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FeCl₂-PPh₃ as an efficient catalytic system for the acceptorless dehydrogenation of amines into imines

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Abstract

In this work, a novel and simple catalytic system including FeCl_2 , PPh_3 and potassium *tert*-butoxide has been employed for the synthesis of imines from amines. In order to prove the catalytic acceptorless dehydrogenation pathway for this transformation, the liberated H₂ gas is detected by NMR spectroscopy. By utilizing this protocol, a variety of arylamines were used successfully for the preparation of corresponding imines in good to excellent yields (on a 1 mmol scale, 73–91% yield for homocoupling, 71 and 91% for heterocoupling).

Keywords Imine · Iron-based catalyst · Dehydrogenation reactions

Introduction

One of the most important developments in organic chemistry is the formation of carbon–nitrogen bonds (Jaiswal et al. 2016). Imines are a significant category of carbon–nitrogen containing compounds because they have different reactivity and many applications in laboratory and industrial processes such as pharmaceuticals, biologically active heterocycles, and natural product (Zanardi et al. 2010; Liu et al. 2009) Active imines are generated as intermediates in reaction process, which due to their abundant application, their selective preparation was studied (Dobereiner & Crabtree. 2010).

The traditional route to prepare of imines implies the reaction of ketones or aldehydes with amines in the presence of Lewis acid catalysts. Imines can also be prepared by the oxidative condensation of amines (Murahashi. 1995; Orito et al. 1998; Yi & Lee. 2009). Another method for producing imines is the coupling of alcohol with amine in the presence of stoichiometric amounts of oxidants which has some disadvantages like the generation of stoichiometric amounts of waste and need to activated alcohols (Gnanaprakasam et al. 2010). To overcome these limitations and to develop more effective way, other methods have been investigated.

Dehydrogenation reaction is one of the best methods for preparation of imines by releasing the molecular hydrogen as a by-product which is a greener method and it has potential applications in the field of organic hydrogen storage materials (Chakraborty et al. 2014a, b; Armaroli & Balzani. 2011; Fukuzumi & Suenobu. 2013) Furthermore, one of the concerns in the contemporary century is the gradual disappearance of fossil fuels and the finding of a clean energy supply that is sustainable and renewable. It has been widely accepted that hydrogen as a fuel can be useful to decrease the energy crisis (Balaraman et al. 2017; Jaiswal et al. 2017) For these reasons, the stable generation of hydrogen is favourable (Largeron et al. 2008; Han et al. 2014; Kwon et al. 2009; Zhang et al. 2013). In recent years, catalysis based on metal complexes (such as Ru, Rh, Ir and Au complexes) is used in many of dehydrogenation reactions but they are scarce and expensive (Sieffert and Bühl 2010; Choi & Doyle. 2007; Li et al. 2011; So et al. 2009) But catalysis based on the relatively abundant and economical first-row transition metals (Fe, Co, Ni and Cu) has become more fascinating and suitable alternative to precious-metal based catalytic systems (Jagadeesh et al. 2014; Chen et al. 2015; Chakraborty et al. 2014a, b). Gopalaiah et al. reported the synthesis of imines by oxidative self- or cross-condensation of primary amines using iron(II) bromide as the catalyst. They used oxygen as an oxidant and water was produced as waste (Gopalaiah et al., 2016).

Herein, we have introduced a novel homogenous catalytic system including FeCl₂, PPh₃ and potassium *tert*-butoxide

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for the acceptorless dehydrogenation of amines into imines. This reaction occurs efficiently in the oxidant free condition and is accompanied by liberation of hydrogen gas as a by-product.

Experimental

General

All reagents were purchased from Sigma-Aldrich and used without further purification. Column chromatography separations were performed on silica gel (220–440 mesh) and aluminium oxide (100–200). The NMR spectra were determined on a Bruker Avance DRX-400 MHz. Elemental microanalysis was performed on a Thermo Finnigan Flash EA 1112 series CHN analyzer. The physical, analytical and spectral data for all compounds are given in the Supplementary material to this paper.

General Procedure

FeCl₂ (11.4 mg, 0.09 mmol), triphenylphosphine (47.2 mg, 0.18 mmol) and *t*-BuOK (11.2 mg, 0.10 mmol (and 2 mmol aniline derivatives in the case of heterocoupling reaction) were placed in a dry Schlenk tube and connected to the vacuum line. The tube was evacuated and filled with nitrogen three times. Freshly degassed mesitylene (3 mL) was injected into the mixture, which was then heated to 160 °C under a N₂ atmosphere and then benzylic amine (2 mmol) was added. The progress of reaction was monitored by thin layer chromatography. After finishing the reaction, the mixture was cooled to room temperature and the product was purified by aluminium oxide (activated) or silica gel column chromatography (96/4 hexane/Et₃N) to give the product. In the case of heterocoupling reaction, benzylic amins (1 mmol) and aniline derivatives (2 mmol) were applied.

Procedure for hydrogen detection

An oven-dried Schlenk tube was charged with FeCl_2 (11.4 mg, 0.09 mmol), triphenylphosphine (47.2 mg, 0.18 mmol) and *t*-BuOK (11.2 mg, 0.10 mmol. The tube was then inserted into an oil bath, vacuum was used and the tube was filled with nitrogen (repeated 3 times). Freshly degassed mesitylene (3 mL) was injected into the mixture and the mixture was heated to 160 °C and then benzylamine (2 mmol) was added. Subsequently, the tube was disconnected from the nitrogen atmosphere and connected to a burette filled with water. After completion of reaction, the hydrogen gas collected in the burette was bubbled through a

septum in a NMR tube filled with toluene-d8. ¹HNMR result showed the presence of hydrogen at 4.65 ppm.

Results and discussion

Primary results on the dehydrogenation of benzylamine using different percentages of iron complexes with phosphine as a ligand in several conditions such as different additives and different amounts of PPh_3 and $FeCl_2$ are shown in Table 1.

At first, the catalytic activity was investigated in different amounts of metal and ligand. When 2 mol% of FeCl₂ was used, the product was formed in low yield (Table1, entry1). Increasing the loading of the catalyst to 9 mol% has improved the yield to 90% (entries 2-5). But, when the catalyst loading was increased over (above) the 9 mol%, no significant change was observed in the efficiency of reaction (Table1, entry 6). Then, different amounts of ligand were investigated, which only 18 mol% of ligand was approved and had good efficiencies (Table1, entries 5, 7 and 9). Further optimization of the reaction was performed by studding the effect of additive on the reaction yields. We understood that in the additive-free condition, the yields are not more than 78% (Table1, entry 17). No improvement was observed by adding 10% MgSO₄, NaH, Na₂CO₃ and K₂CO₃ (Table1, entries 10 and 12–14). By adding 10 mol% of DABCO as an organic additive, an improvement was observed (Table1, entry 11). Finally, with 10% of t-BuOK the yield changed to 90% (Table1, entry 5) clearly showing that additional reactivity by t-BuOK as an additive can be useful.

Additionally, in the absence of PPh₃, the reaction yield was decreased (Table1, entry18). Also, in FeCl₂-free condition, the reaction was prevented and no product was isolated (Table 1, entry 19). Optimization studies showed that FeCl₂ (9 mol%), PPh₃ (18 mol%), *t*-BuOK (10 mol %) and mesitylene (3 ml) at 160 °C are the best combinations for this catalytic system in this reaction.

After optimizing the reaction conditions, the various amines were examined under the mentioned reaction conditions (Table 2). In all the cases, benzylic amines containing electron-withdrawing groups gave lower yields than that with electron-donating groups. (Table2, entries 4–7).

As shown as in the Table 2, the substituted benzylamine with methyl group has an excellent yield. In addition, the existence of reactivity different between benzylamines and aniline derivatives can make it possible to do heterocoupling reaction (Table 2, entries 8 and 9). In order to prevent of forming homocoupling products, 2 mmol of aniline derivatives have been employed. Additionally, the further investigations have been done for the all entries in

Table 1 Optimization of the reaction conditions^a

	NH ₂	FeCl ₂ (X mol%) PPh ₃ (Y mol%)		\sim	
		Additive (Z mol %) Mesitylene			
Entry	FeCl ₂ (x mol%)	PPh ₃ (Y mol%)	Additive (Z mol%)	Time(h)	Yield ^b
1	2	18	t-BuOK,10	48	32
2	4	18	t-BuOK,10	48	41
3	6	18	t-BuOK,10	48	62
4	8	18	t-BuOK,10	35	76
5	9	18	t-BuOK,10	30	90
6	10	18	t-BuOK,10	30	89
7	9	9	t-BuOK,10	48	72
9	9	36	t-BuOK,10	30	78
10	9	18	MgSO ₄ ,10	30	31
11	9	18	DABCO,10	30	81
12	9	18	NaH,10	30	76
13	9	18	Na ₂ CO ₃ ,10	30	59
14	9	18	K ₂ CO ₃ , 10	30	65
15	9	18	t-BuOK,15	30	84
16	9	18	t-BuOK,5	30	63
17	9	18	-	30	78
18	9	_	t-BuOK,10	30	70
19	-	18	t-BuOK,10	30	-

^aReaction conditions: benzylamine (2 mmol), mesitylene (3 mL) at 160 °C. ^bIsolated yields

the additive-free condition. The results are presented in the Table 2.

Observing reduced product or detecting of hydrogen gas is an important evidence for this catalytic dehydrogenative transformation because it can prove that this catalytic system is not an air oxidation. In order to detect hydrogen gas, the catalytic homocoupling reaction of benzyl amine was performed in the optimized reaction condition in the close system (scheme 1). The liberation of H_2 gas was confirmed by ¹HNMR spectroscopy.

Based on the some reported studies (Takallou et al. 2020; Bottaro et al. 2019), a plausible mechanism pathway for FeCl₂-PPh₃ catalytic system in the dehydrogenative coupling of amines is shown in the Scheme 2. In the beginning step of catalytic cycle, benzylic amines in the presence of *t*-BuOK is coordinated to Fe(L) to generate intermediate (1). Then, pursuant to the β -H elimination of (1) a Fe-hydride species (2) and an aldimine intermediate can be generated. Finally, amine can react with aldimine intermediate to obtain corresponding imine.

Conclusions

In conclusion, we have introduced a novel catalytic system which has been applied in the acceptorless dehydrogenation amines into imines. Detection of the liberated hydrogen gas has been confirmed by NMR spectroscopy that can prove the dehydrogenative nature of these reactions. Additionally, the activity of this catalytic system had been examined to synthesize different imines in good to excellent yields. There are some advantages in using this catalytic system including oxidant free reaction condition, using the catalytic amount of additive and catalyst, and also applying the inexpensive earth abundant metal.





Entry	-X	Product	Time (h)	Yield ^b	Yield ^c
1	-H		30	90	78
2	-OMe	MeO OMe	30	89	75
3	-Me	Me	30	91	79
4	-F	F F	36	73	64
5	-Cl		36	75	73
6	-Br	Br	36	75	66
7	-I		36	81	63
8 ^d	-H	OMe	48	71	58
9 ^d	-H	Me	48	72	53

^aReaction conditions: benzylamine (2 mmol), FeCl₂ (9 mol%), PPh₃ (18 mol%), *t*-BuOK (10 mol%), mesitylene (3 mL) at 160 °C. ^bIsolated yields. ^cIsolated yields in the absence of base for 30 h. ^d2 mmol Ar-NH₂ is used



Scheme 1 FeCl₂-PPh₃ catalyzed dehydrogenative coupling of benzylamine



Scheme 2 The plausible mechanism pathway for the FeCl₂-PPh₃ catalytic system in the catalytic dehydrogenative coupling of amines

Supplementary Information The online version contains supplementary material available at https://doi.org/10.1007/s11696-021-01749-x.

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