, entries 2 and 3), indicating that the accessibility to the active sites is more hindered when larger solvent ligands such as ethanol are present. The scope of the reaction was evaluated with substituted ketones (Table 1) showing that InPF-110 displays very good activity; even linear ones yield the corresponding Strecker product at very short reaction times (0.85 h for 2-hexanone, entry 9). Cyclic ketones need longer reaction times (Table 1, entries 10, 13, and 14), and differently substituted acetophenones present only some slight modifications compared to the standard reaction, requiring a longer time than the case with a methyl group in the p-position (Table 1, entry 5).

Table 1. InPF-110-Catalyzed Strecker One-Pot Three Component Reaction[a]

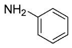
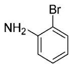
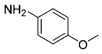
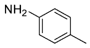
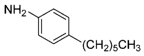
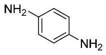


Entry	Activation solvent	Ketone	t (h)	Yield (%)[b]	TON[c]
1	H_2O		3.5	99	198
2	MeOH		4	99	198
3	EtOH		10	99	198
4	MeOH		4	94	188
5	EtOH		14	95	190
6	MeOH		4	89	178
7	EtOH		10	97	194
8	MeOH		4	99	198
9	MeOH		0.85	99	198
10	EtOH		1.5	99	198
11	EtOH		1.5	99	198
12	MeOH		4	99	198
13	EtOH		24	99	198
14	EtOH		24	81	162

[a] Reaction conditions: ketone, aniline, TMSCN (1.1:1:1.1), 0.5 mol % catalyst (from $[In_3O(btb)_2(HCO_2)(L)]$), N_2 atmosphere, 25 °C; catalyst washed with methanol, ethanol, or water. [b] Yield by ^{1}H NMR or GC-MS, from reaction crude. [c] TON = (mmol substrate/mmol catalyst).

The influence of the substituent in aromatic amines has been also studied (Table 2), with excellent yields ($\geq$90%) found for all the explored substrates, including p-phenyldiamine (entry 21). When nonquantitative yields were obtained, only unreacted substrates (entries 16) and/or imine were detected (entries 18, 20, and 22) (see SI Scheme S1). These results demonstrate the large scope of use of InPF-110 in the formation of substituted α-aminonitriles.

Table 2. InPF-110-Catalyzed Strecker One-Pot Three Component Reaction among Acetophenone, Aromatic Anilines, and TMSCN[a]

Entry	Activation solvent	Aniline	t (h)	Yield (%)[b]	TON[c]
1	H_2O		3.5	99	198
2	MeOH		4	99	198
3	EtOH		10	99	198
15	EtOH		28	99	198
16	EtOH		48	64	128
17	MeOH		24	95	190
18	EtOH		24	20	40
19	MeOH		24	90	180
20	EtOH		48	41	82
21[d]	MeOH		24	90	180
22[d]	EtOH		48	20	40

[a] Reaction conditions: acetophenone, amine, TMSCN (1.1:1:1.1), 0.5 mol % catalyst (from $[In_3O(btb)_2(HCO_2)(L)]$), N_2 atmosphere, 25 °C; catalyst washed with methanol or ethanol. [b] Yield by ^{1}H NMR or GC-MS, from reaction crude. [c] TON = (mmol substrate/mmol catalyst). [d] Double amount of acetophenone and TMSCN was added.

A scale-up experiment with a 5-fold larger amount was also performed, affording a 98% yield after 5 h. Also, the catalyst was reused in up to 10 cycles without significant loss of activity (see section 7 of SI). The heterogeneous nature of the catalyst was assessed by performing a leaching test, where the solid was separated from the reaction mixture after 5 min, and then the mother liquid was transferred to an empty Schlenk flask. After 24 h, reaction progress was not observed, which proves that the catalyst is necessary to quantitatively yield the Strecker product.

As we previously described, we noticed that the selection of the solvent employed for the MOF activation influences the material catalytic activity. It should be noted that there is a potential open metal site in the inorganic SBU of InPF-110, which is occupied by this solvent molecule. Indeed, single-crystal X-ray diffraction studies showed the presence of ethanol at such positions, which in addition are forming several hydrogen bonds with other solvent ligand molecules of adjacent SBUs. The differences in the catalytic activity indicate that this metal site is less accessible when ethanol is employed, probably due to its larger bulkiness compared to water or methanol, and/or to a more efficient packing of ethanol ligands in the micropore that prevents its displacement by the substrate molecules. This observation also indicates that, as expected, the MOF catalytic activity is strongly dependent on the metal coordination environment. Thus, a pentacoordinated indium cation, as the one generated after elimination of the adsorbed ligand, should be highly active, although this position is likely occupied by either the remaining solvent ligand or water molecules from moisture. To gain more insight into the interaction between the substrate and catalyst, we performed a single crystal X-ray diffraction study with an MOF crystal that was soaked in a mixture of aniline and acetophenone. The analysis of the diffraction data clearly shows the presence of aniline coordinated to the indium atom with the accessible metal site, partly replacing the solvent ligand (Figure 4). Other areas with high electron density were located inside the channels of the MOF in the vicinity of the SBUs, resembling a phenyl ring.

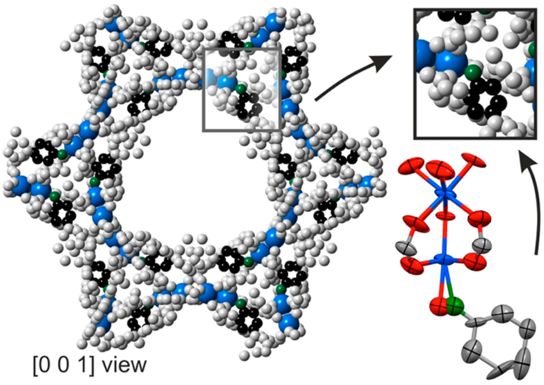


Figure 4. Space filling representation of InPF-110 showing the interaction of the active sites with the aniline. For the sake of clarity, framework atoms are white colored, except the indium ones, which are blue. Aniline carbon and nitrogen atoms are black and green, respectively. A blow up of the area corresponding to an SBU with coordinated aniline is shown in top right corner, and the corresponding ORTEP representation (50% probability) of the atoms is shown below. Aniline atoms are 50% occupied, as well as the oxygen atom coordinated to the indium atom in the absence of aniline.

However, these electron density areas were more diffuse, and acetophenone could not be unambiguously assigned, probably due to its partial occupancy and positional disorder. These findings are significant in view of the fact that the proposed mechanism of the Strecker reaction involves the formation of an intermediate imine species between the carbonyl and the amine derivatives, prior to attack of the silylcyanide compound.[5] In general, the formation of the imine intermediate is considered to go through the carbonyl activation by the Lewis acid site. Nonetheless, this experiment indicates that aniline is directly interacting with the active metal site, suggesting that the formation of the imine group requires not only the activation of the carbonyl group at the Lewis acid center but also the simultaneous presence of the amine at this site. Current research is being carried out to further clarify the reaction mechanism.

■ ASSOCIATED CONTENT

Ⓢ Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/jacs.6b05706.

> Experimental procedure; characterization of InPF-110; single-crystal XRD crystal data and structure refinement for InPF-110, InPF-50, and InPF-110 with coordinated aniline; catalytic experimental procedure; catalytic activity experiments background; catalytic activity data and product characterization (PDF)
>
> Crystallographic data (CIF, CIF, CIF)

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Notes

The authors declare no competing financial interest.

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