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Research Article

SELECTIVE OXIDATION OF SEC-ALCOHOLS CATALYZED BY IRON (III) ALANINE SCHIFF BASE COMPLEX USING MOLECULAR OXYGEN BY MICROWAVE IRRADIATION UNDER SOLVENT FREE CONDITION

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ABSTRACT

A simple and convenient procedure for the oxidation of secondary alcohols to their corresponding carbonyl compounds under solvent free condition is developed using molecular oxygen as the oxidant under microwave irradiation method. By applying iron (III) amino acid Schiff base complex as catalyst a variety of activated and non-activated secondary alcohols were oxidized to ketones in good yield and excellent selectivity under mild conditions. The oxidation reactions performance was evaluated using different amount of catalyst in various solvent systems and at different temperatures.

Keywords: *Secondary Alcohols, Metal Schiff Base Complexes, Solvent Free, Microwave Irradiation, Oxidation*

INTRODUCTION

Currently, the Microwave-Assisted Organic Synthesis (MAOS) is a powerful synthetic tool to carry out the synthesis of a variety of organic compounds (Insuasty *et al.*, 2013; Kappe *et al.*, 2013; Quiroga *et al.*, 2012). Comparing with classical methods, microwave-assisted reactions are non-conventional efficient energy source for synthetic chemistry and have gained importance because of the simplicity in operation, milder reaction conditions, increasing reaction rates, and formation of cleaner products. Moreover, solvent-free microwave-assisted reactions are having more popularity as they provide an opportunity to work under conditions ecologically compatible (Martins *et al.*, 2009; Bougrin *et al.*, 2005; Quiroga *et al.*, 2007).

The selective oxidation of primary and secondary alcohols into the corresponding aldehydes and ketones without forming over-oxidized product is one of the most important transformations for both academic and industrial applications (Vannucci *et al.*, 2012; Lee *et al.*, 2011; Bianchini *et al.*, 2009; Choudhary *et al.*, 2005), still many oxidation processes use are non-environmentally friendly. The carbonyl compounds are used as important precursors and intermediates for many drugs, vitamins, and fragrances (Choudhary *et al.*, 2006).

In traditional oxidation processes, large amounts of toxic and volatile organic solvents and metal oxidants were extensively used including stoichiometric oxidants notably chromium reagents (Luzzio *et al.*, 1988), manganese(IV) oxide (Taylor *et al.*, 2005), activated DMSO (Pfitzner *et al.*, 1963), hypervalent iodine reagents (Nicolaou *et al.*, 2000; Uyanik *et al.*, 2009), ruthenium reagents (Berkowitz *et al.*, 1958), osmium (VIII) oxide (Maione *et al.*, 1984), metal (Gamez *et al.*, 2003; Marko *et al.*, 2004; Jiang *et al.*, 2006; Figiel *et al.*, 2010; Hoover *et al.*, 2011; Kwong *et al.*, 2011; Gunasekaran *et al.*, 2012; Li *et al.*, 2003) or TEMPO-catalyzed oxidation (Sheldon *et al.*, 2004; Liu *et al.*, 2004; Shibuya *et al.*, 2011) which, produce copious amounts of heavy metal wastes. Even some recently reported reactions using transition metal based catalyst such as Cu, Ru, Au, and Pd also afford considerable amounts of toxic metal salts. And all of these methods still have poor atom efficiencies. The need for environmentally benign and clean oxidation reactions remains an important goal of chemical researchers to minimize the amount and toxicity of the released waste. Hence, developing green selective oxidation process for alcohols is still a challenging task in catalysis (Aellig *et al.*, 2012; Feng *et al.*, 2011; Xie *et al.*, 2008). By comparing different oxidation methods, it is apparent that the oxidant used in the respective transformation defines the quality and applicability of the method. Molecular oxygen is an attractive green oxidant and development of synthetic methodologies using molecular oxygen as the sole oxidant is the rewarding goal both from economical and environmental points of view. The use of molecular oxygen with a variety of metal catalysts has been reported in the literature (Tang *et al.*, 1978; Backvall *et al.*, 1991; Yamaguchi *et al.*, 2000; Csjernyik *et al.*, 2002; Kaneda *et al.*, 1998; Kakiuchi *et al.*, 2001; Dijksman *et al.*, 2001). Because dioxygen is inexpensive and water is produced as the only by product. Many catalytic systems have been shown to be capable of catalyzing alcohol oxidation to the corresponding aldehydes and ketones with molecular oxygen.

Therefore, the discovery of new protocol catalyst using molecular oxygen is gathering much attention. In this context, variety of transition metal-based catalysts has been extensively investigated towards the oxidation of alcohols so far. In continuation to our studies on oxidation using molecular oxygen as primary oxidant. Herein, we report the iron (III) amino acid Schiff base complexes as the catalysts for the oxidation of secondary alcohols to corresponding ketones in excellent yields with molecular oxygen as the sole oxidant without using a solvent under microwave (**Scheme 1**).

MATERIALS AND METHODS

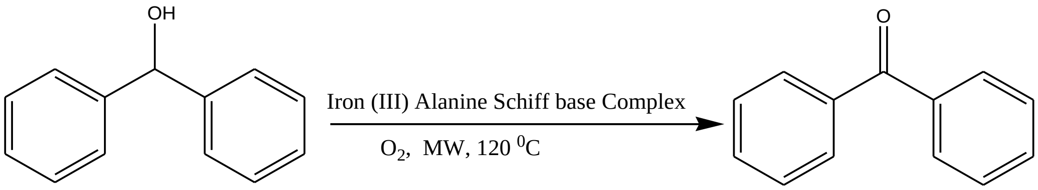
All Secondary alcohols and salicylaldehyde were purchased from (Fluka), the $FeCl_3$, $CoCl_2 \cdot 6H_2O$, $ZnCl_2$, L-alanine, L-phenylalanine, Piperidine, acetone, diethyl ether and petroleum ether were purchased from (Sigma Aldrich) and used as received without further purification. Ethanol, chloroform, acetonitrile and ethyl acetate were purchased from (Loba Chemie). All chemicals and reagents used in the present study were of analytical grade. ^1H NMR spectra of products (Ketones), ligands and complexes were measured on a Brucker 500-DRX Avance spectrometer at 500 MHz using TMS as internal standard. The FTIR spectra were recorded on a Shimadzu JASCO FTIR-460 plus spectrophotometer using KBr pellets or neat. Mass spectra of obtained products were recorded on GC-MS Varian Saturn 2100T**.**

Synthesis of the Amino Acid Schiff Base Metal Complexes

In our laboratory, we synthesized various amino acid Schiff base metal complexes, amino acid metal complexes and applied for the oxidation of cyclohexane, secondary alcohols and other value added products (Merajuddin *et al.*, 2014; Merajuddin *et al.*, 2013; Merajuddin *et al.*, 2013).

General Procedure for Oxidation of Secondary Alcohols to Ketones

Secondary alcohol (1 mmol) and iron (III) alanine Schiff base complex (5 mol%) were taken in a 25 ml double necked round bottomed flask fitted with a gas passing tube and a stirring bar. The mixture was then stirred at room temperature in the presence of molecular sieves (3Å) with oxygen gas bubbled in slow rate for a while later it was kept in microwave irradiation chamber under oxygen atmosphere (**Scheme 1)**. The progress of reaction was monitored by TLC and after completion; the molecular sieves were removed by filtration. The filtrate thus obtained was evaporated under reduced pressure and the residual mass was dissolved in a mixture of ethyl acetate/hexane (1:4) and then passed through a short column of silica gel using hexane/ethyl acetate (4:1) as eluent. Removal of solvent and usual workup gave corresponding ketones, which were identified by comparing their physical and spectral data with those of authentic compounds reported in literature.



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RESULTS AND DISCUSSIONS

To evaluate the catalytic efficiency of various metal Schiff base complexes and simple amino acid metal complexes, the oxidation of benzhydrol was studied as a model reaction with molecular oxygen using different metal Schiff base complexes and simple amino acid metal complexes as catalyst under solvent free system in presence of molecular sieves. These results are presented in **Table 1** and show that iron (III) alanine Schiff base complex (Entry 1) was most efficient catalyst for this transformation. The other amino acid metal complexes have shown moderate yield. In blank experiment (Entry 6) no oxidation was observed under similar conditions in the absence of catalyst.

Table 1: Screening of the different catalysts for oxidation of benzhydrol to benzophenone using molecular oxygen

yrtnE	tsylataC	Yield (%)
1	Iron (III) alanine Schiff base complex	94
2	Iron (II) phenyl alanine Schiff base complex	75
3	xelpmoc eninala norI	72
4	xelpmoc eninala tlaboC	76
5	Zinc alanine complex	65
6	tsylatac tuohtiW	N. R

Further, we explored the efficiency of this method, by carrying out the oxidation of benzhydrol to benzophenone in different organic solvents including without solvent and these results are shown in **Table 2**. Although among the various organic solvents (Entries 1, 2, 3, 5), solvent free system (Entry 4) was found to be more suitable in terms of products as obtained in shorter reaction time.

Table 2: Screening of the solvents for oxidation of benzhydrol to benzophenone using iron (III) alanine Schiff base complex

yrtnE	Catalyst	tnevloS	Yield (%)
1	Iron (III) alanine Schiff base complex	enelyX	15
2	-Do-	elitinotecA	40
3	-Do-	lonahtE	50
4	-Do-	eerf tnevloS	94
5	-Do-	enuloT	30

After conducting the reaction as mentioned above we further evaluated the catalytic effect of iron (III) alanine Schiff base complex, the oxidation of benzhydrol was carried out with different catalyst concentrations 5 mol%, 10 mol%, 20 mol% and 30 mol%, under similar reaction conditions. These results are presented in **Table 3**. A 10 mol% (Entry 2), loading of the catalyst was sufficient to promote the reaction and increased amounts of the catalyst did not lead to any significant changes in the product yield.

Table 3: Effect of the catalyst concentration for the oxidation of benzhydrol to benzophenone using iron (III) alanine Schiff base complex

yrtnE	Catalyst (mol %)	Yield (%)
1	5	65
2	10	94
3	20	70
4	30	68

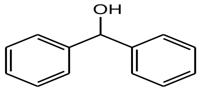
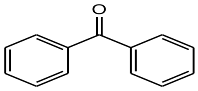
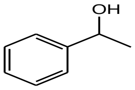
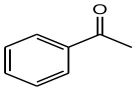
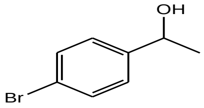
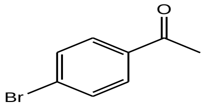
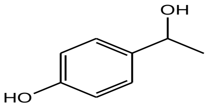
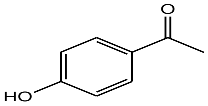
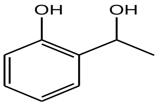
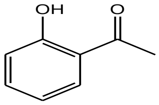
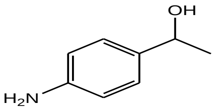
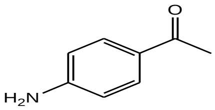
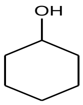
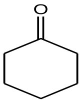
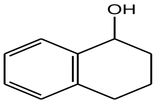
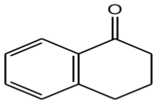
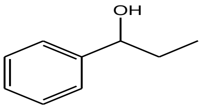
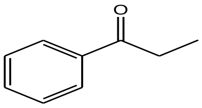
The effect of the reaction temperature was also evaluated and found that the oxidation of benzhydrol to benzophenone was slow at room temperature (Entry 1), moderate at 80 ^{0}C (Entry 3). But similar reaction was conducted efficiently at 120 ^{0}C under microwave gave the benzophenone in 94% yield (Entry 4). Further increase in temperature affected the oxidation adversely in terms of yield of the benzophenone. The results are summarized in **Table 4**.

Table 4: Effect of the reaction temperature for the oxidation of benzhydrol to benzophenone using molecular oxygen with 10 mol% iron (III) alanine Schiff base complex

yrtnE	Temperature (^{0}C)	Yield (%)
1	Room temperature	30
2	60	40
3	80	65
4	120	94
5	140	55

To examine the scope and versatility of the iron (III) alanine Schiff base complex, a wide variety of secondary alcohols including both activated and non-activated were oxidized to their corresponding ketones in excellent yields by simply bubbling molecular oxygen at room temperature into a solution of secondary alcohols and iron (II) alanine Schiff base complex in presence of molecular sieves (3Å). Later, the reaction mixture was transferred to microwave (Milestone MicroSYNTH) irradiation under oxygen atmosphere. These results are summarized in **Table 5**.

Table 5: Oxidation of various alcohols using molecular oxygen catalyzed by iron (III) alanine Schiff base complex under microwave at 120 ^{0}C under solvent free

Entry	Alcohol	Ketone	Time (min)	Yield (%)
1			10	94
2			12	88
3			13	85
4			12	83
5			13	80
6			12	82
7			17	84
8			16	86
9			12	82

Among the various alcohols studied, benzhydrol was found to be the most reactive and required shorter reaction times for their oxidation (Entry 1). Furthermore, aromatic substituted alcohols were found to be more reactive than aliphatic alcohol (Entry 7 and 8). Hydroxyl groups attached directly on the aromatic system did not participate in the reaction. Only secondary alcohols were selectively converted to give the corresponding ketones (Entries 4 and 5). Therefore, the present protocol is showing the usefulness of the chemo selectivity.

Conclusion

Our efforts are successful in developing a simple and eco-friendly catalytic aerobic oxidation procedure for the oxidation of both activated and non-activated alcohols to the corresponding ketones. The simplicity of the system, the non-hazardous nature of the catalyst and the versatility of the method towards a range of activated and non-activated alcohols make iron (III) alanine Schiff base complex an attractive, environmentally friendly synthetic catalytic tool for the oxidation of secondary alcohols to ketones by using molecular oxygen without using solvent under microwave.

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