Framework-Copper-Catalyzed C–N Cross-Coupling of Arylboronic Acids with Imidazole: Convenient and Ligand-Free Synthesis of N-Arylimidazoles

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A convenient and environmentally benign synthesis of N-arylimidazoles has been demonstrated by a straightforward reaction catalyzed by the unsaturated coordination sites of Cu in the copper terephthalate metal–organic framework (Cu(tpa)-MOF). A series of N-arylimidazoles has been synthesized in excellent yields by the C–N cross-coupling reaction of arylboronic acids and imidazoles catalyzed by the Cu(tpa)-MOF using ethanol as a benign solvent. The present ligand-free catalytic system proceeds smoothly under mild conditions, avoids

stoichiometric Cu reagents, tolerates many functional groups, has a wide substrate scope, and is feasible with other nitrogen heterocycles. The stability and heterogeneity of the catalyst is evidenced by the results of a heterogeneity test, and the catalyst can be reused several times without a loss of activity. The easy preparation of the catalyst, its stability, recovery by simple filtration, and reusability reveal Cu(tpa) MOF as a versatile catalyst for academic and industrial applications.

Introduction

Imidazoles are important and versatile compounds that attract wide attention in medicinal chemistry.^[1] Among imidazoles, those that bear a phenyl moiety on the N atom show interesting biological activities^[2] and their subunits are found commonly in pharmaceutically important molecules (Figure 1). In addition, they also have numerous synthetic utilities such as in natural-product synthesis,^[3] as versatile N-heterocyclic carbene precursors,^[4] as a ligand for transition-metal catalysis,^[5] and as room-temperature ionic liquids.^[6]



Figure 1. N-arylimidazole-containing drug molecules.

In general, the synthesis of these moieties can be achieved by one of two methods: (a) the ring-closure reaction of acyclic precursors^[7] or (b) the nucleophilic aromatic substitution of heterocyclic compounds.^[8] The exponential growth in

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transition-metal catalysis facilitates the development of simple synthetic methodologies for the direct coupling of imidazoles with functionalized arenes.^[9] Chan et al.^[10a] and Lam et al.^[11] have investigated Cu in C–N cross-coupling, but high loadings, harsh conditions, and high-boiling-point aprotic solvents are required for the catalytic methods. Although Collman et al.^[12a,b] reported the Cu-catalyzed synthesis of *N*-arylimidazole, the reactions required ligands^[12] and co-oxidants^[13] to maintain the oxidation state of Cu. Various other methodologies and cata-

lysts have been developed using different heterogeneous media^[14] for the N-arylation of imidazole that, in general, require harsh conditions, exhibit poor functional group tolerance, and produce transitionmetal waste, which triggered us to identify a new catalytic system with a simple methodology and a more benign process.

Metal–organic frameworks (MOFs), a new class of crystalline porous materials, have emerged as distinguished heterogeneous catalysts in numerous transformations^[15] because of their unique features such

as stability, tunability, reusability, and high surface areas.^[16] MOF-based catalysts find potential applications in areas from basic synthetic transformations^[17] to large-scale industrial applications.^[18] Although MOFs are studied extensively as catalysts for various organic reactions, the catalytic role of Cubased MOFs is of particular interest because of the presence of coordinatively unsaturated open metal sites^[19] that mimic the coordination and electronic properties of N-heterocyclic Cu coordination complexes in catalysis.^[20] Hence, Cu-based MOFs have been identified as excellent substitutes for the corresponding homogenous counterparts and as replacements for expensive catalysts such as Pd and Rh in organic synthesis.^[21] The potential use of a Cu MOF as a catalyst in C–N



cross-coupling has been little explored.^[22] The synthetic use of boronic acids is becoming more common in coupling reactions as they are more stable, less toxic, and greener^[23] than aryl halides. Boronic acids have a broad substrate scope, however, their utility in MOF-catalyzed coupling reactions is very limited.^[24] Therefore, in the present study, we aim to utilize a simple copper terephthalate MOF^[25] (Cu(tpa)-MOF) as a ligand-free, sustainable catalyst for the facile and benign synthesis of N-arylimidazoles. The exposed apical Cu²⁺ coordination sites, high surface area, and large pore volume of Cu(tpa)-MOF will be expected to catalyze the N-arylation of imidazole using arylboronic acids as electrophiles. Except for very few reports^[24c, 26] on the application of Cu(tpa)-MOF in organic synthesis, to the best of our knowledge this is the first report of Cu(tpa)-MOF as a catalyst for the synthesis of N-arylimidazoles by C–N cross-coupling.

Results and Discussion

To optimize the reaction conditions for the N-arylation of imidazole using Cu(tpa)-MOF as a catalyst, a model reaction was performed to screen various parameters such as the catalyst, solvent, time, temperature, base, and catalyst loading using imidazole (2) with phenylboronic acid (1 a), and the results are listed in Table 1. Without catalyst, the treatment of 2 with 1 a using triethylamine (TEA) as a base and EtOH as the solvent resulted in no reaction.

Table 1. Optimization of the Cu(tpa)-MOF-catalyzed N-arylation of imida- zole ^[a]						
2010.	B(OH) ₂					
	+	Reaction Co Open ves	nditions seel			
	1a	2	3a			
Entry	Solvent	Base	Yield [%] ^[b]			
1	EtOH	TEA	_[c]			
2	Dioxane	TEA	_			
3	ACN	TEA	_			
4	DCM	TEA	trace			
5	DMF	TEA	-			
6	DMSO	TEA	-			
7	MeOH	TEA	99 ^[d]			
8	Water	TEA	47 ^[e]			
9	MeOH/water	TEA	76 ^[f]			
10	EtOH	TEA	51, ^[g] 70, ^[h] 99, ^[i] 99 ^[j]			
11	EtOH	TEA	98, ^[k] 98 ^[l]			
12	EtOH/water	TEA	60, ^[f] 98 ^[m]			
13	EtOH	-	_			
14	EtOH	Na_2CO_3	74			
15	EtOH	K ₂ CO ₃	73			
16	EtOH	Cs ₂ CO ₃	40			
17	EtOH	N,N-diisopropyle	ethylamine 94			
18	EtOH	pyridine	35			
[a] Reaction conditions: 1a (1 equiv.), 2 (1.2 equiv.), Cu(tpa)-MOF (7.6 mol%), base (1.2 equiv.), solvent 3.0 mL, RT, 12 h. [b] Isolated yield. [c] Without catalyst. [d] MOF decomposed. [e] MOF becomes pasty. [f] MeOH/water and EtOH/water ratios are 1:9. Yields in [g] 4 h, [h] 8 h, [i] 12 h, and [j] 24 h. Yields at [k] 60 and [l] 70 °C. [m] EtOH/water ratio is 9:1.						

If the same reaction was performed under identical conditions using Cu(tpa)-MOF as the catalyst, the reaction proceeded smoothly with a good conversion. To choose the optimum solvent for the N-arylation of **2**, various nonpolar and polar solvents, dioxane, acetonitrile (ACN), dichloromethane (DCM), EtOH, MeOH, DMF, DMSO, and water, were investigated, and nonpolar and aprotic polar solvents resulted in poor yields or no reaction. Protic polar solvents, MeOH, EtOH, and water, favor the arylation to give good to excellent yields, however, the high nucleophilicity of MeOH disturbs the framework of Cu(tpa)-MOF, which decomposes during the course of the reaction.

The same phenomenon was noted if water was used as the solvent, and the catalyst became pasty and stuck to the reaction vessel. In EtOH, the reactions went to completion with a very good yield of 99% with a minimum catalyst loading (Table 1, entry 10). Consequently, EtOH was chosen as the reaction medium for this coupling reaction and it does not influence Cu(tpa)-MOF negatively. A survey of solvent section guides^[23, 27] showed that EtOH is a greener solvent than MeOH, and industrial companies, such as Pfizer, Astra Zeneca, GCI-PR, and GSK, rank EtOH as a green solvent for medicinal chemistry^[27] in terms of health, safety, and environmental scores. Although other catalytic systems employ MeOH^[14b, c, h-j] as the medium for N-arylation, the present Cu(tpa)-MOF catalyst in EtOH offers a green methodology to synthesize N-arylimidazole by C-N cross-coupling. However, the catalyst was sensitive to water, and a notable decrease in the yield was observed if an aqueous mixture of solvents was used. The catalyst was highly specific towards N-arylation, and no other homocoupling or conversion of the C-B bond into a C-O bond was found with any protic polar solvents, which was observed in previous studies under identical conditions.^[24c, 28] The reaction was highly time dependent, and shorter reaction times result in moderate conversions (Table 1, entry 10), whereas reaction times of 12 h afford an excellent yield of 99% without any byproducts. The reaction is insensitive to the temperature as it proceeds smoothly at room temperature, and an increase in temperature does not affect the yield. Among the bases screened, the soluble organic base TEA showed the best result in EtOH, and catalyst was inactive in the absence of base. The catalyst loading plays a significant role in the maximization of the yield, and an increase in the catalyst loading results in a rapid enhancement of the yield. Finally, optimization showed that 7.6 mol% catalyst was enough (Figure 2) to obtain a good conversion with the minimum Cu loading (0.06 mmol).

Although Cu(tpa)-MOF catalyzes the N-arylation with a minimum Cu loading, to understand the role of framework Cu, various Cu sources, namely, Cu(NO₃)₂·3 H₂O, Cu(OAc)₂·H₂O, CuSO₄·5 H₂O, Cu(BF₄)₂·H₂O, CuCl, CuCl₂·2 H₂O, and CuCO₃, were screened using TEA in EtOH without any ligands (Table 2). All invariably worked but afforded moderate yields with stoichiometric amounts of the catalysts. In addition, to prove the competence of the catalytic activity of Cu in Cu(tpa)-MOF, N-arylation was performed using various MOFs, such as Cu(bpy)-(H₂O)(BF₄)₂(bpy) (bpy=bipyridine), Cu(btc) (btc = benzene-1,3,5-tricarboxylic acid), MIL-53(Fe), Fe(btc), and IRMOF-3,

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Figure 2. Optimization of the catalyst loading for the N-arylation of imidazole.

Table 2. Various Cu sources in the N-arylation of imidazole. ^[a]						
Entry	Cu source ^[b]	Yield [%] ^[b]				
1	$Cu(NO_3)_2 \cdot 3H_2O$	58				
2	Cu(OAc) ₂ ·H ₂ O	60				
3	CuSO ₄ ·5H ₂ O	61				
4	Cu(BF ₄) ₂ ·H ₂ O	32				
5	CuCl	51				
6	CuCl ₂ ·2H ₂ O	62				
7	CuCO ₃	70				
8	Cu(tpa)-MOF ^[d]	99				
[a] Reaction conditions: 1a (1 equiv.), 2 (1.2 equiv.), [b] Cu salt (1 equiv.), TEA (1.2 equiv.), EtOH (3.0 mL), RT, 12 h. [c] Isolated yield. [d] 7.6 mol%.						

Table 3. Different MOFs as catalysts in the N-arylation of imidazole. $^{[a]}$						
Entry	Other MOFs	Yield [%] ^[b]				
1	Cu(bpy)(H ₂ O) ₂ (BF ₄) ₂ (bpy)-MOF	48				
2	Cu(BTC)-MOF	57				
3	Fe(BTC)-MOF	-				
4	MIL-53(Fe)-MOF	-				
5	IRMOF-3	-				
6	$Cu(NO_3)_2 \cdot 3H_2O$:terephthalic acid ^[c]	26				
[a] Reaction conditions: 1a (1 equiv.), 2 (1.2 equiv.), MOF catalyst 20 wt%, TEA (1.2 equiv.), EtOH (3.0 mL), RT, 12 h. [b] Isolated yield. [c] As a 1:1 physical mixture						

under identical conditions. Among these MOFs, Cu MOFs (Table 3, entry 1 and 2) showed a very poor response, and the other MOFs (Table 3, entry 3–5) were inactive in N-arylation. From this, we inferred that the presence of a high surface area, porous nature, and the catalytic center of Cu ligated by terephthalic acid are responsible for the high catalytic activity of Cu(tpa)-MOF, which was confirmed from the control experiment in which a stoichiometric mixture of Cu(NO₃)₂·3 H₂O and terephthalic acid as the catalyst was used, which afforded poor yields (26%; Table 3, entry 6). These preliminary screening results reveal that Cu(tpa)-MOF acts as a good catalyst in the

presence of the simple and mild base TEA and the solvent EtOH at room temperature.

After the reaction conditions were optimized for the N-arylation of 2 with 1 a using Cu(tpa)-MOF as the catalyst, we used other structurally and electronically diverse arylboronic acids under the optimized conditions to further expand the scope of the present methodology, and the results are highly encouraging (Table 4). Notably, all of the arylboronic acids that bear either electron-donating or electron-withdrawing groups yielded the corresponding N-arylimidazoles in excellent yields, which illustrates that the electronic effect of the substituents is not significant. Boronic acids that possess electron-rich alkyl, alkoxy, and alkenyl groups were used as coupling partners to afford the coupling products 3b-3h in good to excellent yields. Boronic acids that have electron-withdrawing substituents such as halogens, nitro, and nitrile groups reacted guickly and gave excellent yields within the optimized time, and the phenylboronic acid with the strongly electron-withdrawing trifluoromethyl group (3p; Table 4) reacted smoothly without any competing homocoupling.

A marginal decrease in the yield was observed with disubstituted arylboronic acids that possess both electron-donating and -withdrawing substituents (3n and 3o; Table 4) because of electronic reinforcement. Another observation is that Cu(tpa)-MOF was highly insensitive to steric factors and showed good yields, as observed in all ortho-substituted arylboronic acids (3b, 3g, 3j, and 3n; Table 4). A similar trend was observed with fused-ring moieties (3w and 3x; Table 4). Notably, the present methodology tolerates many functional groups, which include formyl, nitrile, and amino groups, as oxidized or hydrolyzed products were not observed (3r-3u; Table 4). Heteroarylboronic acids react nearly as well as arylboronic acids and gave good yields without any impact of the heteroatom on the catalyst. Remarkably, arylboronic acids that contained more polar substituents, such as aryl and alkyl amides, sulfones, and nonpolar ethers, form the respective coupled products in good yields, and the imidazole could be arylated selectively in the presence of amide N atoms.

To expand the scope of this method, we found that the catalyst was also suitable for other π -electron-rich nitrogen heterocycles, such as pyrrole, pyrazole, and benzimidazole, and yielded the corresponding N-arylated product in a good yield (**3ak–3am**; Table 5). Isatin and aromatic primary amine (**3an**, **3ai**, and **3aj**; Table 5) undergo arylation if coupled with **1a** with Cu(tpa)-MOF. However, all of the heterocycles react slowly and require long reaction times, and we found that the catalytic system is totally inactive with indoles and aliphatic amines.

Heterogeneity

In heterogeneous catalysis, during the course of the reaction the leaching of the catalytically active sites into the reaction medium may lead to a homogenous catalytic reaction, so we must question the real heterogeneity of a catalyst. To determine the true heterogeneity of Cu(tpa)-MOF, a control experiment was performed in the C–N cross-coupling reaction between **2** and **1a** by simple filtration at room temperature.





[a] Reaction conditions: Arylboronic acid (1.0 equiv.), imidazole (1.2 equiv.), Cu(tpa)-MOF (7.6 mol%), TEA (1.2 equiv.), EtOH (3.0 mL), RT. All are isolated yields. [b] isolated yield in 1 g batch.

During the course of the reaction under the optimized conditions, the solid catalyst was removed from the reaction mixture by filtration after 4 h and analyzed by using GC as the reaction conversion reached 51%. The reaction of the filtered liquid phase was allowed to proceed under identical conditions for a further 20 h without the solid catalyst at room temperature. At 4 h intervals, sample aliquots were analyzed by using GC, which showed no further increase in the product conversion, which remained at 51% (Figure 3). This confirms that Cu(tpa)-MOF is highly stable under the optimized reaction conditions and does not undergo any structural deformation or decomposition, and no leaching of the catalytically active Cu species into the solution takes place.

These results suggest that the Cu(tpa)-catalyzed N-arylation happens in a heterogeneous manner and there is no contribution from leached species in the liquid phase. These results were supported by inductively coupled plasma optical emission spectroscopy (ICP-OES) of the filtrate from the reaction mixture in ethanol that showed the absence of metal leaching, which demonstrates strongly that Cu(tpa)-MOF is truly heterogeneous.

Reusability

The reusability of the catalyst was also studied. At the end of the reaction, the Cu(tpa)-MOF catalyst was separated by simple filtration, washed with ethanol and excess DMF, and activated at 220 °C. The recovered catalyst was reused subsequently for five times (Figure 4), and a minor loss in the activity of the catalyst was observed with a minor decrease in the product yield.

To confirm the recoverability and reusability of the Cu(tpa)-MOF in the C-N cross-coupling reaction and to understand the structural stability of the catalyst, the recovered catalyst was characterized by using FTIR spectroscopy and powder XRD. The FTIR spectra of the reused samples were recorded after drying at 220°C, and the spectra were similar to that of the fresh catalyst with a strong peak at $\tilde{\nu} = 1640 \text{ cm}^{-1}$ (Figure 5). Even after five consecutive uses, no changes in the IR stretching frequencies were observed. The absence of strong absorption bands in the range of $\tilde{\nu} = 1760 - 1690 \text{ cm}^{-1}$, in which the -COOH vibrations appear, indicates that Cu(tpa)-MOF does not decompose into carboxylic acids during the course of the reaction. This shows that catalyst retains its framework structure and is stable even after five consecutive runs.

In the powder XRD patterns (Figure 6), a very sharp peak at $2\theta = 10.37^{\circ}$ was observed, which indicates that the MOF was highly crystalline in nature and that DMF was coordinated to the Cu center. However in the reused Cu(tpa)-MOF, a new peak appeared at $2\theta = 8.77^{\circ}$, which is caused by the removal

of all coordinated solvent molecules after the activation of the catalyst at 220 °C.^[25] In this study, although the catalyst was activated at 220 °C, a few peaks were retained that indicate the presence of Cu(tpa)-DMF, which shows that the complete removal of coordinated solvent molecules inside the framework is difficult. The diffraction pattern of the reused catalyst demonstrates clearly that Cu(tpa)-MOF retains its crystallinity even after five consecutive reuses. To ensure the crystalline stability of the Cu(tpa)-MOF catalyst, SEM images were recorded to study the external morphology (Figure 7). Both the fresh and



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[a] Reaction conditions: Arylboronic acid (1.0 equiv.), N-heterocycle (1.2 equiv.), Cu(tpa)-MOF (7.6 mol %), TEA (1.2 equiv.) EtOH (3.0 mL), RT, all are isolated yields.



Figure 5. FTIR spectra of fresh and reused Cu(tpa)-MOF. a) Fresh Cu(tpa)-MOF, b) first, c) third, and d) fifth run.



Figure 3. Filtration test for the true heterogeneity of Cu(tpa)-MOF in the N-arylation of imidazole.



Figure 4. Reusability profile of Cu(tpa)-MOF in the N-arylation of imidazole.

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Figure 6. Powder XRD patterns of fresh and reused Cu(tpa)-MOF. a) Fresh Cu(tpa)-MOF, b) first, c) third, and d) fifth run.



Figure 7. SEM images of a, b) fresh Cu(tpa) and c) reused Cu(tpa)-MOF after the fifth run. Scale bars = 2 μm (b and c) and 5 μm (a).



reused catalysts showed the same highly crystalline surface morphology, which remained unaltered even after the fifth reuse.

Terephthalate ligands are coordinated in a bidentate bridging fashion to form a Cu^{II} dimer, with Cu centers separated by 2.63 Å. Each Cu^{II} center is also coordinated to a molecule of DMF to give the Cu^{II} ion a square-planar geometry. In addition, Cu^{II} ions exhibit dynamic Jahn–Teller distortion and can provide open Lewis acid sites that endorse transmetalation followed by the addition of imidazole after deprotonation in C-N coupling. Also, the presence of a high surface area and exposed apical coordination sites on Cu in Cu(tpa)-MOF promote the N-arylation of imidazole with various arylboronic acids. The flexibility of the framework allows Cu to coordinate to arylboronic acids and imidazole, either by expanding the coordination sphere of framework Cu or by displacing the solvent molecules coordinated to unsaturated metal sites without causing framework collapse. As a result of all of these factors, Cu(tpa)-MOF shows a good activity for the C-N coupling reaction. In accordance with previous studies^[29] and our results, a plausible mechanism is proposed (Scheme 1). During the C-N cross-coupling, the solvent molecule coordinated to the Cu center may be replaced by the arylboronic acid. The initial transmetalation of Cu(tpa)-MOF with 1 a would initiate the reaction and generate II through bonding with the coordinatively unsaturated Cu sites. Then 2 coordinates to II in the presence of base to generate III. In the presence of O₂, the Cu^{II} center of Cu(tpa)-MOF in III is oxidized readily to Cu^{II} to form the intermediate IV, which would subsequently undergo reductive elimination to give the N-arylated product and the regenerated catalyst simultaneously. As a result of the rigid framework and paddlewheel coordination geometry of Cu(tpa)-MOF, a bimetallic mechanism is also likely to yield the N-arylated product.

Conclusions

We have demonstrated a green and sustainable method to prepare a series of N-arylimidazoles in excellent yields by the cross-coupling of arylboronic acids with imidazole using the framework Cu present in a copper terephthalate metal-organic framework under heterogeneous conditions. Reactions were performed in an open flask at room temperature without the aid of any ligand or additive and using ethanol as a green solvent. This protocol offers an efficient, highly selective, and sustainable catalyst for C-N cross-coupling reactions with a minimal Cu loading. Importantly, this catalyst could tolerate diverse functional groups and is highly insensitive to hindered substrates. Many N-arylimidazoles were synthesized under heterogeneous conditions. The catalyst is highly stable, shows no metal leaching, and could be recovered by simple filtration. Moreover, the reused catalyst showed no loss in activity. A scale-up has also been achieved successfully with a negligible loss in activity. To our delight, this catalyst may find wide applications in synthetic and medicinal chemistry in industry and academia.

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Scheme 1. Plausible mechanism for the Cu(tpa)-MOF-catalyzed N-arylation of imidazole.

Experimental Section

All reagents and starting materials were purchased commercially from Sigma-Aldrich, Alfa-Aesar, or Merck, and were used as received without any further purification unless otherwise noted. All ^1H and $^{13}\text{C}\,\text{NMR}$ spectra were measured either in CDCI_3 or [D₆]DMSO with TMS as an internal standard by using a 300 MHz on a Bruker spectrometer. ESI-MS was performed by using an LCQ Fleet, Thermo-Fisher Instruments Limited, US. The collision voltage and ionization voltage were -70 V and -4.5 kV, respectively, and N₂ was used as the atomization and desolvation gas. The desolvation temperature was set at 300 °C. The powder XRD patterns of the MOF were recorded by using an XPERT-PRO instrument using CuK_a radiation at RT. FTIR spectra of the MOF were recorded by using a Shimadzu instrument from 4500 to 500 cm⁻¹, and the samples were dispersed using the KBr pellet technique. N₂ physisorption measurements were conducted by using a Micromeritics 2020 volumetric adsorption analyzer system. Samples were outgassed at 200 °C for 12 h. A Netzsch Thermoanalyzer STA 409 was used for



thermogravimetric analysis (TGA) with a heating rate of 10 °C min⁻¹ under a N₂ atmosphere at 50–800 °C. GC was performed by using a Shimadzu instrument with a flame ionization detector (FID) and a ZB-5 column (length = 30 m, inner diameter = 0.25 mm, and film thickness = 0.25 μ m) using a temperature program from 100 to 250 °C at 10 °C min⁻¹. SEM was performed by using a TESCAN VEGA3 instrument using a SE detector and equipped with an EDAX energy-dispersive X-ray spectroscopy (EDX) detector. ICP-OES was performed by using a PerkinElmer OPTIMA 5300 DV.

Synthesis and characterization of Cu(tpa)-MOF

Cu(tpa)-MOF was synthesized by a solvothermal process as reported previously.^[25] Copper nitrate trihydrate (8.45 g, 34.9 mmol) and terephthalic acid (5.80 g, 34.9 mmol) were dissolved in DMF (780 mL) in a 1 L round-bottomed flask, and the mixture was stirred for 30 min. The mixture was transferred into a Teflon-lined autoclave and heated in an air oven to 110 °C for 36 h. After the reaction was over, the autoclave was cooled slowly to RT, and small, fine, blue crystals were recovered. Then the mother liquor was simply decanted, and the crystals were washed with DMF to remove unreacted starting materials and dried in a hot-air oven at 220 °C for 24 h. The product was characterized by FTIR spectroscopy, powder XRD, SEM, EDX, and TGA.

The FTIR spectrum of Cu(tpa)-MOF exhibits a peaks at $\tilde{v} =$ 1666 cm⁻¹, which indicates that a DMF molecule was coordinated to the Cu^{II} center, and the absence of strong absorption bands at $\tilde{\nu} = 1760 - 1690 \text{ cm}^{-1}$ confirmed the deprotonation of carboxylic acid groups in 1,4-benzene dicarboxylic acid. In the powder XRD pattern, the presence of a very sharp peak nearly at $2\theta = 10.37^{\circ}$ indicates that the MOF was highly crystalline in nature, and the observed pattern exactly matches reported and simulated patterns.^[25] Cu(tpa)-MOF was dissolved in dilute HNO₃, and quantitative analysis by ICP-OES showed that 19.93% of Cu was present. EDX analysis of Cu(tpa)-MOF revealed the presence of Cu, C, and O on the framework. Cu(tpa)-MOF is porous in nature, and the surface area and pore volume of the synthesized MOF were calculated from the N₂ adsorption/desorption isotherm data at 77 K. The synthesized MOF has a BET surface area of $625 \text{ m}^2\text{g}^{-1}$ and a pore volume 0.264 cm³g⁻¹, which are good agreement with reported values.^[30] TGA that showed Cu(tpa)-MOF exhibited a good stability in good agreement with previous studies. Freshly synthesized Cu(tpa)-MOF exhibits a gradual weight loss in the initial stage and a sudden decrease from 160 $^\circ\text{C}$ that ends at nearly 270 $^\circ\text{C},$ which indicates the loss of coordinated DMF. The next loss starts nearly at 290 $^\circ\text{C}$ and ends at nearly 350 $^\circ\text{C},$ which was because of the pyrolysis of the MOF. This result revealed that Cu(tpa)-MOF was stable up to 350 °C. The morphology of the Cu(tpa)-MOF was studied by using SEM by coating on conducting carbon tape and using a secondary electron (SE) detector. The SEM images revealed the presence of well-shaped and good-quality crystals, which was in good agreement a previous study.^[26b] The overall analyses of synthesized Cu(tpa)-MOF values agreed accurately with reported values.

General procedure for Cu(tpa)-MOF-catalyzed C-N crosscoupling

The N-arylation of **2** with **1a** was performed in oven-dried glassware. Compound **2** (70 mg, 0.98 mmol, 1.2 equiv.) and **1a** (100 mg, 0.82 mmol, 1.0 equiv.) were added to EtOH (3 mL). Then TEA (0.98 mmol, 1.2 equiv.) was added followed by Cu(tpa)-MOF (20 mg,7.6 mol%; 20 wt%; 0.06 mmol of Cu). The mixture was stirred at RT in an open vessel. The course of the reaction was monitored by TLC, and the catalyst was recovered by simple filtration from the reaction mixture after the completion of the reaction (12 h). The catalyst was washed repeatedly with ethyl acetate to remove the product and any unreacted materials, if present. The filtrate was washed with water, dried with anhydrous sodium sulfate, and concentrated under reduced pressure. The resulting product was purified by passing it over silica gel (60–120 mesh) using petroleum ether/ethyl acetate (3:1) as an eluent to afford 1-phenyl-1*H*-imidazole (**3 a**), which was analyzed by using NMR spectroscopy and ESI-MS. After the extraction of the product, Cu(tpa)-MOF was washed with ethanol and washed repeatedly with DMF and dried in a hot-air oven at 220 °C before reuse.

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FULL PAPERS



Coupling in frameworks: The copper terephthalate metal–organic framework (Cu(tpa)-MOF) is an efficient, reusable, and benign heterogeneous catalyst for the C–N cross-coupling of arylboronic acids with imidazoles. A series of N-arylimidazoles is synthesized in excellent yields catalyzed by the unsaturated coordination sites of Cu in the Cu(tpa)-MOF. The easy preparation of the catalyst, its stability, recovery by simple filtration, and reusability reveal Cu(tpa)-MOF as a versatile catalyst for diverse applications.

Framework-Copper-Catalyzed C–N Cross-Coupling of Arylboronic Acids with Imidazole: Convenient and Ligand-Free Synthesis of N-Arylimidazoles N. Devarajan, P. Suresh*