

A base-free Chan–Lam reaction catalyzed by an easily assembled Cu(II)-carboxylate metal-organic framework

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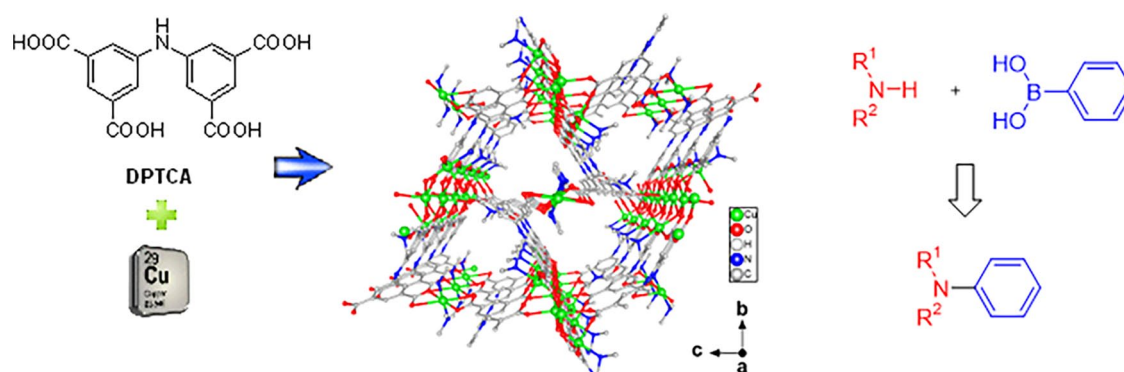
Abstract

A new copper(II) metal-organic framework is constructed as a sustainable copper heterogeneous catalyst. Cu-DPTCA, with high catalytic activity, can effectively promote the Chan–Lam coupling reaction of arylboronic acids and amines without adding any base or additive.

Keywords

amines, arylboronic acid, Chan–Lam reaction, Cu-metal-organic framework, heterogeneous catalysis

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Introduction

Reactions that form C–N bonds are widely used in synthetic chemistry due to the prevalence of this functionality within pharmaceuticals and biologically active natural products.^{1–4} In recent decades, various effective strategies based on transition-metal catalysis for C–N bond formation have been developed, such as Pd-catalyzed Buchwald–Hartwig coupling^{5,6} and Ullmann coupling.⁷ However, these cases mostly involve the expensive transition-metal palladium and harsh reaction conditions (over 100 °C), which restrict their wide applications in industry. However, the Chan–Lam cross-coupling reaction, the oxidative coupling of amines and arylboronic acids catalyzed by Cu salts, represents one of the most powerful and straightforward tools to construct C–N bonds.^{8–13} This process is mild, convenient, and cheap, offering an alternative to complementary methods using

noble metals. So far, various homogeneous Cu catalysts have been used for the Chan–Lam reaction to access *N*-arylamine subunits. Nevertheless, the use of an additional base in a stoichiometric amount is required for regeneration of the active Cu species. Furthermore, homogeneous

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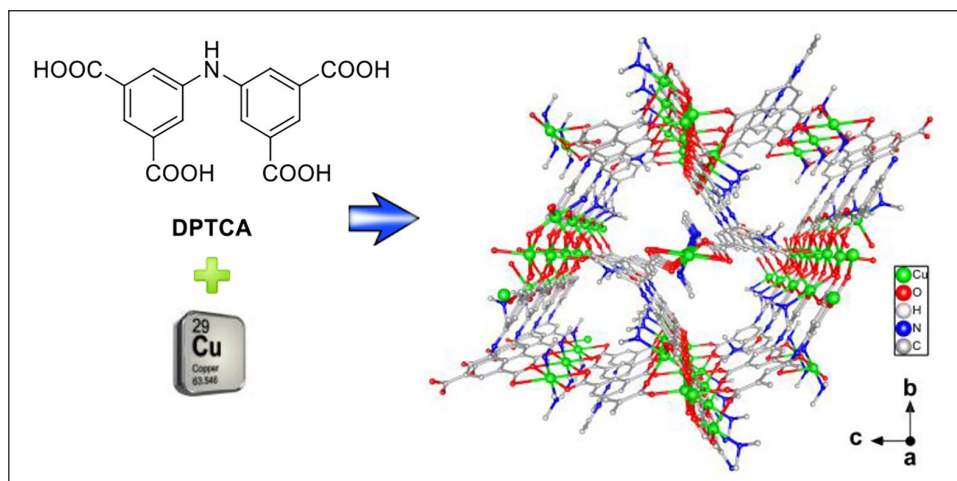


Figure 1. DPTCA ligands are presented and assembled with Cu^{II} , forming a Cu-based framework.

catalytic systems are generally affected by the separation of the products and the metal catalysts, which can be problematic and costly.

In recent years, metal-organic frameworks (MOFs) have emerged as a distinct new option for heterogenization of a metal catalyst for organic synthesis.^{14–19} In comparison with other existing heterogeneous catalytic systems, the design flexibility and framework tunability resulting from the huge variations of metal nodes and organic linkers allow the introduction of different compositions in a single MOF.^{20–25} With this in mind, we anticipated that a MOF containing an amine motif in the organic linker and Cu ion nodes should have two benefits. It may eliminate the need for an additional base, and it may facilitate the recovery and separation of the Cu metal catalyst from products, thereby reducing economic and environmental barriers. To achieve this objective, herein we report the synthesis of a new Cu-DPTCA MOF based on diphenylamine tetracarboxylic acid (DPTCA) and Cu metal (Figure 1, left), named $[\text{Cu}_{2.5}(\text{DPTCA})(\text{OH})(\text{dma})_2(\text{H}_2\text{O})]\cdot 2\text{DMF}$ (abbreviated as Cu-DPTCA), (dma = dimethylamine, DMF = *N,N*-dimethylformamide). With a diphenylamine acid as the linker, DPTCA forms a quad-core structure with a high surface area and large pore volume, providing open metal sites accessible in the catalytic process (Figure 1, right). The MOF was characterized by single-crystal and powder X-ray diffraction, infrared spectroscopy, and thermogravimetric analysis (TGA).

Results and discussion

The asymmetric unit of Cu-DPTCA contains two and a half Cu^{II} ions, one DPTCA ligand molecule, one μ_3 -hydroxyl group, two coordinated dimethylamines, one coordinated water molecule, and two free DMF molecules. Cu-DPTCA features a non-interpenetrated open three-dimensional (3D) porous framework constructed from a tetranuclear Cu(II) cluster $[\text{Cu}_4(\text{CO}_2)_6(\mu_3\text{-OH})_2]$ and DPTCA (Figure 1). Six carboxylate groups from six DPTCA ligands and two μ_3 -hydroxy oxygen atoms link four adjacent Cu(II) ions into tetranuclear clusters. Each DPTCA ligand links four tetranuclear Cu(II) clusters, resulting in the formation of a 3D

porous framework. The effective free volume of Cu-DPTCA is calculated by PLATON analysis as 17.1% of the crystal volume including the free DMF molecules. When viewed from the *a*-axis, Cu-DPTCA has large triangular channels. The structure contains Cu₄ cluster units (Figure 2). The crystallographic data of Cu-DPTCA are summarized in Table 1.

The thermal stability was verified by TGA. A differential thermal weight loss experiment was performed on Cu-DPTCA under an N_2 atmosphere. The temperature range was 30–805 °C, and the temperature ramp rate was 10 °C min^{−1}. The TGA curve (Figure 3) shows that the first mass loss (15%) occurred between 30 and 175 °C due to the loss of coordinated H_2O molecules (theoretical value is 11.3%). Between 175 and 300 °C, it can be seen that the frame structure collapsed and was completely dissociated by 500 °C. The above experimental results show that Cu-DPTCA retains its frame structure and is stable below 300 °C.

To further investigate the porosity of Cu-DPTCA, substrate adsorption experiments were performed with phenylboronic acid (**2**). Cu-DPTCA crystals were soaked in a saturated acetonitrile solution of phenylboronic acid (**2**) for 3 days. Then, the Cu-DPTCA crystals were washed with diethyl ether to remove excess phenylboronic acid (**2**) which was merely absorbed or a coating on the surface of the crystals. Subsequently, the pre-treated Cu-DPTCA crystals were dissolved in $\text{DMSO}-d_6$ and the NMR analysis revealed the presence of phenylboronic acid (**2**). These experimental results clearly showed that the cavity of Cu-DPTCA can accommodate organic molecules of an appropriate size such as phenylboronic acid (**2**); thus, it can potentially act as a heterogeneous catalytic material for organic reactions.

At the outset of the investigation, we were interested in exploring the catalytic potential of Cu-DPTCA for the Chan–Lam coupling reaction. Before catalytic reactions, pre-treatment is required to activate Cu-DPTCA. Thus, the Cu-DPTCA catalyst was immersed in an acetonitrile solution for 24 h for guest molecular exchange and then dried in a vacuum oven (100 °C, 2 h) to remove acetonitrile molecules and solvent molecules inside the Cu-DPTCA catalyst.

Next, phenylboronic acid (**2**) and primary amine **3a** were selected as template substrates to investigate the catalytic

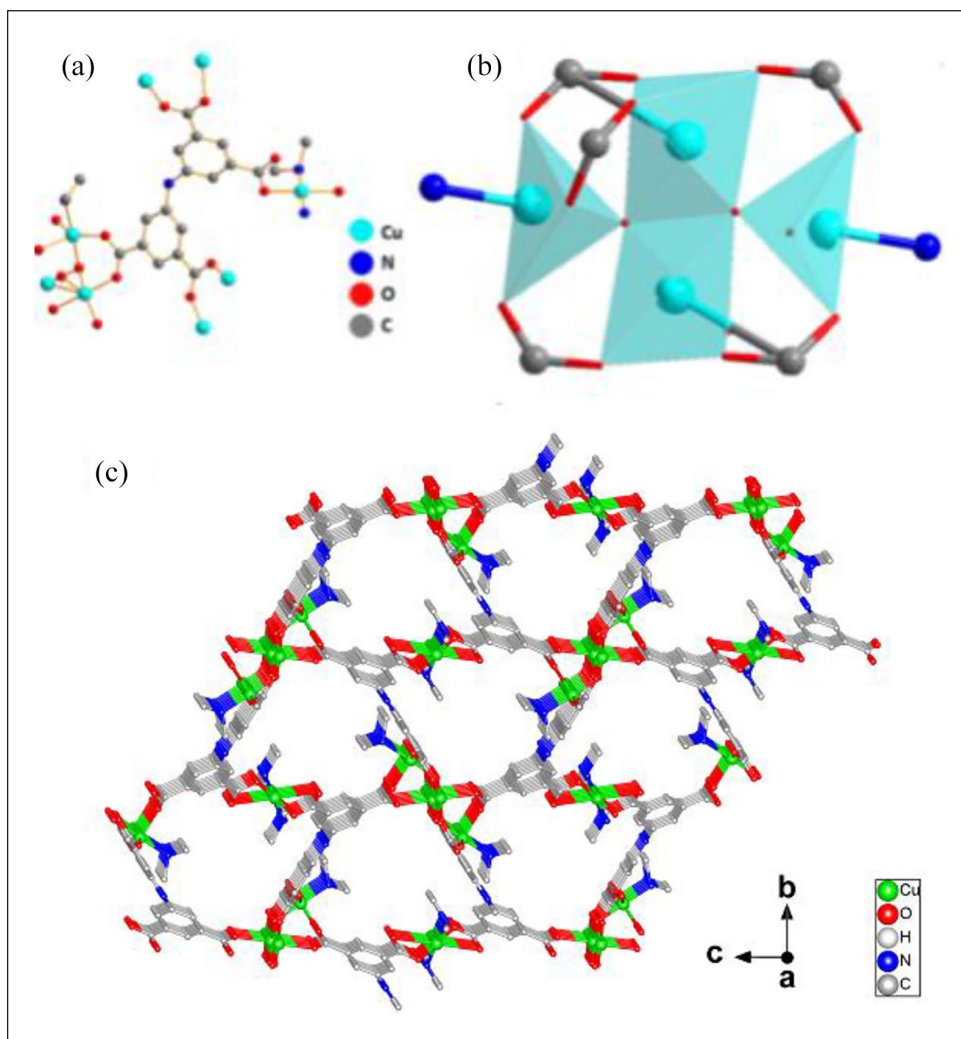


Figure 2. (a) The asymmetric unit of Cu-DPTCA, (b) the tetranuclear Cu cluster in Cu-DPTCA, and (c) the cavity in Cu-DPTCA.

performance of Cu-DPTCA. These reactions were carried out in different solvents at 30°C for 12 h and the experimental results are listed in Table 2. When polar aprotic solvents were used, such as DMF, DMSO, THF, and acetonitrile, the reactions afforded the desired product **4a** in good to excellent yields, because such solvents can significantly enhance the activity of nucleophiles. However, in polar protic solvents such as methanol and ethanol, the yields dropped significantly due to the formation of a large number of unidentified by-products. Among the solvents screened, DMF is the best solvent giving a yield of 86%. In the case of the reaction without Cu-DPTCA, the reaction failed to produce any product indicating that Cu is indispensable for the coupling. Furthermore, the reaction is not sensitive to oxygen or H₂O and can be carried out in open air. It is worth noting that the reactions did not need an additional basic additive.

Under the optimized conditions, the substrate scope of the amines was further investigated, and a number of structurally different amines were selected. Primary aliphatic amines, such as **3c** and **3e**, provided excellent yields of *N*-arylated amines **4c** and **4e** with good yields in short reaction times (within 3 h). Aromatic aniline (**3b**) reacted faster and afforded diarylamine **4b** in 74% yield. Secondary amines, such as morpholine (**3f**) and diphenylamine (**3g**),

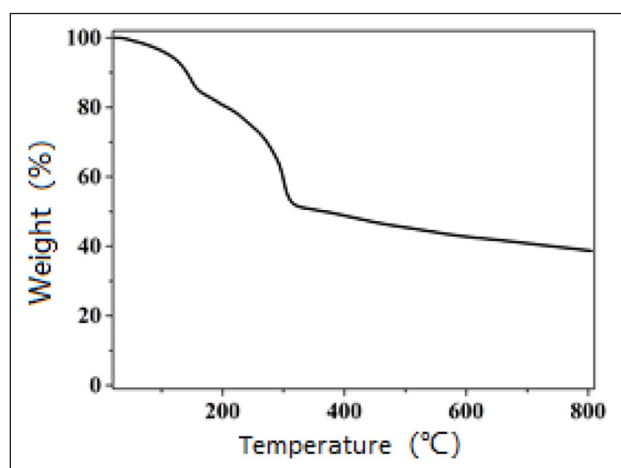
required a longer reaction time (about 12 h) and afforded **4f** and **4g** in satisfactory yields. Interesting, highly reactive allylamine (**3h**) reacted with phenylboronic acid smoothly and produced **4h** in good yield (Table 3).

The advantage of the Cu-DPTCA catalyst over its homogeneous counterparts lies in its facile recovery and reusability. To this end, the Cu-DPTCA catalyst was recovered and used under the optimized conditions for C–N coupling of phenylboronic acid (**2**) and cyclohexylamine **3d**. At the end of each cycle, simple centrifugation of the reaction mixture allowed the separation of the solid-state catalyst from the product-containing solution, and this was repeatedly washed with diethyl ether to remove the product from the pores inside Cu-DPTCA. The same isolated Cu-DPTCA catalysts were recharged with acetonitrile and phenylboronic acid (**2**) and cyclohexylamine **3d** for the next run. In the recycling experiments, we found that the use of acetonitrile as solvent is the best in term of yields and recyclability. The Cu-DPTCA catalyst can be reused for at least three times with near-quantitative conversion and 60%–70% yields. However, it was observed that for the fourth recycling experiment extending the reaction time to 24 h is necessary for better yield of products. This may indicate the loss of the catalyst's reactivity gradually during separation process.

Table 1. Crystallographic data and experimental details.

Complex	Cu-DPTCA
Empirical formula	$C_{26}H_{35}Cu_{2.5}N_5O_{11}$
Formula weight	752.44
Temperature (K)	296.15
Crystal system	Monoclinic
Space group	$P2_1/n$
a (Å)	10.8080(7)
b (Å)	17.4762(9)
c (Å)	19.9289(17)
α (°)	90
β (°)	102.658(4)
γ (°)	90
Volume (Å ³)	3672.7(4)
Z	4
ρ_{calc} (cm ³)	1.361
μ (mm ⁻¹)	1.495
$F(000)$	1546.0
Crystal size (mm ³)	$0.02 \times 0.01 \times 0.01$
Radiation	MoK α ($\lambda = 0.71073$)
2 θ range for data collection (°)	4.19 to 49.994
Index ranges	$-12 \leq h \leq 12, -20 \leq k \leq 20, -19 \leq l \leq 23$
Reflections collected	15,248
Independent reflections	6412 [$R_{\text{int}} = 0.0496, R_{\text{sigma}} = 0.0712$]
Data/restraints/parameters	6412/125/411
Goodness-of-fit on F^2	1.082
Final R indexes ($I \geq 2\sigma(I)$)	$R_1 = 0.0558, wR_2 = 0.1500$
Final R indexes (all data)	$R_1 = 0.0762, wR_2 = 0.1582$
Largest difference peak/hole (e Å ⁻³)	1.67/−1.01

$$R = [\sum ||F_o| - |F_c|| / \sum |F_o|], \quad R_w = [\sum w(|F_o|^2 - |F_c|^2|^2 / \sum w(|F_o|^2)^2]^{1/2}.$$

**Figure 3.** TGA curve of Cu-DPTCA.

Conclusion

In the present work, a new Cu(II)-carboxylate-based MOF $[Cu_{2.5}(DPTCA)(dma)_2(DMF)_2(H_2O)]_n$ has been synthesized by a solvothermal method and characterized by single-crystal and powder X-ray diffraction, infrared spectroscopy, and TGA. Cu-DPTCA has good triangular channels, and the presence of coordinated, unsaturated open metal sites allows it to be used for the Chan–Lam coupling reaction, affording various amine products. It is worth mentioning that this eco-friendly process does not require an additional basic additive and the Cu-DPTCA

Table 2. Optimization of the reaction conditions.^a

Entry	Solvent	Yield
1	DMF	86%
2	DMSO	74%
3	MeCN	66%
4	THF	62%
5	1,4-dioxane	47%
6	MeOH	24%
7	EtOH	31%

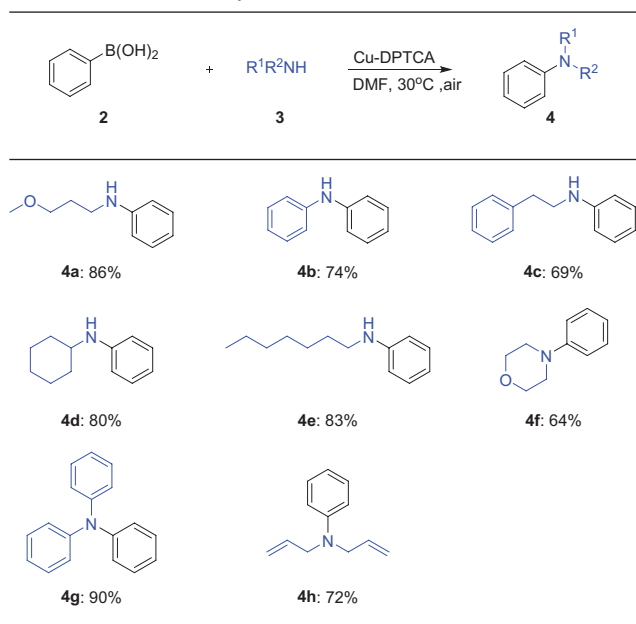
^aReaction conditions: amine (1.5 mmol), arylboronic acid (1 mmol), catalyst Cu-DPTCA (8 μmol based on a paddlewheel unit), DMF (4 mL), and air.

can be easily recovered from the product, and thus the sustainability is significantly improved.

Experimental

Materials and measurements

All solvents and chemical materials used in the synthesis were purchased from commercial sources and were used without further purification. X-ray powder diffraction (PXRD) was recorded with CuK α radiation ($\lambda = 1.54056$ Å) using a Bruker AXS D8 advanced diffractometer at an angle of $2\theta = 5$ – 50° at 293 K.

Table 3. Reaction scope.^{a,b}

^aReaction conditions: amine (1.5 mmol), arylboronic acid (1 mmol), catalyst Cu-DPTCA (8 μmol based on a paddlewheel unit), DMF (4 mL), rt, and air.

^bIsolated yields.

Crystallography

The single-crystal structure was obtained using Bruker d8 Venture SMART-CCD single-crystal diffractometer with MoK α radiation, wavelength (λ) = 0.71073 Å. Diffraction data were collected using the SAMRT and SAINT programs. The test temperature was maintained near 200 K with liquid nitrogen. The crystal structure was solved by direct methods using SHELXTL-97. The full-matrix least-square method was used to refine F^2 (CCDC: 2047623).

Synthesis of Cu-DPTCA

DPTCA (13.8 mg, 0.04 mmol) and copper nitrate hexahydrate (22.0 mg, 0.12 mmol) were placed in a 10-mL glass bottle, and DMF (4 mL) and distilled water (0.5 mL) were added. The resulting mixture was sonicated for 30 min. The bottle was placed in a 25-mL polytetrafluoroethylene-lined autoclave, sealed and placed in a program-controlled oven. The oven was heated to 115 °C for 5.5 h and held for a further 70 h. The oven was cooled to room temperature over 15 h and colorless transparent square crystals were obtained with the chemical formula $\text{C}_{26}\text{H}_{35}\text{Cu}_{2.5}\text{N}_5\text{O}_{11}$. The crystals were filtered and washed with the mother liquor. The yield was 52%.

Cham–Lam reaction

N-arylation of phenylboronic acid and amine, in a typical experimental procedure, Cu-DPTCA (8 μmol) was added to the amine (1.5 mmol) and phenylboronic acid (1 mmol) in DMF (4 mL) at 30 °C, and the mixture was stirred at room temperature for 12 h under an air atmosphere. The progress of the reaction was monitored by TLC, and when the reaction was completed, the mixture was filtered to obtain a crude product. The crude product was purified by silica gel

column chromatography (petroleum ether–EtOAc, 10: 1) to give coupling products 4.

Declaration of conflicting interests

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Supplemental material

Supplemental material for this article is available online.

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