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Synchronizing Substrate Activation Rates in Multicomponent Reactions with Metal–Organic Framework Catalysts

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Abstract: A study on the influence of the cation coordination number, number of Lewis acid centers, concurrent existence of Lewis base sites, and structure topology on the catalytic activity of six new indium MOFs, has been carried out for multicomponent reactions (MCRs). The new indium polymeric frameworks, namely [In₈(OH)₆(popha)₆(H₂O)₄]·3 H₂O (InPF-16), [In(popha)(2,2'-bipy)]·3 H₂O (InPF-17), [In₃(OH)₃-(popha)₂(4,4'-bipy)]·4 H₂O (InPF-18), [ln₂(popha)₂(4,4'bipy)₂]·3H₂O (InPF-19), [In(OH)(Hpopha)]·0.5(1,7-phen) (InPF-**20**), and $[ln(popha)(1,10-phen)] \cdot 4H_2O$ (**InPF-21**) (InPF= indium polymeric framework, H₃popha=5-(4-carboxy-2-nitrophenoxy)isophthalic acid, phen = phenanthroline, bipy = bipyridine), have been hydrothermally obtained by using both conventional heating (CH) and microwave (MW) proce-

Introduction

In terms of new materials development, the last two decades have been captivated by metal–organic frameworks (MOFs), which facilitate the construction of a large variety of interesting structures that have applications in a huge number of fields.^[1–7]MOFs offer great potential as heterogeneous catalysts as they can have active sites within their frameworks, both in the organic linkers and in the metal centers.^[8–10] In our group, we have previously demonstrated that indium-based MOFs might have high catalytic activity in several organic transformations, from simple Lewis acid catalyzed reactions, such as cyanosilylation, acetalization, nitro group reduction, or oxidation of sulfides, to more elaborate ones, such as the one-pot Strecker three-component reaction (S-3CR).^[11–16]

In previous work, we showed that modulation of the ratio of different metals in solid-solution MOFs resulted in changes to their catalytic activity in a multicomponent reaction (MCR).^[16] This demonstrated that MCRs are highly sensitive to the nature

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Supporting information for this article is available on the WWW under http://dx.doi.org/10.1002/chem.201504576. dures. These indium frameworks show efficient Lewis acid behavior for the solvent-free cyanosilylation of carbonyl compounds, the one pot Passerini 3-component (P-3CR) and the Ugi 4-component (U-4CR) reactions. In addition, **InPF-17** was found to be a highly reactive, recyclable, and environmentally benign catalyst, which allows the efficient synthesis of α -aminoacyl amides. The relationship between the Lewis base/acid active site and the catalytic performance is explained by the 2D seven-coordinated indium framework of the catalyst **InPF-17**. This study is an attempt to highlight the main structural and synthetic factors that have to be taken into account when planning a new, effective MOFbased heterogeneous catalyst for multicomponent reactions.

of the catalyst active sites when carried out in one pot, even whilst the framework is not modified. Herein, we have studied the influence of various structural factors over the catalytic activity of MOFs in MCRs, while maintaining the same chemical components.

MCRs have several advantages:^[17] the isolation or purification of intermediate products is not required, superior atom economy, and high variability of substrates. Among numerous types of multicomponent condensations, the Passerini and the Ugi reactions^[18] are highly convergent methods, which allows for the rapid generation of organic drug-like molecule libraries and many different types of biologically active targets.^[19]

The Ugi four-component reaction (U-4CR) is perhaps one of the most important isocyanide-based MCRs.^[19–20] It is a valuable method for generating α -aminoacyl amide derivatives in a very straightforward manner by the condensation of an aldehyde, amine, carboxylic acid, and isocyanide in a one-pot reaction.^[18] Lewis acids are not always required for many of the reported isocyanide-based MCRs; however, to obtain good yields and selectivity in the U-4CR, Lewis acid catalysts do have to be used.^[21–34]

Recently, U-4CRs have been described by using ionic liquids,^[35] and deep eutectic solvent–water systems.^[28, 31–32] In the case of heterogeneous catalysts, fluorite has been employed as a mild acid catalyst under a microwave-assisted method.^[33] The use of a novel magnetic nanocatalyst has also been described, which resulted in a decrease of the reaction time and an improvement of the selectivity of the Ugi products.^[34]

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Based on our previous experience,^[11-16] we have performed a study of the mechanisms of the Passerini and Ugi MCRs by using new indium MOFs, in which various structural and compositional variables are introduced. Thus, we have prepared six new materials by using indium, the V-shaped tripodal ligand 5-(4-carboxy-2-nitrophenoxy) isophthalic acid (H₃popha), and in some cases, the addition of different aromatic amines (Scheme 1). With this strategy, we can study the influence of the cation coordination number (CN), number of Lewis acid/ base centers, concurrent existence of Lewis and/or Brønsted sites, and structure topology on the catalytic activity of the new MOFs, which will give us an insight into the mechanism of these important reactions.^[36] The less-explored^[37-40] H₃popha linker was chosen because of its capability to coordinate to the metal cations through three carboxylate groups in several modes. In addition, the presence of the nitro group breaks not only the symmetry of the molecules but also the electronic likeness of the two aromatic rings (Scheme 1).



Scheme 1. The organic ligand 5-(4-carboxy-2-nitrophenoxy) isophthalic acid (H_3 popha) reacts with indium and nitrogenated auxiliary ligands to form a series of new MOFs.

The differences between conventional heating (CH) and microwave(MW)-assisted hydrothermal synthesis procedures, particle size, and heterogeneous catalysis activity for each MOF material were established. Some of them showed a catalytically efficient evolution from the cyanosilylation reaction to the one-pot Passerini three-component reaction (P-3CR) and the one-pot Ugi four-component reaction (U-4CR) (Scheme 2). To the best of our knowledge, there are no reports on the synthesis of functionalized *N*-acylamino amides by MCRs catalyzed by MOFs.

Results and Discussion

With the purpose of studying the influence of the synthetic procedure on the particle sizes and shapes and subsequently on the catalytic activity of the **InPF** compounds, we performed a study to compare conventional heating with microwave-assisted hydrothermal synthesis; Figure 1 shows the differences





Scheme 2. Different Lewis acid catalyzed reactions: i) cyanosilylation of carbonyl compounds, ii) P-3CR, iii) U-4CR, and iv) Danishefsky reaction.



Figure 1. Comparison between MW and CH reaction conditions to obtain InPF materials.

between the reaction time for each method. Under the MW methodology, we obtained all the new materials as pure phases in higher yields (89–97%) and much shorter reaction times (a decrease of 97–99%) than with the CH protocol. The purity of each sample was confirmed by using PXRD, elemental analysis, and IR spectroscopy (see the Supporting Information).

The dynamic light scattering (DLS) analysis, performed by using water as a solvent at 25 °C, showed a broad range of particle sizes for the **InPF** materials (Table 1, Figure 2). Even

Table 1. Average particle size distribution for the crystalline materials obtained by MW-assisted synthesis.						
Material	No. particle	Particle size distribution range [nm]	% particles in the size range			
InPF-16 InPF-17 InPF-18 InPF-19 InPF-20 InPF-21	2037 2817 2518 2982 2537 3684	355–446 389–616 148–468 355–467 295–446 389–467	78 98 68 41 74 70			

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Figure 2. SEM images of the InPF-17 material synthesized by MW (15000 \times mag, left) and CH (8000 \times mag, right) protocols.

though several reports have suggested that materials with well-defined particle sizes can be obtained by using MW methodology,^[41-46] in our case, for almost all **InPF** materials, the average particle size was around 400 nm, and there was a large variation in their size distribution. The aforementioned advantages of reduced reaction times and higher yields facilitate the material elaboration.

Crystal structures

The crystal structure for each compound was determined by using single-crystal X-ray diffraction; crystals of a suitable size were obtained through the CH hydrothermal synthesis. Details of data collection, refinement, and crystallographic data for the compounds **InPF-16** to **InPF-21** are summarized in Table 2.

Structural description

The tripodal V-shaped ligand H_3 popha possesses several different modes of coordination onto metal centers. Herein, six different coordination modes are possible for the fully deprotonated popha^{3–} linker and one coordination mode for the protonated Hpopha^{2–} species (Figure 3).



Figure 3. Different coordination modes of the popha³⁻ and Hpopha²⁻ organic linker in InPF-16 to InPF-21 materials.

Additionally, the geometrical description of each framework, in terms of linked nodes or SBUs (secondary building units), is presented, which is fundamental to enable rationalization of the corresponding MOF net topology. This study was performed by using the TOPOS program.^[47–49]

InPF-16 material, with formula $[In_8(OH)_6(popha)_6(H_2O)_4]$. 3 H₂O, crystallizes in the triclinic $P\bar{1}$ space group. The asymmetric unit consists of four crystallographically different In^{3+} ions, three molecules of the fully deprotonated popha³⁻ linker, three hydroxyl groups, and two coordinated water molecules (Figure 4).

The molecules of the popha^{3–} linker show three different coordination modes: i) L_1 with $\eta^1 - \eta^2 \mu - \eta^2 \mu$, ii) L_2 with $\eta^2 \mu - \eta^1 - \eta^1$, and iii) L_3 with $\eta^2 \mu - \eta^2 \mu - \eta^2 \mu$ (Figure 3). There are four crystallographically independent indium metal centers, all of which are in

Table 2. Main crystallographic and refinement data for compounds InPF-16 to InPF-21.								
	InPF-16 $C_{45}H_{24}In_4N_3O_{34}$	InPF-17 C ₂₅ H ₁₄ InN ₃ O ₁₁	$\begin{array}{l} \textbf{InPF-18} \\ C_{40}H_{20}In_{3}N_{4}O_{22.64} \end{array}$	InPF-19 $C_{50}H_{28}In_2N_6O_{18.30}$	InPF-20 C _{20.25} H _{8.5} InNO _{10.25}	InPF-21 C ₂₇ H ₁₄ InN ₃ O ₁₀		
$M_{\rm r}$ [g mol ⁻¹]	1609.95	647.21	1263.30	1230.42	551.61	655.23		
<i>T</i> [K]	296	296	296	296	296	293		
λ [Å]	1.54178	0.71073	1.54178	1.54178	1.54178	1.54178		
crystal system	triclinic	triclinic	monoclinic	monoclinic	monoclinic	triclinic		
space group	ΡĪ	ΡĪ	C2/c	P21/n	P21/n	ΡĪ		
a [Å]	11.2976(3)	9.9939(6)	17.363(1)	17.411(1)	7.2776(7)	10.0013(5)		
<i>b</i> [Å]	12.8826(4)	12.3477(8)	14.759(1)	18.452(1)	22.060(2)	12.5596(6)		
c [Å]	18.5044(5)	13.1271(8)	19.890(2)	17.903(1)	15.0234(16)	13.5491(7)		
α [°]	76.122(2)	98.256(1)	90	90	90	100.704(3)		
β [°]	88.327(2)	110.786(1)	95.180(6)	101.309(5)	98.687(6)	105.631(3)		
γ [°]	78.218(2)	110.310(1)	90	90	90	113.311(2)		
<i>V</i> [Å ³]	2558.9(1)	1353.0(1)	5076.0(7)	5640.1(6)	2384.3(4)	1420.6(1)		
Ζ	2	2	4	4	4	2		
$Dx [g cm^{-3}]$	2.089	1.589	1.653	1.455	1.537	1.532		
$\mu \text{ [mm}^{-1}\text{]}$	15.234	0.938	11.4502	7.171	8.422	7.180		
F(000)	1566	644	2444	2457	1086	652.0		
GOF(<i>F</i> 2)	0.977	1.040	0.881	1.043	1.126	1.029		
final P indexes $[l > 2\sigma(h)]$	0.0576	0.0725	0.0823	0.0565	0.0816	0.0874		
initial function indexes $[I > 20(I)]$	0.1644	0.2090	0.2383	0.1839	0.3402	0.2722		

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Figure 4. Top: asymmetric unit of InPF-16. Bottom: polyhedral representation of the 3D structure of InPF-16 with its corresponding IIj topology and its representation of the inorganic secondary building unit.

InO₆-octahedral coordination environments. The environment of one of the indium metallic centers (In1) is formed by two In-O bonds with the two hydroxyl bridge groups, one In-O bond with the monodentate part of the L₁ popha³⁻ linker, and three In–O bonds with the chelate popha³⁻ linker (two L₁ and one L₃). The environment of the second indium metallic center (In2) is formed by two In-O bonds with the bridging hydroxyl groups and four In–O bonds with the chelating popha^{3–} linker (two L_1 and two L_3). The third indium environment (In3) consists of two In-O bonds with the bridging hydroxyl groups, one In-O bond with the monodentate part of the L₂ linker, and three In-O bonds with the chelating popha³⁻ linker (one L_2 and two L_3). The fourth indium environment (In4) exhibits one In-O bond with the bridging hydroxyl group, one In-O bond with the monodentate part of the L₂ coordination mode, two In–O bonds with the chelating popha^{3–} linker (one L₂ and one L₃), and two In-O bonds with the coordinated water molecules. An SBU is formed by four vertex-sharing octahedra (In1 to In4), which are joined through an inversion center to another four indium centers to form eight octahedra clusters in the [001] direction. In1 and In1' share a face, which creates a corrugated geometry. These clusters can be described as rods (defined as a 1-periodic 3D structure with a linear axis that is determined by specifying a point on the axis and its direction)^[50] that are connected through the organic units in all directions; the result is a 3D structure with a 3-periodic bipartite 3,12-IIj topology.

The **InPF-17** material, with formula $[\ln(\text{popha})(2,2'-\text{bipy})]$ -3H₂O, crystallizes in the triclinic $P\overline{1}$ space group. The asymmetric unit consists of one \ln^{3+} ion, one fully deprotonated popha³⁻ linker, and one 2,2'-bipyridine molecule. The indium environment is made up of five In–O bonds with the carboxylate part of the popha³⁻ linker and two In–N bonds with the 2,2'-bipyridine. A weak interaction between In…O6 (2.650(8) Å) is also observed. The [InN2O5] polyhedra are connected through the L₄ $(\eta^1-\eta^2-\eta^2)$ popha³⁻ organic linker to construct square rings of 9.994 Å×9.916 Å dimensions that contain three metal centers. The presence of the blocking bipyridine unit together with the square-shaped rings give rise to 2D layers, which are perpendicular to the (001) plane, that possess an hcb topology of a three-connected uninodal net. The supramolecular network was built up through two types of weak interactions, which increase the dimensionality of the framework and connect the 2D covalent layers along the *a* and *c* axes: i) $\pi \cdot \cdot \pi$ from two neighboring molecules of 2,2'-bipyridine with a distance of 3.832 Å between centroids, which display an offset of 20.79°, and ii) C–HL··· π (dD-A: 3.403 Å), which extend the network along the (001) plane. The final 3D structure shows a dia topology with a four-connected uninodal network (Figure 5).



Figure 5. Top: atomic and polyhedral representation of **InPF-17** structure, which shows the asymmetric unit and a perpendicular view of the 2D layers with the topological representation. Bottom: $\pi \cdot \cdot \pi$ and C–H $\cdot \cdot \pi$ intralayer interactions with the 3D supramolecular net formed and the topology representation.

The InPF-18 material, with formula [In₃(OH)₃(popha)₂(4,4'bipy)]·4H₂O, crystallizes in the monoclinic C2/c space group. The asymmetric unit consists of one and a half crystallographically independent In³⁺ ions, one fully deprotonated popha³⁻ linker, one and a half hydroxyl groups, and half a 4,4'-bipyridine molecule (Figure 6). There are two different environments in the octahedral PBUs (primary building units): [InO₆] and [InN₂O₄]. In the case of the fully deprotonated organic linker, an L₅ $(\eta^2 \mu - \eta^2 \mu - \eta^1)$ coordination is observed. One of the PBUs, $-[InO_6]$ -, is constructed from two In-O bonds with the μ -OH groups, which connect In1-O-In2 and In1-O-In1, and four In-O bonds with the carboxylate groups. Three PBUs have $\eta^2\mu$ -type coordination and only one is monodentate (η^1). The other PBU, -[InN₂O₄]-, has two In-N bonds with the coordinated 4,4'-bipyridine, two In–O bonds with the μ -OH groups, which connect In1-O-In2, and two In-O bonds with the carboxylate groups, which connect ln1-O-ln2 with $\eta^2\mu$ -type coordination. Inorganic chains along the c axis are built from the PBUs that share a vertex through the µ-OH groups. The SBUs





Figure 6. Top: atomic and polyhedral representation of **InPF-18** structure, which shows the asymmetric unit and (010) view of inorganic chains. Bottom: (001) view of the 3D network and the topological representation.

can be described as infinite $(-OH-In-)_{\infty}$ rods with carboxylate O and bipyridine N atoms that complete the octahedral coordination around the indium centers, which results in infinite rods of InO_6 and InN_2O_4 octahedra that share corners (Figure 6). These rods are connected in all direction through the $-C_{10}H_8$ - and the $-C_{14}NO_3H_6$ - linkers, which give rise to a 3D framework. The rods are assembled in a hexagonal packing arrangement going down the (001) plane; in fact, the **InPF-18** 3D arrangement can be described as rod-packing pillared 2D layers with a **3,8118** topology and a 3,10-connected binodal network (Figure 6).^[51]

The InPF-19 material, with formula [In₂(popha)₂(4,4'bipy)₂]·3H₂O, crystallizes in the monoclinic $P2_1/c$ space group. The asymmetric unit consists of two different crystallographic $\ensuremath{\mathsf{In}^{3+}}$ ions, two fully deprotonated popha^{3-} linkers, and two 4,4'-bipyridine molecules (Figure 7). As a result, the formation of two -[InN₂O₆]- PBUs, which contain eight-coordinate indium centers, is observed. They are made up of two In-N bonds with the 4,4'-bipyridine ligands (In1-N: 2.299-2.312 Å and In2-O: 2.325-2.323 Å) and six In-O bonds with the popha-3 linker (In1-O: 2.117-2.473 Å and In2-O: 2.171-2.521 Å). An L_6 (η^2 - η^2 - η^2) fully chelating coordination mode is found for both indium metal centers. Along the c axis, the -[InN₂O₆]- PBUs are connected through the 4,4-bipyridine with In1-In2 distances of 11.695(1) and 11.746(1) Å. Connections along the *a* and *b* axes are made through the popha linker: In1...In1, In2...In2, and two In1...In2 PBUs with distances 15.554, 15.553, 9.693, and 9.695 Å, respectively, which gives rise to a 3D structure. By considering the double connectivity that is showed by the two crystallographically different 4,4-bipyridine along the c axis, the topological study showed a 3D interpenetrated (Class IIa) framework with a dmc 3,4-connected binodal network, which could also be described as the derivated fsc-3,5-Cmce-1 of a 3,5-connected binodal network.[52]

The **InPF-20** material, with formula [In(OH)(Hpopha)] $\cdot 0.5$ (1,7-phen), crystallizes in the monoclinic $P2_1/n$ space group. The asymmetric unit consists of two crystallographically different



Figure 7. Top: atomic and polyhedral representation of InPF-19 structure, which shows the asymmetric unit and its 3D framework. Bottom: two different topological representations of InPF-19.

In³⁺ ions, both of which are placed at inversion centers, one partially deprotonated Hpopha²⁻ linker, and one μ -OH group (Figure 8). Both indium cations exist as $-[InO_6]$ - octahedral units with the following bonds: two In–O bonds with the bridging hydroxyl group (In1–O: 2.079(8) Å and In2–O: 2.095 (7) Å), and four In–O bonds with the carboxylate group (In1–O: 2.182(9)–95(9) Å and In2–O: 2.129(9)–35(11) Å). The PBUs share vertices that form infinite -[In–O-In]- chains along the



Figure 8. Top: asymmetric unit representation of InPF-20. Bottom: polyhedral representation of InPF-20 3D framework and its corresponding cds topology.

a axis; the linker with coordination mode L₇ ($\eta^2\mu$ - $\eta^2\mu$ -COOH) connects these chains through the two carboxylate bridging units along the *b* and *c* axes to build a 3D covalent network, which can be described as a 4-connected uninodal network with a **cds** topology. The protonated part of the popha linker forms an O–H···O synthon (d_{H··O}=2,614 Å) between adjacent molecules of the popha linker.

The InPF-21 material, with formula [In(popha)(1,10phen)]·4H₂O, crystallizes in the triclinic P1 space group. The asymmetric unit consists of one In³⁺ ion, one fully deprotonated popha³⁻ linker, and one 1,10-phenanthroline molecule. Indium cations form [InN₂O₆] octa-coordinated units, which together with the L_6 (η^2 - η^2 - η^2) popha⁻³ linker, give rise to 2D layers that are perpendicular to the (001) plane with an hcb topology in a three-connected uninodal net. The supramolecular network is constructed through two weak interactions, which increase the dimensionality of the framework and connect the 2D covalent layers along the *a* and *c* axes: i) π_{phen} ···H– C_{phen} with two neighboring 1,10-phenanthroline units at a distance of 3.575 Å between the middle phenanthroline ring centroids and the hydrogen atom of one of the carbons from the phenanthroline, and ii) C–HL··· π L (dD-A: 3.388 Å), which extend the network along the (001) plane. The final 3D structure shows a dia topology with a four-connected uninodal network (Figure 9).



Figure 9. Top: atomic and polyhedral representation of **InPF-21** structure, which shows the asymmetric unit and a perpendicular view of a 2D layers with **hcb** topology. Bottom: weak intralayer interactions with the 3D supramolecular net topology representation.

Catalytic activity of InPF materials

Initially, the possible accessible voids for each structure were examined. Only the **InPF-19** material, which does not possess available Lewis acid centers, contains accessible pores (\approx 147–115 Å³), whereas **InPF-17**, **InPF-18**, and **InPF-21** materials only contain small pores (\approx 43 Å³), and **InPF-16** and **InPF-20** catalysts did not contain any pores. This led us to consider that the studied MOFs represent only superficial catalytic systems.

To evaluate the utility, stability, and capacity of these novel indium MOF materials as heterogeneous acid catalysts, we chose to test three different Lewis acid catalyzed organic transformations: i) a two-component cyanosilylation of carbonyl compounds, ii) the Passerini three-component reaction, and iii) the Ugi four-component reaction (Scheme 2). The reactions were carried out with the two MOF catalyst series: those obtained by CH or MW-assisted synthesis; however, no differences between these two InPF catalyst series were found.

The cyanosilylation reaction is a Lewis acid catalyzed carbon-carbon bond formation. Over the years, many catalysts have proved to be excellent for the cyanosilylation of aldehydes; nevertheless, when ketones were used as substrates, only a few heterogeneous catalysts have shown good conversions.^[53-64] Previous studies with indium MOFs have concluded that these materials exhibit good catalytic activity in such reactions with low loadings, mild temperatures, and without solvent.^[14-16]

The cyanosilylation reactions were performed by using low catalytic amounts (1–5 mol%), under an inert atmosphere, without solvent, and at room temperature. The results showed that catalysts with the six or seven-coordinated indium atoms (InPF-16, InPF-17, InPF-18, and InPF-20) gave good yields in short reaction times, whereas those with eight-coordinated indium atoms showed no catalytic activity, which further proves the important role that the Lewis acid active site on the metallic center plays in the reactants activation. Thus, the InPF-19 and InPF-21 materials, which do not possess available Lewis acid sites or any other groups that are suitable to interact with the substrates, were not considered as catalysts in the subsequent studies.

The InPF-16, InPF-17, InPF-18, and InPF-20 materials possess, besides indium Lewis acid sites, Lewis base moieties, such as bridging hydroxyl groups (μ -OH) and/or noncoordinated carbonyl groups (free C=O). This permits two-component catalytic systems, which follow a mechanism that is based on the "dual-activation" phenomenon^[65] in which the carbonyl compound is activated by the interaction with the metal-centered Lewis acid site, and simultaneously, the silyl group is activated by the Lewis basic moieties (Figure 10).

Although the presence of a central oxygen atom between the phenyl rings in the H_3 popha organic ligand could be considered as a Lewis basic moiety, the presence of the nitro group at the *ortho* position in one of the phenyl rings withdraws the charge density from this central oxygen. This delocalizes the electron charge and decreases the basicity of this moiety, but does not seem to show any influence on the catalytic behavior of the **InPF** materials.

By increasing the number of active sites in the catalyst (acid and basic moieties), we expected higher product yields over shorter reaction times. The **InPF-16** material contains eight In clusters, μ -OH moieties, and noncoordinated C=O groups (potential Lewis basic sites) along its framework with an M/CO/OH ratio of 4:3:3 as well as two easily displaceable coordinated water molecules. Consequently, it exhibits an outstanding catalytic activity by reaching 99% yield in just 10 min.

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Figure 10. Proposed mechanism for the InPF-16-catalyzed cyanosilylation of carbonyl compounds.

The **InPF-16** material, which is the superior MOF catalyst for the cyanosilylation reaction, was also tested with the more hindered, reactant-like acetophenone. Although, as expected, the catalyst loading had to be increased for this substrate, the yield was 67% when the reaction was carried out at with 2.5 mol% catalyst loading, at room temperature in only 4 h. Catalyst loading of 5 mol% was necessary to obtain 99% yield over 16 h at room temperature without any solvent (Table 3, entry 1).

The differences in indium CNs and the presence or absence of bridging hydroxyl groups in the structures explains the distinction in the catalytic activity between InPF-17 and InPF-18 materials. In InPF-17, the higher indium CN (seven) together with the absence of μ -OH groups makes it a slower catalyst with moderate yields over longer reaction times (TON: 68) compared with the more active InPF-18 catalyst (Table 3, entry 2 vs. 3). The latter contains inorganic chains –[In–O–In]– of six connected indium cations, bridging hydroxyl groups,

and the free C=O groups (M/C=O/OH ratio=3:2:3 for InPF-18 and M/C=O ratio=1:1 for InPF-17) along its framework.

After the first catalytic reaction, the **InPF-20** crystalline structure was not preserved, which means that interaction between the reactants and the catalyst affects its framework (see the Supporting Information). Therefore, this material was not considered for subsequent studies, because the structure–activity relationship could not be established.

Once a good catalytic behavior was demonstrated for the **InPF-16**, **-17** and **-18** materials in the cyanosilylation transformation, the catalytic efficiency of these materials was evaluated in two multicomponent organic reactions: the Passerini (P-3CR) and the Ugi reactions (U-4CR).

The Passerini reaction is an isonitrile-based MCR that yields α -acyloxy carboxamides in a one-pot synthesis from an aldehyde, isonitrile, and carboxylic acid. The carbonyl group is one of the most critical reactants because of the pronounced reactivity of the isonitrile carbon atom towards the electrophilic sp² carbon center; this reaction can be time consuming with low yields if it is not carried out with a strong carboxylic acid or an unusually electrophilic carbonyl compound.^[66]

We carried out the Passerini reaction by using the one-pot methodology, at room temperature, without any solvent, and with 1 mol% of catalyst. InPF-16, InPF-17, and InPF-18 materials demonstrated good catalytic activities (Table 3, entries 1-3). Taking into account the dual-activation phenomena that was manifested before by these catalysts (see above), and considering their basic and acid moieties placed along their frameworks, we propose the following catalytic mechanism: i) Lewis acid activation of the carbonyl compound and Lewis base activation of the OH group of the benzoic acid, ii) attack of the oxygen of the OH group onto the isocyanide sp carbon, iii) subsequent coordination onto the sp³ carbon of the activated carbonyl compound, and iv) protonation of the intermediate product and its release from the catalyst. Finally, the free intermediate undergoes a 1,4-O \rightarrow O acyl transfer to give the expected 2-cyclohexylamino-2-oxo-1-phenylethylbenzoate product (Figure 11).

Entry	Catalyst	Catalytic reaction ^[a]							
	(indium CN, dimensionality)	Cyanosilylation ^[b]			Passerini 3CR ^[c]		Ugi 4CR ^[d]		
	-	Benzaldehyde		Acetophenone		Yield [%] ([h])	TON ^[e]	Yield [%]	TON ^[e]
		Yield [%] ([h])	TON ^[d]	Yield [%] ([h])	TON ^[e]				
1	InPF-16 (6, 3D)	99 (0.17)	99	99 (16)	20	89 (0.5)	89	traces	-
2	InPF-17 (7, 2D)	67 (18)	68	53 (24)	11	86 (0.7)	86	92	92
3	InPF-18 (6, 3D)	85 (18)	83	80 (24)	16	83 (0.7)	83	67	67
4	InPF-20 (6, 3D)	71 (12)	87	76 (24)	15	66 (1.0)	66	89	89
5	Blank	28 (24)	-	-	-	50 (24)	-	40	-

[a] All reactions were tested at least 3 times by using different fresh batches of manufactured catalysts. [b] Carbonyl compound (0.001 mol), TMSCN (0.001 mol), and catalyst (1 mol% for benzaldehyde, 5 mol% for acetophenone), without solvent, N₂ atmosphere, T=25 °C, t=10 min–24 h. Yields were determined by GC-MS. [c] Benzaldehyde (0.001 mol), benzoic acid (0.001 mol), cyclohexyl isocyanide (0.001 mol), catalyst (1 mol%), without solvent, T=25 °C, t=30 min–2 h. Yields were determined by ¹H NMR without further purification. [d] Benzaldehyde (0.001 mol), benzoic acid (0.001 mol), aniline (0.001 mol), cyclohexyl isocyanide (0.001 mol), benzoic acid (0.001 mol), aniline (0.001 mol), cyclohexyl isocyanide (0.001 mol), benzoic acid (0.001 mol), aniline (0.001 mol), cyclohexyl isocyanide (0.001 mol), benzoic acid (0.001 mol), aniline (0.001 mol), cyclohexyl isocyanide (0.001 mol), benzoic acid (0.001 mol), aniline (0.001 mol), cyclohexyl isocyanide (0.001 mol), benzoic acid (0.001 mol), aniline (0.001 mol), cyclohexyl isocyanide (0.001 mol), benzoic acid (0.001 mol), aniline (0.001 mol), cyclohexyl isocyanide (0.001 mol), benzoic acid (0.001 mol), aniline (0.001 mol), cyclohexyl isocyanide (0.001 mol), and catalyst (1 mol%) in EtOH (0.5 mL), T=25 °C; t=2 h; The progress of the reaction was monitored by GC-MS until disappearance of the substrates; the final solid product was analyzed by ¹H NMR without further purification. [e] mmol substrate per mmol catalyst.

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Figure 11. Proposed mechanism for InPF-16-catalyzed Passerini reaction.

Unexpectedly, the TON value of **InPF-17**, which displayed the lowest activity in the cyanosilylation reaction, was found to be similar to those of **InPF-16** and **InPF-18** in the P-3CR (Table 3, indium CN is six in the former compounds and seven in the latter). This indicates that in MCRs the metal CN is not the only key factor in reaching a good level of catalytic activity. As several substrates are involved in the reaction, it seems reasonable to think that synchronization in their activation is required to yield the final product with high selectivity. To prove this point the catalysts were tested in the four-component Ugi 4CR.

The increment in the reactants number, such as in the U-4CR, allows us to observe the catalytic activation processes that arise under InPF catalysis. The reaction was performed according to a one-pot methodology at room temperature with a catalyst loading of 1 mol%, and this led to good yields of the expected products. Among various solvents that were screened, we found ethanol to be the best choice for this reaction. Usually, when this reaction was carried out without a catalyst, the condensation of an aldehyde, amine, carboxylic acid, and isocyanide is achieved through a cascade mechanism that favors transformation of the imine and to finally obtain the α aminoacyl amide derivative, albeit at lower yields (Table 3, entry 4). The proposed catalytic mechanism for the U-4CR by using the InPF materials as catalysts also relies upon the dualactivation phenomena, which is based on presence of both basic and acidic moieties. The Lewis acid activation of the carbonyl reactant is followed by the intermediate imine formation and its subsequent activation at the same Lewis acid site. The OH group from the benzoic acid is activated by the Lewis basic component of the catalyst and attacks the sp carbon of the isocyanide derivative, which simultaneously coordinates to the sp² carbon of the activated imine. This is followed by protonation of this second intermediate and its release from the catalyst. Finally, this intermediate undergoes a 1,4-O \rightarrow N acyl transfer known as the "mumm rearrangement", which results



Figure 12. Proposal mechanism for indium-mediated U-4CR by using the 2D InPF-17 as the catalyst.

in the expected *N*-(-(cyclohexylaminocarbonyl)(phenyl)methyl)-*N*-phenylbenzamide product (Figure 12).

The Lewis acid centers that are present in the **InPF** material frameworks activate both the carbonyl and intermediate imine fragments. This occurs faster with the **InPF-17** catalyst than with the **InPF-18** material.

With the aim of proposing one of the crucial steps of the Ugi mechanism and checking if the benzoic acid and cyclohexyl isocyanide coupling was possible, we carried out the Danishefsky reaction (Scheme 2, iv),⁶⁷ which was performed under exactly the same conditions that were employed for the U-4CR (RT, ethanol, 1 mol% of **InPF-17**). By monitoring the reaction by GC-MS over time, we observed that no *N*-formyl amide was formed, which ruled out this species as an intermediate in the U-4CR. In the case of the **InPF-16** catalyst, the imine intermediate showed no reaction after 2 h, and only traces of the expected Ugi product were observed.

In the view of these results and based on the structural features of the catalyst, we have tentatively established a parameter $0 \le x \le 1$ that is based on the Lewis base/acid active site ratio, which could explain the differences in the activity for each catalyst in the Ugi 4CR. To the best of our knowledge, there are no other examples in the literature of MOF-catalyzed Ugi reactions; therefore, this parameter has only been tested in the compounds that are presented herein.

The maximum CN of indium cations is eight; therefore, we define the number of Lewis acid sites (LA) as eight minus the actual CN of each indium atom plus the number of coordinated water ligands (O_L) (easily displaced by the reactants to generate additional active sites): $LA = \sum n(8-CN+O_L)$, in which n = number of In cations per formula. The number of Lewis basic sites (LB) is defined as the number of OH groups plus the non-



coordinated carboxylate C=O groups per formula. Upon scrutiny of the LB/LA ratio (x) for the catalytically active materials (InPF-16, InPF-17, InPF-18), it was apparent that the closer the value was to 1, the better the catalytic behavior was. This would support the hypothesis that a synchronization of the substrates' activation rates was required.

Thus, **InPF-17** material (x = 1) owns equal amounts of Lewis acid and base active sites and showed an excellent catalytic activity, with the highest TON for the studied 4CR. **InPF-18** material (x = 0.8) also displayed good activity, but the TON value was the second highest, and **InPF-16** (x = 0.6) hardly showed any catalytic activity. As expected, **InPF-19** and **InPF-21** MOFs (x = 0) did not show any catalytic activity.

The recyclability of the best indium catalysts (InPF-16 and InPF-17) was also tested: catalysts were recovered after centrifugation, washed several times with ethanol and acetone, dried at 130 °C, and reused. Even after four catalytic cycles, the catalytic activity was maintained with only a small decrease, which was probably due to the loss of material during the recovery of each catalyst (see the Supporting Information). The crystalline structure of both materials did not suffer from any alteration; hot filtration experiments confirmed that InPF-16 and InPF-17 are truly heterogeneous catalysts.

Conclusions

A series of 6 new indium MOFs with different chemical and structural characteristics (indium CNs, Lewis acid active centers, concurrent existence of Lewis bases) have been obtained. Their structures and topological nets were determined.

The MOFs were synthesized by using CH and MW hydrothermal synthesis. The same pure phases we obtained with both methods with hardly any variation of the synthetic conditions. The particle size–catalytic behavior relationship was studied for both MOF series, and it showed no dependence of the catalytic activity on the synthetic method. The advantages of the MW procedure, which include reduced reaction times and higher yields, make this the favorable method for synthesis of the materials.

Structural and topological studies of every compound allowed us to propose certain catalytic mechanisms for the tested reactions.

From our catalytic studies on these six new **In-MOFs** we can make the following conclusions:

For cyanosilylation reactions, in which there only are two reactants, the factor that drives the reaction yield is the indium CN; therefore, the catalytic activity decreases in the following way: InPF-16 > InPF-18 > InPF-17. InPF-19 and InPF-21 materials did not show any catalytic activity because both of them possess indium CNs of 8, which means that no Lewis acid active sites are present.

In the three-component Passerini reaction, InPF-16, InPF-18, InPF-17 catalysts, which all possess active sites, show a similar level of activity. InPF17, which has the lowest catalytic activity in the cyanosilylation reaction, displays a similar activity to the other catalysts in the P-3CR, which suggests that synchronization of the reactants' activation rates would be the driving

force in this reaction. To prove that the larger the number of substrates, the more significant their synchronization rates become, we tested the catalysts in the Ugi 4CR. We concluded that the driving force was the synchronization of the substrates' activation rates, because the order of catalytic activity went in the opposite direction to that of the two-component cyanosilylation: InPF-16 < InPF-18 < InPF-17.

We cautiously proposed a parameter $0 \le x \le 1$ that was based on the Lewis base/acid active site ratio, which explains our results in the 4CR. The closer to 1 the *x* value is, the better the catalytic behavior of the MOF. Thus, the catalyst **InPF-17** (x=1) possesses equal amounts of acid and base active sites and shows excellent catalytic activity, with the highest TON out of all the catalysts that were studied in the 4CR. **InPF-18** (x=0.8) also presents good catalytic activity with the second highest TON value, whereas **InPF-16** (x=0.6) hardly shows any catalytic activity. As expected, **InPF-19** and **InPF-21** MOFs (x=0) do not show any catalytic activity.

This study highlights that multicomponent complex reactions require heterogeneous catalysts with very specific structural features, which can be delivered by MOFs though a planned synthetic strategy.

Experimental Section

General information

All reagents, 5-(4-carboxy-2-nitrophenoxy)isophthalic acid (H₃popha), 1,10-phenanthroline monohydrate (1,10-phen), 1,7-phenanthroline (1,7-phen), 4,4'-bipyridine (4,4'-bipy), 2,2'-bipyridine (2,2'-bipy), and [In(OAc)₃], and solvents that were employed were commercially available and used as received without further purification.

Characterization methods

IR spectra were recorded from KBr pellets in the range 4000-250 cm⁻¹ on a Bruker IFS 66 V/S. Thermogravimetric and differential thermal analyses (TGA/DTA) were performed by using the Seiko TG/DTA 320U equipment in a temperature range between 25 and 1000 °C in air (flow rate = 100 mLmin⁻¹, heating rate = 10 °C min⁻¹). A PerkinElmer CNHS Analyzer 2400 was employed for the elemental analysis. Powder X-ray diffraction (PXRD) patterns were measured with a Bruker D8 diffractometer (step size = 0.02° , exposure time = 0.5 s per step). PXRD measurements were used to check the purity of the obtained microcrystalline products by a comparison of the experimental results with the simulated patterns obtained from single-crystal X-ray diffraction data. The residues of the compounds after TGA were analyzed by PXRD and compared with reported Inorganic Crystal Structure Database (ICSD)^[68] patterns. DLS particle size analysis was performed by using the VASCO particle size analyzer with a refraction index of 1.6 for the analyzed particles, by using water as the solvent (refraction index = 1.33, viscosity = 0.894), and by employing the statistic mode with a time limit of 30 acquisitions at 15 seconds per acquisition.

Preparation of InPF materials

All compounds were synthesized under hydrothermal conditions, by using conventional heating (CH) and microwave heating (MW). The CH was performed in a conventional oven at temperatures be-

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tween 150 and 180 °C. The MW-assisted synthesis was performed in a CEM- Discover Class S n/s DC5363 apparatus by using a dynamic method, during which the temperature was fixed, the power was set to a maximum of 200 W, and the pressure reached up to 18 bar to allow the MW source to reach the setup temperature.

[In₈(OH)₆(popha)₆(H₂O)₄]·3H₂O (InPF-16), CH synthesis: A mixture of H_3 popha (0.089 g, 0.256 mmol) and $ln(OAc)_3$ (0.100 g, 0.343 mmol) in water (6 mL) was transferred to a Teflon-lined stainless steel autoclave and heated at 170 °C for 72 h. After cooling to room temperature, the crystals that had formed were isolated by filtration and washed with distilled water, ethanol, and acetone to give colorless crystals of InPF-16 (0.781 g, 95%). MW synthesis: A mixture of H₃popha (0.030 g, 0.085 mmol) and In(OAc)₃ (0.033 g, 0.114 mmol) in water (2 mL) was placed in a glass vial and submitted to MW radiation by using a dynamic method at 170°C with vigorous stirring (30 min, 200 W, 10 bar), which led to formation of the product InPF-16 (0.265 g, 97%). Elemental analysis calcd (%) for C₉₀H₅₆In₈N₆O₆₇ (3211.96 g mol⁻¹): C 33.65, H 1.76, N 2.62; found: C 33.68, H 1.72, N 2.68; IR (KBr): $\tilde{v} = 3636$ (O–H, coordinated), 3539 (O-H, coordinated H₂O), 3231 (O-H, free H₂O), 3078 and 3088 (C-H, aromatic)L, 1633 and 1613 (C=O)L, 1586 (C=C, aromatic)L, 1562 (N-O)as, 1458 (OCO)s, 1419 (OCO)as, 1410 (C-C)as, 1351 and 1313 (N-O)s, 1259 and 1229 (C-O)as, 1143 (C-C)s, 777, 767, and 712 cm⁻¹ $\delta oop(C-H)L$ (L: linker, s: symmetric, as: asymmetric); TGA (air, flow rate = 100 mLmin⁻¹): initial weight loss (of \approx 5%) started at 100°C, which was due to the loss of coordinated and physisorbed water molecules; at $\approx\!420\,^\circ\text{C}$ a 60% loss of material had occurred; the final residue that remained at \approx 800 °C corresponded to 35% of the material that was converted into In_2O_3 (ICSD_ 640179).

[In(popha)(2,2'-bipy)]·3H2O (InPF-17), CH synthesis: A mixture of H₃popha (0.119 g, 0.343 mmol), 2,2'-bipy (0.047 g, 0.343 mmol), and In(OAc)₃ (0.100 g, 0.343 mmol) in distilled water (12 mL) was heated in a Teflon-lined stainless steel autoclave at 150 °C for 24 h. After cooling to room temperature, the newly formed crystals were isolated by filtration and washed with distilled water, ethanol, and acetone to give light violet crystals of InPF-17 (0.177 g, 79%). MW synthesis: H₃popha (0.040 g, 0.114 mmol), 2,2'-bipy (0.016 g, 0.114 mmol), In(OAc)₃ (0.033 g, 0.114 mmol), and water (2 mL) were placed in a glass vial and submitted to MW radiation by using a dynamic method at 160 °C with vigorous stirring (30 min, 200 W, 9 bar), which led to formation of the product InPF-17 (0.067 g, 90%). Elemental analysis calcd (%) for C₂₅H₂₂InN₃O₁₃ (687.27 g mol⁻¹): C 43.69, H 3.22, N 6.11; found: C 43.56, H 3.10, N 5.90; IR (KBr): $\tilde{\nu}$ = 3620, 3559 (O–H, H₂O), 3449 (C–H, aromatic, 2,2'bipy), 3115 and 3083 (C-H, aromatic)L, 1619 and 1602 (C=O)L, 1579 (C=C, aromatic)L, 1562 (N-O)as, 1530 (C=N, 2,2'-bipy), 1496 and 1477 (OCO)s, 1458 and 1444 (OCO)as, 1382 v(C-C)as, 1349 and 1319 (N-O)s, 1264 and 1253 (C-O)as, 1176 and 1164 (C-C)s, 921 and 836 δoop(C–H, 2,2'-bipy), 779, 771, and 759 cm⁻¹ $\delta oop(C-H)L$; TGA (air, 100 mLmin⁻¹): Initial weight loss started at temperatures <100°C, which was due to the loss of water molecules that had been physisorbed inside the material framework (total loss = $\approx 8\%$); a 70% loss of material was observed at pprox430°C; the final residue that remained at pprox800°C corresponded to 22% of the material that had been converted into In_2O_3 (ICSD_ 640179).

 $[In_3(OH)_3(popha)_2(4,4'-bipy)]-4H_2O$ (InPF-18), CH synthesis: a mixture of H₃popha (0.119 g, 0.343 mmol), 4,4'-bipy (0.047 g, 0.343 mmol), and In(OAc)_3 (0.100 g, 0.343 mmol) in distilled water (10 mL) was heated in a Teflon-lined stainless steel autoclave at 180 °C for 18 h. After cooling to room temperature, colorless crystals formed were isolated by filtration and washed with distilled

water, ethanol, and acetone to give colorless crystals of InPF-18 (0.350 g, 81%). MW synthesis: H₃popha (0.040 g, 0.114 mmol), 4,4'bipy (0.016 g, 0.114 mmol), In(OAc)₃ (0.033 g, 0.114 mmol), and water (2 mL) were placed in a glass vial and submitted to MW radiation by using a dynamic method at 180 °C with vigorous stirring (30 min, 200 W, 11 bar) to give the product InPF-18 (0.096 g, 96%). Elemental analysis calcd (%) for $C_{40}H_{31}In_3N_4O_{25}$ (1312.14 g mol⁻¹): C 36.61, H 2.38, N 4.27; found: C 36.47, H 2.66, N 4.22; IR (KBr): $\tilde{\nu} =$ 3610 (O-H, coordinated), 3447 (O-H, H₂O), 3076 (C-H, aromatic)L, 1645 and 1625 (C=O)L, 1590 (C=C, aromatic)L, 1576 (N-O)as, 1532 (C=N, 4,4'-bipy), 1499 and 1451 (OCO)s, 1417 (OCO)as, 1390 (C-C)as, 1353 and 1307 (N-O)s, 1271 and 1255 (C-O)as, 1224 and 1142 (C-C)s, 905 and 856 δoop(C-H, 4,4'-bipy), 777, 759, and 716 cm⁻¹ δ oop(C–H)L; TGA (air, 100 mLmin⁻¹): Initial weight loss started at $< 100 \,^{\circ}$ C, which was due to the loss of water molecules that had been physisorbed inside the framework (total loss = \approx 7%); at \approx 250°C a loss of 3% was observed, which corresponded to loss of the hydroxyl groups in the framework; at \approx 450 °C a final loss of 60% of the material occurred. The final residue that remained at \approx 800 °C corresponded to the 30% of the material that was converted into In₂O₃ (ICSD_640179).

[In₂(popha)₂(4,4'-bipy)₂]·3H₂O (InPF-19), CH synthesis: a mixture of H₃popha (0.119 g, 0.343 mmol), 4,4'-bipy (0.047 g, 0.343 mmol), and In(OAc)₃ (0.100 g, 0.343 mmol) in a mixed solution of EtOH/ H₂O (11 mL, 1.2:1) was heated in a Teflon-lined stainless steel autoclave at 165 °C for 18 h. After cooling to room temperature, crystals were isolated by filtration and washed with distilled water, ethanol, and acetone to give colorless crystals of InPF-19 (0.308 g, 73%). MW synthesis: H₃popha (0.040 g, 0.114 mmol), 4,4'-bipy (0.016 g, 0.114 mmol), In(OAc)₃ (0.033 g, 0.114 mmol), and water (2 mL) were placed in a glass vial and submitted to MW radiation by using a dynamic method at 155 °C with vigorous stirring (10 min, 200 W, 9 bar) to give the product InPF-19 (0.119 g, 85%). Elemental analysis calcd (%) for $C_{50}H_{28}In_2N_6O_{18}$ (1230.42 g mol⁻¹): C 48.80, H 2.29, N 6.83; found: C 48.22, H 1.91, N 6.23; IR (KBr): 3414 (O-H, H2O), 3243 (C-H, aromatic, 4,4'-bipy), 3121 and 3097 (C-H, aromatic)L, 1614 and 1600 (C=O)L, 1564 (N-O)as, 1537 (C=N, 4,4'-bipy), 1493 and 1466 (OCO)s, 1420 and 1407 (OCO)as, 1385 (C-C)as, 1347 and 1321 (N-O)s, 1258 and 1225 (C-O)as, 1163 and 1122 (C-C)s, 977 and 928 δoop(C–H, 4,4'-bipy), 778, 750, and 727 cm⁻¹ δoop(C–H)L; TGA (air, 100 mLmin⁻¹): Initial weight loss started at \approx 100 °C, which was due to the loss of water molecules that had been physisorbed inside the framework (total loss = \approx 5%); at \approx 420 °C the loss of 66% of material was observed; the final residue that remained at $\approx\!800\,^\circ\text{C}$ corresponded to 29% of material that had been converted into In₂O₃ (ICSD_640179).

[In(OH)(Hpopha)]-0.5 (1,7-phen) (InPF-20), CH synthesis: a mixture of H₃popha (0.119 g, 0.343 mmol), 1,7-phen (0.061 g, 0.343 mmol), and In(OAc)₃ (0.100 g, 0.343 mmol) in distilled water (10 mL) was heated in a Teflon-lined stainless steel autoclave at 175 °C for 48 h. After cooling to room temperature, crystals were isolated by filtration and washed with distilled water, ethanol, and acetone to give colorless crystals of InPF-20 (0.095 g, 58%). MW synthesis: H₃popha (0.040 g, 0.114 mmol), 1,7-phen (0.017 g, 0.057 mmol), In(OAc)₃ (0.033 g, 0.114 mmol), and water (2 mL) were placed in a glass vial and submitted to MW radiation by using a dynamic method at 175°C with vigorous stirring (90 min, 200 W, 9 bar) to give the product InPF-20 (0.038 g, 70%). Elemental analysis calcd (%) for $C_{21}H_{12}lnN_2O_{10}$ (567.15 g mol⁻¹): C 44.47, H 2.13, N 4.94; found: C 43.50, H 2.47, N 4.83; IR (KBr): 3637 (O-H, coordinated), 3608 (O-H)L, 3389 (C-H, aromatic, 1,7-phen), 3232 and 3103 (C-H, aromatic)L, 1688, 1619, and 1598 (C=O)L, 1567 (N-O)as, 1552 (C= N, 1,7-phen), 1538 and 1493 (OCO)s, 1459 and 1417 (OCO)as, 1394

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(C–C)as, 1304 (N–O)s, 1267 and 1257 (C–O)as, 1143 and 1111 (C–C)s, 1078 and 976 $\delta oop(C-H$, phen), 777, 759, and 707 cm⁻¹ $\delta oop(C-H)L$; TGA (air, 100 mL min⁻¹): Initial weight loss started at ≈ 200 °C, and the final residue that remained at ≈ 800 °C corresponded to 31% of the material that had been converted into In₂O₃ (ICSD_640179).

[In(popha)(1,10-phen)]·4H₂O (InPF-21), CH synthesis: a mixture of H₃popha (0.119 g, 0.343 mmol), 1,10-phen (0.061 g, 0.343 mmol), and In(OAc)₃ (0.100 g, 0.343 mmol) in distilled water (8 mL) was heated in a Teflon-lined stainless steel autoclave at 160 °C for 72 h. After cooling to room temperature, crystals were isolated by filtration and washed with distilled water, ethanol, and acetone to give yellow crystals of InPF-21 (0.220 g, 91%). MW synthesis: H₃popha (0.040 g, 0.114 mmol), 1,10-phen (0.034 g, 0.114 mmol), In(OAc)₃ (0.033 g, 0.114 mmol), and water (2 mL) were placed in a MW glass vial and submitted to MW radiation by using a dynamic method at 160 °C with vigorous stirring over 60 min at 200 W and 7 bar to give the product InPF-21 (0.072 g, 96%). Elemental analysis calcd (%) for C₂₇H₂₂lnN₃O₁₃ (711.3 g mol⁻¹): C 45.59, H 3.12, N 5.91; found: C 45.86, H 2.86, N 5.79; IR (KBr): 3455 (O-H, H₂O), 3248 (C-H, aromatic, 1,10-phen), 3081 (C-H, aromatic)L, 1621 and 1606 (C=O)L, 1590 (C=C, aromatic)L, 1563 (N-O)as, 1527 (C=N, 1,10-phen), 1496 and 1456 (OCO)s, 1432 and 1403 (OCO)as, 1383 (C-C)as, 1348 and 1311 (N–O)s, 1263 and 1252 (C–O)as, 1150 and 1107 (C–C)s, 1074 and 982 δoop(C–H, phen), 779, 748, and 724 cm⁻¹ δoop(C–H)L; TGA (air, 100 mLmin⁻¹): Initial weight loss started at \approx 100 °C, which was due to the loss of water molecules that had been physisorbed inside the framework (total loss \approx 7%), and at \approx 450 °C the loss of 68% of material was observed. The final residue at pprox 800 °C corresponded to 25% of the material that had been converted into In₂O₃ (ICSD_640179).

General procedure for the catalytic activity experiments

All catalysts were previously treated at 130 °C for 12 h to guarantee the absence of adsorbed solvent molecules. The purity and crystallinity of the catalysts was confirmed by PXRD before and after each catalytic reaction.

Catalytic cyanosilylation of aldehydes: Catalytic amounts of **InPF-16** to **InPF-21** (10 mg, 1 mol%) were placed in a Schlenk tube under nitrogen atmosphere without solvents with the corresponding carbonyl compound (1 equiv); trimethylsilyl cyanide (1.5 equiv) was then added dropwise by syringe. The mixture was stirred at room temperature until disappearance of the aldehyde (0.08–1 h, monitored by GC).

Catalytic cyanosilylation of ketones: Catalytic amounts of **InPF-16** to **InPF-20** (1, 2.5, and 5 mol%) were placed in a Schlenk tube under a nitrogen atmosphere with the corresponding ketone (1 equiv); trimethylsilyl cyanide (1.1 equiv) was then added dropwise by syringe. The mixture was stirred and heated at room temperature until disappearance of the ketone (24–72 h, monitored by GC).

Catalytic One Pot Passerini-3CR: Catalytic amounts of **InPF-16** to **InPF-20** (1 mol%) were placed in a Schlenk tube with benzoic acid (1 equiv), benzaldehyde (1 equiv), and cyclohexyl isocyanide (1 equiv) was then added dropwise by syringe. The mixture was stirred vigorously at room temperature until the precipitation of the solid product (2 h, monitored by ¹H NMR).

General procedure for catalytic One Pot Ugi-4CR: Catalytic amounts of **InPF-16**, **InPF-17**, **InPF-18**, and **InPF-20** (1 mol%) were placed in a Schlenk tube with ethanol (1 mL). Benzoic acid (1 equiv), benzaldehyde (1 equivt), aniline (1 equiv), and cyclohexyl isocyanide (1 equiv) were added dropwise by syringe. The mixture

was vigorously stirred at room temperature until the precipitation of the solid product (2–3 h, monitored by 1 H NMR and GC-MS).

X-ray structure determination

The single-crystal X-ray data for compounds **InPF-16** to **InPF-21** were obtained on a Bruker four circle kappa-diffractometer equipped with a Cu INCOATED microsource, operated at 30 W power (45 kV, 0.60 mA) to generate Cu_{Kα} radiation ($\lambda = 1.54178$ Å), and a Bruker VANTEC 500 area detector (microgap technology).

Diffraction data were collected by exploring over a hemisphere of the reciprocal space in a combination of φ and ω scans to reach a resolution of 0.86 Å, using a Bruker APEX2^[69] software suite (each exposure of 40 s covered 1° in $\omega).$ Unit cell dimensions were determined for least-squares fit of reflections with $l > 20\sigma$. A semi-empirical absorption and scale correction based on equivalent reflection was carried out by using SADABS.^[70] The space-group determination was carried out by using XPREP.^[71] The structures were solved by direct methods. The final cycles of refinement were carried out by full-matrix least-squares analyses with anisotropic thermal parameters of all non-hydrogen atoms. The hydrogen atoms were fixed at their calculated positions by using distances and angle constraints. All calculations were performed by using SMART^[72] and APEX2^[69] software for data collection, SAINT^[70] for data reduction, and $\mathsf{SHELXTL}^{\scriptscriptstyle[71]}$ to resolve and refine the structure details. CCDC 1424185 (InPF-20), 1424083 (InPF-16), 1424084 (InPF-17), 1424085 (InPF-18), 1424026 (InPF-21), and 1424055 (InPF-19) contain the supplementary crystallographic data for this paper. These data are provided free of charge by The Cambridge Crystallographic Data Centre.

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- H. Furukawa, K. Cordova, M. O'Keeffe, O. M. Yaghi, Science 2013, 341, 1230444.
- [2] R. E. Morris, P. S. Wheatley, Angew. Chem. Int. Ed. 2008, 47, 4966–4981; Angew. Chem. 2008, 120, 5044–5059.
- [3] G. Férey, Chem. Soc. Rev. 2008, 37, 191.
- [4] M. E. Medina, A. E. Platero-Prats, N. Snejko, A. Rojas, A. Monge, F. Gándara, E. Gutiérrez-Puebla, M. A. Camblor, *Adv. Mater.* 2011, 23, 5283–5292.
- [5] A. U. Czaja, N. Trukhan, U. Müller, Chem. Soc. Rev. 2009, 38, 1284-1293.
- [6] A. Corma, H. García, F. X. Llabrés i Xamena, Chem. Rev. 2010, 110, 4606– 4655.
- [7] C. Aakeröy, N. R. Champness, C. Janiak, CrystEngComm 2010, 12, 22-43.
- [8] J. Y. Lee, O. K. Farha, J. K. Roberts, A. Scheidt, S. T. Nguyen, J. T. Hupp, *Chem. Soc. Rev.* 2009, 38, 1450–1459.
- [9] A. Dhakshinamoorthy, M. Alvaro, H. Garcia, Chem. Commun. 2012, 48, 11275-11288.
- [10] L. Bromberg, Y. Diao, H. Wu, S. A. Speakman, T. A. Hatton, *Chem. Mater.* 2012, 24, 1664–1675.

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- [11] B. Gómez-Lor, E. Gutiérrez-Puebla, M. Iglesias, M. A. Monge, C. Ruiz-Valero, N. Snejko, *Inorg. Chem.* 2002, 41, 2429–2432.
- [12] F. Gándara, B. Gómez-Lor, E. Gutiérrez-Puebla, M. Iglesias, M. A. Monge, D. M. Proserpio, N. Snejko, *Chem. Mater.* 2008, 20, 72–76.
- [13] B. Gómez-Lor, E. Gutiérrez-Puebla, M. Iglesias, M. A. Monge, C. Ruiz-Valero, N. Snejko, Chem. Mater. 2005, 17, 2568–2573.
- [14] L. M. Aguirre-Díaz, M. Iglesias, N. Snejko, E. Gutiérrez-Puebla, M. A. Monge, CrystEngComm 2013, 15, 9562–9571.
- [15] L. M. Aguirre-Díaz, M. Iglesias, N. Snejko, E. Gutiérrez-Puebla, M. A. Monge, *RSC Adv.* 2015, *5*, 7058–7065.
- [16] L. M. Aguirre-Díaz, F. Gándara, M. Iglesias, N. Snejko, E. Gutiérrez-Puebla, M. A. Monge, J. Am. Chem. Soc. 2015, 137, 6132–6135.
- [17] M. José Climent, A. Corma, S. Iborra, RSC Adv. 2012, 2, 16-58.
- [18] I. Ugi, Angew. Chem. Int. Ed. Engl. 1962, 1, 8–21; Angew. Chem. 1962, 74, 9–22.
- [19] A. Dömling, I. Ugi, Angew. Chem. Int. Ed. 2000, 39, 3168-3210; Angew. Chem. 2000, 112, 3300-3344.
- [20] M. Krasavin, V. Parchinsky, A. Shumsky, I. Konstantinov, A. Vantskul, *Tetrahedron Lett.* 2010, *51*, 1367–1370.
- [21] H. Kunz, W. Pfrengle, J. Am. Chem. Soc. 1988, 110, 651-652.
- [22] S. Lehnhoff, M. Goebel, R. M. Karl, R. Klösel, I. Ugi, Angew. Chem. Int. Ed. Engl. 1995, 34, 1104–1107; Angew. Chem. 1995, 107, 1208–1211.
- [23] K. Oertel, G. Zech, H. Kunz, Angew. Chem. Int. Ed. 2000, 39, 1431 1433; Angew. Chem. 2000, 112, 1489–1491.
- [24] G. F. Ross, E. Herdtweck, I. Ugi, Tetrahedron 2002, 58, 6127-6133.
- [25] G. V. Shanbhag, S. M. Kumbar, T. S. Joseph, B. Halligudi, *Tetrahedron Lett.* 2006, 47, 141 – 143.
- [26] Y. Zhang, J. P. Donahue, C. J. Li, Org. Lett. 2007, 9, 627-630.
- [27] W-.M. Dai, H. Li, Tetrahedron 2007, 63, 12866-12876.
- [28] I. Kanizsai, S. Gyonfalvi, Z. Szakonyi, R. Sillanpaa, F. Fulop, Green Chem. 2007, 9, 357–360.
- [29] F. Bonnaterre, M. Bois-Choussy, J. Zhu, Beilstein J. Org. Chem. 2008, 4, 1-8.
- [30] H. M. Hügel, Molecules 2009, 14, 4936-4972.
- [31] S. Kaur, V. Singh, G. Kumar, J. Singh, ARKIVOC (Gainesville, FL, U.S.) 2011, 2, 151–160.
- [32] N. Azizi, S. Dezfooli, M. M. Hashemi, C. R. Chim. 2013, 16, 1098-1102.
- [33] I. Mohanram, J. Meshram, A. Shaikh, B. Kandpal, Synth. Commun. 2013, 43, 3322-3328.
- [34] M. Ghavami, M. Koohi, M. Z. Kassaee, J. Chem. Sci. 2013, 125, 1347– 1357.
- [35] C. Janiak, AIMS Material Science **2014**, *1*, 41–44.
- [36] J. Jiang, O. M. Yaghi, Chem. Rev. 2015, 115, 6966-6997.
- [37] S.-N. Zhao, S.-Q. Su, X.-Z. Song, M. Zhu, Z.-M. Hao, X. Meng, S.-Y. Song, H.-J. Zhang, Cryst. Growth Des. 2013, 13, 2756–2765.
- [38] G.-Z. Liu, X.-L. Li, L.-Y. Xin, L.-Y. Wang, CrystEngComm 2012, 14, 5315-5321.
- [39] S. Su, S. Wang, X. Song, S. Song, C. Qin, M. Zhu, Z. Hao, S. Zhao, H. Zhang, *Dalton Trans.* 2012, *41*, 4772–4779.
- [40] Z.-G. Gu, X.-X. Xu, W. Zhou, C.-Y. Pang, F.-F. Bao, Z. Li, Chem. Commun. 2012, 48, 3212–3214.
- [41] J. Klinowski, F. A. Almeida Paz, P. Silva, J. Rocha, Dalton Trans. 2011, 40, 321–330.
- [42] Z.-J. Lin, Z. Yang, T.-F. Liu, Y.-B. Huang, R. Cao, Inorg. Chem. 2012, 51, 1813–1820.
- [43] Z. Lin, D. S. Wragg, R. E. Morris, Chem. Commun. 2006, 42, 2021-2023.

- [44] P. Amo-Ochoa, G. Givaja, P. J. S. Miguel, O. Castillo, F. Zamora, *Inorg. Chem. Commun.* 2007, 10, 921–924.
- [45] W. Liu, L. Ye, X. Liu, L. M. Yuan, X. Lu, J. Jiang, Inorg. Chem. Commun. 2008, 11, 1250–1252.
- [46] P. Silva, A. A. Valente, J. Rocha, F. A. Almeida Paz, Cryst. Growth Des. 2010, 10, 2025 – 2028.
- [47] V. A. Blatov, A. P. Shevchenko, V. N. Serezhkin, J. Appl. Crystallogr. 2000, 33, 1193.
- [48] V. A. Blatov, L. Carlucci, G. Ciani, D. M. Proserpio, *CrystEngComm* 2004, 6, 378-395.
- [49] V. A. Blatov, A. P. Shevchenko, D. M. Proserpio, Cryst. Growth Des. 2014, 14, 3576-3586.
- [50] M. O'Keeffe, S. Andersson, Acta Crystallogr. Sect. A 1977, 33, 914-923.
- [51] T. G. Mitina, V. A. Blatov, Cryst. Growth Des. 2013, 13, 1655-1664.
- [52] V. A. Blatov, D. M. Proserpio, Acta Crystallogr. Sect. A 2009, 65, 202–212.
- [53] Y. Ogasawara, S. Uchida, K. Yamaguchi, N. Mizuno, Chem. Eur. J. 2009, 15, 4343–4349.
- [54] A. Procopio, G. Das, M. Nardi, M. Oliverio, L. Pasqua, ChemSusChem 2008, 1, 916–919.
- [55] K. Iwanami, J. C. Choi, B. Lu, T. Sakakura, H. Yasuda, Chem. Commun. 2008, 1002–1004.
- [56] W. K. Cho, J. K. Lee, S. M. Kang, Y. S. Chi, H. S. Lee, I. S. Chio, Chem. Eur. J. 2007, 13, 6351–6358.
- [57] S. Huh, H. T. Chen, J. W. Wiench, M. Pruski, V. S. Y. Lin, Angew. Chem. Int. Ed. 2005, 44, 1826–1830; Angew. Chem. 2005, 117, 1860–1864.
- [58] K. Yamaguchi, T. Imago, Y. Ogasawara, J. Kasai, M. Kotani, N. Mizuno, Adv. Synth. Catal. 2006, 348, 1516–1520.
- [59] B. Karimi, L. Ma'Mani, Org. Lett. 2004, 6, 4813-4815.
- [60] K. Higuchi, M. Onaka, Y. Izumi, Bull. Chem. Soc. Jpn. 1993, 66, 2016– 2032.
- [61] S. Martín, R. Porcar, E. Peris, M. I. Burguete, E. García-Verdugo, S. V. Luis, Green Chem. 2014, 16, 1639–1647.
- [62] N. A. Guerra-Navarro, L. N. Palacios-Grijalva, D. Ángeles-Beltrán, G. E. Negrón-Silva, L. Lomas-Romero, E. González-Zamora, R. Gaviño-Ramírez, J. Navarrete-Bolaños, *Molecules* **2011**, *16*, 6561–6576.
- [63] B. Thirupathi, M. K. Patil, B. M. Reddy, Appl. Catal. A: General 2010, 384, 147–153.
- [64] S. Horike, M. Dincă, K. Tamaki, J. R. Long, J. Am. Chem. Soc. 2008, 130, 5854–5855.
- [65] C. Xu, I. Yu, P. Mehrkhodavandi, Chem. Commun. 2012, 48, 6806-6808.
- [66] Q. Xia, B. Ganem, Org. Lett. 2002, 4, 1631-1634.
- [67] X. Li, S. J. Danishefsky, J. Am. Chem. Soc. 2008, 130, 5446-5448.
- [68] Inorganic Crystal Structure Database, ICSD.
- [69] APEX2; Bruker-AXS: Madison, WI, 2006.
- [70] Siemens SAINT Data Collection and Procedure Software for the SMART System, Siemens Analytical X-ray Instruments, Inc., Madison, WI, 1995.
- [71] Siemens SHELXTL, Version 5.0, Siemens Analytical X-ray Instruments Inc., Madison, WI, **1995**.
- [72] Software for the SMART System V5. 0.4 and SHELXTL V 5.1, Bruker-Siemens Analytical X-ray Instrument Inc., Madison, WI, 1998.

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