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Graphical Abstract

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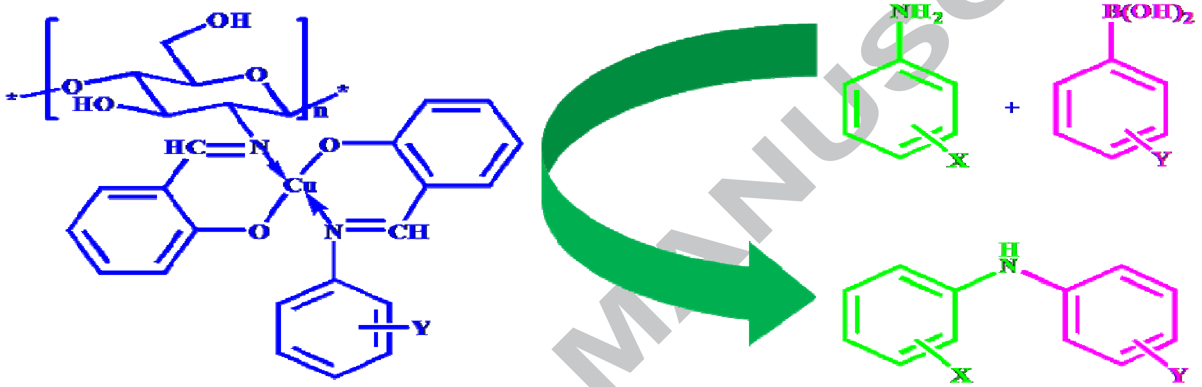

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Synthesis and development of Chitosan anchored Copper(II) Schiff base complexes as heterogeneous catalysts for *N*-arylation of amines

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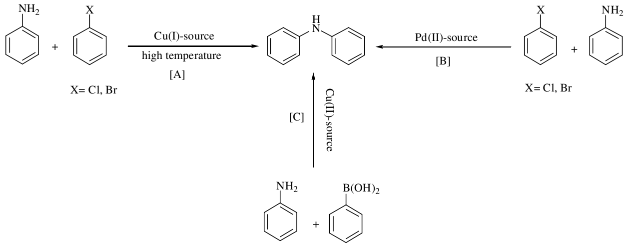
ABSTRACT

The Chitosan anchored Cu(II) Schiff base complexes (C_1 to C_3) have been synthesized and characterized by FTIR, UV, FE-SEM, EDAX, TGA, AAS and elemental analysis. These complexes have been found to be efficient and recyclable heterogeneous catalysts for Chan-Lam C-N coupling reaction of various aromatic/aliphatic amines with arylboronic acid under mild reaction conditions. These complexes can be easily filtered out from the reaction medium and reused up to five times without significant loss of catalytic activity.

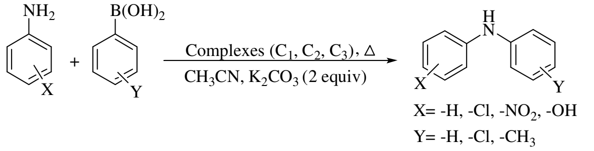
Introduction

The *N*-arylation of amines is currently an active area of research in organic synthesis due to its applications in the synthesis of a variety of biologically active compounds, agrochemicals, HIV-1 protease inhibitors and in material science.[1-2] Due to wide range of applications of these compounds, several protocols for C-N bond formation have emerged over the years. Mainly, three important protocols for C-N coupling reactions have been reported to-date namely, Ullmann coupling reaction[3], Buchwald-Hartwig amination[4] and Chan-Lam couping[5] (Scheme 1). Ullmann-type protocol involves the coupling of amines with aryl halides in the presence of Cu(I) source.[6] However, this protocol suffers from certain disadvantages, such as harsh reaction conditions, high temperature (~150-200℃), moderate yield, use of stochiometric amount of copper reagent and formation of by-products. In order to circumvent these drawbacks, use of copper(I) salts with several ligands such as 1,10-phenanthroline[7], L-proline[8], (±)-trans-1,2-cyclohexyldiamine[9] etc were introduced. However, none of the modifications could address the problems of high temperature and prolong reaction time.[10] Considering the drawbacks of this reaction, Buchwald and Hartwig, in 1994, devised a new protocol for the coupling of amines with aryl halides for C-N bond formation in the presence of catalytic amount of Pd(II).[11]Although palladium compounds were used with spectacular success as catalysts for C-N bond formation[4], these catalysts were unable to catalyze the coupling reaction of an electron rich or *o*-substituted aryl halides with aromatic amines. However, spectacular success has been achieved using very small loading of Pd (ca 0.01 mol%) in Buchwald-Hartwig amination reaction. Therefore, it mitigates the cost factor. Subsequently, in 1998, Chan and Lam reported a new protocol for C-N bond formation by the arylation of amines with arylboronic acid at room temperature in the presence of Cu(II) source.[12,13] This protocol has several advantages over the classical Ullmann coupling reaction and Pd-catalyzed Buchwald-Hartwig amination. It involves mild reaction conditions and use of weak bases. The low toxicity, high thermal stability and structural diversity of arylboronic acid were found to be inherent advantages over the use of aryl halides. The protocol did not require any ligands. Later on, the protocol has been modified by the use of various additives, such as TEMPO, pyridine-N-oxide and molecular oxygen.[14] Recently, Bora and co-workers developed a Cu(II)-Salen type complex for the *N*-arylation of anilines and imidazole with arylboronic acids at room temperature.[15] However, these protocols are homogeneous in nature, where an efficient separation and subsequent recycling of the homogeneous catalyst remains a challenge and an economic concern. Heterogeneous catalysis is of importance in the chemical industries due to easy separable and reuse upto several times.[16] Here in, our interest lies in the development of novel heterogeneous catalyst for C-N coupling reactions of amines with arylboronic acid under milder reaction conditions.

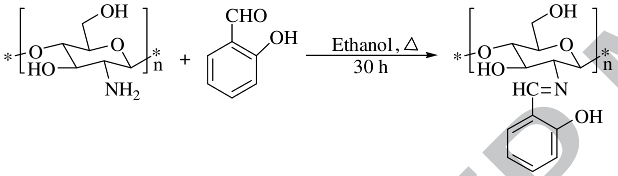
Recently, Chitosan has emerged as a novel support for anchoring transition metal complexes. It is the second most abundant natural co-polymer, obtained by alkaline deacetylation of chitin.[17] The renaissance of interest in the Chitosan arises mainly due to the presence of free amino group, which can easily be subjected to variety of chemical modifications such as carboxymethylation, acylation, sulfation, enzymatic substitution, metal chelation, cyanoethylation, nitration, phosporylation and Schiff's base formation.[18-21] Chitosan anchored metal Schiff base complexes have been reported as good catalysts for cyclopropanation[22], olefin oxidation[23] and C–C coupling reactions.[24] Importantly, the Chitosan anchored Metal Schiff base complexes have been found to be more potent than the Chitosan metal complexes only.[25] Prompted by these reports, we herein, describe the synthesis and development of Chitosan anchored Copper(II) Schiff base complexes as heterogeneous catalysts for Chan-Lam coupling reactions (**Scheme 2**).



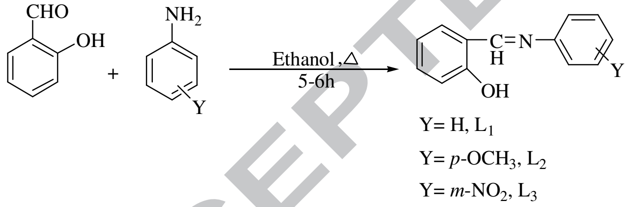
Scheme 1. Schematic representation of [A] Ullmann coupling reaction, [B] Buchwald-Hartwig amination reaction, and [C] Chan-Lam coupling reaction.



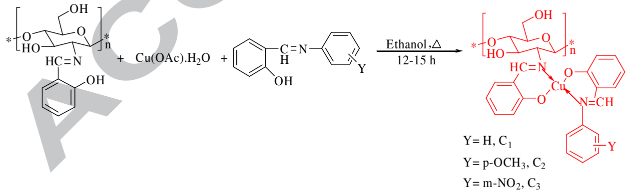
Scheme 2. Chan-Lam coupling of N-aryl/alkyl amines with different arylboronic acids in presence of a base and catalyst.



(3a) Schiff base of Chitosan (L)



(3b) Schiff base Ligands (L_1, L_2, L_3)



(3c) Complexes (C_1, C_2, C_3)

Scheme 3. General procedure: (a) Schiff base of Chitosan (L), (b) Schiff base Ligand (L_1, L_2, L_3), and (c) Chitosan anchored Cu(II) Schiff base complexes (C_1, C_2, C_3)

Results and Discussion

Schiff base of Chitosan (L) was prepared by the reaction of Chitosan and salicyaldehyde in ethanol under reflux (Scheme 3a). Schiff base Ligands (L_1, L_2, and L_3) were prepared by reacting salicyaldehyde and substituted aniline under reflux (Scheme 3b). The Chitosan anchored Cu(II) Schiff base complexes (C_1, C_2, C_3) were prepared by the reaction of Schiff base of Chitosan (L) with Cu(OAc).H_2O and Schiff base (L_1 or L_2 or L_3) in ethanol under reflux for 12-15hr (Scheme 3c). The structural features of Chitosan, its Schiff base (L) and complexes were elucidated by FTIR, UV, FE-SEM, EDAX, TGA, AAS and elemental analyses.

The FTIR data of Chitosan, its Schiff base (L), Schiff base ligands (L_1 to L_3) and complexes (C_1 to C_3) are given in Table 1. The representative FTIR spectra of Chitosan, its Schiff base (L), complex (C_3) and Schiff base (L_3) are shown in Figure 1. A comparison of IR spectra of Chitosan and its Schiff base (L), indicates the absence of -NH_2 band and presence of two additional bands at 1632 cm^{-1}and 1212 cm^{-1}, which were assigned to the stretching modes of azomethine (C=N) group and phenolic (C-O) groups, respectively. The FTIR studies indicate the formation of Schiff base of Chitosan (L). The FTIR spectra of free Schiff base (L_3), indicates peaks at 1622 cm^{-1} and 1520 cm^{-1} characteristics of azomethine (C=N) group and aromatic –NO_2 group, respectively, and confirm the formation of Schiff base (L_3). However, the IR spectra of complex (C_3) indicate the presence of few additional bands at 1614 cm^{-1} and 1523 cm^{-1}. The shifting of υ(C=N) to lower wave number (ca.~10-15 cm^{-1}) confirms the coordination of Cu(II) metal ion with azomethine nitrogen atom of the Schiff's base.[26]

Table 1. Selected FTIR data of Chitosan, its Schiff base (L), Schiff base ligands (L_1 to L_3) and complexes (C_1 to C_3).

COMPOUNDS	$\upsilon(NH_2)$	$\upsilon(OH)$	$\upsilon(C=N)$	$\upsilon(C-O)$	$\upsilon(M-N)$
CHITOSAN	1653	3163	-	-	-
(L)	-	3428	1632	1212	-
L_1	-	3426	1635	1262	-
L_2	-	3320	1630	1215	-
L_3	-	3148	1622	1267	-
C_1	-	3442	1622	-	439
C_2	-	3440	1622	-	438
C_3	-	3155	1614	-	455

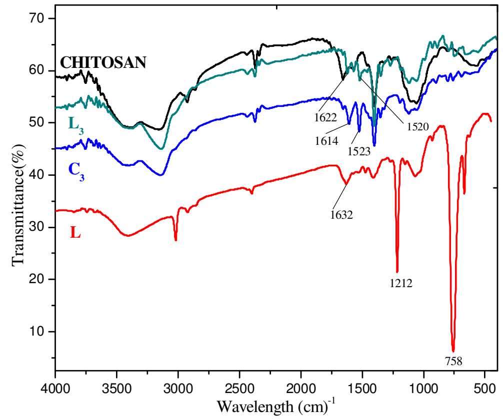


Figure1. FT-IR spectra of (a) Chitosan, (b) L, (c) C_3, (d) L_3

The UV-Visible spectra of the Schiff base of Chitosan (L) and its complex (C_3) are depicted in Figure 2. The observed λ_{max}

value from electronic spectra of the complexes is used to predict the geometry around the central metal ion. The electronic spectra of (L) show two significant bands below 400 nm. This might be due to n-π* and π-π* transition of azomethine C=N group and aromatic C=C group of benzene ring, respectively. The electronic spectra of complexes observed slight shift in the position and intensity of these bands. This might be due to coordination of metal ion with ligand. The charge transfer transition from metal to ligand may also contribute to these absorption bands below 400 nm in the complexes.[27] The electronic spectra of the complexes show an additional band between 500-600 nm, which is the characteristic band, arises from d-d transitions. The electronic spectra of the complex (C_3) show only one broad band ~535 nm, which suggest the square planar geometry of the complex. Generally, Copper(II) square planar complexes are expected to show three spin allowed transitions namely, ${}^2B_{1g} \rightarrow {}^2A_{1g}$ (dx^2-$y^2 \rightarrow dz^2$), ${}^2B_{1g} \rightarrow {}^2B_{2g}$ (dx^2-$y^2 \rightarrow dxy$) and ${}^2B_{1g} \rightarrow {}^2E_g$ (dx^2-$y^2 \rightarrow dxz, dyz$) and dx^2-y^2 in a ground state.[28] These three bands may overlap inside the broad band appeared in complexes due to similar energy of these transitions.

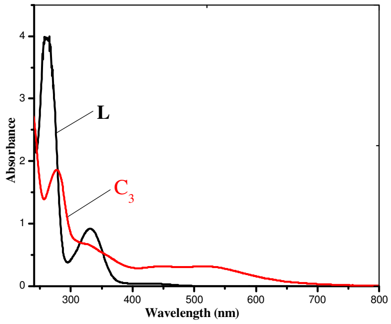


Figure 2. UV- Visible spectra of Schiff base of Chitosan (L) and Complex (C_3)

The FE-SEM micrographs of Chitosan, its Schiff base (L) and complexes (C_1 to C_3) are depicted in Figure 3. FE-SEM image of Chitosan displays the smooth and even surface. However, the FE-SEM micrograph of (L) indicates the rough surface and this might be due to the chemical modification of Chitosan through the condensation of salicyaldehyde with free amino group of Chitosan. The FE-SEM micrograph of complexes (C_1 to C_3) also indicates the rough surface and this might be due to the imprinting of metal ion on the modified Chitosan.[29] Energy dispersive X-ray spectroscopy (EDAX) analysis data for the Chitosan, its Schiff base ligand (L) and complexes (C_1 to C_3) are given in Figure 4. The EDAX spectra of complexes show the presence of copper in the complex.

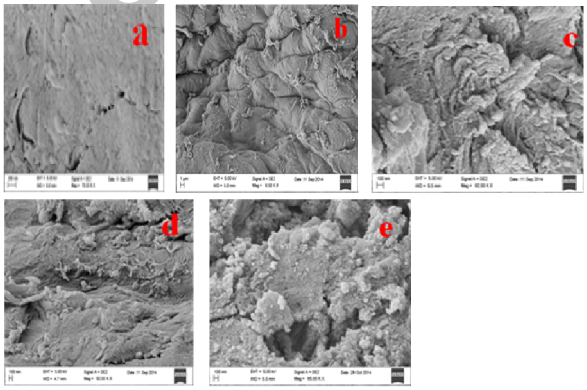


Figure 3. FE-SEM micrographs of (a) Chitosan, (b) Schiff base of Chitosan (L), (c) Complex (C_1), (d) Complex (C_2) and (e) Complex (C_3)

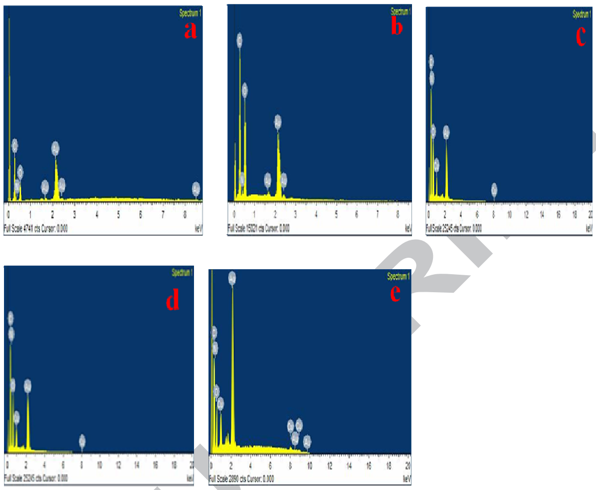


Figure 4. EDAX analysis of (a) Chitosan, (b) Schiff base of Chitosan (L), (c) Complex (C_1), (d) Complex (C_2) and (e) Complex (C_3)

The TGA study is used to explain the thermal stability and mode of decomposition of ligand and complexes. The TGA thermogram of (L) and complexes (C_1 to C_3) are depicted in Figure 5. The TGA thermogram of L shows two mass loss stages. The initial mass loss (~13%) up to 100 ℃ may be due to hygroscopic nature of the Chitosan unit. The maximum and significant second mass loss (~49%) occurs at higher temperature (325-350°C) and can be attributed to the dehydration, depolymerisation along with decomposition of acetylated and deacetylated unit of Chitosan.[30] However, the TGA thermogram of complexes (C_1 to C_3) display first mass loss (~8%), (~12%) and (~5%), respectively, ~100 ℃ is due to physically absorbed water. The second mass loss (~34%), (~44%) and (~29%), respectively, occur at (260-280°C), (300-330°C) and (280-300 ℃), respectively. This might be due to the introduction of a metal ion on polymer matrix, which obstructs the chain packing and cause loosening of the packed structure. Thus (L) decomposes at higher temperature and thermally more stable than the complexes (C_1 to C_3).

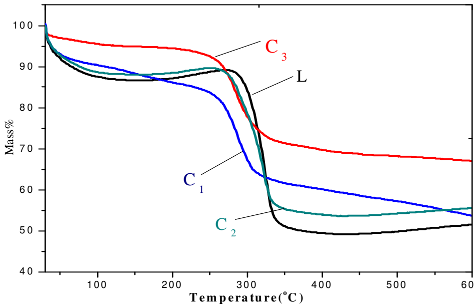


Figure 5. TGA thermogram of Schiff base of Chitosan (L) and Complexes (C_1 to C_3)

The elemental analysis data of Chitosan and its Schiff base (L) are used to calculate the degree of substitution (DS) in Chitosan. It is apparent from the elemental analysis (Table 2) that the observed micro analytical data (C, H and N) of the compounds are closely comparable to the theoretical data. The DS of Schiff base Ligand (L) to $-NH_2$ group on Chitosan was estimated by the equation, proposed by Inukai et al.[31]

$$DS = \frac{a(C/N)m - (C/N)o}{n}$$

Where (C/N)m is the C/N ratio of modified Chitosan, (C/N)o is the ratio of original Chitosan and 'a' and 'n' are the number of nitrogen and carbon introduced after Schiff base modification, respectively. C/N ratio of Chitosan and its Schiff base Ligand (L) are calculated as 5.22 and 11.81, respectively. The calculated DS for Chitosan is 0.65.

Table 2. Elemental analysis data of Chitosan, Schiff base ligand (L) and complexes (C_1 to C_3).

Compound	Calculated (%) (Found) (%)			
	C	H	N	Cu
Chitosan	44.72 (44.80)	6.38 (6.32)	8.69 (8.54)	-
L	58.86 (58.89)	5.70 (5.21)	5.28 (4.93)	-
C_1	62.22 (61.35)	5.40 (5.38)	4.89 (4.23)	10.97 (10.36)
C_2	61.12 (60.99)	5.46 (5.19)	4.60 (4.38)	10.43 (10.31)
C_3	59.59 (59.16)	5.35 (5.21)	4.62 (4.80)	10.79 (10.65)

Based upon AAS analysis, the copper content are found to be (21 mg), (23 mg) & (24 mg) per litre for C_1, C_2 & C_3 complexes, respectively, against calculated value of (26 mg), (27 mg) & (30 mg), respectively.

After full characterization of the complexes, the catalytic activity of the complexes (C_1 to C_3) was explored for Chan-Lam C-N coupling reaction of amines with arylboronic acid. In order to optimize conditions, the reaction of aniline (1mmol) and phenylboronic acid (2mmol) was chosen as a model reaction in acetonitrile using K_2CO_3 as a base. When the reaction was carried out without catalyst at room temperature for 48 hr (Table 3, entry 1), no product was isolated. The same reaction under reflux also did not afford any product (Table 3, entry 2). The reaction was also performed in the presence of neat Chitosan (50 mol% and 100 mol%) in acetonitrile at room temperature and under reflux. No trace of product could be isolated from the reaction mixture (Table 3, entries 3-6). It clearly indicates that Chitosan itself does not catalyze the reaction. The reaction was performed in the presence of the complex (C_1) at room temperature (Table 3, entry 7), no product was isolated. Subsequently, the reaction was performed in presence of 3.5 mol% of the complex (C_1, C_2, C_3), respectively, under reflux, to afford the desired products in 63%, 54% and 71% yield, respectively (Table 3, entries 8-10). Among the three complexes (C_1 to C_3), C_3 afforded good yield product under the reflux. To optimize the catalyst loading, the reaction was carried out in the presence of 8 mol% of the complex (C_3) instead of 3.5 mol%, the yield of the product was increased from 71 to 85% (Table 3, entry 11). However, when the catalyst load was increased to 12 mol%, no significant improvement in the yield was observed (Table 3, entry 12).

Table 3. Optimization of the catalysts (C_1, C_2, C_3) for Chan-Lam coupling reaction of aniline (1mmol) and phenylboronic acid (2mmol) in acetonitrile using K_2CO_3 as a base.

Entry	Catalyst	Catalyst Load (mol%)	Time (h)	Temp (°C)	Yield (%)[a]
1	-	-	48	rt	-
2	-	-	48	reflux	-
3	Chitosan	50	48	rt	-
4	Chitosan	50	36	reflux	-
5	Chitosan	100	36	rt	-
6	Chitosan	100	36	reflux	-
7	C_1	3.5	36	rt	-
8	C_1	3.5	24	reflux	63
9	C_2	3.5	24	reflux	54
10	C_3	3.5	24	reflux	71
11	C_3	08	09	reflux	85
12	C_3	12	10	reflux	83

[a]Isolated yield after work up

In order to find out the best solvent for the reaction (Table 4, entry 1-5), the reaction was conducted in a number of solvents, e.g. H_2O, CH_3CN, $CH_3COOC_2H_5$, CH_3OH and C_2H_5OH. Out of these solvents, H_2O was found to be the worst solvent (Table 4, entry 1). On the other hand, CH_3CN was found to be the best solvent (Table 4, entry 2). The other solvent such as, $CH_3COOC_2H_5$, CH_3OH and C_2H_5OH gave poor yields of 53%, 35% and 38%, respectively (Table 4, entries 3-5).

Table 4. Study of solvent effect on the coupling reaction of aniline (1mmol) with phenylboronic acid (2mmol) in presence of optimized catalyst (C_3) (8 mol%).

Entry	Solvent	Time (h)	Yield (%) [a]
1	H_2O	48	-
2	CH_3CN	09	85
3	$CH_3COOC_2H_5$	19	53
4	CH_3OH	36	35
5	CH_3CH_2OH	36	38

[a]Isolated yield after work up

In order to find out the best base, the reaction was carried out with different bases such as K_2CO_3, Na_2CO_3, $NaHCO_3$ and Cs_2CO_3 (Table 5, entry 1-7). The best yield (85%) was obtained in case of 2 equivalent of K_2CO_3 (Table 5, entry 2). The reaction did not afford any product in the absence of base (Table 5, entry 1). The reaction was also carried out with 1.0 and 1.5 equiv of K_2CO_3, to afford 61% and 73% yields, respectively (Table 5, entry 6-7). However, $NaHCO_3$ gave only trace mount of product (Table 5, entry 4). On the other hand, Cs_2CO_3 gave only 45% (Table 5, entry 5) within 24 h. Therefore, K_2CO_3 was found to be the best base for the reaction.

Table 5. Screening of base for the coupling reaction of aniline (1mmol) with phenylboronic acid (2mmol).

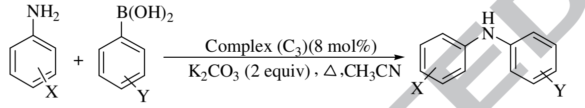
Entry	Base (equiv)	Time (h)	Yield (%)[a]
1	Without base	30	-
2	K_2CO_3 (2)	09	85
3	Na_2CO_3 (2)	36	29
4	$NaHCO_3$ (2)	36	Trace
5	Cs_2CO_3 (2)	22	45
6	K_2CO_3 (1.0)	19	61
7	K_2CO_3 (1.5)	15	73

[a]Isolated yield after work up

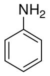
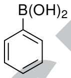
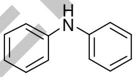
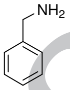
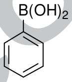
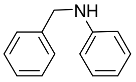
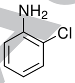
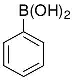
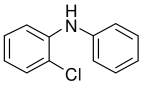
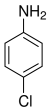
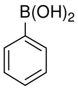
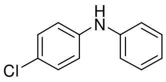
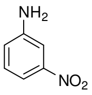
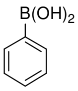
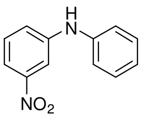
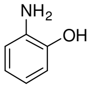
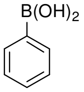
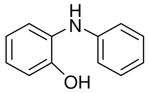
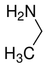
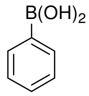
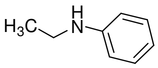
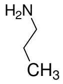
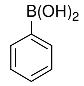
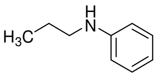
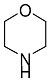
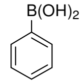
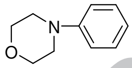
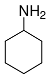
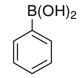
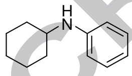
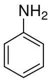
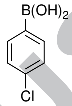
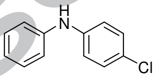
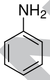
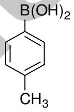
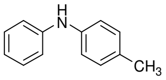
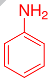
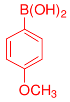
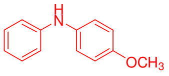
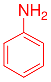
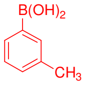
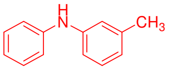
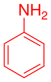
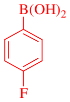
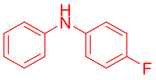
With the optimized conditions in our hand, we further extend the scope of the reaction to various aromatic and aliphatic amines with phenylboronic acid bearing either electron-donating group (EDG) or electron-withdrawing group (EWG). The results obtained, are summarized in (Table 6, entry 1-15). The products were obtained as colourless/yellow oil to colourless/yellow/red crystalline solids, soluble in common organic solvents such as $CHCl_3$, CH_3OH and C_2H_5OH and were fully characterized by ^1H NMR and Mass spectra. The data were in close agreement with the literature values.[32]

Aliphatic amines were found to be comparatively less reactive and took longer reaction time than aromatic amines (Table 6, entries 7, 8). The aromatic amines bearing EWG such as $-NO_2$, and -Cl, afforded corresponding diaryl amines in high isolated yields (72 - 85%, Table 6, entries 3-5). The *meta*-position of EWG in amine (Table 6, entry 5) gave higher yield than corresponding *ortho*- and *para*-positions (Table 6, entries 3, 4). However, the aromatic amines bearing –OH afforded corresponding product in high yield (Table 6, entry 6). Benzylamine, cyclohexylamine and morpholine gave yields (71%, 72% and 84%), respectively (Table 6, entries 2, 9 and 10). Electron rich and electron withdrawing group at *meta* and *para*-position of the phenylboronic acid were also tested. The electron donating group enhanced the yield while low yields were obtained with electron withdrawing group (Table 6, entry 11-15). The plausible reason for such substituents effect is that the oxidation of Cu(II) complexes, bearing electron withdrawing substituent, to Cu(III) is less facile as compared to electron donating substituents. The presence of electron withdrawing groups either on aryl boronic acids or amines retards the formation of putative Cu(III)-intermediate and hence influence the yield of the products[12,33].

Table 6. The reaction of various aromatic and aliphatic amines with phenylboronic acid under optimized reaction conditions



X= -H, -Cl, $-NO_2$, -OH
Y= -H, -Cl, $-CH_3$

Ent -ry	Amines	Aryl boronic acid	Products[a]	Time (h)	Yeild (%)[b]
1	 **1a**	 **2a**	 **3a**	9	85
2	 **1b**	 **2a**	 **3b**	12	71
3	 **1c**	 **2a**	 **3c**	18	72
4	 **1d**	 **2a**	 **3d**	18	74
5	 **1e**	 **2a**	 **3e**	15	82
6	 **1f**	 **2a**	 **3f**	12	82
7	 **1g**	 **2a**	 **3g**	24	66
8	 **1h**	 **2a**	 **3h**	24	69
9	 **1i**	 **2a**	 **3i**	11	84
10	 **1j**	 **2a**	 **3j**	11	72
11	 **1k**	 **2b**	 **3k**	18	77
12	 **1l**	 **2c**	 **3l**	14	81
13	 **1m**	 **2d**	 **3m**	14	80
14	 **1n**	 **2e**	 **3n**	13	78
15	 **1o**	 **2f**	 **3o**	13	74

[a] Purity determined by TLC & ^1H NMR
[b] Isolated yield after work up

Furthermore, the recyclability of Complex (C_3) was checked by choosing the reaction of aniline and phenylboronic acid as a model reaction. After completion of reaction, the catalyst could easily be separated out by filtration from the aqueous layer, and then washed with diethyl ether for the subsequent batch reaction. It is apparent from Figure 6 that the complex (C_3) could be re-used up to five cycles with no significant loss of catalytic activity.

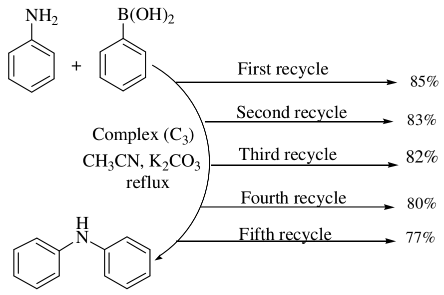


Figure 6. Recyclability of the catalyst

Conclusion

In summary, Schiff base of Chitosan (L), Schiff base ligands (L_1, L_2, and L_3) and the resultant Chitosan anchored Copper(II) Schiff base complexes (C_1, C_2, and C_3) have been synthesized and characterized by various spectroscopic and instrumental techniques. All the three complexes (C_1 to C_3) were found to be good heterogeneous catalyst for Chan-Lam C-N coupling reactions. However, the best results were obtained with complex C_3. The complex C_3 contains an electron withdrawing NO_2 group which presumably enhances the Lewis acidity of the complex. The novelty of the work is that the catalyst can be easily filtered out and reused at least for five times with no significant loss of the catalytic activity.

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References

1. (a) Negwer, M. In *Organic-Chemical Drugs and their Synonyms (An International Survey)*, seventh ed.; Akademie Verlag GmbH: Berlin, Germany. **1994**; (b) Shirota, Y. *J. Mater. Chem.* **2000**, 10, 1-25; (c) Barlow, S.; Marder, S. R. *Adv. Funct. Mater.* **2003**, 15, 517-518; (d) Tu, S.; Xu, L. H.; Ye, L. Y.; Wang, X.; Sha, Y.; Xiao, Z. Y. *J. Agrio. Food Chem.* **2008**, 56, 5247-5253; (e) Goodson, F. E.; Hartwig, J. F. *Macromolecules* **1998**, 31, 1700-1703; (f) Goodson, F. E.; Hauck, S. I.; Hartwig, J. F. *J. Am. Chem. Soc.* **1999**, 121, 7527-7530; (g) Naya, L.; Larrosa, M.; Rodriguez, R.; Cruces, J. *Tetrahedron Lett.* **2012**, 53, 769-772.

2. (a) Hong, Y.; Senanayake, C. H.; Xiang, T.; Vandenbossche, C. P.; Tanoury, G. J.; Bakale, R. P.; Wald, S. A. *Tetrahedron Lett.* **1998**, *39*, 3121-3124; (b) Buckingham, J. B. *In Dictionary of Natural Products*; CRC Press, **1994**, 1; (c) Craig, P. N. *In Comprehensive Medicinal Chemistry*; Drayton, C. J., Ed.; Pergamon Press: New York, **1991**, Vol. 8; (d) Ley, S. V.; Thomas, A. W. *Angew. Chem. Int. Ed.* **2003**, *42*, 5400; (e) Wiglenda, T.; Gust, R. *J. Med. Chem.* **2007**, *50*, 1475.

3. (a) Ullmann, F. *Ber. Dtsch. Chem. Ges*. **1903**, 36, 2382–2384; (b) Goodbrand, H. B.; Hu, N-X. *J. Org. Chem.* **1999**, *64*, 670-674; (c) Ullmann, F. Chem. Ber. **1904**, *37*, 853-854.

4. (a) Guram, A. S.; Buchwald, S. L. *J. Am. Chem. Soc.* **1994**, 116, 7901–7902; (b) Paul, F.; Patt, J.; Hartwig, J. F. *J. Am. Chem. Soc.* **1994**, 116, 5969–5970; (c) Hartwig, J. F. *Angew. Chem. Int.* Ed. **1998**, 37, 2046–2067; (d) Kiyomori, A.; Marcoux, J-F.; Buchwald, S. L. *Tetrahedron Lett.* **1999**, 40, 2657; (e) Wolfe, J. P.; Wagaw, S.; Marcoux, J. F.; Buchwald, S. L. *Acc. Chem. Res*. **1998**, 31, 805–818.

5. (a) Chan, D. M. T.; Monaco, K. L.; Wang, R.-P.; Winters, M. P. *Tetrahedron Lett.* **1998**, 39, 2933-2936. (b) Lam, P. Y. S.; Clark, C. G.; Saubernt, S.; Adams, J.; Winters, M. P.; Chan, D. M. T.; Combs, A. *Tetrahedron Lett*. **1998**, 39, 2941-2944; (c) Lam, P. Y. S.; Vincent, G.; Bonne, D.; Clark, C. G. *Tetrahedron Lett.* **2003**, 44, 4927; (d) Evans, D. A.; Katz, J. L.; West, T. R. *Tetrahedron Lett*. **1998**, 39, 2937-2940; (e) Singh, K. N.; Raghuvanshi, D. S.; Gupta, A. K. *Org. Lett*. **2012**, 14 (17), 4326-4329.

6. Ullmann, F.; Illgen, E. *Ber. Dtsch. Chem. Ges*. **1914**, 47, 380–383

7. Tang, B.; Guo, S.; Zhang, M.; Li, *J. Synthesis* **2008**, 1707- 1716.

8. Chouhan, G.; Wang, D.; Alper, H. *Chem. Commun.* **2007**, 4809–4811.

9. Antilla, J. C.; Klapars, A.; Buchwald, S. L. *J. Am. Chem. Soc*. **2002**, 124, 11684–11688.

10. Rao, R. K.; Naidu, A. B.; Jaseer, E. A.; Sekar, G. *Tetrahedron* **2009**, 65, 4619-4624.

11. (a) Buchwald, S. L. *Angew. Chem. Int*. Ed. **2008**, 47, 6338; (b) Hartwig, J. F. Acc. Chem. Res. **2008,** 41, 1534; (c) Shen, Q.; Shekhar, S.; Stambuli, J. P.; Hartwig, J. F. *Angew. Chem. Int.* Ed. **2005**, 44, 1371–1375; (d) Hartwig, J. F. *Synlett.* **2006**, 1283; (e) Surry, D. S.; Buchwald, S. L. *Angew. Chem. Int*. Ed. **2008**, 47, 6338; (f) Surry, D. S.; Buchwald, S. L. *Chem. Sci.* **2011**, 2, 27-50; (g) Tardiff, B. J.; Mc Donald, R.; Ferguson, M. J.; Stradiotto, M. J. *Org. Chem.* **2012**, 77, 1056-1071; (h) Meiries, S.; Speck, K.; Cordes, D. B.; Slawin, A. M. Z.; Nolan, S. P. *Organometallics* **2013**, 32, 330-339.

12. (a) Rao, K. S.; Wu, T.-S. *Tetrahedro*n **2012**, 68, 7735-7754.

13. (a) Lam, P. Y. S.; Vincent, G.; Clark, C. G.; Deudon, S.; Jadhav, P. K. *Tetrahedron Lett.* **2001**, 42, 3415-3418; (b) For a recent review of Chan–Lam coupling, see: Qiao, J. X.; Lam, P. Y. S. *Synthesis* **2011**, 829–856; (c) Antilla, J. C.; Buchwald, S. L. *Org. lett.* **2001**, 3, 2077-2079; (d) Mondal, M.; Sarmah, G.; Gogoi, K.; Bora. U. *Tetrahedron Lett.* **2012**, 53, 6219-6222.

14. (a) Lam, P. Y. S.; Vincent, G.; Bonne, D.; Clark, C.G. *Tetrahedron Lett*. **2003**, 44, 4927-4931; (b) Inamoto, K.; Nozawa, K.; Kadokawa, J.; Kondo, Y. *Tetrahedron Lett.* **2012**, 68, 7794-7798; (c) Collman, J. P.; Zhong, M.; Zhang, C.; Costanzo, S. J. *Org. Chem.* **2006**, 66, 7892-7897.

15. Gogoi, A.; Sarmah, G.; Dewan, A.; Bora, U. *Tetrahedron Lett*. **2014**, 55, 31-35.

16. (a) Kumari, S.; Shekhar, A.; Mungse, H. P.; Khatri, O. P.; Devendra D. D. *RSC Adv.* **2014**, 4, 41690–41695; (b) Kumari, S.; Shekhar, A.; Devendra D. D. *RSC Adv.* **2014**, 4, 61187–61192.

17. (a) Muzzarelli, R. A. A. Chitin. *Pergamon Press, Oxford.* **1977**, 83-252; (b) Rinaudo, M. Chitin and chitosan: Properties and applications. *Progress in*

Polymer Science **2006**, 31(7), 603–632; (c) Mathur, N. K; Narang, C. K. *J. Chem. Edu.* **1990**, 67(11), 938.

18. (a) Reddy, K. R.; Rajgopal, K.; Maheshwari, C. U., Katam, M. L. *New j. Chem.* **2006**, 30, 1549-1552; (b) Moore, G. K.; Roberts, G. A. F. *Int. J. Biol. Macromol.* **1981**, 3, 337-340.(c) Muzzarelli, R.; Baldassarre, V.; Conti, F.; Ferrara, P.; Biagini, G.; Gazzanelli, G.; Vasi, V. *Biomaterials* **1988**, 9, 247–252; (d) Binsu, V. V.; Nagarale, R. K.; Shahi, V. K.; Ghosh, P. K. *React. Funct. Polym.* **2006**, 66, 1619–1629; (e) Mohamed, R. M.; Fekry, A. M. *Int. J. Electrochem. Sci.* **2011**, 6, 2488–2508.

19. (a) Demetgul, C.; Serin, S. *Carbohydr. Polym.* **2008**, 72, 506–512; (b) Cervera, M. F.; Heinamaki, J.; Rasanen, M.; Maunu, S. L.; Karjalainen, M.; Acosta, O. M. N.; Colarte, A. I.; Yliruusi, J. *Carbohydr. Polym.* **2004**, 58, 401–408.

20. (a) Chang, Y.; Wang, Y.; Zha, F.; Wang, R. *Polym. Adv. Technol.* **2004**, 15, 284–286; (b) Santos, J. E.; Dockal, E. R.; Cavalheiro, E. T. G. *Carbohydr. Polym.* **2005**, 60, 277–282;

21. (a) Tong, J.; Li, Z.; Xia, C. *J. Mol. Catal. A* **2005**, 231, 197–203; (b) Anan, N. A.; Hassan, S. M.; Saad, E. M.; Butler, I. S.; Mostafa, I. S. *Carbohydrate Research* **2011**, 346, 775-793.

22. Sun, W.; Xia, C.G.; Wang, H. W. *New J. Chem.* **2002**, 226, 755-758.

23. Xue, L.; Zhou, D. J.; Tang, L. *React. Funct. Polym.* **2004**, 58, 117-121.

24. Hu, D. D.; Cui, Y. L.; Dong, X. L. *React. Funct. Polym.* **2001**, 48, 201-207.

25. (a) Shen, C.; Xu, J.; Yu, W.; Zhang, P. *Green Chem.* **2014**, 16, 3007; (b) Yi, S. S.; Lee, D. H.; Sin, E.; Lee, Y. S. *Tetrahedron lett.* **2007**, 48, 6771-6775.

26. (a) Dubey, R. K.; Mishra, C. M.; Mishra, A. N. *Indian J. Chem.* **2005**, 44A, 1169; (b) De, R. L.; Bera, K.; *Indian J. Chem.* **2000**, 39A, 1098; (c) Khera, B, Sharma, A. K.; Kaushik, N. N. *Polyhedron* **1983**, 2, 1177; (d) Haddad, H. H.; Hammadi, H. N. *Der Pharma Chimica.* **2014**, 6(6), 68-72.

27. (a) Antony, R.; Manickam, S. T. D.; Saravanan, K.; Karuppasamy, K.; Balakumar, S. *J. Mol. Str.* **2013**, 1050, 53-60; (b) Raman, N.; Selvan, A.; Sudharsan, S. *Spectrochim. Acta A.* **2011**, 79, 873-883.

28. Chikate, R. C.; Belapure, A. R.; Padhye, S. B.; West, D. X. *Polyhedron* **2005**, 24, 889.

29. (a) Yang, Z.; Zhuang, L.; Tan, G. J. *Appl. Polym. Sci.* **2002**, 85, 530; (b) Demetgul, C.; Serin, S. *Carbohydr. Polym.* **2008**, 72, 506-512.

30. (a) Hu, H.; Wang, X.; Wang, J.; Liu, F.; Zhang, N.; Xu, C. *Appl. Surf. Sci.* **2011**, 257, 2637-2642; (b) Antony, R.; David, S. T.; Saravanan, K.; Karuppasamy, K.; Balakumar, S. *Spectrochim. Acta A: Molecular and biomolecular* **2013**, 103, 423-430.

31. Inukai, Y.; Chinen, T.; Matsuda, T.; Kaida, Y.; Yasuda, S. J. *Analytica Chimica Acta.* **1998**, 371(2-3), 187-193.

32. (a) Raghuvanshi, D. S.; Gupta, A. K.; Singh, K. N. *Org. Lett.* **2012**, 14, 4326-4329; (b) Kantam, M. L.; Venkanna, G. T.; Sridhar, C.; Sreedhar, B; Choudary, B. M. *J. Org. Chem.* **2006,** 71, 9522; (c) Chen, S.; Huang, H.; Liu, X.; Shen, J.; Jiang, H.; Liu, H. *J. Comb. Chem.* **2008**, 10, 358-360; (d) Wang, X.; Jang H.-Y. *J. Bull. Korean Chem. Soc.* **2012**, 33(5), 1785; (e) Mondal, M.; Sarmah, G.; Gogoi, K.; Bora. U. *Tetrahedron Lett.* **2012**, 53, 6219-6222; (f) Zhu, X.; Zhang, Q.; Su, W. *RSC Adv.* **2014**, 4, 22775-22778.

33. Yoo, W.-J.; Tsukamoto, T.; Kobayashi, S. *Angew Chem. Int. Ed.* **2015**, 54, 1-5.

- Three new Chitosan anchored Copper(II) Schiff base complexes (C_1 to C_3) have been synthesized.
- The complexes were found to be efficient heterogeneous catalyst for Chan-Lam coupling reaction.
- The catalyst can be easily filtered out and reused at least for five times.