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Covalent Imine Polymers

Triazine-Based Mesoporous Covalent Imine Polymers as Solid Supports for Copper-Mediated Chan–Lam Cross-Coupling N-Arylation Reactions

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Abstract: The synthesis of a novel mesoporous covalent imine polymeric (MCIPs) material, involving simple Schiff-base chemistry, is reported. This highly functionalised nitrogen-rich material acts as a good support for immobilising Cu^{II} ions, exhibiting excellent catalytic activity in promoting the Chan–Lam cross-coupling reaction between biologically active amines and arylboronic acids. The performance of this catalyst is also evident from its broad substrate scope, high stability, real heterogeneity, mild reaction conditions and reusability without loss of activity. The observed results will provide additional scope on the design and catalytic applications of this emerging class of materials.

Introduction

The creation of pores with desired dimensions, in the form of frameworks, is a challenging task in materials chemistry. Among various porous materials, metal–organic frameworks (MOFs)[1] and porous organic frameworks (POFs)[2] are considered to be of interest in the fields of gas storage and catalysis.[1,2] In particular, covalently linked POFs have attracted considerable attention as unique and emerging materials. A number of different types of POFs, such as covalent organic frameworks (COFs),[3] conjugated microporous polymers (CMPs),[4] polymers of intrinsic microporosity (PIM),[5] element–organic frameworks (EOFs),[6] triazine-based organic frameworks (CTFs),[7] porous polymer networks (PPN),[8] covalent organic polymers (COP)[9] and porous aromatic frameworks (PAFs),[10] among others, have been reported. These materials have advantages, such as relatively high thermal stability, high specific surface area, low density, ease of synthesis from simple compounds and retaining their porosity even after boiling in water for one week.[2–10] In addition, one of the most attractive aspects of POFs is the promise of tuning structures and properties through rational chemical design and synthesis. These properties allow potential applications[8a,10,11] in gas storage, explosive detection, drug release and catalysis. Consequently, the development of multifaceted functionality into porous networks is one of the frontline areas of research, potentially leading to the synthesis of new materials with diverse applications. For example, incorporation of catalytically active sites, such as metals, onto the nitrogen-rich porous-organic-framework surfaces may be beneficial to enhance the catalytic performance, as well as the stability, of the supported materials.[12]

The synthesis of porous carbon-based material catalysts has immense potential in the advancement of sustainable substitutes over existing MOFs, zeolite and metal oxides.[13] Jang et al. have extensively reported that nitrogen-doped carbon nanotubes (CNTs) are used to stabilize the palladium nanoparticles,[14] which are used as a catalyst for the Heck reaction and hydrogenation. Thomas et al. have demonstrated a nitrogen-rich covalent triazine framework as a good catalytic support for glycerol oxidation.[15] Recently, Wang et al. have reported palladium-loaded covalent organic frameworks as catalysts for

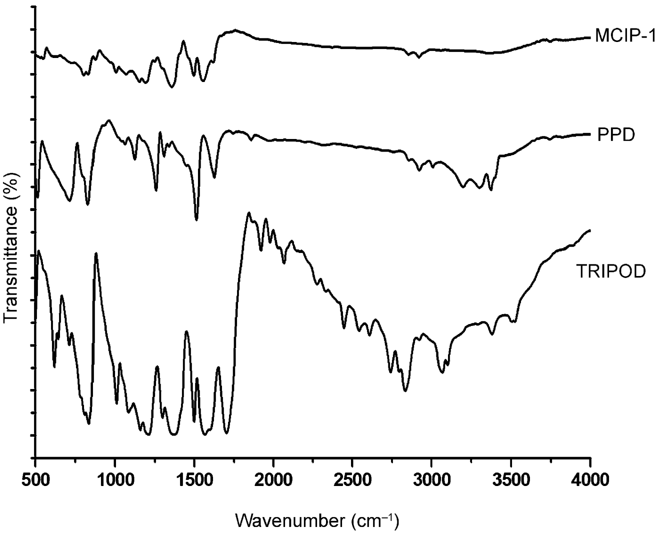

Figure 1. FTIR spectra of 2,4,6-tris(*p*-formylphenoxy)-1,3,5-triazine (TRIPOD), *p*-phenylenediamine (PPD) and MCIP-1.

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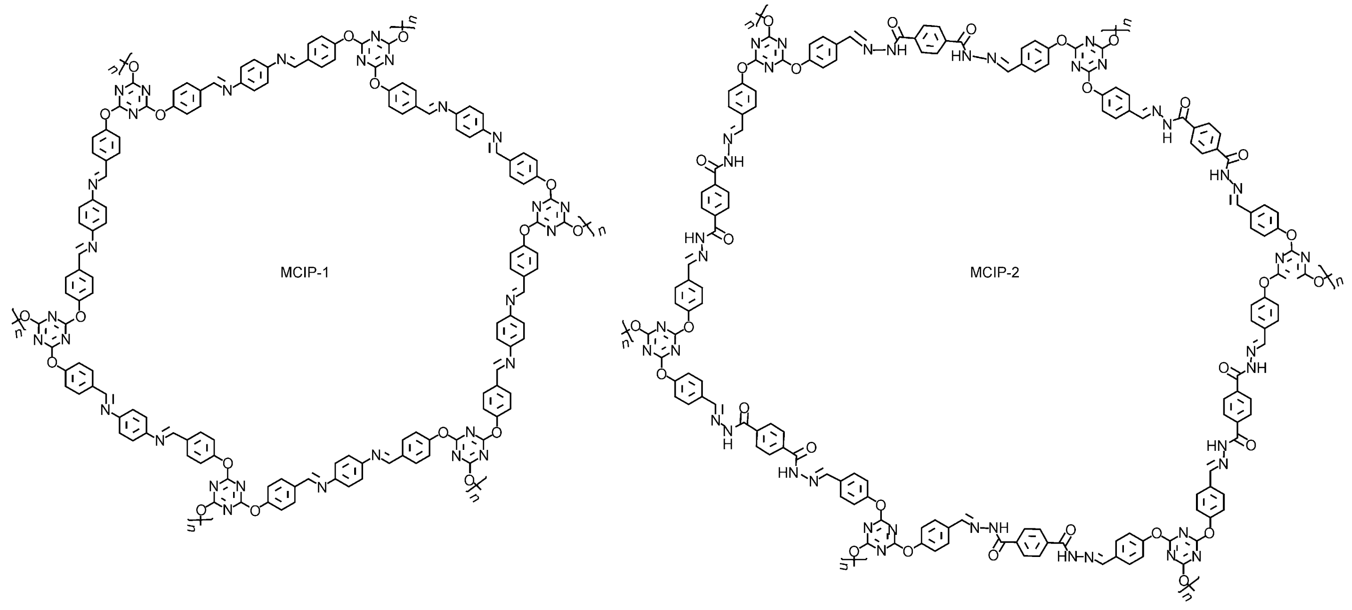


Scheme 1. Schematic representation of MCIP-1 and MCIP-2.

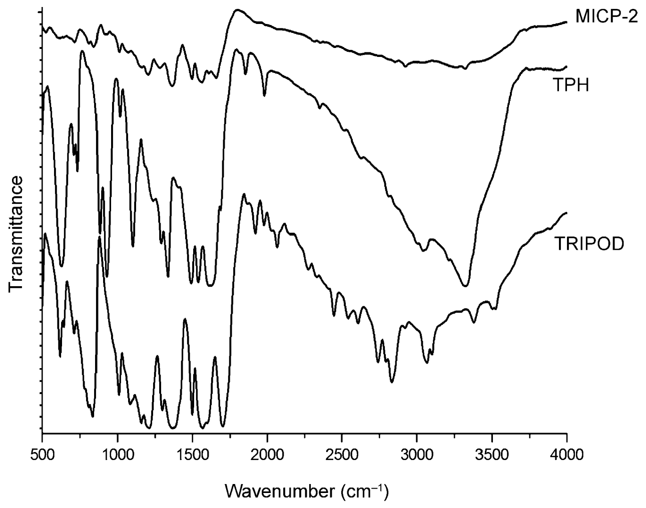


Figure 2. FTIR spectra of 2,4,6-tris(*p*-formylphenoxy)-1,3,5-triazine (TRIPOD), terephthalodihydrazide (TPH) and MCIP-2.

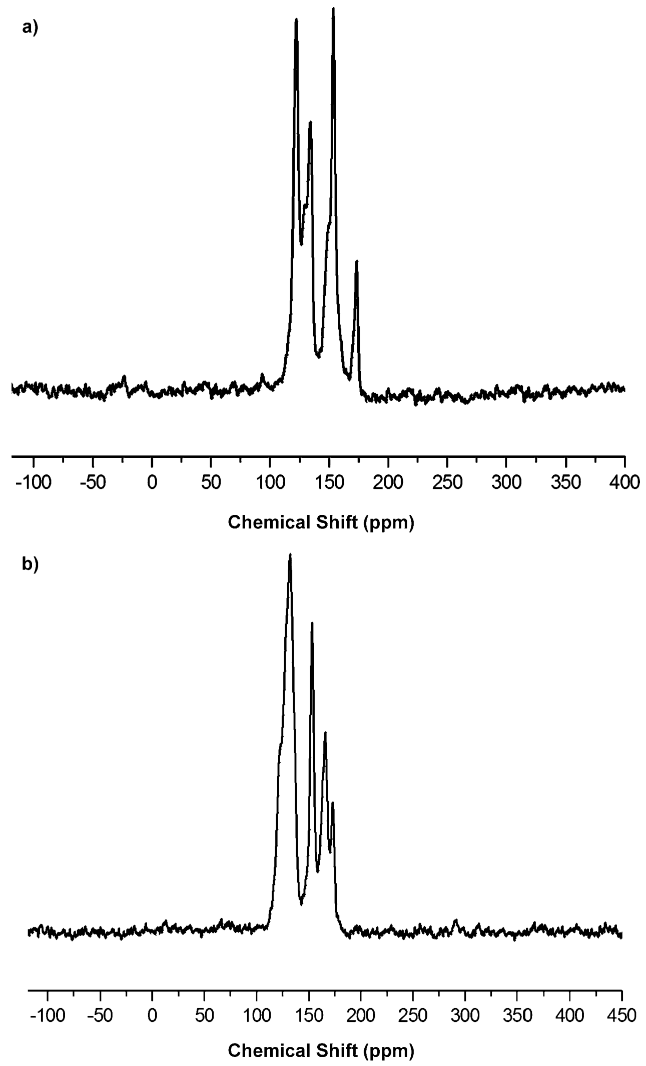


Figure 3. ^{13}C CP-MAS NMR spectrum of a) MCIP-1 and b) MCIP-2.

Suzuki coupling reactions.[11e] Bhaumik et al. have extensively reported triazine-functionalised mesoporous polymers[12] and nitrogen-rich porous covalent imine (CIN) frameworks,[16] for supporting palladium species, as catalysts for C–C cross-coupling reactions, and acid-group-containing porous organic polymers as catalysts for the synthesis of 3-benzhydrylindole.[11c] More recently, Zhang et al. have demonstrated the mesoporous poly(melamine–formaldehyde) material as an efficient catalyst for chemoselective acetalisation of aldehydes.[17] Encouraged by these results, herein we report a copper-loaded mesoporous covalent imine polymer (MCIP) as a unique heterogeneous protocol to achieve the oxidative Chan–Lam cross-coupling reaction of diverse boronic acids with biologically active amines.

Transition-metal-catalysed C–N cross-coupling reactions have immense utility in organic synthesis to develop several pharmacophore and drug analogues.[18] Generally, these aromatic C–N moieties were synthesised by the aromatic nucleophilic substitution of nitrogen nucleophiles with aryl halides, or the Ullmann coupling reaction,[18] by using stoichiometric amounts of copper metal at high temperature. Furthermore, these procedures utilize an expensive and air-sensitive palladium source for C–N cross-coupling,[19] thus, limiting their application in large-scale and laborious catalyst-separation processes. Consequently, the development of milder, more environmentally friendly conditions and a cheap and efficient catalyst is desirable. In this context, Chan–Lam cross-coupling involves the copper-promoted coupling of amines with wide range of commercially available arylboronic acids, and has emerged as a powerful tool for C–N bond formation under mild reaction conditions.[20] Though this coupling is reported with nitrogen nucleophiles,[21] to the best of our knowledge, there is no report describing the formation of biologically active *N*-arylflavones from flavones and arylboronic acids. These features prompted us to study the N-arylation of aminoflavones and heterocyclic amines by using arylboronic acids to yield biologically important N-aryl derivatives; the observed results are discussed below.

Results and Discussion

The imine-functionalised mesoporous covalent imine polymers (MCIPs) were synthesised by Schiff-base chemistry involving a trialdehyde–triazine derivative and diamine (Scheme 1). The synthesised materials were characterized by using FTIR, ^{13}C cross-polarization magic-angle spinning (CP-MAS) NMR spectroscopy, Field-emission scanning electron microscopy (FE-SEM), elemental microanalysis, powder XRD (PXRD), thermogravimetric analysis (TGA) and nitrogen-gas-adsorption studies. The synthesised MCIP-1 and MCIP-2 materials are insoluble in water and common organic solvents, such as DMF, THF, DMSO, acetone, and others.

Fourier transform infrared (FTIR) spectroscopy of MCIP-1 and MCIP-2 shows a strong C=N stretching at 1560 and 1592 cm^{-1}, respectively, (Figure 1 and Figure 2), indicating the formation of an imine bond. The band at 1500 cm^{-1}, representing the triazine ring, is present in both MCIP-1 and MCIP-2 materials. Meanwhile, the aldehyde (1703 cm^{-1}) and amine (3420 and 3358 cm^{-1}) bands of MCIP-1 and MCIP-2 had disappeared completely on comparison with the spectra of the starting materials (Figure 1 and 2).

The ^{13}C CP-MAS NMR spectral data of MCIP-1 and MCIP-2 (Figure 3) clearly confirmed their chemical structure. The solid-state NMR spectrum of MCIP-1 shows six peaks at $\delta = 122.4$, 129.0, 134.5, 148.6, 153.8, and 173.5 ppm (Figure 3 a). The peak at 153.8 ppm corresponds to the carbon atom of the C=N bond obtained from the condensation reaction of trialdehyde and diamine. The peak at 173.5 ppm corresponds to the triazine carbon atom. The signals at 122.4, 129.0, 134.5 and 148.6 ppm can be assigned to the carbon atoms of the phenyl rings. There was no peak present at around 190 ppm. These results clearly confirm the absence of unreacted aldehyde.

Similarly, in the solid-state NMR spectra of MCIP-2, the characteristic peak of a C=N bond appears at 153.4 ppm (Figure 3 b). Data from the solid-state NMR spectra of MCIP-1 and MCIP-2 are given in the Supporting Information (Tables S1 and S2).

FE-SEM describes the morphology of the MCIP-1 and MCIP-2 materials (Figure 4). Images in Figures 4 a and 4 b clearly indicate that MCIP-1 adopts a sheet-like morphology, whereas those of MCIP-2 (Figure 4 c and 4 d) clearly indicate that MCIP-2 adopts a uniform needle-like morphology. These observations indicate that the condensation of aldehyde and amines leads

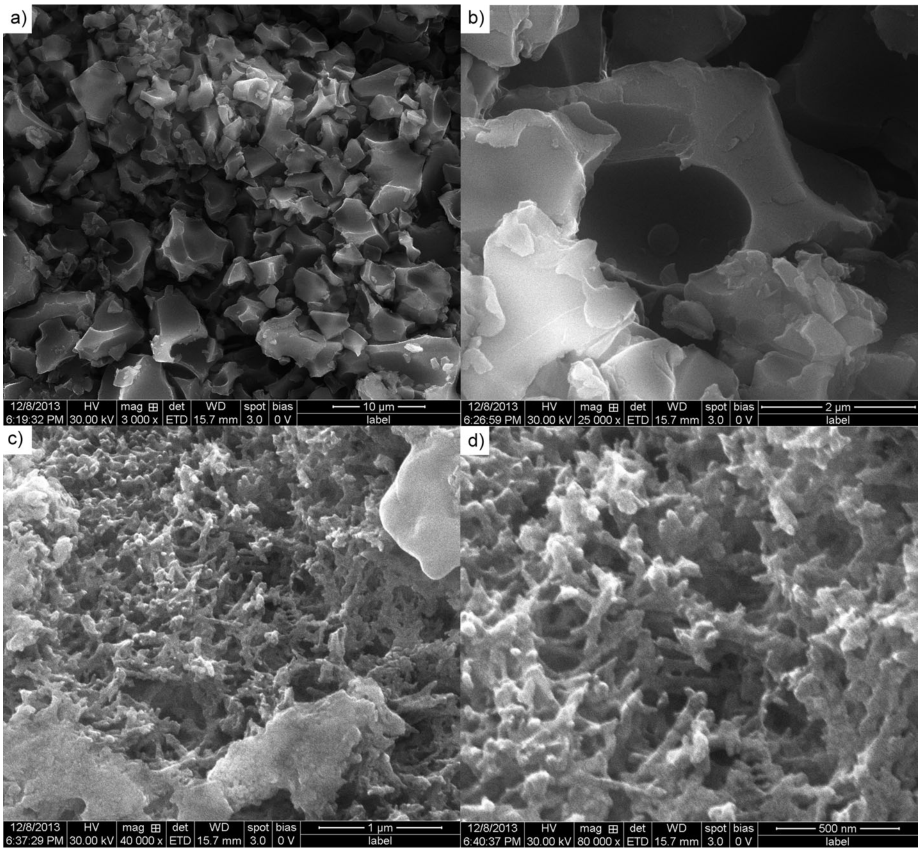


Figure 4. FE-SEM images of the synthesised a,b) MCIP-1 and c,d) MCIP-2.

to a uniform morphology and a certain degree of structural regularity.

The regularity and crystallinity of the structure of MCIP-1 and MCIP-2 materials are further confirmed by powder PXRD analysis (Figure 5). The obtained PXRD pattern of MCIP-1 indicates a partial crystallinity and the set of peaks in the range of 9 to 40°, suggests that the framework has a certain degree of order (Figure 5a). Similarly, the PXRD pattern of MCIP-2 indicates a structure with partial crystallinity and shows a certain degree of order in the range 10 to 40° (Figure 5b).

The thermal stability of MCIP-1 and MCIP-2 was analysed TGA under a nitrogen atmosphere (Figure 6). As shown in Figure 6, MCIP-1 exhibits almost no weight loss below 300 °C, suggesting no loss of guest. The framework decomposition of MCIP-1 was observed at about 350 °C. Subsequently, the weight gradually decreases, by up to 50% at 600 °C. TGA of Cu/MCIP-1 also demonstrated a good thermal stability up to 200 °C. Similarly, Figure 8 clearly shows that MCIP-2 is stable up to 250 °C.

The porosity and surface area of the above materials were measured by nitrogen adsorption–desorption analysis at 77 K (Figure 7 and 8). These isotherms are closely related to a type-IV isotherm, which is indicative of characteristic mesoporous materials.[22] From the Brunauer–Emmett–Teller (BET) isotherms, the surface areas are found to be 174 m^2g^{-1} and 187 m^2g^{-1} for MCIP-1 and MCIP-2, respectively. These values are very close to that of mesoporous materials,[22] but still well within the values of other materials. Pore-size-distribution plots of both MCIP-1 and MCIP-2 (insets of Figure 7 and 8) display a pore width of 32.4 and 44.3 Å, respectively.

As the synthesised MCIP-1 material has large number of nitrogen atoms, from the triazine and imine groups, it can be used as a metal-ion stabiliser. MCIP-1 was stirred with copper(II) acetate in CH_2Cl_2 solvent at room temperature for 48 h to prepare the copper-loaded MCIP-1 (Cu/MCIP-1) catalyst, which was characterized by powder XRD (see the Supporting Information, Figure S1), energy-dispersive X-ray (EDX), atomic-absorption spectroscopy (AAS), inductively coupled plasma atomic-emission spectroscopy (ICP-AES), TGA and X-ray photoelectron spectroscopy (XPS) analysis. A comparison of the powder XRD patterns of MCIP-1 and Cu/MCIP-1 shows that the structure of MCIP-1 was maintained after the treatment with copper acetate. Elemental analysis by AAS indicated a 2.58 $mmol\,g^{-1}$ copper loading in Cu/MCIP-1. From ICP-AES analysis the copper concentration in Cu/MCIP-1 was found to be 2.60%. The SEM-EDX results suggest ≈2.53 wt% of copper in Cu/MCIP-1 (see the Supporting Information, Table S3).

XPS spectra (Figure 9a and 9b) show the Cu $2p_{3/2}$ core level of fresh and reused Cu/MCIP-1 catalyst, respectively. The binding-energy values of the fresh and reused catalyst are summarized in Table 1. Cu $2p_{3/2}$ XPS of the fresh Cu/MCIP-1 catalyst exhibits a sharp peak at 934.5±0.1 eV and a strong satellite peak on the higher binding-energy site (above 940 eV), indicating the existence of divalent copper species, in good agreement with the characteristic peak of Cu^{II} in literature reports.[23] Similarly, the XPS spectrum (of Cu $2p_{3/2}$) of the reused Cu/MCIP-1 catalyst also exhibits a strong binding-energy peak, in the same region as the fresh catalyst, with strong satellite peaks. These results clearly confirm that after completion of the reac-

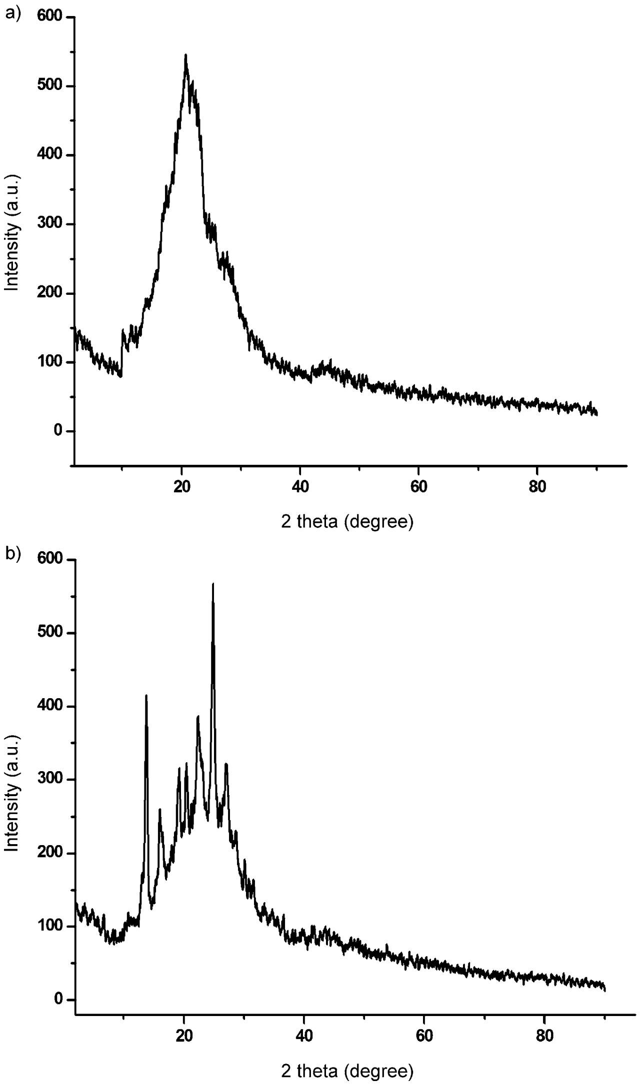


Figure 5. Powder XRD pattern of a) MCIP-1 and b) MCIP-2.

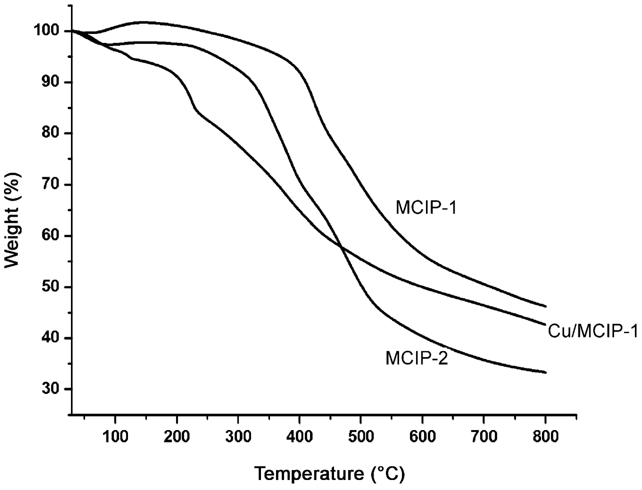


Figure 6. TGA of MCIP-1, Cu/MCIP-1 and MCIP-2.

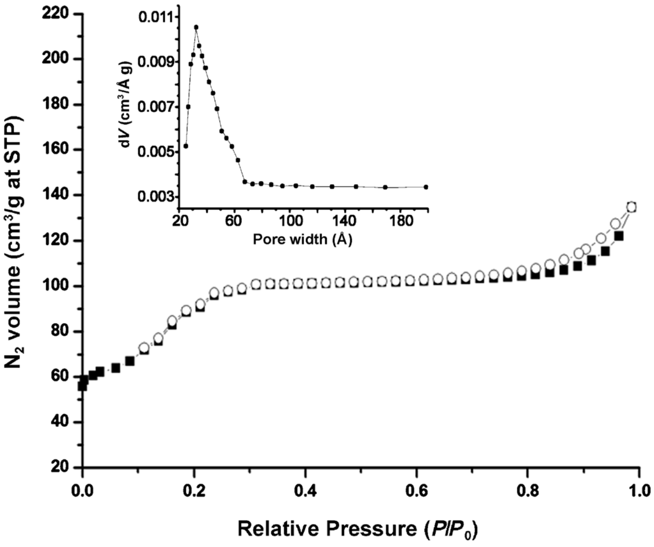


Figure 7. Nitrogen adsorption–desorption isotherm of MCIP-1 (solid square: adsorption; empty circle: desorption). Pore-size distribution of MCIP-1 (inset).

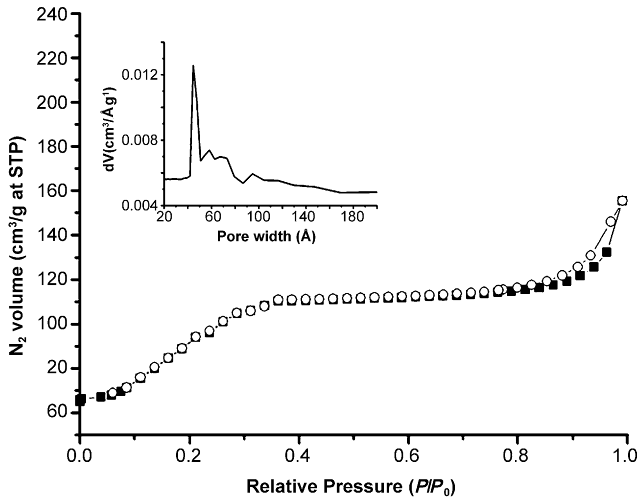


Figure 8. Nitrogen adsorption–desorption isotherm of MCIP-2 (solid square: adsorption; empty circle: desorption). Pore size distribution of MCIP-2 (inset).

tion, the catalyst retains its original valence (Cu^{II}) and provides a strong support for the structural integrity of the catalyst.

The XPS spectra (Figure 10 and Figure 11) describe the N 1s and O 1s core-level spectra of the fresh and reused Cu/MCIP-1 catalyst. A binding energy of 532.5 eV for the C–O–C bond (O 1s core level) is reported in the literature.[24] Interestingly, the O 1s value for the fresh and reused Cu/MCIP-1 catalyst appears at 531.8 ± 1 eV. Similarly, the triazine unit (N 1 s core level) is reported to have a binding energy of 398.9 eV.[25] The N 1s core-level binding energy of the fresh and reused Cu/MCIP-1 catalyst appears at 400.4 ± 1 eV. These values clearly demonstrate that copper metal binds strongly to nitrogen as well as oxygen atoms.

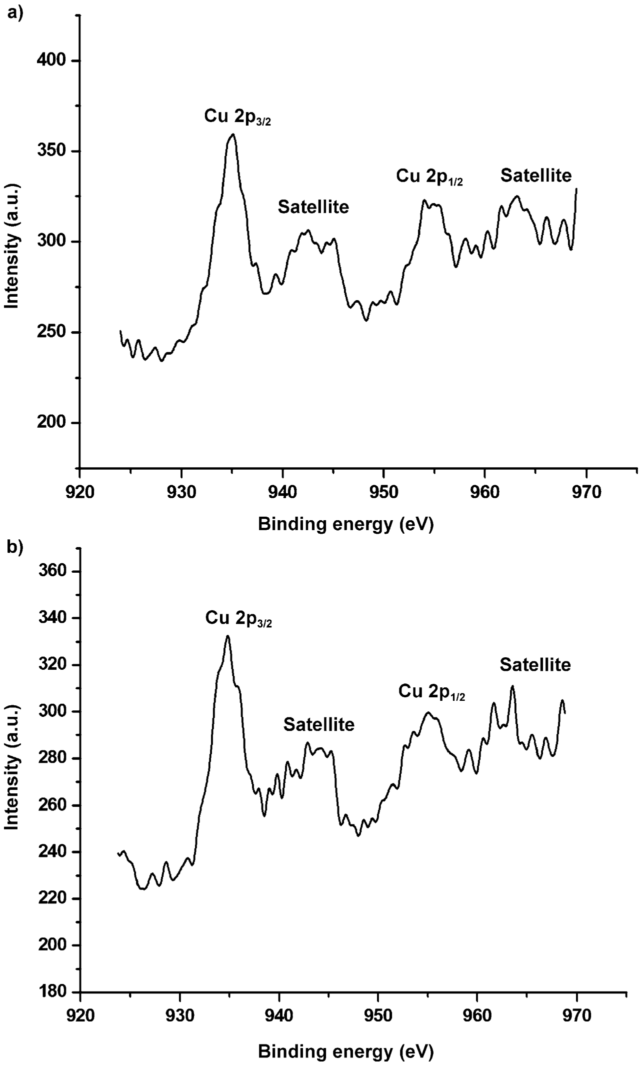


Figure 9. Cu 2p$_{3/2}$ core level XPS spectra of a) fresh and b) reused Cu/MCIP-1.

Table 1. Cu 2p$_{3/2}$ XPS parameters of fresh, reused Cu/MCIP-1 and reported catalysts.

Catalyst	BE of Cu 2p$_{3/2}$ [eV]	FWHM [eV]
fresh Cu/MCIP-1	934.5 ± 1	3.8
reused Cu/MCIP-1	934.4 ± 1	3.8
CuZnAl-HT[23a]	934.6	3.8
Malachite[23a]	934.6	3.3
CuO[23b]	933.8	3.6
Cu metal[23a]	932.7	1.7

BE = binding energy; FWHM = full width half maximum.

The catalytic activity of this heterogeneous Cu/MCIP-1 material was established in the Chan–Lam cross-coupling reaction of biologically relevant amines with boronic acids. It is relevant to note here that the potential industrial applications of this reaction, using other homogeneous copper catalysts to produce pharmacologically relevant derivatives, is quite limited because of the difficulties in separating and recycling the cata-

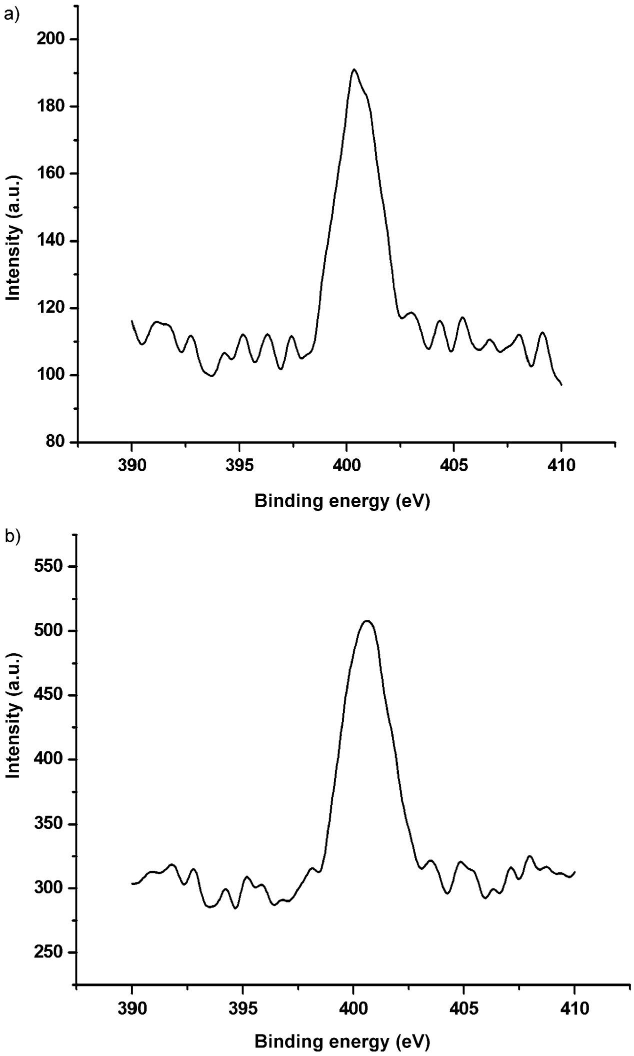


Figure 10. N 1 s core level XPS spectra of a) fresh and b) reused Cu/MCIP-1.

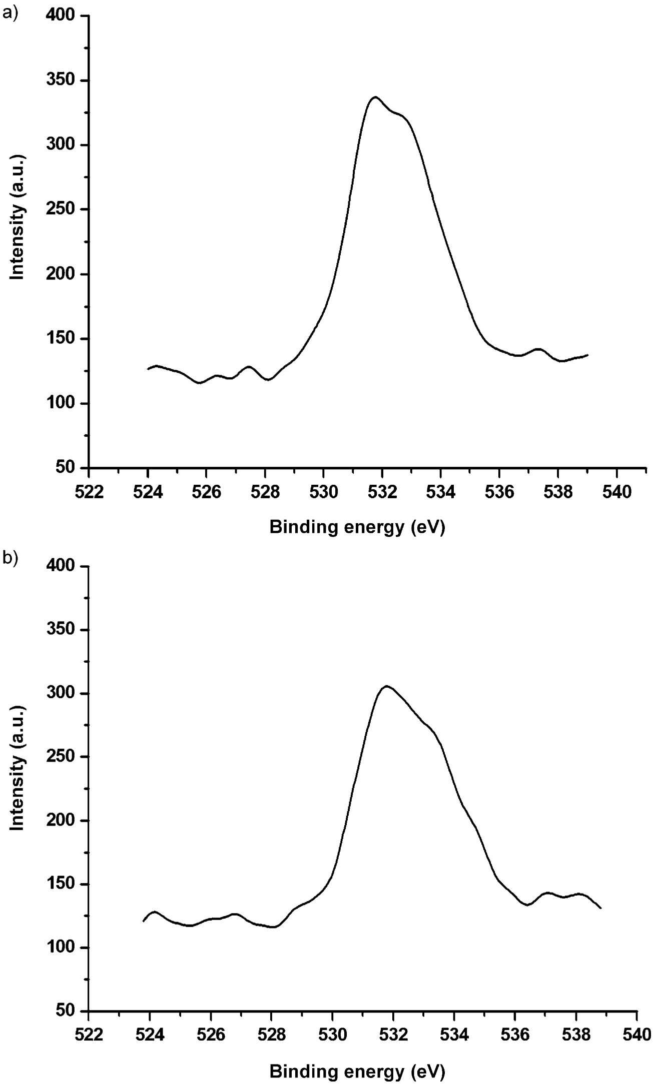


Figure 11. O 1 s core level XPS spectra of a) fresh and b) reused Cu/MCIP-1.

lyst from the reaction mixture. Catalytic studies are restricted to Cu/MCIP-1 and are not extended to Cu/MCIP-2 because amides are known to undergo Chan–Lam N-arylation.

Preliminary studies to screen the catalytic system were carried out by using the reaction of phenylboronic acid with 7-aminoflavone (Table 2). All reactions were conducted under an oxygen atmosphere (by using a balloon) at room temperature. In the absence of a catalyst, with only MCIP-1 and under an inert atmosphere (absence of oxygen), no product was obtained (Table 2, entries 1, 2 and 24). These results clearly highlight the specific role of the copper catalyst in the Chan–Lam cross-coupling N-arylation reaction. When the reactions were conducted in the presence of other common Cu^{II} sources, such as $Cu(OAc)_2$, $CuSO_4{\cdot}5H_2O$ and $CuCl_2$, the desired product was obtained in 68, 17 and 32% yields, respectively (Table 2, entries 3–5). When Cu^{I} sources, such as CuCl and CuI, were used as catalysts, only trace amounts of the coupled product were observed (Table 2, entries 6 and 7). Our interest in heterogeneous solid catalysts, to increase reactivity and reusability, promoted us to use Cu/MCIP-1 in CH_2Cl_2, with K_2CO_3 as a base, and the desired product was formed in 70% yield (Table 2, entry 8). When other inorganic bases were used, similar results were observed (Table 2, entries 9 and 10). Interestingly, when organic bases, such as NEt_3 and pyridine, were used, higher yields were obtained (Table 2, entries 11 and 12). From a toxicity point of view, NEt_3 is a better choice of base than pyridine for this cross-coupling reaction. Other solvents, such as methanol, MeCN, DMF, DMSO and toluene were also employed, but showed no improvement in yield (Table 2, entries 13–17). When the reaction was conducted in 1,2-dichloroethane (DCE), excellent yields were obtained (Table 2, entries 18 and 21). Water was found to be a poor solvent for this cross-coupling reaction (Table 2, entry 20). When the reaction was carried out in the presence of $Cu(OAc)_2$ and organic bases (NEt_3 and pyridine), the desired product was obtained in 75 and 80% yields, respectively (Table 2, entries 19 and 22). When the reaction was conducted in atmospheric oxygen (in an open flask), a 78% yield was observed (Table 2, entry 23).

Table 2. Optimisation studies for N-arylation of 7-aminoflavone.[a]

Entry	Catalyst	Base	Solvent	Time [h]	Yield [%][b]
1	–	K_2CO_3	CH_2Cl_2	16	nil
2	MCIP-1	K_2CO_3	CH_2Cl_2	16	nil
3[c]	$Cu(OAc)_2$	K_2CO_3	CH_2Cl_2	16	68
4[c]	$CuSO_4{\cdot}5H_2O$	K_2CO_3	CH_2Cl_2	16	17
5[c]	$CuCl_2$	K_2CO_3	CH_2Cl_2	16	32
6[c]	CuCl	K_2CO_3	CH_2Cl_2	16	trace
7[c]	CuI	K_2CO_3	CH_2Cl_2	16	trace
8	Cu/MCIP-1	K_2CO_3	CH_2Cl_2	16	70
9	Cu/MCIP-1	Cs_2CO_3	DCE	16	64
10	Cu/MCIP-1	K_3PO_4	DCE	16	65
11	Cu/MCIP-1	NEt_3	CH_2Cl_2	16	88 (89.5)[h]
12	Cu/MCIP-1	pyridine	CH_2Cl_2	16	90 (91.9)[h]
13	Cu/MCIP-1	NEt_3	MeOH	16	74
14	Cu/MCIP-1	NEt_3	MeCN	16	62
15	Cu/MCIP-1	NEt_3	DMF	16	43
16	Cu/MCIP-1	NEt_3	DMSO	16	41
17	Cu/MCIP-1	NEt_3	toluene	16	47
18	Cu/MCIP-1	NEt_3	DCE	16	91 (93.8)[h]
19[c]	$Cu(OAc)_2$	NEt_3	DCE	16	75
20	Cu/MCIP-1	NEt_3	water	16	25
21	Cu/MCIP-1	pyridine	DCE	16	93 (94.8)[h]
22[c]	$Cu(OAc)_2$	pyridine	DCE	16	80
23[d]	Cu/MCIP-1	NEt_3	DCE	16	78
24[e]	Cu/MCIP-1	NEt_3	DCE	16	nil
25	Cu/MCIP-1	NEt_3	DCE	14, 12, 10, 8	91, 91, 83, 67
26[f]	Cu/MCIP-1	NEt_3	DCE	12	91, 91, 76, 49
27[g]	Cu/MCIP-1	NEt_3	DCE	12	91, 69, 26

[a] Reaction conditions: 7-Aminoflavone (0.5 mmol), phenylboronic acid (0.6 mmol), catalyst (50 mg), solvent (2 mL), base (100 mol%) O_2 balloon, room temperature (RT); [b] Isolated yield based on 7-aminoflavone; [c] 10 mol% of catalyst; [d] Atmospheric oxygen; [e] N_2 atmosphere; [f] Yield of the reaction carried out with 50, 40, 30, 20 mg of Cu/MCIP-1, respectively; [g] Yield of the reaction carried out with 100, 50, 0 mol% of base, respectively; [h] Yield obtained by HPLC analysis.

The influence of other experimental parameters, such as reaction time, amount of catalyst and base, were also optimized. Increasing the reaction time from 8 to 12 h increased the overall yield from 67 to 91% (Table 2, entry 25). The yield of the desired product increased rapidly with an increase in the amount of the catalyst. On increasing the amount of catalyst to 40 mg, the product was obtained in excellent yield, but further addition of catalyst had no positive effect on the overall yield of product (Table 2, entry 26). Table 2, entry 27, shows that the concentration of base plays an important role in this heterogeneous copper-catalysed Chan–Lam cross-coupling reaction. In the absence of a base, only 26% yield was obtained after 12 h, and only 69% yield was observed when 50 mol% of base was added. These observations show that the optimum conditions for this reaction are the use of Cu/MCIP-1 as a catalyst, in DCE under an O_2 atmosphere (balloon), at room temperature for 12 h.

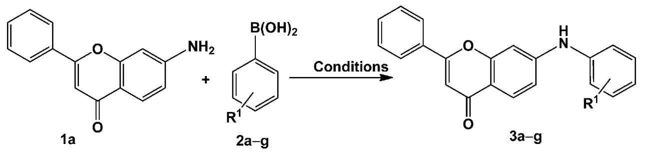
Motivated by these results, we explored the scope of the cross-coupling reaction of 7-aminoflavone (**1 a**) with various arylboronic acids (**2 a**–**g**). All of the arylation reactions proceeded cleanly in excellent yields. As depicted in Table 3, compound **1 a** was coupled easily with arylboronic acids bearing electron-withdrawing and electron-donating *p*- and *m*- substituents, providing the corresponding N-arylated flavones in good to excellent yields. Interestingly, halogen-substituted arylboronic acids were also tolerated in the N-arylation reaction, affording compounds **3 f** and **3 g** in 80 and 78% yields.

In a further set of experiments, we have investigated the scope and generality of this method, with respect to 6-aminoflavone (**1 b**). As depicted in Table 4, compound **1 b** was easily coupled with arylboronic acids bearing both electron-donating and electron-withdrawing substituents. Arylboronic acids with electron-withdrawing substituents gave a somewhat lower amount of product than those with electron-donating groups. It is pertinent to note that the presence of halogen substituents, as in **3 f**, **3 g**, **4 f** and **4 g**, provides a handle for further structural diversifications using this metal-catalysed cross-coupling reaction.

The scope of this protocol was further extended to the coupling reaction of substituted arylboronic acids with 8-aminoquinoline (**1 c**) to give the corresponding products in good to excellent yield; the results are summarized in Table 5. Compound **1 c** was coupled readily with electronically diverse boronic acids. Interestingly, all the examined substrates underwent clean conversion to the desired N-arylated aminoquinolines, the only noticeable difference was in the reaction time. Substituting both electron-donating and electron-withdrawing groups at the *p*- and *m*- positions gave very good yield. However, *o*-substituted arylboronic acid gave a lower yield of product owing to steric hindrance.

Based on the above results and previous reports,[20d,21a] a plausible mechanistic pathway for the present cross-coupling N-arylation reaction, involving a Cu^I/Cu^{III} cycle, is depicted in Scheme 2. The first step involves the coordination of Cu/MCIP-1 to amine **1** to form a Cu^{II} complex, **A**. The second step in-

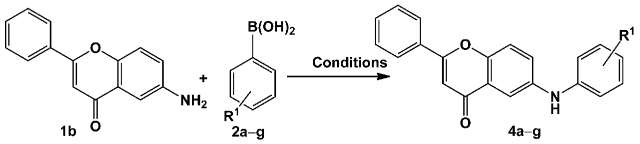
Table 3. N-Arylation of 7-aminoflavone with various arylboronic acids.[a]



Entry	7-Aminoflavone (**1 a**)	Arylboronic acid (**2 a**–**2 g**)	Product (**3**)	Yield [%]	TON[b]
1	**1 a**	$C_6H_5B(OH)_2$ (**2 a**)	**3 a**	91	54
2	**1 a**	4-C_2H_5-$C_6H_4B(OH)_2$ (**2 b**)	**3 b**	93	55
3	**1 a**	4-OCH_3-$C_6H_4B(OH)_2$ (**2 c**)	**3 c**	90	53
4	**1 a**	3-OCH_3-$C_6H_4B(OH)_2$ (**2 d**)	**3 d**	87	51
5	**1 a**	3-CH_3-C6$H_4B(OH)_2$ (**2 e**)	**3 e**	89	53
6	**1 a**	4-Cl-$C_6H_4B(OH)_2$ (**2 f**)	**3 f**	80	47
7	**1 a**	4-F-$C_6H_4B(OH)_2$ (**2 g**)	**3 g**	78	46

[a] Reaction conditions: 7-Aminoflavone (0.5 mmol), boronic acid (0.6 mmol), Cu/MCIP-1 (40 mg), NEt_3 (100 mol%), DCE (2 mL), O_2 balloon, RT; Yield based on 7-aminoflavone. [b] TON = turnover number.

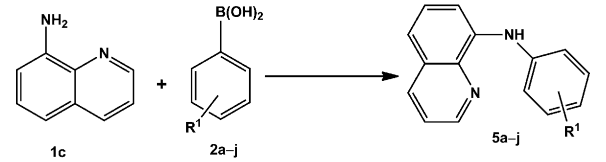
Table 4. N-Arylation of 6-aminoflavone with various arylboronic acids.[a]



Entry	6-Aminoflavone (**1b**)	Arylboronic acid (**2a–2g**)	Products (**4**)	Yield [%]	TON[b]
1	**1b**	**2a**	**4a**	93	55
2	**1b**	**2b**	**4b**	90	53
3	**1b**	**2c**	**4c**	91	54
4	**1b**	**2d**	**4d**	89	53
5	**1b**	**2e**	**4e**	90	53
6	**1b**	**2f**	**4f**	81	48
7	**1b**	**2g**	**4g**	77	45

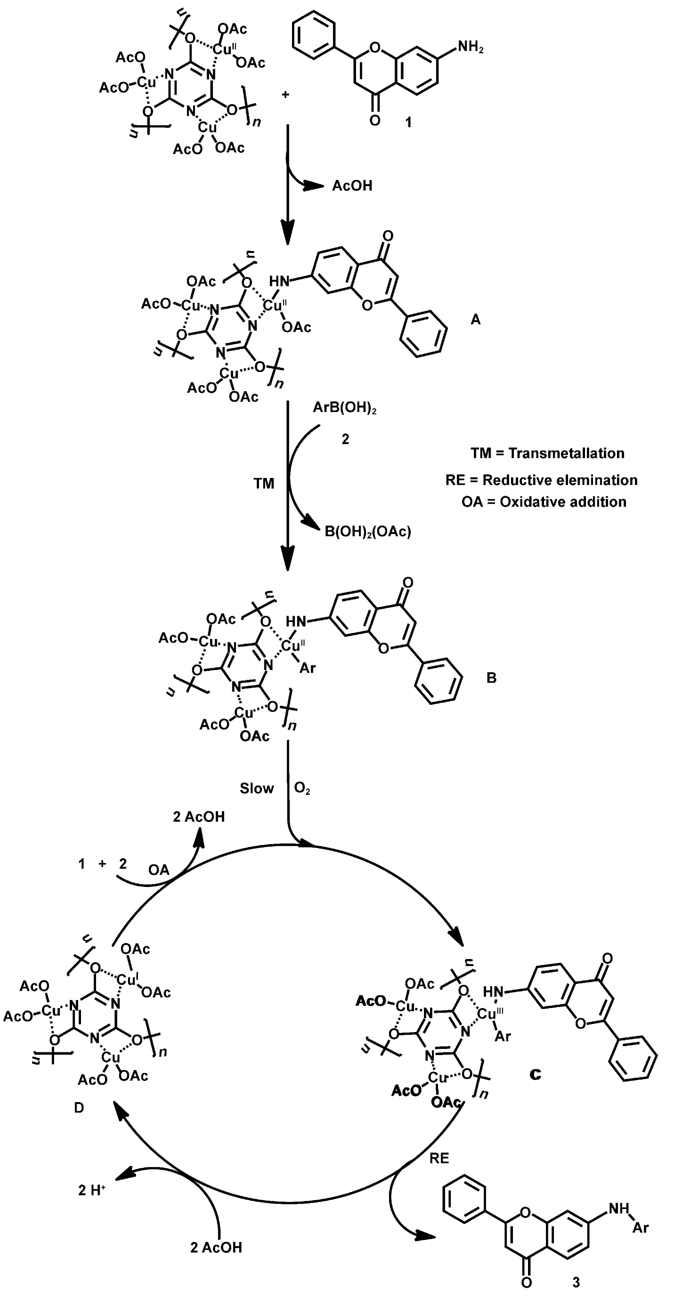
[a] Reaction conditions: 6-Aminoflavone (0.5 mmol), boronic acid (0.6 mmol) Cu/MCIP-1 (40 mg), NEt_3 (100 mol%), DCE (2 mL), O_2 balloon, RT; Yield based on 6-aminoflavone. [b] TON = turnover number.

Table 5. N-Arylation of 8-aminoquinoline with various arylboronic acids.[a]



Entry	8-Aminoquinoline (**1c**)	Arylboronic acid (**2a–2j**)	Products (**5**)	Yield [%]	TON[b]
1	**1c**	**2a**	**5a**	94	56
2	**1c**	**2b**	**5b**	93	55
3	**1c**	**2c**	**5c**	90	53
4	**1c**	**2d**	**5d**	88	52
5	**1c**	**2e**	**5e**	90	53
6	**1c**	**2f**	**5f**	84	50
7	**1c**	**2g**	**5g**	80	47
8	**1c**	3-CN-$C_6H_4B(OH)_2$ (**2h**)	**5h**	78	46
9	**1c**	3-NO_2-$C_6H_4B(OH)_2$ (**2i**)	**5i**	76	45
10	**1c**	2-Cl-5-OCH_3-$C_6H_4B(OH)_2$ (**2j**)	**5j**	58	34

[a] Reaction conditions: 8-Aminoquinoline (0.5 mmol), boronic acid (0.6 mmol), Cu/MCIP-1 (40 mg), NEt_3 (100 mol%), DCE (2 mL), O_2 balloon, RT; Yield based on 8-aminoquinoline. [b] TON = turnover number.



Scheme 2. Plausible mechanistic pathway for Chan–Lam N-arylations.

volves transmetalation of the arylboronic acid, **2**, with complex **A**, resulting in an arylated Cu^{II} complex, **B**. Complex **B** then undergoes oxidation to form a Cu^{III} species, **C**, which undergoes reductive elimination to form the Cu^{I} complex, **D**, and the N-arylated products. Subsequently, oxidative addition of **1** and **2** to the Cu^{I} complex, **D**, generates the Cu^{III} species, **C**, thereby propagating the Cu^{I}/Cu^{III} cycle.

As recyclability is important for industrial applications, the reuse performance of Cu/MCIP-1 was also investigated. In this context, the reusability of Cu/MCIP-1 was investigated in the Chan–Lam cross-coupling reaction under the optimized conditions, as given in Figure 12. After completion of the reaction, the products were extracted with CH_2Cl_2, dried with anhydrous sodium sulfate, and concentrated under reduced pressure. The recovered Cu/MCIP-1 was washed three times with CH_2Cl_2, and activated under vacuum at room temperature for 1 h. Only a marginal decrease in the activity of the catalyst was observed after four cycles.

To verify whether the catalyst is truly heterogeneous, or whether some metal-leached copper species is present in the filtrate, Sheldon's test[26] was performed. The reaction was carried out under the optimized conditions and the Cu/MCIP-1 catalyst was filtered from the reaction mixture at 67% yield of desired N-arylation product formation (Table 6). After removal of the Cu/MCIP-1 catalyst, the filtrate was stirred for a further four hours and no further increase in yield was observed. The absence of metal leaching was also confirmed by AAS analyses

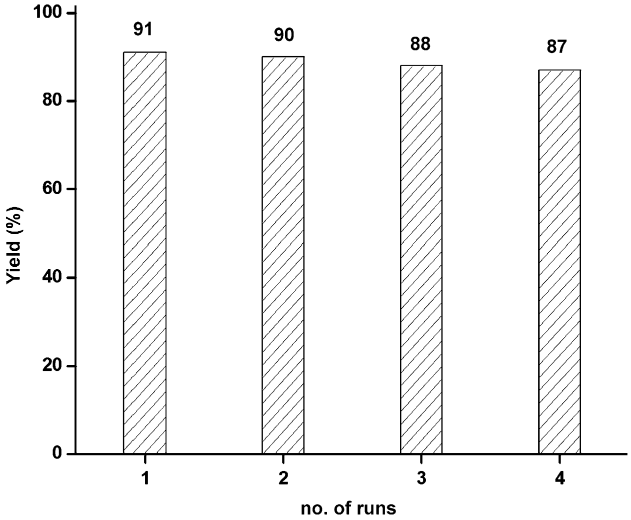


Figure 12. Reusability of Cu/MCIP-1 catalyst.

Table 6. Sheldon test.

Catalyst	Yield [%]		
	8 h	8, then 4 h	Reused catalyst
Cu/MCIP-1	67	67	91

Reaction conditions: 8-Aminoquinoline (0.5 mmol), boronic acid (0.6 mmol), Cu/MCIP-1 (40 mg), NEt_3 (100 mol%), DCE (2 mL), O_2 balloon, RT; yield based on 8-aminoquinoline.

and ICP-AES of the filtrate from the reaction mixture, and also of the filtrate from a stirred solution of Cu/MCIP-1 in DCE, under the same reaction conditions. This result was also further confirmed by SEM-EDX analysis. The SEM-EDX results suggested ≈ 2.53 and $\approx 2.50\%$ of copper metal was present in fresh and reused Cu/MCIP-1, respectively (see the Supporting Information, Figures S2, S3 and Tables S3, S4). These results demonstrate clearly that Cu/MCIP-1 is truly heterogeneous in nature.

To investigate whether any metal leaching did occur, the following control experiment was also performed. Cu/MCIP-1 (0.040 g) was added to a mixture of 7-aminoflavone (0.5 mmol), phenylboronic acid (0.6 mmol) and NEt_3 (100 mol%), in DCE (2 mL), and the mixture was stirred at room temperature for 12 h. After completion of the reaction, the reaction mixture was filtered. The filtrate, and reused Cu/MCIP-1 (dissolved in H_2SO_4), were analysed by AAS and ICP-AES. The results of these analyses showed that the copper concentration in the filtrate was below the detectable limit. In the reused Cu-MCIP-1 (dissolved in H_2SO_4), the copper concentration was found to be 2.54 mmol g^{-1} from AAS analysis and 2.59% from ICP-AES analysis. These results clearly show that that no leaching of copper takes place from the solid to the liquid phase. These results further prove that catalyst is heterogeneous in nature.

Conclusion

We have developed two new imine-functionalised MCIPs from relatively cheap starting materials and industrially important building blocks by Schiff-base chemistry. This copper-loaded MCIP-1 material showed excellent catalytic activity in Chan–Lam cross-coupling N-arylation under mild reaction conditions. In all cases, removal of the catalyst consists of a simple filtration. The catalyst is highly stable, shows no metal leaching and can be reused without loss of catalytic activity. To the best of our knowledge, the C–N bond of biologically active flavones was reported for the first time in a solid catalyst system. The observed results will provide further motivation for design and catalytic applications of this novel class of materials. Further studies of the applications of the MCIP-2 material are currently underway.

Experimental Section

Synthesis of MCIP-1

2,4,6-Tris(*p*-formylphenoxy)-1,3,5-triazine (TRIPOD) was prepared according to the published procedure.[27] A round-bottomed flask fitted with a condenser was charged with TRIPOD (2 mmol) and *p*-phenylenediamine (3 mmol) in THF and mesitylene (1:1, 30 mL), at 120 °C for 72 h. After the formation of a solid, the reaction mixture was filtered and the solid washed with methanol, acetone and CH_2Cl_2 (each solvent 100 mL) to remove unreacted aldehyde and diamine. Finally, the product was dried under vacuum to obtain the desired solvent-free material with 85% yield. Elemental analysis calcd (%) for $C_{33}H_{24}N_6O_3$: C 71.73, H 4.38, N 15.20; found C 69.95, H 4.88, N 13.94.

Synthesis of catalyst (Cu/MCIP-1)

In a typical experiment, a mixture of copper acetate (40 mg) in CH_2Cl_2 and MCIP-1 material (500 mg) was stirred at room temperature for 48 h. After the formation of a greenish-brown solid, the reaction mixture was filtered and the solid was washed with methanol, acetone and CH_2Cl_2 to remove any unreacted copper acetate. The solid was dried under vacuum to obtain the designed solvent-free catalyst. Powder XRD, EDX and AAS, ICP-AES and X-ray photoelectron spectroscopy (XPS) analyses of the catalyst suggested the presence of Cu^{II} metal. The stability of the catalyst was confirmed by TGA. The Cu/MCIP-1 material was dissolved in H_2SO_4, diluted and analysed with AAS. The results show that copper content in Cu/MCIP-1 is 2.58 mmol g^{-1}. After the fourth cycle, the copper content in Cu-MCIP-1 (dissolved in H_2SO_4) was found to be 2.54 mmol g^{-1}.

Cu/MCIP-1-catalysed Chan–Lam cross-coupling N-arylation

In a typical reaction, a mixture of Cu/MCIP-1 (40 mg), amines (0.5 mmol) and arylboronic acids (0.6 mmol) was added to 2 mL of DCE under an oxygen atmosphere (balloon), at room temperature for 16 h. The progress of the reaction was monitored by TLC analysis. After completion of the reaction, the reaction mixture was treated with CH_2Cl_2 (10 mL), the catalyst was removed by filtration and the filtrate was extracted with distilled water. The organic layer was then dried over anhydrous sodium sulfate. After the organic solvent was evaporated under vacuum, the residues were purified by column chromatography silica gel (60–120 mesh), affording the corresponding pure N-arylated products. The recovered catalyst was thoroughly washed with CH_2Cl_2 and activated under vacuum at room temperature for 1 h, before being reused.

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Keywords: cross-coupling · copper · covalent imine polymers · heterogeneous catalysts · mesoporous materials · Schiff bases

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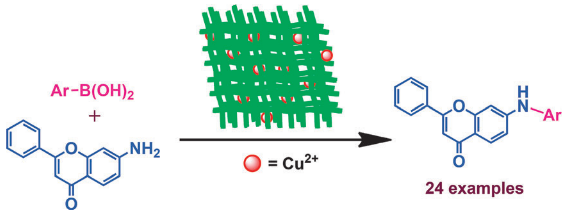
FULL PAPER



Immobilising Copper: A novel mesoporous covalent imine polymeric (MCIP) material, involving simple Schiff-base chemistry, is reported. This highly functionalised nitrogen-rich material acts as a good support for immobilising Cu^{II} ions, exhibiting excellent catalytic activity in promoting the Chan–Lam cross-coupling reaction between biologically active amines and arylboronic acids (see scheme).

Covalent Imine Polymers

*P. Puthiaraj, K. Pitchumani**

■■–■■

Triazine-Based Mesoporous Covalent Imine Polymers as Solid Supports for Copper-Mediated Chan–Lam Cross-Coupling N-Arylation Reactions