

Polymeric 2,6-bis(benzimidazol-2-yl)pyridine-RuCl₃ complex as a catalyst for aerobic oxidative self-condensation of amines to imines

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A polymer ruthenium complex pbbp-RuCl₃ has been easily synthesized from the direct coordination of RuCl₃ with polymer constituted by tridentate 2,6-bis(benzimidazol-2-yl)pyridine unit (pbbp). As a heterogeneous catalyst, pbbp-RuCl₃ showed high efficiency in aerobic oxidative self-condensation of primary amines to imines. This heterogeneous catalyst can be easily recovered and exhibits good reusability in the reaction.

Keywords: pbbp-RuCl₃, Aerobic oxidation, Amines, Self-condensation, Imines

Imines are very important intermediates in the synthesis of many biologically and pharmaceutically active compounds via reactions such as cycloadditions, reductions, condensations and additions¹⁻⁷. The traditional method to obtain imines is the condensation reaction of carbonyl compounds with primary amines promoted by an acid catalyst. Due to importance of imines for organic and pharmaceutical syntheses, many alternative methods for the synthesis of imines have been developed such as oxidative cross-coupling between amines and alcohols⁸⁻¹⁴, oxidation of secondary amines¹⁵⁻¹⁷, and oxidative self-condensation of primary amines¹⁸⁻²⁴. Among all the protocols, the oxidative self-condensation of primary amines to imines has the advantages of amine as the only material and ready availability of amines. Various catalysts or catalytic systems including metal²²⁻²⁶, metal-free^{27,28}, photo²⁹⁻³², and bio-inspired³³⁻³⁶ ones have been developed with a promising future for the synthesis of imines. Amongst these, the transition metal-based catalytic systems can tolerate wide range of substrates, and afford imines in good yields. However, the homogeneous catalysts suffer from the disadvantage of difficulty of separation of the catalyst from the reaction mixture leading to impossible recycling. Therefore, it is essential to develop simple catalysts with both advantages of high efficiency and recyclability for the aerobic oxidation of primary

amines to imines. Heterogenization of homogeneous catalysts is expected to attain this end. It was reported that a polymer (abbreviated as pbbp) with a 2,6-bis(benzimidazol-2-yl)pyridine moiety can coordinate with ruthenium to afford several polymer-metal complexes with good thermal stabilities³⁷. This polymer can be readily obtained by the condensation reaction between pyridine-2,6-dicarboxylic acid and 3,3'-diaminobenzidine tetrahydrochloride dihydrate in the presence of polyphosphoric acid. Herein, we use this polymer both as a ligand and a supporter to synthesize an immobilized ruthenium complex pbbp-RuCl₃ for the self-condensation of primary amines to imines. As expected, this immobilized ruthenium complex showed good activity and recyclability in the aerobic oxidative self-condensation of amines to imines.

Materials and Methods

All the reagents and solvents were commercially available and used as received without further purification. RuCl₃·3H₂O was obtained from Xi'an Kaili Chemical Company. The amines were purchased from Alfa Aesar China (Tianjin) Co., Ltd. The polymer pbbp was synthesized according to reported procedures³⁷.

¹H NMR spectra were collected with TMS as internal standard on a Bruker AC-P 400 spectrometer. FTIR spectra were obtained from a Bruker Vector 22

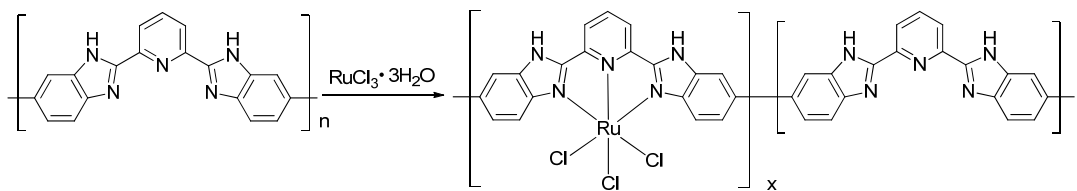
type instrument in the range of 4000–400 cm⁻¹ using KBr pellets. Thermogravimetric analysis was carried out using SDT/Q600 thermogravimetric analyzer at a temperature range of 20 °C to 1200 °C with a temperature ramp of 10 °C/min under air. The ruthenium contents of the catalyst samples were analyzed using a Perkin-Elmer Opfima 7300V type ICP-AES instrument. During the analysis, accurately weighed sample was carefully added into a flask, followed by addition of appropriate volumes of nitric acid and perchloric acid. The mixture was heated until the sample was completely dissolved. The resulting clear solution was then subjected to analysis.

Synthesis of pbbp-RuCl₃

A solution of pbbp (0.93 g, 3 mmol) in DMAC (200 mL), was taken and RuCl₃·3H₂O (0.79 g, 3 mmol) in DMAC (40 mL) under nitrogen atmosphere was added to it. The resulting solution was stirred at 80 °C for 4 h. The mixture was then cooled to room temperature and a dark brown solid precipitate was obtained. The solid was collected by filtration, and washed thoroughly with DMAC and methanol successively to afford the polymer complex pbbp-RuCl₃ (1.20 g, yield 77%).

Catalytic aerobic oxidative self-condensation of amines

In a typical process, a 5 mL two-necked flask equipped with a magnetic stirrer was taken and pbbp-RuCl₃ (0.073 g, 0.01 mmol) and primary amine (5 mmol) were added to it successively at room temperature. Oxygen as oxidant was introduced from a top balloon. Then, the temperature was raised to 100 °C and the contents maintained at this temperature until the completion of the reaction. The progress of the reaction was monitored by GC. Finally, the imine product was obtained by column chromatography of the reaction mixture on silica gel using *n*-hexane/EtOAc (10:1) as eluent. Characterization data for the products are given in Supplementary Data, Table S1.



Synthesis route and structure of pbbp-RuCl₃.

Results and Discussion

Synthesis of pbbp-RuCl₃

The synthesis route and structure of pbbp-RuCl₃ are shown in Scheme 1. The synthesis procedure of pbbp-RuCl₃ is same as that of its homogeneous counterpart 2,6-bis(2-benzimidazol-2-yl)pyridine ruthenium trichloride (bbp-RuCl₃)³⁷. As in the formation of bbp-RuCl₃, the bbp moiety in the polymer pbbp coordinated with RuCl₃ to afford the polymer complex pbbp-RuCl₃.

Characterization

The pbbp-RuCl₃ complex was characterized by FTIR. For comparison the spectra of the polymer pbbp, 2,6-bis(benzimidazol-2-yl)pyridine (bbp) and bbp-RuCl₃ were also taken. As shown in Fig. 1, pbbp and bbp exhibit similar spectra, but the wave numbers of the characteristic bands shift in some degree. The bands at 1665–1550 cm⁻¹ are assigned to the C=N stretching in the imidazole and pyridine ring, and the broad absorption bands around 3300–2750 cm⁻¹ are ascribed to the imino N-H stretching³⁷. The spectrum of pbbp-RuCl₃ is close to

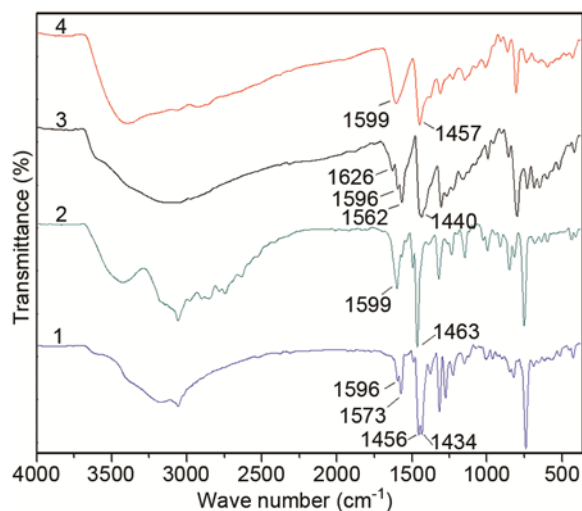


Fig. 1 — FTIR spectra of bbp (1), bbp-RuCl₃ (2), pbbp (3), and pbbp-RuCl₃ (4).

Scheme 1

that of bbp-RuCl_3 , and both spectra show a strong band at 1606 cm^{-1} and a series of bands around $3300\text{--}2750\text{ cm}^{-1}$. The characteristic bands of the spectra of bbp-RuCl_3 and pbbp-RuCl_3 shown in Fig. 1 are identical to the ones of bbp-RuCl_3 reported in literature³⁷. The FTIR characterization results indicate that a bbp-RuCl_3 unit is present in the skeleton of the polymer complex pbbp-RuCl_3 .

ICP was employed to determine the ruthenium content, which was found to be 13.9%, it can be thus estimated that the percentage of complexation in pbbp-RuCl_3 is about 60%, or the ratio of x to y in Scheme 1 is about 60:40.

The thermal stability of pbbp-RuCl_3 was evaluated by thermogravimetric analysis (TGA). The TG and

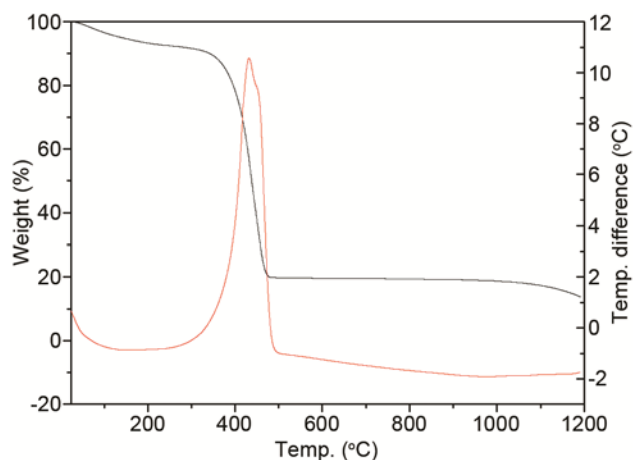


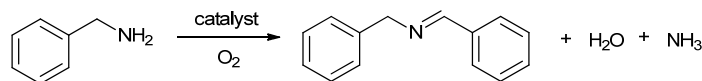
Fig. 2 — TG and DSC curves of the thermal degradation of pbbp-RuCl_3 .

DSC plots of pbbp-RuCl_3 as shown in Fig. 2 indicate that an initial endothermic stage occurs in the range of 50 to 200 °C for the sample of pbbp-RuCl_3 with a weight loss of about 7%, which can be ascribed to the desorption of physisorbed water. The second stage taking place in the temperature range of 300 to 500 °C corresponds to the exothermic oxidative degradation of the complex. A weight loss of about 70% takes place in this stage. The results indicate that the pbbp-RuCl_3 as a catalyst is stable in the catalytic run below 300 °C.

Catalytic aerobic oxidation of amines to imines

The catalytic performance of pbbp-RuCl_3 in the aerobic oxidative self-condensation of amines to imines was evaluated using benzylamine as a model substrate. Initial experiments disclosed that the reaction could proceed under solvent-free and atmospheric oxygen pressure conditions. The parameters influencing the reaction were therefore screened under solvent-free and atmospheric oxygen pressure conditions. As shown in Table 1, no reaction was observed in the absence of pbbp-RuCl_3 (Table 1, entry 1), indicating the necessity of pbbp-RuCl_3 in the reaction. In the case of catalyst loading of 0.1 mol%, the conversion of benzylamine reached 83.9% with a selectivity of 94.9% of the corresponding imine *N*-(benzylidene)benzylamine in 4 h at 110 °C (Table 1, entry 2). Increasing the catalyst loading to 0.2 mol%, the conversion increased and reached up to 99% with a selectivity of 97.9% of the imine under the same reaction conditions

Table 1 — Optimization of conditions for oxidative coupling of benzylamine to imines



Entry	Temp. (°C)	Catalyst (mol%)	Time (h)	Conversion (%) ^a	Selectivity (%) ^a
1	110		10	0	0
2	110	0.1	4	83.9	94.9
3	110	0.2	4	99.0	97.9
4	110	0.3	4	98.1	96.2
5	110	0.4	4	96.1	98.7
6	110	0.5	4	98.9	93.1
7	90	0.2	10	94.0	97.4
8	100	0.2	7	99.3	97.0
9	120	0.2	3.5	98.6	94.3

reaction conditions: benzylamine (5 mmol), atmospheric oxygen pressure

^aconversion and selectivity were determined by GC.

(Table 1, entry 3). Further increasing the catalyst loading could not accelerate the reaction, on the contrary, excessive catalyst loading led to the decrease of selectivity (Table 1, entries 5, 6). The effect of reaction temperature was then examined under the catalyst loading of 0.2 mol%. When the reaction was performed at 90 °C, the conversion was 94% with a selectivity of 97.4% of the imine in 10 h (Table 1, entry 7). Increasing the reaction temperature can accelerate the reaction (Table 1, entries 3, 7-9), and the reaction was completed in 7 h with a selectivity of 97.0% of the imine at 100 °C (Table 1, entry 8). Further increase of reaction temperature led to the decrease in selectivity of the imine (Table 1, entry 9).

Based on the above results, it can be concluded that the optimal reaction conditions for the reaction are: substrate 5 mmol, reaction temperature 100 °C, catalyst loading 0.2 mol% of substrate, and atmospheric oxygen pressure. Under the optimal reaction conditions, the conversion of benzylamine reached up to 99.3% with a selectivity of 97% of N-(benzylidene)benzylamine in 7 h in the absence of any solvents.

To screen its versatility, the catalyst pbbp-RuCl₃ was applied to the aerobic oxidative self-condensation of other primary amines under the optimal conditions. As shown in Table 2, all the substituted primary benzylamines, including the ones bearing both electron-withdrawing and electron-donating groups, were converted to the corresponding imines in good to excellent GC yields. However, the electronic properties of the substituents have some effects on the reaction. Generally, the electron-withdrawing substituent enhanced the reactivity of the substrate, and the electron-donating substituent reduced the reactivity of the substrate (Table 2, entries 1, 2, 5, 8-10). The reactivity of the substrate was also related to the positions of the substituent on the phenyl groups. The *ortho*-substituted benzylamine exhibited low reactivity compared to the *para*-substituted one due to the steric hindrance between the substituent and hydroxymethyl group (Table 2, entries 2, 4, 5, 7). For instance, *p*-chlorobenzylamine was converted to its corresponding imine in only 5 h, but in the case of *o*-chlorobenzylamine as substrate under the same conditions 23 h were required (Table 2, entries 5, 7). The reactivity of *meta*-substituted benzylamine was situated between those of *para*- and *ortho*-substituted ones. In some cases, aldehydes as by-products

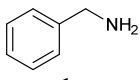
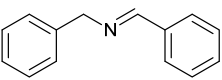
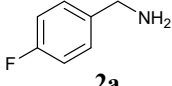
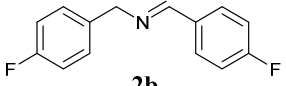
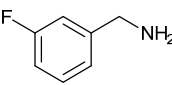
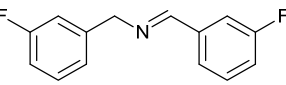
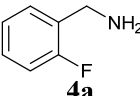
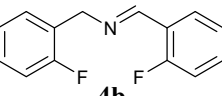
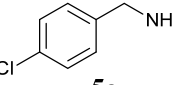
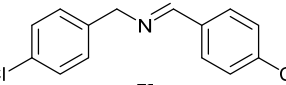
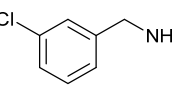
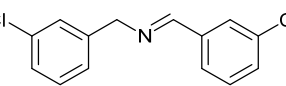
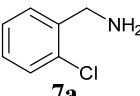
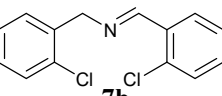
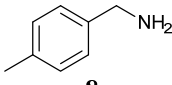
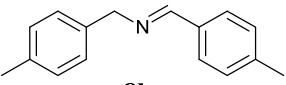
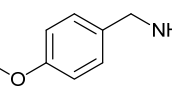
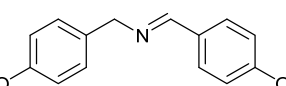
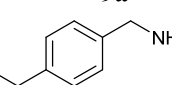
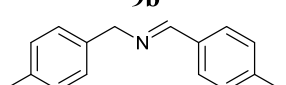
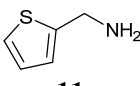
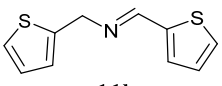
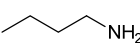
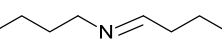
were observed, which led to the decrease of the selectivity of imines (Table 2, entries 4, 6, 7). The aldehydes were derived from the hydrolysis of imines under the reaction conditions.

The catalyst pbbp-RuCl₃ also exhibited high activity in the aerobic oxidative self-condensation of heterocyclic amines. 2-Thiolyl methylamine, one representative of the heterocyclic amines, was smoothly oxidized to its corresponding imine in high yield in 11 h (Table 2, entry 11). Generally, heterocyclic amines including 2-thiolyl methylamine were poor substrates in the aerobic oxidative self-condensation to imines catalyzed by copper based catalysts³⁸. Poor results were obtained in the self-condensation of non-activated aliphatic amines to imines under the same reaction conditions (Table 2, entries 12, 13). In the case of *n*-butylamine as substrate the conversion was only 40.5% with a selectivity of imine of 44.7%, and no pure product could be separated by column chromatography (Table 2, entry 12). Similar results were also observed in the case of cyclopropyl methylamine as substrate.

Recyclability

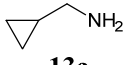
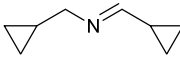
Recycling experiments were carried out to evaluate the stability and reusability of the catalyst in the aerobic oxidative self-condensation of benzylamine. The catalyst remained insoluble under the reaction conditions, and hence could be easily recovered by simple filtration. The recovered catalyst was washed extensively with methanol and dried at 100 °C thoroughly, and then subjected to the next run. The conversion decreased with the recycle times, but not obviously in the first four runs (Table 3). For instance, the conversion decreased only by 1.6% in the second run compared to the first run. However, the conversion decreased sharply in the fifth run, and the conversion was only 87.5%. It should be noted that the selectivity remained almost constant throughout the recycle runs. The above results indicate that the catalyst can be recycled at least four times without a large decrease in its activity. The decrease of the catalyst's activity can be ascribed to the leaking of ruthenium, which was confirmed by analyzing the ruthenium content of the reaction mixture after each run. The leaking rate of ruthenium in each catalytic run is shown in Table 3.

Table 2 — pbbp-RuCl₃ catalyzed oxidation of different amines to imines

$\text{R-CH}_2\text{-NH}_2 \xrightarrow[\text{neat, 100 }^\circ\text{C}]{\text{pbbp-RuCl}_3 (0.2\text{mol}\%) / \text{O}_2} \text{R-CH}_2\text{-N=CH-R}$						
Entry	Substrate 1a-13a	Product 1b-13b	Time (h)	Conv. (%) ^a	Selectivity (%) ^a	Yield (%) ^b
1	 1a	 1b	7	99.3	97.0	96.3 (79.0)
2	 2a	 2b	9	98.7	96.0	94.8 (74.1)
3	 3a	 3b	16	97.5	97.8	95.4 (70.9)
4	 4a	 4b	17	>99	87.3	86.4 (66.7)
5	 5a	 5b	5	97.5	98.5	96.0 (70.2)
6	 6a	 6b	19	>99	89.6	88.7 (62.2)
7	 7a	 7b	23	>99	94.6	93.7 (71.0)
8	 8a	 8b	10	>99	98.7	97.7 (76.4)
9	 9a	 9b	12	86.8	>99	85.9 (62.3)
10	 10a	 10b	14	98.2	>99	97.2 (71.2)
11	 11a	 11b	11	98.9	93.1	92.1 (65.1)
12	 12a	 12b	8	40.5	44.7	18.10

(Contd.)

Table 2 — pbbp-RuCl₃ catalyzed oxidation of different amines to imines (*Contd.*)

Entry	Substrate	Product	Time (h)	Conv. (%) ^a	Selectivity (%) ^a	Yield (%) ^b
13	 13a	 13b	6	58.8	34.1	20.1

reaction conditions: primary amine (5 mmol), pbbp-RuCl₃ (0.01 mmol), reaction temperature 100 °C, atmospheric oxygen pressure

^aconversions and selectivity were determined by GC

^bdata in parentheses represent isolated yields.

Table 3 — Recycling of pbbp-RuCl₃ in aerobic oxidative self-condensation of benzylamine

Run	Conversion (%) ^a	Selectivity (%) ^a	Leaking rate (%) ^b
1	98.3	96.9	3.38
2	96.7	96.7	2.63
3	95.5	94.8	2.31
4	93.7	96.7	2.21
5	87.5	96.6	2.07

reaction condition: benzylamine (20 mmol), catalyst (0.04 mmol), reaction temperature 100 °C, reaction time 7 h, atmospheric oxygen pressure

^adetermined by GC

^bpercentage of ruthenium in filtrate with that of catalyst loading in the first run.

Conclusions

The complex pbbp-RuCl₃ was easily synthesized and showed high activity and selectivity in the aerobic oxidative self-condensation of some primary amines to the corresponding imines. This polymer ruthenium complex can be recovered easily and reused four times without significant decrease in its activity. The gradual decrease of its activity is due to the leaking of ruthenium from the polymer during the catalytic runs.

Supplementary Data

Supplementary data associated with the article are available in the electronic form at [http://www.niscair.res.in/jinfo/ijca/IJCA_57A\(10\)1242-1248_SupplData.pdf](http://www.niscair.res.in/jinfo/ijca/IJCA_57A(10)1242-1248_SupplData.pdf).

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