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FULL PAPER

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Highly reusable support-free copper(II) complex of *para*-hydroxy-substituted salen: Novel, efficient and versatile catalyst for C—N bond forming reactions

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An air-stable, highly active and versatile method for C—N bond forming reactions is reported. Under mild conditions using a highly reusable support-free Cu(II)–salen complex, structurally diverse *N*-aryl-substituted compounds were obtained via direct C—N bond forming reaction of HN-heterocycles with aryl iodides or three-component C—N bond forming reaction of 2-bromobenzaldehyde, aniline derivatives and sodium azide in good to excellent yields. C—N bond forming reaction for benzimidazole derivatives was also performed in the presence of the catalyst under ambient conditions. A series of hybrid benzimidazoles bearing morpholine, tetrazole and quinoxaline backbones were produced using this method. All reactions were performed in short times under air. The Cu(II) catalyst could be reused up to eight times in the direct cross-coupling reaction of 9*H*–carbazole with iodobenzene without any decrease in its catalytic activity.

KEYWORDS
C—N bond forming reactions, Cu(II) catalyst, N-heterocyclic compounds, reusable support-free catalyst, versatile method

1 | INTRODUCTION

Recently, the Cu(II) complex-catalysed formation of C—N bonds has received high priority in the design of N-arylated products and proved to be challenging to medicinal chemists. The C—N bond construction strategies employ pre-activated starting materials such as aryl halides using metal complexes to react with N-source nucleophiles. Various C—N bond forming reactions have been carried out using a variety of metal complexes under mild conditions in relatively cost-effective manners.[1] In recent decades, developing efficient procedures under nearly solvent-free conditions (low amount of solvent) or using environmentally benign solvents for purification and isolation of products and catalyst has been of great strategic importance.[2] Pd,[3] Co[4] and Ni[5] complexes have been well explored for the Buchwald–Hartwig amination reaction. However, these methods need ligands including N-heterocyclic carbenes, phosphine and many others which are non-reusable, air-sensitive, highly expensive and toxic.[6]

N-Aryl-substituted heterocycles which have many biological activities can be prepared using a variety of procedures including direct C—N bond forming reaction of HN-heterocycles with aryl iodides or three-component C—N bond forming reaction of 2-bromobenzaldehyde, aniline derivatives and sodium azide.

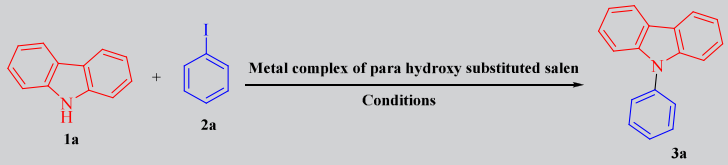
Most procedures for indazole derivatives which play an increasingly important role in modern drug discovery give mixtures of 1*H*- and 2*H*–indazoles. In this regard, some researchers have focused on the selective synthesis of 2*H*–indazoles which are discussed below.

A procedure based on copper-catalysed intramolecular N—N bond formation through 2*H*–indazoles from easily accessible starting materials was reported by Rao and co-workers.[7] Substituted 2*H*–indazoles were synthesized via condensation and reductive cyclization of nitrobenzaldehydes

and anilines promoted by tri-*n*-butylphosphine.[8] A [3 + 2] dipolar cycloaddition of sydnones and arynes was employed to afford a series of 2*H*–indazoles.[9] A one-pot multicomponent synthesis of highly regioselective 2*H*–indazoles via consecutive condensation and C—N and N—N bond formations was reported by Kumar et al.[10]

Benzimidazole derivatives[11] have also proved to have a broad range of pharmacological activities such as antimicrobial, antifungal, antiviral, anti-helmintic, anti-HIV, antioxidant, antihistaminic, antiulcer, anticancer, cardiotonic, antihypertensive, angiotensin I receptor antagonism, proton-pump inhibition and anti-inflammatory. These types of compounds are generally produced from the condensation–dehydration of *o*-phenylenediamines with carboxylic acid derivatives under strong acid and high-temperature conditions. These compounds are also prepared from aldehydes

TABLE 1 Results of reactions under various conditions[a]



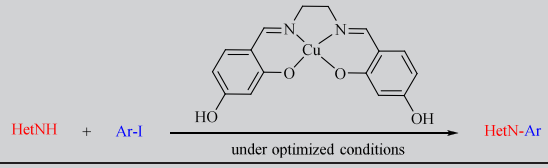
Entry	Metal–salen complex (amount, Mol%)	Base (amount, mmol)	Solvent (amount, ml)	Temperature (°C)	Time (h)	Yield (%)[b]
1	—	$(CH_3)_3CONa$ (2.0)	DMSO (2.0)	120	24.0	0
2	$Cu(OAc)_2$ (10)	$(CH_3)_3CONa$ (2.0)	DMSO (2.0)	120	24.0	31
3	**Cu(II)–salen (10)**	**$(CH_3)_3CONa$ (2.0)**	**DMSO (2.0)**	**120**	**12.0**	**94**
4	Cu(II)–salen (10)	$(CH_3)_3CONa$ (2.0)	Peg (2.0)	120	24.0	39
5	Cu(II)–salen (10)	$(CH_3)_3CONa$ (2.0)	Xylene (2.0)	Reflux	24.0	0
6	Cu(II)–salen (10)	K_2CO_3 (2.0)	Water (2.0)	Reflux	24.0	0
7	Cu(II)–salen (10)	$(CH_3)_3CONa$ (2.0)	Ethyl acetate (2.0)	Reflux	24.0	3
8	Cu(II)–salen (10)	$(CH_3)_3CONa$ (2.0)	Acetonitrile (2.0)	Reflux	24.0	0
9	Cu(II)–salen (10)	$(CH_3)_3CONa$ (2.0)	—	120	12.0	88
10	Cu(II)–salen (10)	K_2CO_3 (2.0)	—	120	24.0	33
11	Cu(II)–salen (10)	K_3PO_4 (2.0)	—	120	24.0	61
12	Cu(II)–salen (10)	NaOH (2.0)	—	120	24.0	12
13	Cu(II)–salen (10)	Et_3N (2)	—	120	24.0	27
14	Cu(II)–salen (10)	$(CH_3)_3CONa$ (2.0)	—	110	24.0	88
15	Cu(II)–salen (10)	$(CH_3)_3CONa$ (2.0)	—	80	24.0	0
19	Cu(II)–salen (7)	$(CH_3)_3CONa$ (2.0)	—	110	24.0	89
20	Cu(II)–salen (5)	$(CH_3)_3CONa$ (2.0)	—	110	24.0	66
21	Cu(II)–salen (7)	$(CH_3)_3CONa$ (2.0)	—	120	12.0	87
22	Cu(II)–salen (7)	$(CH_3)_3CONa$ (2.0)	0.2	120	12.0	94
23	Cu(II)–salen (7)	NaOH (2.0)	2.0	120	7	91
24	**Cu(II)–salen (7)**	**NaOH (2.0)**	**0.2**	**120**	**7**	**91**
25	Cu(II)–salen (7)	NaOH (2.0)	0.2	100	10	89
26	Cu(II)–salen (7)	NaOH (2.0)	0.2	80	14	Trace
27	Cu(II)–salen (10)	Cs_2CO_3 (2.0)	0.2	120	12	95
28	Zn(II)–salen (10)	$(CH_3)_3CONa$ (2.0)	—	120	24.0	10
29[c]	Co(III)–salen (10)	$(CH_3)_3CONa$ (2.0)	—	120	24.0	0
30	Mn(II)–salen (10)	$(CH_3)_3CONa$ (2.0)	—	120	24.0	0

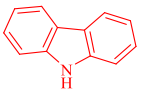
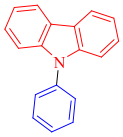
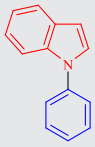
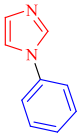
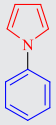
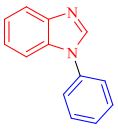
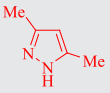
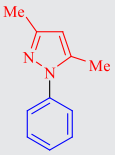
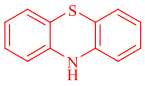
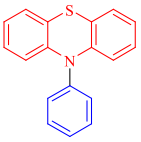
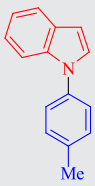
[a]Reaction conditions: 9*H*–carbazole (1.0 mmol), iodobenzene (1.2 mmol), base, solvent and metal–salen complex.

[b]Isolated yield.

[c]The partner anion of this complex is acetate ion.

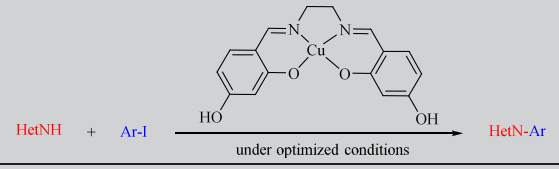
TABLE 2 Direct C–N bond forming reaction of various structurally diverse N-unsubstituted compounds (1.0 mmol) and aryl iodides (1.2 mmol) in the presence of NaOH (2.0 mmol) and highly reusable support-free Cu(II)–salen complex (7 mol%) under nearly solvent-free conditions[a]

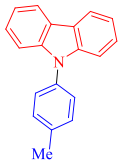
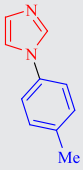
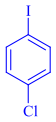
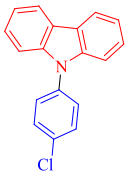
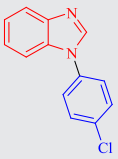
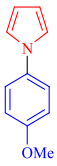


Entry	N-unsubstituted compound	Aryl halide	Product	Time (h)	Yield (%)[b]	Ref.
1	 **1a**	 **2a**	 **3a**	7.0	91	[1e]
2	 **1b**	**2a**	 **3b**	6.5	90	[1f]
3	 **1c**	**2a**	 **3c**	7.0	87	[1f]
4	 **1d**	**2a**	 **3d**	6.5	91	[1g]
5	 **1e**	**2a**	 **3e**	7.0	88	[1b]
6	 **1f**	**2a**	 **3f**	7.0	88	[1b]
7	 **1g**	**2a**	 **3g**	8.0	69	[1b]
8	**1b**	 **2b**	 **3h**	6.0	91	[7m]

(*Continues*)

TABLE 2 (Continued)



Entry	N-unsubstituted compound	Aryl halide	Product	Time (h)	Yield (%)[b]	Ref.
9	**1a**	**2b**	 **3i**	7.0	90	[1e]
10	**1c**	**2b**	 **3j**	7.0	87	[1j]
11	**1a**	 **2c**	 **3k**	8.0	90	[1e]
12	**1e**	**2c**	 **3l**	7.0	89	
13	**1d**	 **2d**	 **3m**	8.0	87	[2i]
14	**1b**	 **2e**	**3b**	12	34	[1f]

[a]Reaction conditions: aryl iodide (1.2 mmol) and N-heterocyclic compound (1.0 mmol) in the presence of NaOH (2.0 mmol) and Cu(II) catalyst (7 mol%) at 120 °C.

[b]Isolated yield.

instead of carboxylic acids with subsequent oxidation using various oxidative reagents. A literature survey has also revealed the importance of quinoxalines as having miscellaneous pharmaceutical and biological activities.[12] They are realized from both natural and synthetic origins and are also known for their biomedical potential, including as anti-asthmatic, anti-inflammatory, antihypertensive and antibacterial agents. According to longstanding research for finding new bioactive benzimidazoles containing morpholine and tetrazole backbones,[13] numerous benzimidazole compounds incorporating morpholine and tetrazole have been produced in this study. A series of benzimidazole–morpholine molecules have been proved to elicit anti-inflammatory effect by blocking activity of Lck.[13] Benzimidazole nucleus can be substituted with tetrazole to explore the development of antihypertensive drugs.[14]

Because of low reusability of homogeneous metal complexes, the anchoring of these catalysts onto various solid

supports has been found to increase their reusability. These solid materials are widely used for heterogenization of homogeneous catalysts, since they have good stability and mechanical resistance. Although they are acceptable as catalyst supports, investigation of reusable support-free metal complexes for use umder mild conditions is of great interest. Most complexes are soluble in organic solvents and so they should be supported on reusable materials; supporting in this way is time-consuming and causes pollution and also increases costs. In this regard, there is still a need to develop metal complexes without immobilizing them onto any solid support as suitable catalysts in organic reactions. Very important complex catalysts can be found in the field of recoverable metal complex catalysts under homogenous conditions where they can be precipitated by adding suitable solvent.[15] Based on this concept, numerous carefully modified salen complexes have been synthesized so that they can be easily recovered after precipitation with a specific solvent.

As mentioned, a number of approaches for the synthesis of these types of compounds have been reported, but more environmentally benign, general and efficient methods are still needed. With these considerations in mind, based on our previous studies, which focused on the synthesis of salen complexes as catalysts and their applications in organic reactions,[16] herein we report our attempts to develop C─N bond forming reactions using a mononuclear Cu(II)–salen complex as an inexpensive, efficient and versatile catalyst.

2 | RESULTS AND DISCUSSION

As part of our continuing interest in the development of Cu-based procedures[17] for organic reactions, a very simple and new C─N bond forming methodology based on the use of a Cu(II)–salen complex as a versatile catalyst has been developed, which could represent an improvement in efficiency and convenience over previously reported methods.

To determine the efficiency of our catalyst, 9*H*–carbazole (1.0 mmol) and iodobenzene (1.2 mmol) were selected as model substrates and investigated under various conditions (Table 1). In the absence of the catalyst, the starting substrates were isolated, and C─N bond formation did not proceed (Table1, entry 1). When the Cu(II) catalyst was employed, the reaction also did not proceed well, whereas the yield of product increased to 94% by using the Cu(II)–salen complex (7 mol%) (Table 1, entries 2 and 3). These results prompted us to investigate our complex in C─N bond forming reactions.

In the next step, the effect of various solvents was studied for the model reaction. It was found that the reaction gave good to excellent yields in dimethylsulfoxide (DMSO) and under solvent-free or nearly solvent-free conditions, while lower yield or no yield of N-substituted product was obtained in other solvents including poly(ethylene glycol) (PEG 400), xylene, water, ethanol and acetonitrile (Table 1). In continuation of our research, the effect of various bases and temperatures was screened via this C─N cross-coupling reaction and the results showed that reactions proceeded well when using sodium *tert*-butoxide and sodium hydroxide as base (Table 1, entries 9–13 and 23–27). In the next step, various metal complexes were also used, but, among them, the Cu(II) complex is still the best option (Table 1, entries 24 and 28–30). Finally, the catalyst loading was screened and 7 mol% of catalyst was chosen (Table 1, entries 9 and 19–21). As evident from Table 1, the best result was achieved by carrying out the reaction using Cu(II)–salen (7 mol%), sodium hydroxide as base (2 mmol) under nearly solvent-free conditions (0.2 ml) at 120 °C for 7 h (Table 1, entry 24).

TABLE 3 Results of reactions under different conditions[a]

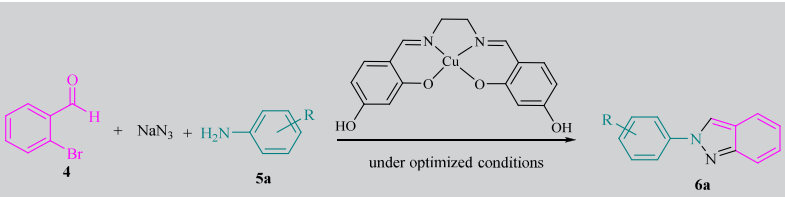
Entry	Metal–salen complex (amount, Mol%)	Solvent (amount, ml)	Temperature (°C)	Time (h)	Yield (%)[b]
1	—	DMSO (3.0)	120	24.0	0
2	**Cu(II)–salen (7.0)**	**DMSO (3.0)**	**120**	**12.0**	**81**
3	Cu(II)–salen (7.0)	DMSO (1.0)	120	12.0	80
4	Cu(II)–salen (7.0)	DMSO (3.0)	100	12.0	80
5	Cu(II)–salen (5.0)	DMSO (3.0)	120	12.0	75
6	Cu(II)–salen (10.0)	DMF (3.0)	120	12	81
7	Cu(II)–salen (10)	Water (1.0)	Reflux	24.0	0
8	Cu(II)–salen (10)	Peg (400) (2.0)	130	12.0	77
9	Zn(II)–salen (10)	—	120	24.0	0
10	Co(III)–salen (10)	—	120	24.0	0
11	Mn(II)–salen (10)	—	120	24.0	0

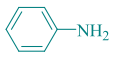
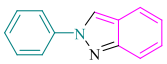
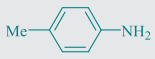
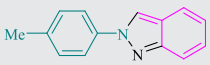
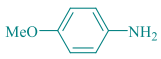
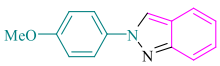
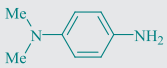
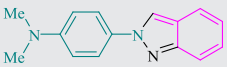
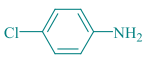
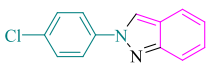
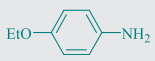
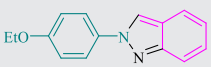
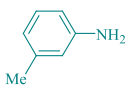
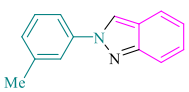
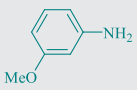
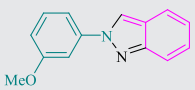
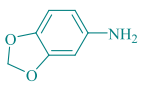
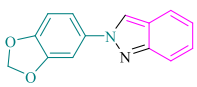
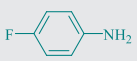
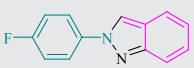
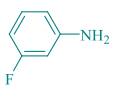
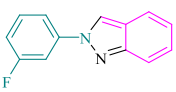
[a]Reaction conditions: 2-bromobenzaldehyde, sodium azide, aniline, solvent, and metal–salen complex.

[b]Isolated yield.

The scope and generality of this cross-coupling reaction catalysed by the Cu(II)–salen complex were explored using a variety of aryl iodides and N-heterocyclic compounds. In all cases, cross-coupling reactions afforded the desired N-substituted products **3a–3 m** in good to excellent yields (Table 2). The usefulness of this catalyst in a three-component

TABLE 4 Synthesis of 2*H*–indazole derivatives from various aromatic amines, sodium azide, and 2-bromobenzaldehyde in the presence of support-free Cu(II)–salen complex as a highly reusable catalyst under nearly solvent-free conditions at 120°C[a]



Entry	Aromatic or aliphatic amine	Product	Yield (%)[b]	Ref.
1	 **5a**	 **6a**	81, 0[c], 0[d], 0[e]	[15]
2	 **5b**	 **6b**	82	[15]
3	 **5c**	 **6c**	85	[19c]
4	 **5d**	 **6d**	83	[19c]
5	 **5e**	 **6e**	77	[19c]
6	 **5f**	 **6f**	83	[19c]
7	 **5g**	 **6g**	85	[19c]
8	 **5h**	 **6h**	80	[19c]
9	 **5i**	 **6i**	81	[19c]
10	 **5j**	 **6j**	80	
11	 **5k**	 **6k**	81	

[a]Reaction conditions: amine (1.0 mmol), NaN_3 (1.1 mmol) and 2-bromobenzaldehyde (1.0 mmol) for 8 h.

[b]Isolated yield.

[c]Reaction performed using Co(III)–salen.

[d]Reaction performed using Mn(II)–salen.

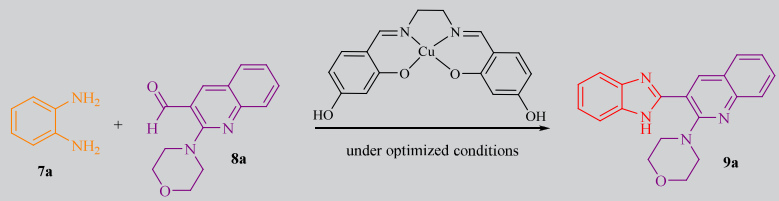
[e]Reaction performed using Zn(II)–salen.

C—N bond forming reaction to produce 2-phenyl-2*H*-indazole derivative from 2-bromobenzaldehyde, sodium azide and aniline was investigated under various conditions (Table 3). The reaction performed well when using 7.0 mol% catalyst at 120 °C under nearly solvent-free conditions (0.3 ml of DMSO). With these reaction conditions in hand, we then explored the scope of this Cu(II) complex of *para*-hydroxy-substituted salen in various indazole syntheses. In all cases, C—N and N—N bond formation reactions produced desired products **6a**–**6 k** with good to excellent yields (Table 4). The reaction was also investigated using other metal–salen complexes, but the best result was obtained using the Cu–salen complex (Table 3, entries 9–11).

Many drugs including albendazole, omeprazole, thiabendazole as antihelminthics; lansoprazole, pantoprazole as proton pump inhibitors; telmisartan as antihypertensive; astemizole as antihistaminic; candesartan, cilexitil and mebendazole have been prepared via optimization of substituents around the benzimidazole nucleus. According to the importance of this heterocyclic compound for some activities, there are many reports in the literature.[11] In continuation of our previous researches and with an aim of helping medicinal chemists in developing heterocyclic-based analogues, there is a need to couple various bioactive heterocyclic compounds using a mild and simple method. Herein we report an efficient protocol for the synthesis of some novel hybrid benzimidazoles bearing 2-morpholin-4-ylquinoline and [1,2,4] triazolo[4,3-a]quinolone backbones via benzimidazole formation catalysed by the reusable Cu(II)–salen complex as the key step. In order to establish the optimum reaction conditions, the condensation reaction between 2-morpholin-4-ylquinoline-3-carbaldehyde (**8a**; 1.0 mmol) and *o*-phenyldiamine (**7a**; 1.0 mmol) was studied varying the parameters such as catalyst loading, solvent and temperature. Initially, the effect of solvent was examined and among the solvents tested, EtOH was the most suitable reaction media for the condensation reaction of **8a** with **7a** (Table 5, entries 6 and 10). Lower yields were obtained for desired substituted benzimidazole **9a** using solvents such as CH_3CN, $CHCl_3$, CH_2Cl_2, tetrahydrofuran (THF) and dimethylformamide (DMF) (Table 5). In the next step, we found that the loading level of the hydroxy-substituted Cu(II)–salen complex also had an effect on the yield of product. According to Table 5 (entries 6–8), 5 mol% catalyst was needed for benzimidazole synthesis. It should be noted that if the amount of catalyst loading was decreased the yield of **9a** decreased, whereas increasing the Cu(II)–salen complex concentration did not lead to a considerable increase in the yield. Increasing the temperature was found to be efficient for decreasing the reaction time; 50 °C was chosen according to green chemistry concepts (Table 5, entry 6). At the end of the reaction the catalyst was recovered by centrifugation and the solvent was evaporated. The remaining solid mixture was recrystallized from acetonitrile to afford desired product; because of high yield of products, most products were purified by recrystallization (Table 5).

To study the scope and limitation of this method, several reactions were performed employing condensation of

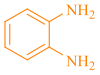
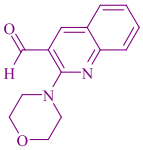
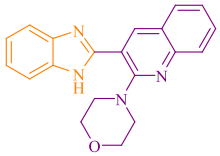
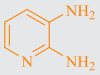
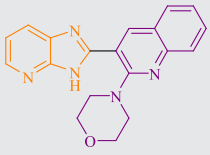
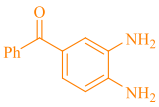
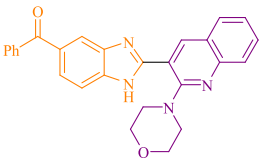
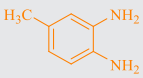
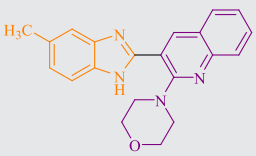
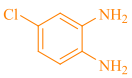
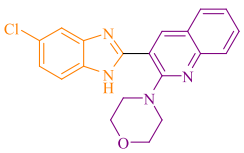
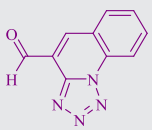
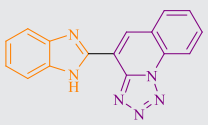
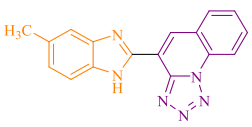
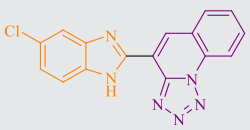
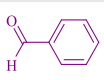
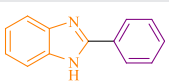
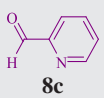
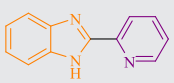
TABLE 5 Copper-catalysed condensation reaction of *o*-phenyldiamine (**7a**, 1.0 mmol) and morpholin-4-ylquinoline-3-carbaldehyde (**8a**, 1.0 mmol) under various conditions



Entry	Solvent	Catalyst (Mol%)	Temp. (°C)	Time (h)	Yield (%)[a]
1	CH_3CN	5	25	24	54
2	THF	5	25	24	45
3	$CHCl_3$	5	25	24	10
4	CH_2Cl_2	5	25	24	11
5	DMF	5	25	24	<10
6	EtOH	5	25	15	80
7	EtOH	3	25	24	62
8	EtOH	10	25	15	80
9	**EtOH**	**5**	**50**	**6**	**86**
10	EtOH	5	70	6	86

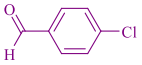
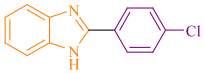
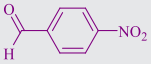
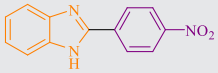
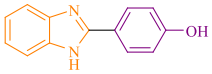
[a]Isolated yield.

TABLE 6 Synthesis of benzimidazole derivatives from various aldehydes and *o*-phenyldiamines[a]

Entry	*o*-Phenyldiamine	Aldehyde	Product	Time (h)	Yield (%)[b]	Ref.
1	 **7a**	 **8a**	 **9a**	6	86	
2	 **7b**	**8a**	 **9b**	6	80	
3	 **7c**	**8a**	 **9c**	6	81	
4	 **7d**	**8a**	 **9d**	6	85	
5	 **7e**	**8a**	 **9e**	6	81	
6	**7a**	 **8b**	 **9f**	6	82	
7	**7d**	**8b**	 **9g**	6	85	
8	**7e**	**8b**	 **9h**	6	86	
9	**7a**	 **8c**	 **9i**	3	88	[12b]
10	**7a**	 **8c**	 **9j**	3	89	[12b]

(*Continues*)

TABLE 6 (Continued)

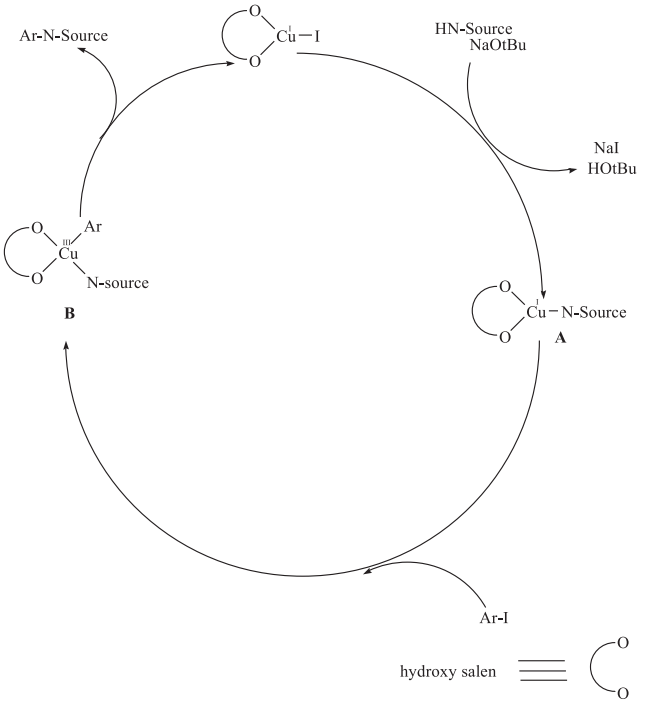
Entry	*o*-Phenyldiamine	Aldehyde	Product	Time (h)	Yield (%)[b]	Ref.
11	**7a**	 **8c**	 **9k**	3	89	[12b]
12	**7a**	 **8c**	 **9l**	3	90	[12b]
13	**7a**	 **8c**	 **9m**	3	81	[12b]

[a]Reaction conditions: *o*-phenyldiamine (1.0 mmol), aldehyde (1.0 mmol), ethanol (5 ml), catalyst (5 mol%) at 50 °C.

[b]Isolated yield.

structurally diverse aldehydes with *o*-phenylenediamines. Initially, benzimidazoles bearing 2-morpholin-4-ylquinoline and [1,2,4]triazolo[4,3-a]quinolone backbones were generated from starting materials with good to excellent yields (Table 6). Using the optimized conditions, some other benzaldehydes and *o*-phenylenediamines bearing electron-donating and electron-withdrawing groups were reacted to give the corresponding products. It was found that the nature and electronic properties of the substituents on the aromatic ring of aldehydes affected the conversion rate, and aromatic aldehydes with electron-donating groups on the aromatic ring reacted faster (Table 6).

Similar to previous reports, we propose a plausible mechanism for the Cu(II)–salen complex-catalysed C─N bond formation reaction.[1–6,19] Although metals are not active enough for the cross-coupling reactions, coordinated metals can increase the rate and yield of organic reactions. It is well known that in the absence of a suitable ligand, no or low yield of product was obtained. Firstly, in the presence of base, N-source compound can be coordinated to the metal centre by its electron pair. In the next step, oxidative addition produces **B** in which arene and halide are both ligated to the metal centre. Finally, reductive elimination generates a C─N bond and regenerates the Cu(II)–salen catalyst (Scheme 1).



SCHEME 1 Proposed mechanism for synthesis of N-substituted compounds catalysed by Cu(II)–salen complex

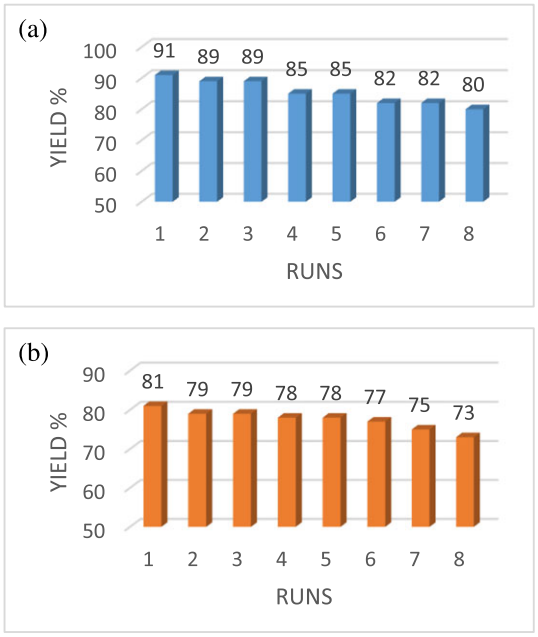


FIGURE 1 Catalytic activity of Cu(II)–salen complex in eight cycles for (a) reaction of 9*H*–carbazole (**1a**; 1.0 mmol) with iodobenzene (**2a**; 1.2 mmol) and (b) three-component C─N bond forming reaction of 2-bromobenzaldehyde, aniline derivative (**5a**) and sodium azide under optimized reaction conditions

The possibility of recycling the catalyst was examined using the reaction of 9*H*–carbazole (**1a**; 1.0 mmol) and iodobenzene (**2a**; 1.2 mmol) under nearly solvent-free conditions at 120 °C. The catalyst recovery was also investigated for the three-component C—N bond forming reaction of 2-bromobenzaldehyde (**4**), aniline (**5a**) and sodium azide. The recovered Cu(II) complex was reused eight times in each of these two C—N bond forming reactions (Figure 1). Upon completion, ethyl acetate (30 ml) was added to the reaction mixture and shaken vigorously. Finally, insoluble catalyst was centrifuged. In the third reaction, it was recovered several times for the model reaction. In this case in order to reuse the catalyst, the reaction mixture was centrifuged and washed with ethanol. After drying under reduced pressure, the recovered catalyst was used for further runs.

Kinetic curves (conversion versus time) of five recycling runs of the reaction between **1a** (1.0 mmol) and **2a** (1.2 mmol) were also plotted (Figure 2).to compare the

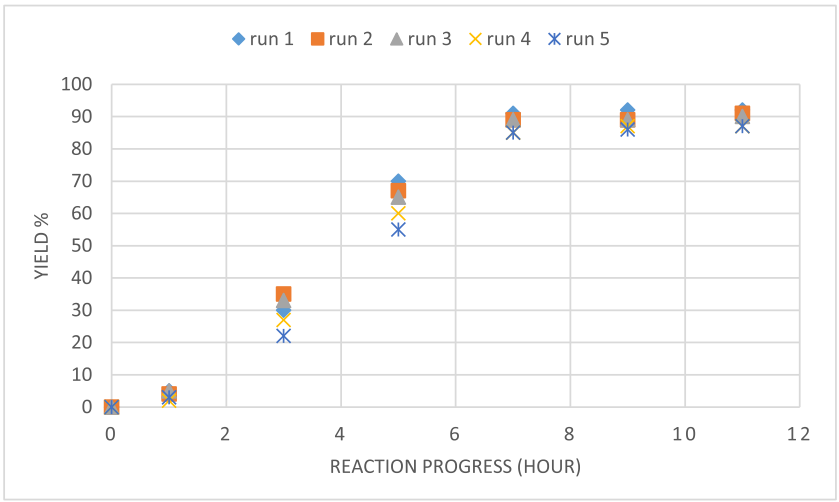


FIGURE 2 Conversion versus time for five recycling runs of reaction of 9*H*–carbazole (**1a**; 1.0 mmol) with iodobenzene (**2a**; 1.2 mmol) under optimized reaction conditions

TABLE 7 Literature screening: comparison of various types of C—N bond forming reaction

	Starting materials	Reagents and conditions	Ref.
Direct C—N bond forming reaction of HN-heterocycles with aryl halides	Indole and iodobenzene	CuI (10 mol%), K_2CO_3 (2 equiv.), glycerol as solvent, DMSO as additive (1 mmol), 120 °C, 24 h, 88%	[6g]
	Imidazole and iodobenzene	Polymer anchored Cu catalyst (0.05 g), K_2CO_3 (2.0 equiv.), DMSO, 120 °C, N_2 atmosphere, 12 h, 95%	[1h]
	Indole and iodobenzene	CuI (10 mol%), 1,2-diamine (20 mol%), Cs_2CO_3 (2 equiv.), DMF, 130 °C, 6 h, 93%	[6s]
	Indole and *o*-dihalobenzenes	CuI (10 mol%), benzotriazole (20 mol%), K_3PO_4 (2 equiv.), DMSO, 120 °C, 30 h, 65%	[6a]
	Imidazole and 4-iodotoluene	Cu_2O (10 mol%), 2,2-dihydroxy-1*H*-indene-1,3 (2*H*)-dione (20 mol%), KOH (2 equiv.), DMSO, 110 °C, Ar atmosphere, 24 h, 91%	[6c]
	Indole, iodobenzene	CuO nanoparticles (5 mol%), K_2CO_3 (1 equiv.), DMF, reflux, 8 h, 98%	[6i]
Three-component C—N bond forming reaction of 2-bromobenzaldehyde, aniline derivatives and sodium azide	2-Bromobenzaldehyde, aniline, and NaN_3	CuO nano (2.5 mol%), Cs_2CO_3 (2 eqiv.), DMSO, 120 °C, 2.5 h, 87%	[20a]
	2-Bromobenzaldehyde, aniline, and NaN_3	Cu–Al hydrotalcites, DMSO, 120 °C, 6 h, 91%	[18]
	2-Bromobenzaldehyde, aniline, and NaN_3	Cu_2O nano (5 mol%), PEG, 120 °C, 6 h, 90%	[17c]
	2-Bromobenzaldehyde, aniline, and NaN_3	CuI (15 mol%), TMEDA (15 mol%), DMSO, 120 °C, 12 h, 98%	[20b]
C—N bond forming reaction towards benzimidazole derivatives	o-Phenylenediamine and 4-chlorobenzaldehyde	$CuFe_2O_4$ nanoparticles (*ca* 13 mol%), toluene, 110 °C, O_2, 24 h, 92%	[21a]
	o-Phenylenediamine and benzaldehyde	Cu(II)-TD@ $nSiO_2$ (10 mg, 0.34 mol% cu(II)), EtOAc, 50 °C, 25 min, 95%	[21b]
	4-me-o-phenylenediamine and benzaldehyde	CuI nano (10 mol%), CH_3CN, r.t., O_2, 1 h, 91%	[21c]

activity of the catalyst in each cycle. For this purpose, the reaction between **1a** and **2a** was selected under optimized conditions to evaluate the reactivity of the catalytic system for every cycle.

The amounts of Cu leaching into products were detected through inductively coupled plasma analysis for the two reactions. Results indicate that 1.49 and 1.78% (for first and second reaction, respectively) of copper content was leached during the eight reaction cycles. Although, hydroxy-functionalized salen ligand and normal salen ligand produced the desired product in the same yield, for several reasons we used hydroxy-functionalized salen ligand. One reason is the function of the hydroxy group of the complex where the reusability of the catalyst greatly increases in comparison with simple Cu–salen complex. A second reason is that leaching during the process was much decreased. For all reactions, the infrared (IR) spectra of the catalyst and the recovered catalyst exhibit ν(N═C) band at around 1620 cm $^{-1}$ and ν(*p*-OH) band at around 2500–2900 cm^{-1}.

Finally, a comparison with other copper catalysts is needed for these C─N bond forming reactions to reveal some advantages of the present catalytic system over most others in terms of higher yield and shorter reaction time (Table 7).

3 | CONCLUSIONS

In summary, a highly active, air-stable and versatile procedure for C─N bond forming reactions for synthesis of *N*-aryl compounds under nearly solvent-free conditions was developed. This system shows several advantages including commercially available starting materials, easy purifications and nearly solvent-free and mild conditions. In addition, we explored the synthesis of some hybrid molecules (benzimidazoles bearing 2-morpholin-4-ylquinoline and [1,2,4]triazolo[4,3-a]quinolone backbones) via benzimidazole formation catalysed by the reusable Cu(II) complex as the key step. Further investigations of the application of these efficient metal catalysts in other transition metal-catalysed reactions are in progress in our laboratory.

4 | EXPERIMENTAL

Chemical materials and solvents were purchased from Aldrich, Fluka and Merck. IR spectra were obtained using a Shimadzu FT-IR 8300 spectrophotometer. NMR spectra were recorded with a Bruker Avance DPX-250 (^{1}H NMR, 250 MHz; ^{13}C NMR, 62.9 MHz) spectrometer in pure deuterated solvents with tetramethylsilane as an internal standard. Mass spectra were obtained with a Shimadzu GCMS-QP 1000 EX instrument at 70 or 20 eV. Melting points were determined in open capillary tubes with a Büchi-535 circulating oil melting point apparatus. Column chromatography was carried out on short columns of silica gel 60 (70–230 mesh) in glass columns.

4.1 | General procedure for direct synthesis of N-substituted compounds from various structurally diverse N-unsubstituted compounds and aryl iodides in presence of NaOH and Cu(II)–salen complex

To a mixture of N-heterocycles (1.0 mmol), aryl iodides (1.2 mmol) and NaOH (2.0 mmol) was added Cu(II)–salen complex (7.0 mol%) and stirred at 120 °C under nearly solvent-free conditions. Progress of reactions was monitored by TLC using *n*-hexane–ethyl acetate. Upon completion, ethyl acetate (30 ml) was added to the reaction mixture and shaken vigorously. Finally, insoluble catalyst was centrifuged. After separation of the catalyst, the organic layer was washed with deionized water (3 × 20 ml) and brine (3 × 20 ml). The organic layer was dried ($CaCl_2$) and evaporated *in vacuo* to give the crude product, which was purified by silica gel column chromatography employing *n*-hexane–ethyl acetate.

4.2 | General procedure for synthesis of 2*H*–indazole derivatives in presence of Cu(II)–salen complex

To a mixture of 2-bromobenzaldehyde (1.0 mmol), amine (1.0 mmol) and NaN_3 (1.1 mmol) was added Cu(II)–salen complex (7 mol%) and stirred at 120 °C under solvent-free conditions. Progress of reactions was monitored by TLC using *n*-hexane–ethyl acetate. Upon completion, ethyl acetate (30 ml) was added to the reaction mixture and shaken vigorously. Finally, insoluble catalyst was centrifuged. After separation of the catalyst, the organic layer was washed with deionized water (3 × 20 ml) and brine (3 × 20 ml). The organic layer was dried ($CaCl_2$) and evaporated *in vacuo* to give the crude product, which was purified by silica gel column chromatography employing *n*-hexane–ethyl acetate as eluent.

4.3 | General procedure for synthesis of benzimidazoles

To a mixture of aldehyde (1.0 mmol) and diamine (1.0 mmol) was added Cu(II)–salen complex (5 mol%) and stirred at 50 °C in ethanol (5 ml). Progress of reactions was monitored by TLC using *n*-hexane–ethyl acetate. Upon completion, the catalyst was centrifuged and after that products (**9a–9 h**) were purified by recrystallization from acetonitrile; other products were purified by silica gel column chromatography employing *n*-hexane–ethyl acetate as eluent.

4.4 | Analytical data

4.4.1 | 2-(3-Fluorophenyl)-2*H*–indazole

Yellow solid; m.p. 80–82 °C. ^{1}H NMR ($CDCl_3$, 250 MHz, δ, ppm): 7.00–7.08 (m, 2H), 7.26 (t, J = 6.50, 1H), 7.37–7.46 (m, 1H), 7.61–7.72 (m, 4H), 8.34 (s, 1H). ^{13}C NMR ($CDCl_3$, 62.9 MHz, δ, ppm): 108.5, 1.8.9, 114.9, 116.1, 116.2, 118.0, 120.4, 122.8, 127.2, 131.0, 165.2. Anal. Calcd for $C_{13}H_9FN_2$ (212.22) (%): C, 73.57; H, 4.27; N, 13.20. Found (%): C, 73.61; H, 4.30; N, 13.17.

4.4.2 | 2-(4-Fluorophenyl)-2*H*–indazole

Yellow solid; m.p. 95–97 °C. ^{1}H NMR ($CDCl_3$, 250 MHz, δ, ppm): 7.00–7.28 (m, 4H), 7.20 (d, J = 8.50, 1H), 7.69 (d, J = 8.75, 1H), 7.75–7.81 (m, 2H), 8.25 (s, 1H). ^{13}C NMR ($CDCl_3$, 62.9 MHz, δ, ppm): 116.3, 116.6, 117.9, 120.3, 120.5, 122.6, 122.7, 122.8, 126.9, 149.8, 160.0, 164.0. Anal. Calcd for $C1_3H_9FN_2$ (212.22) (%): C, 73.57; H, 4.27; N, 13.20. Found (%): C, 73.63; H, 4.29; N, 13.24.

4.4.3 | 2-(4-ethyl-phenyl)-2*H*–indazole

^{1}H NMR ($CDCl_3$, 250 MHz, δ, ppm): 1.32 (t, J = 7.5 Hz, 3H), 2.78 (q, J = 7.5 Hz, 2 H), 7.09–7.46 (m, 5H), 7.66–7.83 (m, 3 H), 8.41 (s, 1 H). ^{13}C NMR ($CDCl_3$, 62.9 MHz, δ, ppm): 15.5, 28.9, 117.9, 118.2, 120.5, 120.7, 122.40, 126.8, 127.5, 129.4, 146.1.

4.4.4 | 3-(1*H*–benzo[*d*]imidazol-2-yl)-2-morpholinoquinoline

Grey solid; m.p. 248–249 °C. ^{1}H NMR ($CDCl_3$, 250 MHz, δ, ppm): 3.27 (t, J = 4.5, 4H), 3.90 (t, J = 4.5, 4H), 7.31–7.35 (m, 2H), 7.41–7.47 (m, 1H), 7.51–7.55 (m, 1H), 7.66–7.72 (m, 1H), 7.78 (d, J = 8.2, 1H), 7.85–7.94 (m, 2H), 8.96 (s, 1H), 11.30 (s, 1H). ^{13}C NMR ($CDCl_3$, 62.9 MHz, δ, ppm): 51.4, 66.8, 121.9, 124.0, 124.8, 127.5, 129.2, 132.6, 143.1, 149.2, 158.7, 189.9. IR (KBr, cm^{-1}): 586 (w), 617 (w), 748 (s), 848 (w), 918 (w), 964 (m), 1041 (m), 1118 (s), 1226 (m), 1272 (m), 1319 (w), 1365 (m), 1427 (s), 1488 (m), 1558 (m), 2831 (w), 2962 (w), 3055 (w). Anal. Calcd for $C_{20}H_{18}N_4O$ (330.38) (%): C, 72.71; H, 5.49; N, 16.96. Found (%): 72.73; H, 5.40; N, 16.88.

4.4.5 | 3-(3*H*-Imidazo[4,5-*b*]pyridin-2-yl)-2-morpholinoquinoline

Yellow solid; m.p. 178–179 °C. ^{1}H NMR ($CDCl_3$, 250 MHz, δ, ppm): 3.41–3.42 (m, 4H), 3.89–3.90 (m, 4H), 7.39 (t, J = 7.0, 1H), 7.62–7369 (m, 1H), 7.78–7.92 (m, 2H), 8.10–8.14 (m, 2H), 8.71 (s, 1H), 8.77 (s, 1H). ^{13}C NMR ($CDCl_3$, 62.9 MHz, δ, ppm): 56.3, 71.4, 114.0, 127.4, 129.6, 132.4, 133.3, 135.6, 138.1, 142.1, 142.8, 145.2, 152.6, 153.1, 153.8, 159.5, 164.6. IR (KBr, cm^{-1}): 586 (m), 694 (m), 748 (s), 825 (m), 948 (s), 1110 (s), 1149 (m), 1195 (m), 1242 (m), 12625 (m), 1357 (m), 1419 (m), 1505 (m), 1612 (s), 1658 (m), 2839 (m), 2916 (w), 2962 (w), 3178 (m), 3278 (m), 3386 (w), 3456 (m). Anal. Calcd for $C_{19}H_{17}N_5O$ (331.37) (%): C, 68.87; H, 5.17; N, 21.13. Found (%): C, 68.89; H, 5.22; N, 21.16.

4.4.6 | (2-(2-morpholinoquinolin-3-yl)-1*H*–benzo[d]imidazol-5-yl)(phenyl)methanone

Yellow solid; m.p. 178–179 °C. ^{1}H NMR ($CDCl_3$, 250 MHz, δ, ppm): 3.20–3.22 (m, 4H), 3.83 (s, 4H), 7.40–7.87 (m, 12H), 8.88–8.95 (m, 1H), 11.57 (s, 1H). ^{13}C NMR ($CDCl_3$, 62.9 MHz, δ, ppm): 51.11, 66.87, 110.88, 117.39, 119.54, 122.82, 123.58, 125.44, 125.64, 127.81, 128.10, 130.74, 133.53, 139.94, 143.40, 146.95, 149.60, 158.13. IR (KBr, cm^{-1}): 585 (w), 620 (w), 642 (m), 662 (w), 693 (s), 766 (m), 791 (m), 832 (w), 846 (w), 879 (m), 897 (w), 930 (m), 953 (m), 1037 (m), 1063 (w), 1083 (w), 1149 (m), 1181 (m), 1228 (m), 1259 (w), 1325 (m), 1362 (s), 1409 (s), 1448 (s), 1491 (s), 1522 (s), 1559 (w), 1570 (w), 1598 (w), 1617 (s), 2849 (s), 2918 (s), 2960 (m), 3060 (m), 3293 (br), 3422 (br). Anal. Calcd for $C_{27}H_{22}N_4O_2$ (434.49) (%): C, 74.64; H, 5.10; N, 12.89. Found (%): C, 74.67; H, 5.02; N, 12.97.

4.4.7 | 3-(5-methyl-1*H*-benzo[*d*]imidazol-2-yl)-2-morpholinoquinoline

Yellow solid; m.p. 227–228 °C. ^{1}H NMR ($CDCl_3$, 250 MHz, δ, ppm): 2.52 (s, 3H), 3.28 (t, J = 4.7, 4H), 3.91 (t, J = 4.5, 4H), 7.15 (dd, J_1 = 1.2, J_2 = 8.2, 1H), 7.33–7.48 (m, 2H), 7.64–7.66 (m, 1H), 7.68–7.75 (m, 1H), 7.82 (d, J = 8.0, 1H), 7.93 (d, J = 8.5, 1H), 8.97 (s, 1H), 11.11 (s, 1H). ^{13}C NMR ($CDCl_3$, 62.9 MHz, δ, ppm): 21.3, 50.7, 66.5, 117.1, 125.1, 125.2, 127.4, 127.6, 130.2, 139.2, 146.4, 157.7. IR (KBr, cm^{-1}): 456 (w), 475 (m), 499 (w), 603 (m), 621 (m), 635 (w), 707 (w), 751 (s), 784 (s), 810 (s), 846 (m), 879 (w), 913 (w), 924 (w), 954 (w), 1039 (s), 1015 (m), 1116 (s), 1147 (w), 1205 (w), 1231 (s), 1205 (s), 1300 (m). Anal. Calcd for $C_{21}H_{20}N_4O$ (344.41) (%): C, 73.23; H, 5.85; N, 16.27. Found (%): C, 73.25; H, 5.90; N, 16.31.

4.4.8 | 3-(5-Chloro-1*H*-benzo[*d*]imidazol-2-yl)-2-morpholinoquinoline

Grey solid; m.p. 238–240 °C. ^{1}H NMR ($CDCl_3$, 250 MHz, δ, ppm): 3.22 (t, J = 4.5, 4H), 3.87 (t, J = 4.7, 4H), 7.23–7.28 (m, 1H), 7.39–7.45 (m, 2H), 7.64–7.75 (m, 3H), 7.89 (d, J = 8.2, 1H), 8.88 (s, 1H), 11.40 (s, 1H). ^{13}C NMR

($CDCl_3$, 62.9 MHz, δ, ppm): 51.31, 66.93, 117.01, 123.74, 125.56, 125.93, 127.96, 128.19, 130.98, 140.03, 147.08, 158.13. IR (KBr, cm^{-1}): 601 (m), 621 (m), 703 (m), 724 (w), 752 (s), 785 (s), 812 (s), 879 (m), 863 (m), 925 (s), 940 (m), 954 (m), 1039 (m), 1056 (m), 1065 (m), 1118 (s), 1147 (m), 1205 (w), 1226 (s), 1257 (m), 1298 (m), 1321 (m), 1361 (s), 1410 (w), 1432 (w), 1599 (m), 1616 (m), 2833 (m), 2852 (m), 2959 (m). Anal. Calcd for $C_{20}H_{17}ClN_4O$ (364.83) (%): C, 65.84; H, 4.70; N, 15.36. Found (%): C, 65.91; H, 4.68; N, 15.09.

4.4.9 | 4-(1*H*–benzo[*d*]imidazol-2-yl)tetrazolo [1,5-*a*]quinoline

Yellow solid; m.p. 277–280 °C. ^{1}H NMR ($CDCl_3$, 250 MHz, δ, ppm): 7.25–7.39 (m, 2H), 7.58–7.61 (m, 1H), 7.73–7.85 (m, 2H), 7.88–7.96 (m, 1H), 8.09 (d, J = 7.5, 1H), 9.07 (s, 1H), 11.76 (s, 1 H). ^{13}C NMR ($CDCl_3$, 62.9 MHz, δ, ppm): 111.8, 116.9, 119.7, 123.14, 124.4, 128.8, 130.0, 132.1. IR (KBr, cm^{-1}): 477 (s), 504 (w), 633 (s), 664 (m), 712 (m), 756 (s), 913 (s), 961 (m), 1008 (m), 1097 (m), 1141 (m), 1161 (m), 1193 (m), 1208 (m), 1231 (m), 1257 (m), 1285 (m), 1314 (s), 1337 (s), 1374 (m), 1410 (s), 1441 (m), 1456 (m), 1517 (s), 1544 (s), 1581 (m), 1605 (s), 3064 (m), 3328 (s). Anal. Calcd for $C_{16}H_{10}N_6$ (286.29) (%): C, 67.12; H, 3.52; N, 29.35. Found (%): C, 67.07; H, 3.59; N, 29.50.

4.4.10 | 4-(5-methyl-1*H*-benzo[*d*]imidazol-2-yl)tetrazolo[1,5-*a*]quinoline

Yellow solid; m.p. 241–242 °C. ^{1}H NMR ($CDCl_3$, 250 MHz, δ, ppm): 2.46 (s, 3H), 7.04 (t, J = 8.0, 1H), 7.26–7.30 (m, 1H), 7.39–7.48 (m, 1H), 7.74 (t, J = 7.5, 1H), 7.89 (t, J = 7.7, 1H), 8.06 (d, J = 7.7, 1H), 8.65 (d, J = 8.2, 1H), 8.97 (s, 1H), 11.56 (s, 1H). ^{13}C NMR ($CDCl_3$, 62.9 MHz, δ, ppm): 21.83, 111.03, 114.6, 116.7, 119.0, 124.0, 125.0, 125.8, 128.6, 129.8, 130.2, 130.4, 131.7, 134.1, 141.7, 144.7, 145.5. IR (KBr, cm^{-1}): 468 (s), 490 (s), 596 (s), 671 (br), 713 (w), 729 (m), 750 (s), 773 (m), 798 (s), 863 (m), 906 (m), 945 (m), 1012 (w), 1100 (s), 1126 (m), 1140 (m), 1212 (s), 1280 (s), 1316 (s), 1337 (m), 1398 (m), 1539 (br), 2915 (s), 3255 (s). Anal. Calcd for $C_{17}H_{12}N_6$ (300.32) (%): C, 67.99; H, 4.03; N, 27.98. Found (%): C, 67.91; H, 4.08; N, 30.02.

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REFERENCES

[1] a) D. S. Surry, S. L. Buchwald, *Chem. Sci.* **2010**, *1*, 13; b) H. Sharghi, P. Shiri, *Synthesis* **2015**, *47*, 1131; c) J. Hu, Y. Cheng, Y. Yang, Y. Rao, *Chem. Commun.* **2011**, *47*, 10133; d) D. H. R. Bartona, J.-P. Fineta, J. Khamsia, *Tetrahedron Lett.* **1988**, *29*, 1115; e) F. Chen, N. Liu, E. Jia, B. Dai, *RSC Adv.* **2015**, *5*, 51512; f) K. R. Reddy, N. S. Kumar, B. Sreedhar, M. L. Kantam, *J. Mol. Catal. A* **2006**, *252*, 136; g) Z.-L. Xu, H.-X. Li, Z.-G. Ren, W.-Y. Du, W.-C. Xu, J.-P. Lang, *Tetrahedron* **2011**, *67*, 5282; h) S. M. Islam, S. Mondal, P. Mondal, A. S. Roy, K. Tuhina, M. Mobarok, *Inorg. Chem. Commun.* **2011**, *14*, 1352; i) R. Sridhar, M. Yedukondalu, N. Chandrasekhar, M. V. Basaveswara Rao, *Am. J. Mater. Sci.* **2011**, *1*, 98; j) H. Chen, D. Wang, X. Wang, W. Huang, Q. Cai, K. Ding, *Synthesis* **2010**, *9*, 1505.

[2] a) M. A. P. Martins, C. P. Frizzo, D. N. Moreira, L. Buriol, P. Machado, *Chem. Rev.* **2009**, *109*, 4140; b) E. C. Gaudino, D. Carnaroglio, K. Martina, G. Palmisano, A. Penoni, G. Cravotto, *Org. Process Res. Dev.* **2015**, *19*, 499; c) K. Tanaka, *Solvent-Free Organic Synthesis*, 2nd ed., Wiley-VCH, Weinheim **2009**; d) M. Bakherad, A. Keivanloo, S. Samangooei, *Tetrahedron Lett.* **2012**, *53*, 5773; e) A. F. Asachenko, K. R. Sorochkina, P. B. Dzhevakov, M. A. Topchiy, M. S. Nechaev, *Adv. Synth. Catal.* **2013**, *355*, 3553.

[3] D. W. Old, M. C. Harris, S. L. Buchwald, *Org. Lett.* **2000**, *2*, 1403.

[4] B. Y.-H. Tana, Y.-C. Teo, *Org. Biomol. Chem.* **2014**, *12*, 7478.

[5] S. S. Kampmann, A. N. Sobolev, G. A. Koutsantonis, S. G. Stewart, *Adv. Synth. Catal.* **2014**, *356*, 1967.

[6] a) S. Díez-González, *Catal. Sci. Technol.* **2011**, *1*, 166; b) A. K. Verma, J. Singh, R. C. Larock, *Tetrahedron* **2009**, *65*, 8434; c) Y.-Z. Huang, J. Gao, H. Ma, H. Miao, J. Xu, *Tetrahedron Lett.* **2008**, *49*, 948; d) F. Xue, C. Cai, H. Sun, Q. Shen, J. Rui, *Tetrahedron Lett.* **2008**, *49*, 4386; e) A. K. Verma, J. Singh, V. K. Sankar, R. Chaudhary, R. Chandra, *Tetrahedron Lett.* **2007**, *48*, 4207; f) S. Haneda, Y. Adachi, M. Hayashi, *Tetrahedron* **2009**, *65*, 10459; g) Z. Xi, F. Liu, Y. Zhou, W. Chen, *Tetrahedron* **2008**, *64*, 4254; h) D. K. T. Yadav, S. S. Rajak, B. M. Bhanage, *Tetrahedron Lett.* **2014**, *55*, 931; i) N. V. Suramwar, S. R. Thakare, N. N. Karade, N. T. Khaty, *J. Mol. Catal. A* **2012**, *359*, 28; j) J. Mao, J. Guo, H. Song, S.-J. Ji, *Tetrahedron* **2008**, *64*, 1383; k) N. Panda, A. K. Jena, S. Mohapatra, S. R. Rout, *Tetrahedron Lett.* **2011**, *52*, 1924; l) S. M. Islam, N. Salam, P. Mondal, A. S. Roy, K. Ghosha, K. Tuhina, *J. Mol. Catal. A* **2014**, *387*, 7; m) R. K. Rao, A. B. Naidu, E. A. Jaseer, G. Sekar, *Tetrahedron* **2009**, *65*, 4619; n) H. Yang, C. Xi, Z. Miao, R. Chen, *Eur. J. Org. Chem.* **2011**, 3353; o) B. Sreedhar, K. B. S. Kumar, P. Srinivas, V. Balasubrahmanyam, G. T. Venkanna, *J. Mol. Catal. A* **2007**, *265*, 183; p) L. Xin, B. Weiliang, *J. Org. Chem.* **2007**, *72*, 3863; q) H.-J. Cristau, P. P. Cellier, J.-F. Spindler, M. Taillefer, *Eur. J. Org. Chem.* **2004**, 695; r) C.-A. Jon, K. Artis, L.-B. Stephen, *J. Am. Chem. Soc.* **2002**, *124*, 11684; s) H. Chen, M. Lei, L. Hu, *Tetrahedron* **2014**, *70*, 5626; t) Q. Zhang, X. Wang, C. Cheng, R. Zhu, N. Liu, Y. Hu, *Org. Biomol. Chem.* **2012**, *10*, 2847; u) S. Jindabot, K. Teerachanan, P. Thongkam, S. Kiatisevi, T. Khamnaen, P. Phiriyawirut, S. Charoenchaidet, T. Sooksimuang, P. Kongsaeree, P. Sangtrirutnugul, *J. Organometal. Chem.* **2014**, *750*, 35; v) D. Urankar, B. Pinter, A. Pevec, F. D. Proft, I. Turel, J. K. Smrlj, *Inorg. Chem.* **2010**, *49*, 4820; w) E. Amadio, A. Scrivanti, M. Bortoluzzi, M. Bertoldini, V. Beghetto, U. Matteoli, G. Chessa, *Inorg. Chim. Acta* **2013**, *405*, 188.

[7] J. Hu, Y. Cheng, Y. Yang, Y. Rao, *Chem. Commun.* **2011**, *47*, 10133.

[8] N. E. Genung, L. Wei, G. E. Aspnes, *Org. Lett.* **2014**, *16*, 3114.

[9] Y. Fang, C. Wu, R. C. Larock, F. Shi, *J. Org. Chem.* **2011**, *76*, 8840.

[10] M. R. Kumar, A. Park, N. Park, S. Lee, *Org. Lett.* **2011**, *13*, 3542.

[11] a) Y. Bansal, O. Silakari, *Bioorg. Med. Chem.* **2012**, *20*, 6208; b) H. Sharghi, M. Aberi, M. M. Doroodmand, *Adv. Synth. Catal.* **2008**, *350*, 2380; c) H. Sharghi, M. H. Beyzavi, M. M. Doroodmand, *Eur. J. Org. Chem.* **2008**, 4126; d) Q. A. McKellar, E. Scott, W. J. Vet, *Pharmacol. Ther.* **1990**, *13*, 223; e) A. A. Spasov, I. N. Yozhitsa, L. I. Bugaeva, V. A. Anisimova, *Pharm. Chem. J.* **1999**, *33*, 232; f) A. A. Spasov, I. N. Yozhitsa, L. I. Bugaeva, V. A. Anisimova, *Pharm. Chem. J.* **1999**, *33*, 232; g) J. F. Rossignol, H. Maisonneuve, *Ann. Trop. Med. Parasitol.* **1984**, *78*, 135; h) A. Patil, S. Ganguly, S. Surana, *Rasayan J. Chem.* **2008**, *1*, 447; i) A. K. Dubey, P. K. Sanyal, *Online Vet. J.* **2010**, *5*, 63; j) M. Boiani, M. González, *Mini Rev. Med. Chem.* **2005**, *5*, 409; k) B. Narasimhan, D. Sharma, P. Kumar, *Med. Chem. Res.* **2012**, *21*, 269.

[12] M. Sabat, J. C. VanRens, M. J. Laufersweiler, T. A. Brugel, J. Maier, A. Golebiowski, B. De, V. Easwaran, L. C. Hsieh, R. L. Walter, M. J. Mekel, A. Evdokimov, M. Janusz, *J. Bioorg. Med. Chem. Lett.* **2006**, *16*, 5973.

[13] a) R. A. Rane, S. Naithani, R. D. Natikar, S. Verma, T. Arulmoli, US Patent 20130303782, **2013**; b) G. Navarrete-Vázquez, L. Yépez, A. Hernández-Campos, A. Tapia, F. Hernández-Luis, R. Cedillo, J. González, A. Martínez-Fernández, M. Martínez-Grueiro, R. Castillo, *Bioorg. Med. Chem.* **2003**, *11*, 4615.

[14] a) D. Hamied, R. N Kankan, D. R. Rao, Patent EP 1085019 A1; b) R. B. Uttarwar, R. B. Nawale, P. B. Shamkuwar, *J. Chem. Pharm. Res.* **2013**, *5*, 41.

[15] a) J. Hu, Q. Wu, W. Li, L. Ma, F. Su, Y. Guo, Y. Qiu, *ChemSusChem* **2011**, *4*, 1813; b) A. Zulauf, M. Mellah, X. Hong, *Dalton Trans.* **2010**, *39*, 6911.

[16] a) H. Sharghi, M. Aberi, M. M. Doroodmand, *Adv. Synth. Catal.* **2008**, *350*, 2380; b) H. Sharghi, M. Aberi, M. M. Doroodmand, J. Iranian, *Chem. Soc.* **2012**, *9*, 189.

[17] a) H. Sharghi, M. H. Beyzavi, A. Safavi, M. M. Doroodmand, R. Khalifeh, *Adv. Synth. Catal.* **2009**, *351*, 2391; b) H. Sharghi, R. Khalifeh, M. M. Doroodmand, *Adv. Synth. Catal.* **2009**, *351*, 207; c) H. Sharghi, P. Shiri, M. Aberi, *Synthesis* **2014**, *46*, 2489; d) H. Sharghi, M. Aberi, *Synlett* **2014**, *25*, 1111.

[18] A. N. Prasad, R. Srinivas, B. M. Reddy, *Catal. Sci. Technol.* **2013**, *3*, 654.

[19] a) Y. Jiang, D. Ma, in *Copper-Mediated Cross-Coupling Reactions*, (Eds: G. Evano, N. Blanchard), John Wiley, Hoboken, NJ **2014**, 3; b) A. Casitas, X. Ribas, in *Copper-Mediated Cross-Coupling Reactions*, (Eds: G. Evano, N. Blanchard), John Wiley, Hoboken, NJ **2014**, 253.

[20] a) N. Khatun, A. Gogoi, P. Basu, P. Das, B. K. Patel, *RSC Adv.* **2014**, *4*, 4080; b) M. R. Kumar, A. Park, N. Park, S. Lee, *Org. Lett.* **2011**, *13*, 3542.

[21] a) D. Yang, X. Zhu, W. Wei, N. Sun, L. Yuan, M. Jiang, J. Youac, H. Wang, *RSC Adv.* **2014**, *4*, 17832; b) M. Nasr-Esfahani, I. Mohammadpoor-Baltork, A. R. Khosropour, M. Moghadam, V. Mirkhani, S. Tangestaninejad, *J. Mol. Catal. A* **2013**, *13*, 243; c) P. L. Reddy, R. Arundhathi, M. Tripathia, D. S. Rawat, *RSC Adv.* **2016**, *6*, 53596.

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