Communications in Science and Technology 10(2) (2025) 439–446

COMMUNICATIONS IN
SCIENCE AND TECHNOLOGY
Homepage: cst.kipmi.or.id

HKUST-1-catalyzed Chan–Evans–Lam C–O coupling under mild conditions with catalyst reusability

Muhamad R. S. Sidik[a], Irwan Kurnia[a], Yessi Permana[b], Ubed S. F. Arrozi[c], Wirawan Ciptonugraha[d], Witri Wahyu Lestari[e], Yudha P. Budiman[a,*]

[a]*Department of Chemistry, Universitas Padjadjaran, Sumedang 45363, Indonesia*
[b]*Inorganic and Physical Chemistry Research Division, Institut Teknologi Bandung, Bandung 40132, Indonesia*
[c]*Department of Chemistry, State University of Malang, Malang 65145, Indonesia*
[d]*Chemistry Education, Universitas Sebelas Maret, Surakarta 57126, Indonesia*
[e]*Department of Chemistry, Universitas Sebelas Maret, Surakarta 57126, Indonesia*

Article history:
Received: 19 November 2025 / Received in revised form: 19 December 2025 / Accepted: 21 December 2025

Abstract

The Chan–Evans–Lam coupling refers to a valuable method for constructing C–O and C–N bonds under mild conditions. Nevertheless, the development of efficient and reusable heterogeneous catalysts remains limited. In this study, we investigated copper-based metal–organic frameworks as catalysts for C–O bond formation between 4-methoxyphenylboronic acid and phenol. The study revealed that HKUST-1 exhibited a significant enhancement in performance when compared to Cu-BDC, yielding up to 86% at room temperature and demonstrating superior accessibility of Cu^{2+} active sites. A systematic optimization of reaction parameters identified NEt_3 as the most effective base, DCM as the optimal solvent, and a mild temperature increase to 40 °C as the key factor enabling a maximum yield of 94%. Studies on recyclability demonstrated that HKUST-1 exhibited high catalytic performance over multiple cycles without significant structural degradation, as confirmed by PXRD analysis. Overall, this work highlights HKUST-1 as an efficient, robust, and reusable heterogeneous catalyst for Chan–Evans–Lam C–O coupling, thus demonstrating its potential for sustainable synthetic applications.

Keywords: Chan–Evans–Lam; arylboronic acids; HKUST-1; copper; metal-organic frameworks

1. Introduction

The Chan–Evans–Lam coupling is a method for forming carbon–heteroatom bonds (C–N or C–O) between organoborons and nucleophilically functionalized compounds, such as amines or alcohols, using copper-based catalysts [1]. As its name implies, this reaction can be viewed as a unification of three separate transformations that operate via a similar mechanism. While all of them employed arylboronic acids as one of the coupling partners, their differences lay in the nature of the complementary partner nucleophile (Fig. 1). Dominic Chan's group focused on aliphatic amines [2], David Evans' group explored phenol-based compounds [3], and Patrick Lam's group introduced aromatic amines [4]. The reaction proceeds under significantly milder conditions, frequently at room temperature and ambient atmosphere, compared to more established methods such as the Ullmann–Goldberg coupling and the Buchwald–Hartwig amination [5–8].

The Chan–Evans–Lam reaction is widely regarded as an oxidative coupling process, wherein two nucleophilic partners undergo coupling in place of the traditional electrophile–nucleophile setup observed in classical cross-coupling reactions (Fig. 2) [9]. Copper-catalyzed Ullmann–Goldberg coupling reactions mostly operate under demanding conditions, requiring stoichiometric catalyst amounts in the presence of additional ligands, elevated temperatures, and prolonged reaction times [10–13]. The utilization of a palladium catalyst in the Buchwald–Hartwig amination negates some of these disadvantages while introducing several others, such as palladium's toxicity, limited natural abundance, and high cost [14,15]. To address these challenges, the Chan–Evans–Lam proposed the substitution of aryl halides with arylboronic acids, thereby enabling the use of catalytic amounts of copper under much milder, stable, and less toxic conditions [16–18]. While the utilization of arylboronic acids serves to transform the reaction into an oxidative coupling, a process that requires the presence of an oxidant, atmospheric oxygen is typically sufficient to oxidize the metal complex [9,19].

---

* Corresponding author.
Email: y.p.budiman@unpad.ac.id
https://doi.org/10.21924/cst.10.2.2025.1837

The Chan–Evans–Lam coupling is of significant importance in both organic and medicinal chemistry seeing that many biologically relevant molecules feature amine and/or ether linkages [20]. To illustrate this, coumarin is a pivotal building block for numerous pharmacologically active compounds and can be synthesized via *O*-arylation [21,22]. Nucleosides such as inosine and guanosine that regulate metabolic pathways can also be obtained through *N*-arylation of purine-based nucleosides [23,24]. Another example is berberine, a bioactive alkaloid employed in modern medicine for its antimicrobial and anti-inflammatory properties, which can also be synthesized through this reaction strategy [25,26]. Overall, the versatility of the Chan–Evans–Lam coupling in forming C–N and C–O bonds underscores its significance as a synthetic tool for constructing biologically active molecules. Its broad substrate scope and mild reaction conditions render it particularly valuable for applications in both pharmaceutical synthesis and drug discovery.

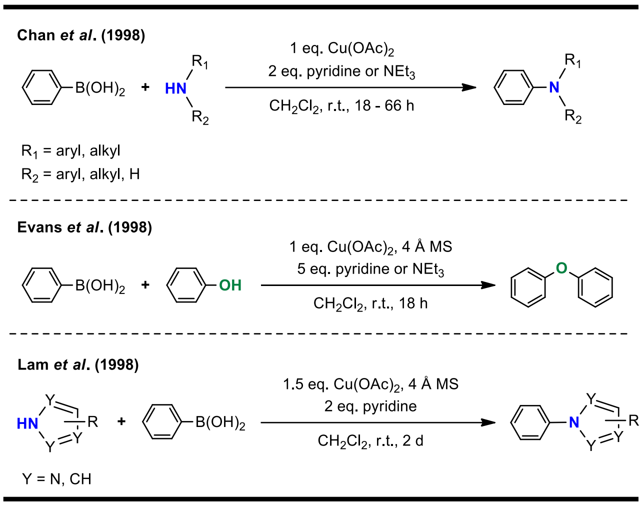


Fig. 1. Classical Chan-Evans-Lam C-N and C-O coupling reactions using homogeneous copper catalysts

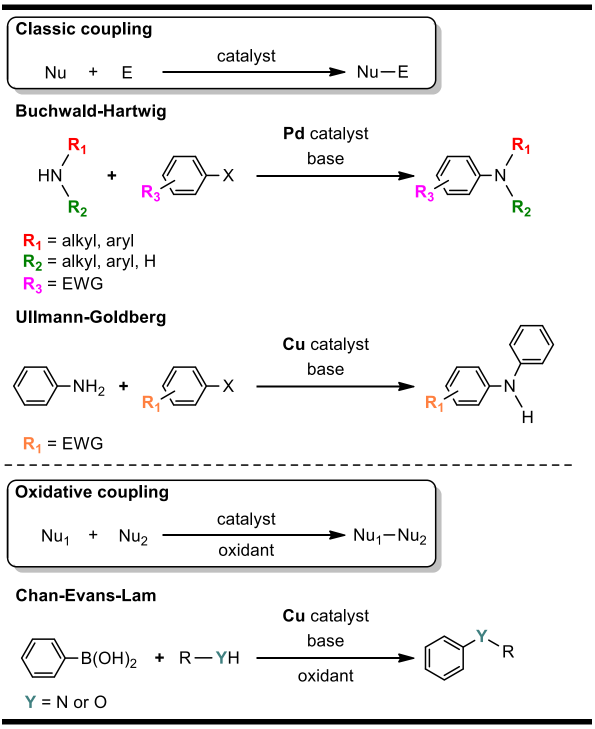


Fig. 2. Classical and oxidative coupling comparison

Extensive studies of Chan–Evans–Lam frequently employ a homogeneous catalytic system. This approach is constrained by difficulties related to the recovery and recyclability of the catalyst [54,56,60,61]. Therefore, heterogeneous catalysts are often favored over their homogeneous counterparts to address sustainability concerns. Metal–organic frameworks (MOFs) have been identified as holding significant potential as heterogeneous catalysts for the Chan–Evans–Lam coupling reaction. The catalytic activity exhibited by these materials can be attributed to the presence of accessible metal active sites and organic linkers within a porous framework that provides a high surface area [27,74]. This combination of hybrid inorganic–organic building blocks that form coordinated porous frameworks, in conjunction with the intrinsic rigidity of its structures, opens a wide range of potential functional properties [28]. Furthermore, the capacity to recover and reuse MOFs, after the reaction process, enhances their economic and environmental advantages [29]. Copper-based MOFs, such as HKUST-1 and Cu-BDC, have been extensively utilized in various organic transformations, such as oxidative cyclization [30], Suzuki coupling [31], alcohol oxidation [32], and organoboron homocoupling [33]. The distinction between HKUST-1 and Cu-BDC arises from the nature of their organic linkers, which significantly affect the resulting framework morphology. HKUST-1 is constructed from 1,3,5-benzene tricarboxylic acid (BTC), forming a highly porous three-dimensional structure, while Cu-BDC is based on 1,4-benzene dicarboxylic acid (BDC), yielding a more planar coordination network [34–36]. Both MOFs exhibit unfavorable catalytic performance under moist conditions [49,62], a similar phenomenon to that observed in Chan–Evans–Lam coupling reactions [63]. The process of the Chan–Evans–Lam coupling is typically characterized by a Cu(II)/Cu(III) cycle in which this cycle involves the transmetalation of the arylboronic acid to a Cu(II) species, followed by oxidation to a Cu(III) intermediate and subsequent reductive elimination resulting in the formation of the C–N or C–O bond [1]. The catalytic cycle is determined by several factors, including accessibility of the copper centers [64], the rate of transmetalation [65], and the stability of high-valent Cu(III) species [66]. In heterogeneous systems, these factors are governed by the porosity, substrate diffusion, and metal site exposure.

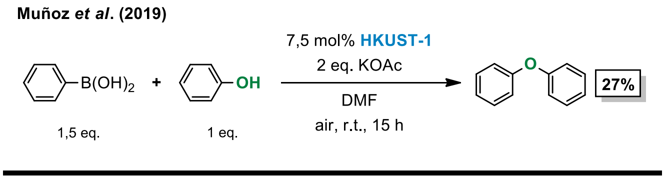


Fig. 3. Previous studies on Chan-Evans-Lam C-O coupling reactions catalyzed by Cu-MOF materials

The utilization of MOF for C–N based Chan–Evans–Lam reaction has been extensively studied [37–40]; however, its C–O variants remain relatively underexplored. The use of HKUST-1 and Cu-BDC in the Chan–Evans–Lam coupling reaction has been documented in numerous reports. A review of the existing studies on their catalytic applications indicates a considerable potential for the enhancement of reaction efficiency and product yield. Anbu and Dhakshinamoorthy investigated the Chan–Evans–Lam coupling between arylboronic acids and benzimidazole employing HKUST-1 as a catalyst, achieving up to 93% yield of the desired C–N coupling product [41]. Nonetheless, the methodology employed by these researchers did not extend to the formation of C–O bonds. In a subsequent study, Muñoz *et al.* employed HKUST-1 to catalyze reactions between arylboronic acids and aniline or phenol, but the obtained product of the C–O coupling only reached 27% (Fig. 3) [42]. Meanwhile, Khosravi *et al.* reported a Cu-BDC catalyst modified with a BPY ligand for the purpose of facilitating coupling reactions between arylboronic acid and aniline to yield the C–N coupling product. The introduction of the BPY ligand has been demonstrated to enhance the three-dimensional morphology of the Cu-BDC framework, thereby improving reactant accessibility to the Cu^{2+} active sites [43]. As such, this prompted us to further explore the potential of these catalysts for the C–O variant of the Chan–Evans–Lam coupling.

This study builds upon prior studies on the use of HKUST-1 and Cu-BDC as catalysts in the homocoupling of arylboronic acids and its subsequent protodeboronation studies [33,44]. The present work focuses on the optimization of the HKUST-1 catalytic system to promote C–O bond formation via the Chan–Evans–Lam reaction.

2. Materials and Methods

2.1. Material

The materials utilized in this study include 4-methoxyphenylboronic acid (Sigma-Aldrich, 95%), acetonitrile (Sigma-Aldrich, gradient grade for liquid chromatography), dichloromethane (Sigma Aldrich, 99.8%), dimethylformamide (Sigma-Aldrich, ACS Grade), ethyl acetate (Sigma-Aldrich, 99%), *n*-hexane (Sigma-Aldrich, 99%), phenol (Sigma-Aldrich, 99%), potassium carbonate (Merck, 99%), synthesized Cu-BDC, synthesized HKUST-1, toluene (Sigma Aldrich, 99.8%), triethylamine (Sigma-Aldrich, 99.5%).

2.2. Chan–Evans–Lam coupling with Cu-MOF

The present procedure was adapted from the original Evans *et al.* method and the previously reported Muñoz *et al.* method in which HKUST-1 was used as the catalyst [3,42]. In a glovebox under a nitrogen atmosphere, 0.15 mmol of phenol was added into a dried Schlenk tube already equipped with a stirring bar. The tube was then sealed by means of a rubber septum prior to be transferred outside of the glovebox. Following the connection of the tube to a Schlenk line, 0.1 mmol of 4-methoxyphenylboronic acid was added, along with 10–30 mol% of HKUST-1 or Cu-BDC catalyst previously synthesized in accordance with the reported literature from Lestari *et al.* and Carson *et al.* [34,75]. The reaction was then completed with 2 equivalent of base and 3 mL of solvent. Subsequently, the reaction mixture was subjected to stirring following the completion of the requisite evaluation of the time and temperature. The solvent was then separated from the catalyst using a centrifuge after which it was evaporated in vacuo. The removal of solvent from the catalyst was performed by means of a CenLee 200K centrifugator at 8000 rpm for duration of five minutes. Subsequently, the catalyst underwent a washing comprising three cycles of centrifugation. The obtained supernatant was concentrated in vacuo using a rotary evaporator at a maximum temperature of 40°C. The residue was then purified by means of column chromatography on silica gel. This procedure entailed the use of hexane for the removal of any residue prior to the isolation of the desired coupling product. The latter was obtained through the use of a mixture of hexane and ethyl acetate in a ratio of 8:2.

2.3. Characterization

High-angle X-ray diffraction patterns were obtained on a Rigaku Miniflex 600 D/teX Ultra diffractometer with Cu Kα radiation. Infrared spectra were recorded on a Nicolet 380 FT-IR spectrometer as solids, using an ATR unit, and reported in cm^{-1}. GC-MS analyses were performed using an Agilent 7890A gas chromatograph (column: DB-5MS 5% phenylmethylsiloxane, 30 m, Ø 0.25 mm, film 0.25 μm; *injector: 200 °C; oven: 40 °C (2 min), 40 °C to 280 °C (20 °C min^{-1}) (5 min) *; carrier gas: He (1 mL min^{-1}) equipped with an Agilent 5977B GC/MSD operating in EI mode.

NMR spectra were recorded at 298 K using a Bruker Avance I 500 (^1H NMR, 500 MHz) spectrometer. The chemical shift of the ^1H NMR are reported as a function of TMS with the reference made via the residual proton resonances of the relevant deuterated solvent ($CDCl_3$: 7.26 ppm)

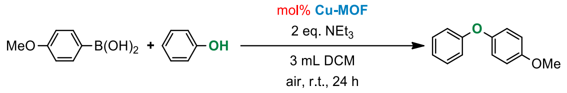
(1-methoxy-4-phenoxybenzene) ^{1}H NMR (500 MHz, $CDCl_3$) δ = 7.29 (*dd*, 2H, $^3J_{H,H}$ = 8 Hz, $^3J_{H,H}$ = 7 Hz; Ar-H), 7.04 (*t*, 1H, $^3J_{H,H}$ = 7 Hz; Ar-H), 6.98 (*d*, 2H, $^3J_{H,H}$ = 9 Hz; Ar-H), 6.94 (*d*, 2H, $^3J_{H,H}$ = 8 Hz; Ar-H), 6.88 (*d*, 2H, $^3J_{H,H}$ = 9 Hz; Ar-H), 3.81 (*s*, 3H, OCH_3); **GCMS**: [t = 10.936 min] m/z: 199.9 $[M]^+$. Spectoscopy data matched those in the literature [59].

3. Results & Discussions

The selection of a suitable catalyst system between HKUST-1 and Cu-BDC for this reaction was first evaluated. It was hypothesized that both catalysts would be suitable for the reaction, as previous studies have reported the formation of Chan–Evans–Lam side products on a homocoupling of arylboronic acids in the presence of cyclohexamine bases [45,46]. Utilizing the coupling between 4-methoxyphenylboronic acid and phenol in an open-air condition as a model system, we examined the reaction under varying catalyst loadings (see Table 1). Control experiments conducted in the absence of either Cu-MOF produced no detectable amount of the desired coupling product (see Table 1, entries 1 & 5). When 30 mol% of each catalyst was introduced, the reaction proceeded with results, affording the yields of 86% with HKUST-1 and 40% with Cu-BDC (Table 1, entries 2 & 6), with confirmation of the coupling product conducted via GCMS and ^{1}H-NMR (Fig. 4). A clear trend was observed when the catalyst loading was reduced by 10 mol%, as the yield of the coupling product decreased accordingly (see Table 1, entries 3–4 & 7–8). While a linear correlation between catalyst loading and reaction yield might be anticipated for an ideal first-order dependence on catalyst concentration, the present system likely deviates from strict linearity. In heterogeneous MOF-catalyzed reactions, factors such as substrate diffusion within the porous framework, partial occupation of active sites, and catalyst–substrate contact efficiency can influence the apparent reaction rate [67]. At higher catalyst loadings, the increased density of exposed Cu^{2+} centers has been shown to increase the probability of effective transmetalation and formation of high-valent Cu(III) intermediates, thereby accelerating productive catalytic cycles. The enhanced performance of HKUST-1 could be attributed to its structure, where the open and more accessible Cu^{2+} reactive sites within HKUST-1 framework facilitate substrate coordination and activation more efficiently than the more sterically restricted Cu^{2+} centers present in Cu-BDC [47]. Several studies have reported that Cu-BDC has the capacity to undergo structural rearrangement when its coordinating solvents are removed, whether through heating, solvent exchange, or even simple recovery after multiple catalytic cycles. In such conditions, the framework tends to collapse into a more compact structure, in which Cu and O atoms from adjacent sheet-like layers form new bonds, thereby restricting the access of the metal centers to external molecules [34,48–51]. Given that Chan–Lam coupling relies on various copper oxidation state cycling, the redox flexibility of HKUST-1, in which partial formation of Cu^+ species from Cu^{2+} paddle-wheel units under reaction conditions has been reported, may facilitate the attainment of a high catalytic product yield [68]. Given the requirement of molecular oxygen in Chan–Evans–Lam coupling, the porosity of HKUST-1 and its coordinatively unsaturated Cu site have been known to enhance oxygen diffusion during the catalytic reaction [33,69,70]. Therefore, HKUST-1 was selected as the catalyst for subsequent experiments.

Having identified the best catalyst for the reaction, we then examined the influence of several parameters, including the selection of bases, solvents, temperatures, and reaction times (see Table 2). The addition of a base was found to be pivotal for the reaction to proceed. In its absence, no coupling product was observed (see Table 2, entry 1), whereas introducing a base enabled the desired product formation. This observation is consistent with the findings of Duparc *et al*., who reported that bases play a crucial role in enhancing product yields by activating the nucleophile, whether an amine or an alcohol, through deprotonation process [52]. Similar conclusions were drawn in previous studies employing HKUST-1 and Cu-BDC-BPY, which likewise demonstrated the necessity of a base for efficient coupling [41,43]. West *et al*. further proposed that the base functions to neutralize intermediates formed during the disproportionation step of the Chan–Evans–Lam mechanism, thereby preventing re-protonation of the deprotonated nucleophile and facilitating productive catalysis [1].

Table 1. Screening of both Cu-MOF catalysts type on the Chan–Evans–Lam coupling reaction[a]



No.	Catalyst loadings (mol%)	Catalyst	Yield[b] (%)
1	-	HKUST-1	-
2	30		86
3	20		44
4	10		23
5	-	Cu-BDC	-
6	30		40
7	20		32
8	10		14

[a]Reaction conditions: 4-methoxyphenylboronic acid (0.1 mmol), phenol (0.15 mmol), and Cu-MOFs catalysts (0 – 30 mol%). [b]Isolated yields by column chromatography.

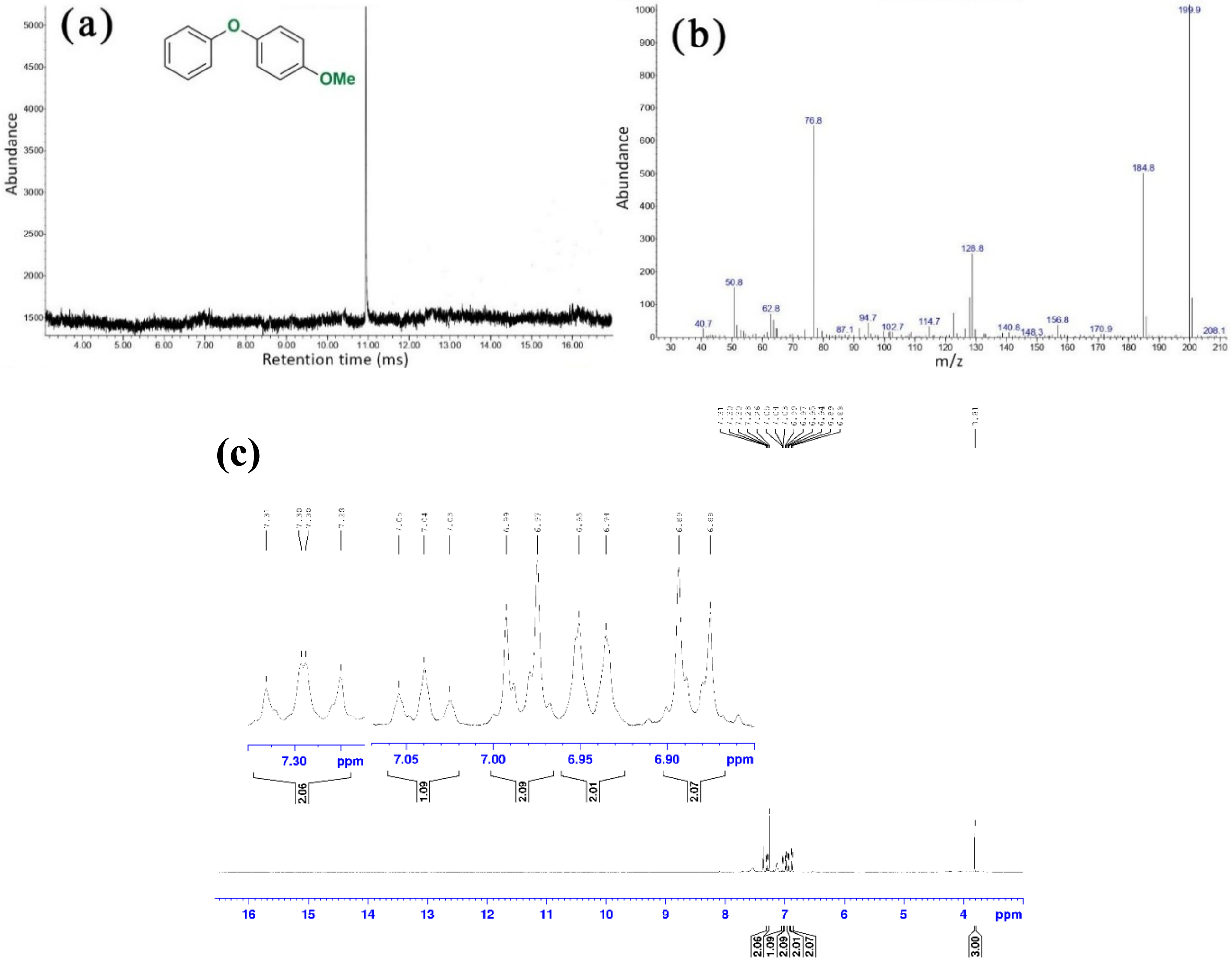
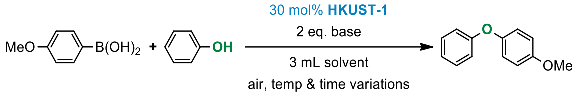


Fig. 4. (a) GC, (b) MS, and (c) ^{1}H-NMR spectra of the Chan-Evans-Lam product: 1-methoxy-4-phenoxybenzene

The present study examined the influence of both inorganic and organic bases, each of which has been previously reported to facilitate a decent product formation in Chan–Evans–Lam couplings. It was observed that NEt$_3$—an organic base—provided a substantially higher yield in comparison to the inorganic base K$_2$CO$_3$ (see Table 2, entry 2 & 3). This distinction may be attributed to the limited solubility of inorganic bases within the reaction solvent, which can reduce their effectiveness in facilitating nucleophile phenol activation and, by extension, the overall rate of product formation. Based on these results, NEt$_3$ was selected as the base for the subsequent stage of the research.

Table 2. Screening of bases, solvents, temperature, and reaction time on the Chan–Evans–Lam coupling[a]



No.	Base	Solvents	Temp (°C)	Time (h)	Yield[b] (%)
1	-	DCM	r.t.	24	-
2	NEt$_3$	DCM	r.t.	24	86
3	K$_2$CO$_3$	DCM	r.t.	24	45
4	NEt$_3$	acetonitrile	r.t.	24	42
5	NEt$_3$	DMF	r.t.	24	57
6	NEt$_3$	toluene	r.t.	24	75
7	NEt$_3$	DCM	40	24	94
8	NEt$_3$	DCM	60	24	13
9	NEt$_3$	DMF	60	24	trace
10	NEt$_3$	DCM	40	24	68[c]
11	NEt$_3$	DCM	40	15	70
12	NEt$_3$	DCM	40	6	34

[a]Reaction conditions: 4-methoxyphenylboronic acid (0.1 mmol), phenol (0.15 mmol), and HKUST-1 (30 mol%). [b]Isolated yields by column chromatography. [c]In the presence of Cu-BDC (30 mol%) as the catalyst.

Several solvents were selected based on their polarity and their relevance in previous studies. Polar protic solvents were avoided, as our previous studies indicated that they could promote undesired side reactions of arylboronic acids, such as hydroxylation of the C–B bond [33,44]. The utilization of acetonitrile and DMF yielded moderate yields of 42% and 57%, respectively (see Table 2, entries 4 & 5). In contrast, toluene yielded a significantly enhanced outcome, yielding the desired coupling product in a 75% yield (Table 2, entry 6), though it was still lower than the yield obtained previously with DCM. This trend can be attributed to the coordination nature of DMF and acetonitrile, in which their O and N atom lone pairs can interact with the open metal sites of HKUST-1. This interaction potentially occupies the coordination environment, thereby hindering substrate access to the catalytic Cu^{2+} centers [47,49]. Within the pores of HKUST-1, it is proposed that DCM molecules can access the internal framework more effectively due to their smaller size and lower steric bulk compared to toluene. This may contribute to the superior catalytic performance as observed. In addition, the slightly polar nature of DCM offers a more favorable balance between solubility of the starting materials and its reactivity, allowing the components to dissolve efficiently while preserving high catalytic activity. Whereas the nonpolar feature of toluene has the capacity to suppress the effect of unwanted protodeboronation products from organoborons which could result in a comparable yield to that the desired reaction, which is more favorable [71,72].

Room temperature proved sufficient to facilitate the reaction, as most Chan–Evans–Lam couplings are recognized to proceed under ambient conditions. However, the objective of this study was to determine whether a modest increase in thermal energy could further enhance the reaction efficiency, as several studies have reported improved outcomes at elevated temperatures [53–56]. As the reaction temperature was elevated to 40 °C using a silicone oil bath, the yield increased substantially to 94% (see Table 2, entry 7). This temperature was selected to remain close to the boiling point of DCM, thereby enabling gentle heating without compromising the solvent system. Following this, the reaction temperature was elevated to 60 °C while all other conditions remained constant. At this higher temperature, however, the arylboronic acid became more prone to protodeboronation, resulting in a significant decrease in the desired product formation (see Table 2, entry 8). Increasing the temperature enhances the interaction of the arylboronic acid species with the Cu^{2+} sites of HKUST-1, which could promote the desired C–O bond formation at a faster rate. However, as the temperature increased further, the Cu–aryl species became susceptible to fast protonolysis from weak proton sources rather than the desired pathway as its activation barrier was easier to reach [73]. Consequently, the unfavorable and irreversible protodeboronation pathway predominates at 60 °C, leading to reduced coupling yields. This finding is in line with our previous study that deeply explored the protodeboronation aspect using HKUST-1 as the catalyst [44]. As a confirmation, we conducted the reaction in DMF, which possessed a significantly higher boiling point to withstand the applied temperature. However, the results still demonstrated a trace amount of protodeboronated byproduct, with only trace amounts of the desired coupling product being detected (see Table 2, entry 9). We also applied the newfound parameter to the previously conducted reaction with Cu-BDC, which resulted in a moderate improvement in yield, reaching up to 68% (see Table 2, entry 10). Although Cu-BDC exhibits a larger increase in yield upon increasing the temperature (see Table 1, entry 6 and Table 2, entry 10), this behavior is likely to reflect the alleviation of kinetic and mass-transfer limitations associated with its more planar coordination framework and restricted Cu^{2+} site accessibility [29]. Mild thermal activation enhances substrate diffusion and may partially increase framework flexibility, thereby facilitating the reaction more readily. In contrast, HKUST-1 possesses intrinsically accessible Cu^{2+} sites within its three-dimensional porous structure, enabling efficient catalysis already at ambient temperature and resulting in only a modest relative improvement upon heating despite higher absolute yields [49]. The final parameter we examined was reaction time, and a clear trend emerged as shorter reaction times led to noticeably reduced yields (see Table 2, entries 11 & 12).

To evaluate the reusability of HKUST-1, three successive runs of the model reaction were performed with the temperature elevated to a slight degree. These consecutive reactions were found to yield the Chan–Evans–Lam product with consistently high efficiency, exhibiting only a slight decline across cycles (Fig. 5). The PXRD patterns of pure HKUST-1, as well as the first, and the second reuse cycles, demonstrate that the characteristic diffraction peaks of HKUST-1 are largely retained throughout multiple catalytic cycles (see Fig. 6). The preserved peak positions and overall peak profiles indicate that the crystalline framework of HKUST-1 remains structurally intact after being subjected to repeated reaction conditions.

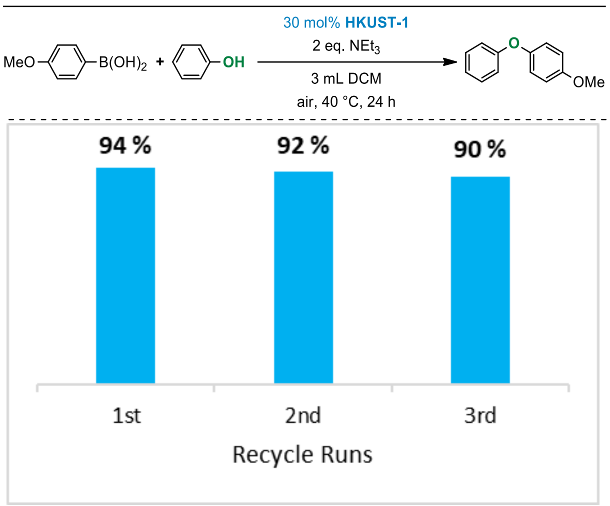


Fig. 5. Recyclability study of HKUST-1 over three consecutive runs of the Chan–Evans–Lam reaction between 4-methoxyphenylboronic acid (0.3 mmol) and phenol (0.45 mmol). Reaction yields were determined after purification by column chromatography

Minor variations in peak intensity can be observed in the reused samples as these changes are commonly attributed to surface adsorbates, partial pore blockage, or slight loss of crystallinity rather than framework collapse [57,58].

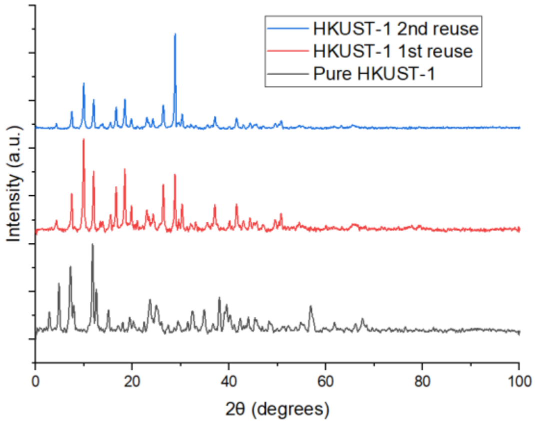


Fig. 6. PXRD patterns of pure and recycled HKUST-1 over three consecutive runs

Consistent with these observations, our previous research demonstrated negligible copper leaching from HKUST-1 under comparable reaction conditions, as determined by AAS. This result provides further evidence for the structural stability of the framework and the retention of active copper sites during catalysis [44]. Overall, the PXRD data confirm that HKUST-1 exhibits excellent structural stability and is suitable for reuse in Chan–Evans–Lam coupling reactions.

4. Conclusion

In summary, this present study demonstrated that HKUST-1 served as an effective heterogeneous catalyst for promoting C–O bond formation in the Chan–Evans–Lam coupling between 4-methoxyphenylboronic acid and phenol. A comparative evaluation with Cu-BDC revealed that the superior catalytic efficiency of HKUST-1 arose from its more accessible Cu^{2+} active sites and greater structural robustness, enabling more efficient substrate coordination. A systematic optimization of reaction parameters established that the use of NEt_3 as a base, DCM as the preferred solvent, and a mild elevation of temperature to 40 °C collectively provided the highest yields, achieving up to 94% of the desired coupling product. The recyclability studies further confirmed the practical applicability of HKUST-1 in heterogeneous catalysis. Across three consecutive reaction cycles, the catalyst exhibited consistently high product yields with only minimal performance loss, while PXRD analysis verified that the structural integrity of the MOF remained intact. The results of this study emphasize the potential of HKUST-1 as a sustainable and reusable catalytic platform for Chan–Evans–Lam couplings, offering an environmentally friendly catalyst to its traditional homogeneous copper systems. Overall, this work provides a valuable contribution valuable to the field by offering novel insight into the area of MOF-based catalytic optimization. Furthermore, it establishes a foundation for the expansion of the use of HKUST-1 to encompass a more extensive range of carbon–heteroatom bond-forming transformations. Further expansion of the substrate scope will be explored in future studies.

Acknowledgment

Y. P. B. acknowledges financial support from Universitas Padjadjaran through the Indonesian Research Collaboration (RKI: 1101/UN6.3.1/PT.00/2025) and the Competency Research Grant for Lecturers at Universitas Padjadjaran (RKDU: 4622/UN6.D/PT.00/2025).

References

1. M. J. West, J. W. B. Fyfe, J. C. Vantourout and A. J. B. Watson, *Mechanistic Development and Recent Applications of the Chan–Lam Amination*, Chem. Rev. 119 (2019) 12491–12523.
2. D. M. T. Chan, K. L. Monaco, R.-P. Wang and M. P. Winteres, *New N- and O-arylations with phenylboronic acids and cupric acetate*, Tetrahedron Lett. 39 (1998) 2933–2936.
3. D. A. Evans, J. L. Katz and T. R. West, *Synthesis of Diaryl Ethers through the Copper-Promoted Arylation of Phenols with Arylboronic Acids. An Expedient Synthesis of Thyroxine*, Tetrahedron Lett. 39 (1998) 2937–2940.
4. P. Y. S. Lam, C. G. Clark, S. Saubern, J. Adams, M. P. Winters and D. M. T. Chan et al., *New aryl/heteroaryl C–N bond cross-coupling reactions via arylboronic acid/cupric acetate arylation*, Tetrahedron Lett. 39 (1998) 2941–2944.
5. F. Ullmann, *Ueber eine neue Bildungsweise von Diphenylaminderivaten*, Ber. Dtsch. Chem. Ges. 36 (1903) 2382–2384.
6. I. Goldberg, *Ueber Phenylirungen bei Gegenwart von Kupfer als Katalysator*, Ber. Dtsch. Chem. Ges. 39 (1906) 1691–1692.
7. A. S. Guram, R. A. Rennels and S. L. Buchwald, *A Simple Catalytic Method for the Conversion of Aryl Bromides to Arylamines*, Angew. Chem. Int. Ed. 34 (1995) 1348–1350.
8. J. Louie and J. F. Hartwig, *Palladium-catalyzed synthesis of arylamines from aryl halides. Mechanistic studies lead to coupling in the absence of tin reagents*, Tetrahedron Lett. 36 (1995) 3609–3612.
9. I. Funes-Ardoiz and F. Maseras, *Oxidative Coupling Mechanisms:*

Current State of Understanding, ACS Catal. 8 (2018) 1161–1172.

10. C. Sambiagio, S. P. Marsden, A. J. Blacker and P. C. McGowan, *Copper catalysed Ullmann type chemistry: from mechanistic aspects to modern development*, Chem. Soc. Rev. 43 (2014) 3525–3550.
11. Q. Yang, Y. Zhao and D. Ma, *Cu-Mediated Ullmann-Type Cross-Coupling and Industrial Applications in Route Design, Process Development, and Scale-up of Pharmaceutical and Agrochemical Processes*, Org. Process Res. Dev. 26 (2022) 1690–1750.
12. M. N. Lavagnino, T. Liang and D. W. C. MacMillan, *HARC as an open-shell strategy to bypass oxidative addition in Ullmann–Goldberg couplings*, Proc. Natl. Acad. Sci. USA 117 (2020) 21058–21064.
13. G. J. Sherborne, S. Adomeit, R. Menzel, J. Rabeah, A. Brückner and M. R. Fielding et al., *Origins of high catalyst loading in copper(i)-catalysed Ullmann–Goldberg C–N coupling reactions*, Chem. Sci. 8 (2017) 7203–7210.
14. J. M. Dennis, N. A. White, R. Y. Liu and S. L. Buchwald, *Pd-Catalyzed C–N Coupling Reactions Facilitated by Organic Bases: Mechanistic Investigation Leads to Enhanced Reactivity in the Arylation of Weakly Binding Amines*, ACS Catal. 9 (2019) 3822–3830.
15. S. McCarthy, D. C. Braddock and J. D. E. T. Wilton-Ely, *Strategies for sustainable palladium catalysis*, Coord. Chem. Rev. 442 (2021) 213925.
16. J.-Q. Chen, J.-H. Li and Z.-B. Dong, *A Review on the Latest Progress of Chan-Lam Coupling Reaction*, Adv. Synth. Catal. 362 (2020) 3311–3331.
17. R. Hajinasiri, *Arylboronic acids in organic synthesis*, J. Mol. Struct. 1336 (2025) 142029.
18. N. de J. Hiller, N. A. do A. e Silva, T. A. Tavares, R. X. Faria, M. N. Eberlin and D. de L. Marins, *Arylboronic Acids and their Myriad of Applications Beyond Organic Synthesis*, Eur. J. Org. Chem. 2020 (2020) 4841–4877.
19. M. G. J. Doyle and R. J. Lundgren, *Oxidative cross-coupling processes inspired by the Chan–Lam reaction*, Chem. Commun. 57 (2021) 2724–2731.
20. I. Munir, A. F. Zahoor, N. Rasool, S. A. R. Naqvi, K. M. Zia and R. Ahmad, *Synthetic applications and methodology development of Chan-Lam coupling: a review*, Mol. Divers. 23 (2019) 215–259.
21. A. Medda, G. Pal, R. Singha, T. Hossain, A. Saha and A. R. Das, *Expedient Synthesis of Biologically Potent Aryloxycoumarins and (Aryloxyimino)ethylcoumarins via Copper(II)-Promoted Chan–Lam Coupling Reaction*, Synth. Commun. 43 (2013) 169–181.
22. F. Saadati, A. M. Chahardehi, N. Jamshidi, N. Jamshidi and D. Ghasemi, *Coumarin: A natural solution for alleviating inflammatory disorders*, Curr. Res. Pharmacol. Drug Discov. 25 (2024) 100202.
23. J. J. Strouse, M. Jeselnik, F. Tapaha, C. B. Jonsson, W. B. Parker and J. B. Arterburn, *Copper catalyzed arylation with boronic acids for the synthesis of N1-aryl purine nucleosides*, Tetrahedron Lett. 46 (2005) 5699–5702.
24. R. Ledesma-Amaro, R. M. Buey and J. L. Revuelta, *Increased production of inosine and guanosine by means of metabolic engineering of the purine pathway in Ashbya gossypii*, Microb. Cell Fact. 14 (2015) 58–66.
25. P. J. Wickhorst, M. Blachnik, D. Lagumdzija and H. Ihmels, *Synthesis of 10- O-aryl-substituted berberine derivatives by Chan-Evans-Lam coupling and investigation of their DNA-binding properties*, Beilstein J. Org. Chem. 17 (2021) 991–1000.
26. A. R. Utami, I. P. Maksum and Y. Deawati, *Berberine and Its Study as an Antidiabetic Compound*, Biology 12 (2023) 973–987.
27. F. R. Mansour, S. F. Hammad, I. A. Abdallah, A. Bedair, R. M. Abdelhameed and M. Locatelli, Applications of metal organic frameworks in point of care testing, Trends Anal. Chem. 172 (2024) 117596.
28. H. Furukawa, K. E. Cordova, M. O'Keeffe and O. M. Yaghi, *The chemistry and applications of metal-organic frameworks*, Science 341 (2013) 1230444.
29. A. Bavykina, N. Kolobov, I. S. Khan, J. A. Bau, A. Ramirez and J. Gascon, *Metal–Organic Frameworks in Heterogeneous Catalysis: Recent Progress, New Trends, and Future Perspectives*, Chem. Rev. 120 (2020) 8468–8535.
30. G. H. Dang, Y. T. H. Vu, Q. A. Dong, D. T. Le, T. Truong and N. T. S. Phan, *Quinoxaline synthesis via oxidative cyclization reaction using metal–organic framework Cu(BDC) as an efficient heterogeneous catalyst*, Appl. Catal. A: Gen. 491 (2015) 189–195.
31. S. Rostamnia, H. Alamgholiloo and X. Liu, *Pd-grafted open metal site copper-benzene-1,4-dicarboxylate metal organic frameworks (Cu-BDC MOF's) as promising interfacial catalysts for sustainable Suzuki coupling*, J. Colloid Interface Sci. 469 (2016) 310–317.
32. B.-C. Li, J.-Y. Lin, J. Lee, E. Kwon, B. X. Thanh and X. Duan et al., *Size-Controlled Nanoscale Octahedral HKUST-1 as an Enhanced Catalyst for Oxidative Conversion of Vanillic Alcohol: The Mediating Effect of Polyvinylpyrrolidone*, Colloids Surf. A: Physicochem. Eng. Asp. 631 (2021) 127639.
33. Y. P. Budiman, M. Rashifari, S. Azid, I. Z. Ghafara, Y. Deawati and Y. Permana et al., *HKUST-1-Catalyzed Homocoupling of Arylboronic Acids*, ChemistrySelect 9 (2024) e202304913.
34. C. G. Carson, K. Hardcastle, J. Schwartz, X. Liu, C. Hoffmann, and R. A. Gerhardt et al., *Synthesis and Structure Characterization of Copper Terephthalate Metal–Organic Frameworks*, Eur. J. Inorg. Chem., 2009 (2009) 2338–2343.
35. X. Ma, L. Wang, H. Wang, J. Deng, Y. Song and Q. Li et al., *Insights into Metal-Organic Frameworks HKUST-1 Adsorption Performance for Natural Organic Matter Removal from Aqueous Solution*, J. Hazard Mater. 424 (2022) 126918.
36. S. Taheri, H. Mollabagher and S. A. H. Mousavi, *Metal Organic Framework Cu-BDC as an Efficient and Reusable Catalyst for One-Pot Synthesis of Benzophenazine Derivatives*, Polycycl. Aromat. Comp. 42 (2022) 6523–6536.
37. N. Cao, Y. Tong, J. Xie, H. Ma and S. Go, *MOF-253·$Cu(OAc)_2$ as a heterogeneous catalyst for N-arylation of heterocycles*, J. Org. Chem. 1033 (2025) 123641.
38. X. Zhang, J. Qin, R. Ma and L. Shi, *A base-free Chan–Lam reaction catalyzed by an easily assembled Cu(II)-carboxylate metal-organic framework*, J. Chem. Res. 45 (2021) 795–799.
39. A. Goswami, P. Dutta and K. Biradha, *Metal–organic frameworks with open metal sites act as efficient heterogeneous catalysts for Knoevenagel condensation and the Chan–Lam coupling reaction*, CrystEngComm. 25 (2023) 5092–5099.
40. R. M. Bora, L. Kyndiah, P. Borah, S. Chingangbam, J. B. Jadav and R. Devan et al., *Copper-Functionalized MIL-101(Cr): An Efficient, Reusable, and Heterogeneous Catalyst for Chan–Lam Coupling and Amide Bond Formation*, ChemistrySelect 10 (2025) e202500513.
41. N. Anbu & A. Dhakshinamoorthy, *$Cu_3(BTC)_2$ metal-organic framework catalyzed N-arylation of benzimidazoles and imidazoles with phenylboronic acid*, J. Ind. Eng. Chem. 65 (2018) 120–126.
42. A. Muñoz, P. Leo, G. Orcajo, F. Martínez and G. Calleja, *URJC-1-MOF as New Heterogeneous Recyclable Catalyst for C-Heteroatom Coupling Reactions*, ChemCatChem. 11 (2019) 3376–3380.
43. A. Khosravi, J. Mokhtari, M. R. Naimi-Jamal, S. Tahmasebi and L. Panahi, $Cu_2(BDC)_2(BPY)$–MOF: an efficient and reusable heterogeneous catalyst for the aerobic Chan–Lam coupling prepared via ball-milling strategy, RSC Adv. 7 (2017) 46022–46027.
44. Y. P. Budiman, M. R. S. Sidik, M. D. Permana, K. Haikal, I. I. Widiyowati and Y. Permana et al., *Catalytic efficiency of Cu-MOFs: HKUST-1 and CuBDC for the protodeboronation of aryl boronic acids*, RSC Adv. 15 (2025) 29453–29461.
45. O. M. Yaghi, A. U. Czaja, B. Wang and Z. Lu, *Oxidative homo-coupling reactions of aryl boronic acids using a porous copper metal-organic framework as a highly efficient heterogeneous catalyst*, US Patents 2012.
46. P. Puthiaraj, P. Suresh and K. Pitchumani, *Aerobic homocoupling of arylboronic acids catalysed by copper terephthalate metal–organic frameworks*, Green Chem. 16 (2014) 2865–2675.
47. M. Todaro, L. Sciortino, F. M. Gelardi and G. Buscarino, *Determination of Geometry Arrangement of Copper Ions in HKUST-1 by XAFS During a Prolonged Exposure to Air*, J. Phys. Chem. C. 21 (2017) 24853–24860.
48. I. Luz, F. X. Llabrés i Xamena and A. Corma, *Bridging homogeneous and heterogeneous catalysis with MOFs: Cu-MOFs as solid catalysts for three-component coupling and cyclization reactions for the synthesis of propargylamines, indoles and imidazopyridines*, J. Catal. 285 (2012)

285–291.

49. H. K. Kim, W. S. Yun, M.-B. Kim, J. Y. Kim, Y.-S. Bae and J.-D. Lee, *A Chemical Route to Activation of Open Metal Sites in the Copper-Based Metal–Organic Framework Materials HKUST-1 and Cu-MOF-2*, J. Am. Chem. Soc. 137 (2015) 10009–10015.
50. Y. Jing, Y. Yoshida, P. Huang and H. Kitagawa, *Reversible One- to Two- to Three-Dimensional Transformation in CuII Coordination Polymer*, Angew. Chem. Int. Ed. 61 (2022) e202117417.
51. H. Eguchi, S. Kato, S. Maegawa, F. Itoigawa and K. Nagata, *Solid-lubrication properties of copper benzene-1,4-dicaboxylate, a metal–organic framework with a two-dimensional layered crystal structure*, RSC Appl. Interfaces 2 (2025) 451–459.
52. V. H. Duparc, G. L. Bano and F. Schaper, *Chan–Evans–Lam Couplings with Copper Iminoarylsulfonate Complexes: Scope and Mechanism*, ACS Catal. 8 (2018) 7308–7325.
53. L. Zhang, G. Zhang, M. Zhang and J Cheng, *$Cu(OTf)_2$-Mediated Chan-Lam Reaction of Carboxylic Acids to Access Phenolic Esters*, J. Org. Chem. 75 (2010) 7472–7474.
54. J. D. Grayson, F. M. Dennis, C. C. Robertson and B. M. Partridge, *Chan–Lam Amination of Secondary and Tertiary Benzylic Boronic Esters*, J. Org. Chem. 86 (2021) 9883–9897.
55. S. A. Rossi, K. W. Shimkin, Q. Xu, L. M. Mori-Quiroz and D. A. Watson, *Selective Formation of Secondary Amides via the Copper-Catalyzed Cross-Coupling of Alkylboronic Acids with Primary Amides*, Org. Lett. 15 (2013) 2314–2317.
56. J. C. Vantourout, R. P. Law, A. Isidro-Llobet, S. J. Atkinson and A. J. B. Watson, *Chan–Evans–Lam Amination of Boronic Acid Pinacol (BPin) Esters: Overcoming the Aryl Amine Problem*, J. Org. Chem. 81 (2016) 3942–3950.
57. S. S.-Y. Chui, S. M.-F. Lo, J. P. H. Charmant, A. G. Orpen and I. D. Williams, *A Chemically Functionalizable Nanoporous Material $[Cu_3(TMA)_2(H_2O)_3]$*n, Science 283 (1999) 1148–1150.
58. A. Dhakshinamoorthy and H. Garcia, *Cascade Reactions Catalyzed by Metal Organic Frameworks*, ChemSusChem. 7 (2014) 2392–2410.
59. K. Kikushima, N. Miyamoto, K. Watanabe, D. Koseki, Y. Kita, and T. Dohi, *Ligand- and Counterion-Assisted Phenol O-Arylation with TMP-Iodonium(III) Acetates*, Org. Lett. 24 (2022), 1924–1928
60. S. Sueki and Y. Kuninobu, *Copper-Catalyzed N- and O-Alkylation of Amines and Phenols using Alkylborane Reagents*, Org. Lett. 15 (2013) 1544–1547.
61. E. M. Miller and M. A. Walczak, *Copper-Catalyzed Oxidative Acetilzation of Boronic Esters: An Umpolung Strategy for Cyclic Acetal Synthesis*, J. Org. Chem. 85 (2020) 8230–8239.
62. J. B. DeCoste, G. W. Peterson, B. J. Schindler, K. L. Killops, M. A. Browe and J. J. Mahle, *The effect of water adsorption on the structure of the carboxylate containing metal-organic frameworks Cu-BTC, Mg-MOF-74, and UiO-66*, J. Mater. Chem. A. 1 (2013) 11922–11932.
63. P. Y. S. Lam, D. Bonne, G. Vincent, C. G. Clark and A. P. Combs, *N-Arylation of α-Aminoesters with p-Tolylboronic Acid Promoted by Copper(II) Acetate*, Tetrahedron Lett. 44 (2003) 1691–1694.
64. J. C. Vantourout, H. N. Miras, A. Isidro-Llobet, S. Sproules and A. J. B. Watson, *Spectroscopic Studies of the Chan–Lam Amination: A Mechanistic-Inspired Solution to Boronic Ester Reactivity*, J. Am. Chem. Soc. 139 (2017) 4769–4779.
65. T. Pooventhiran, N. Khilari and D. Koley, *Mechanistic Avenues in the Chan–Lam–Based Etherification Reaction: A Computational Exploration*, Chemistry 29 (2023) e202302983.
66. L. M. Huffman and S. S. Stahl, *Carbon–Nitrogen Bond Formation Involving Well-Defined Aryl–Copper(III) Complexes*, J. Am. Chem. Soc 130 (2008) 9196–9197.
67. C. H. Sharp, B. C. Bukowski, H. Li, E. M. Johnson, S. Ilic and A. J. Morris et al., *Nanoconfinement and mass transport in metal-organic frameworks*, Chem. Soc. Rev. 50 (2021) 11530–11558.
68. A. Ahmed, C. M. Robertson, A. Steiner, T. Whittles, A. Ho and V. Dhanak et al., *Cu(I)Cu(II)BTC, a microporous mixed-valence MOF via reduction of HKUST-1*, RSC Adv. 6 (2016) 8902–8905.
69. J. B. DeCoste, M. H. Weston, P. E. Fuller, T. M. Tovar, G. W. Peterson and M. D. LeVan et al., *Metal–Organic Frameworks for Oxygen Storage*, Angew. Chem. Int. Ed. Engl. 53 (2014) 14092–14095.
70. P. Guo, C. Froese, Q. Fu, Y.-T. Chen, B. Peng and W. Kleist et al., *CuPd Mixed-Metal HKUST-1 as a Catalyst for Aerobic Alcohol Oxidation*, J. Phys. Chem. C 122 (2018) 21433–21440.
71. J. Sherwood, J. H. Clark, I. J. S. Fairlamb and J. M. Slattery, *Solvent effects in palladium catalysed cross-coupling reactions*, Green Chem. 21 (2019) 2164–2213.
72. L. Li, S. Zhao, A. Joshi-Pangu, M. Diane And M. R. Biscoe, *Stereospecific Pd-Catalyzed Cross-Coupling Reactions of Secondary Alkylboron Nucleophiles and Aryl Chlorides*, J. Am. Chem. Soc. 136 (2014) 14027–14030.
73. P. A. Cox, M. Reid, A. G. Leach, A. D. Campbell, E. J. King and G. C. Lloyd-Jones, *Base-Catalyzed Aryl-$B(OH)_2$ Protodeboronation Revisited: From Concerted Proton Transfer to Liberation of a Transient Aryl Anion*, J. Am. Chem. Soc. 139 (2017) 13156–13165.
74. M. P. Puspitasari, J. H. Pratama, R. A. Nugroho, W. W. Lestari, Y. Kemala and T. E. Saraswati, *Efficient degradation of methyl orange through photo-Fenton processes with MIL-100(Fe) modified Fe_3O_4 (Fe_3O_4@MIL-100(Fe)) catalyst*, Commun. Sci. Tech. 9 (2024) 252–261.
75. W. W. Lestari, M. Adreane and H. Suwarno, *Enhanced Hydrogen Storage Capacity Over Electro-synthesized HKUST-1*, J. Math. Fund. Sci. 49 (2017) 213–224.