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## Original Research Article

# Transition metals as efficient catalysts for transesterification of $\beta$ -keto esters under solvent-free conditions

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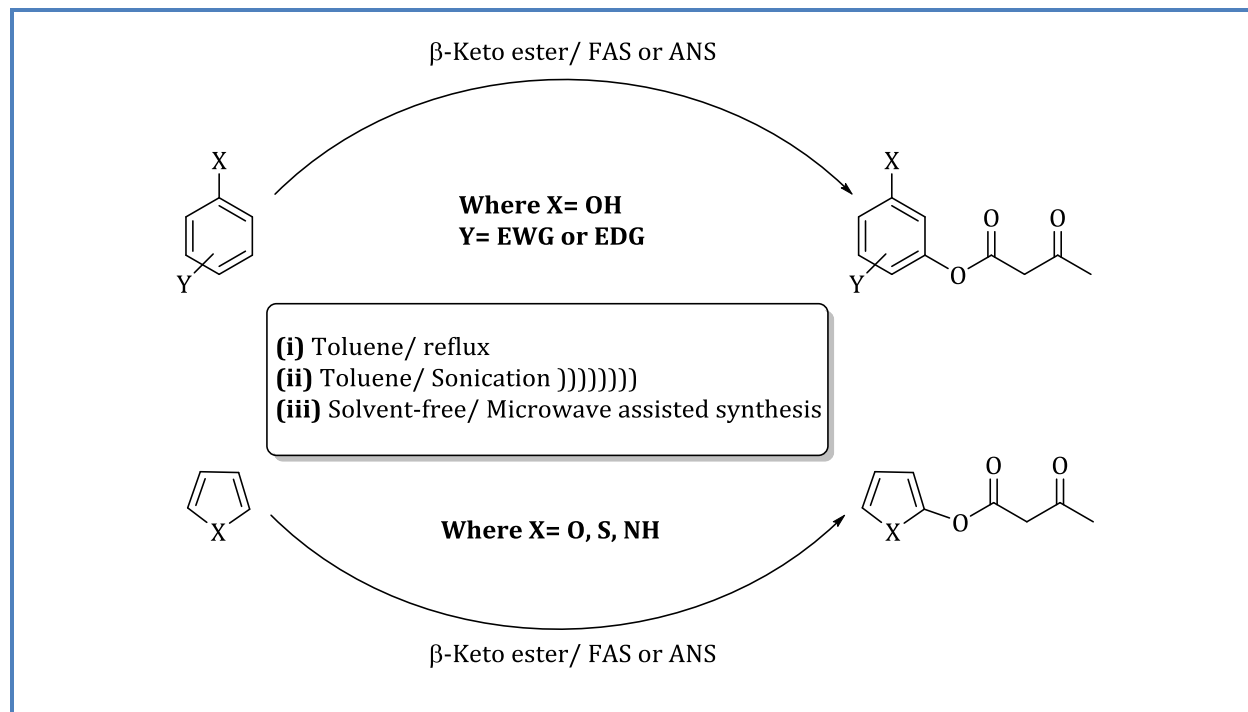
### KEYWORDS

Transesterification  
Transition metals  
 $\beta$ -Keto esters  
Solvent-free

### ABSTRACT

Transition metals (Ferrous ammonium sulphate and ammonium nickel sulphate) complexes have been proved to be efficient catalysts for transesterification of  $\beta$ -keto esters with various aromatic and hetero aromatic alcohols under solvent-free microwave conditions. However, in toluene media, the transesterification reaction was also conducted in both conventional reflux and sonication conditions, but, solvent-free condition microwave irradiation technique was found to be more efficient for transesterification with reduced reaction times and moderate yields. The inclination in reaction rates was found to be very less in solvent-free microwave assisted synthesis when compared to other conventional methods.

## Graphical Abstract



## Introduction

An organic process in which the organic group of an ester and an organic group of an alcohol are exchanged can be referred as transesterification [1]. Predominantly, transesterification reactions are catalysed in the presence of acids [2], bases [3] and, sometimes, enzymes [4]. As these catalysts are highly corrosive and are not eco-friendly, a large number of industrial waste has been produced and sent as eluent. Recently, many transformations have been reported earlier in the literature in order to promote transesterification of  $\beta$ -keto esters by using several catalysts such as zeolites [5], Amberlysts [6] and several heterogeneous catalysts [7]. During the past two decades, there have been continuous efforts diverted towards the selection of a suitable catalyst to promote the design of a clean, fast, efficient, and selective synthetic protocol and thereby to address environmental issues [8, 9]. As a result, there has been an ever increasing demand for metal ions or metal-based species as reaction promoters which can serve the purpose in small amounts and can also be recycled. However, many catalysts that are derived from heavy or rare metals cannot serve the purpose for large-scale applications due to their drawbacks such as toxicity and prohibitive prices. But, over the years, transition metal ions and metal complexes have been the sources for exploring suitable catalysts because many of them are easy available, environmentally safe and economically viable [10].

Transition metals can both lend electrons to and take electrons from other molecules. By giving and taking electrons so easily, transition metal catalysts speed up reactions. Transition metals exhibit different oxidation states and due to their ability to change oxidation states so easily, they are used in organic transformations. It is worth mentioning that iron is one of the most profuse transition metals on earth and also one of the most inexpensive and environmentally friendly materials. Moreover, many iron salts and complexes are either commercially available, or can be easily prepared as described in the literature [11].

Moreover, ferrous ammonium sulphate (FAS) is one of the most easily available desk top chemicals, and economically cheap, but not much focus has been paid to explore as catalyst. Nevertheless, a perusal of literature revealed that ferrous ammonium sulphate (FAS) could be used as a catalyst in several reactions in addition to the estimation of persulfate [12–14].

In addition to this, as a comparative study, we have also used the nickel complexes as a catalyst for transesterification. Nickel, belonging to the same block (d-block) as that of Iron, has been serving as a sustainable metal used in the preparation of stainless steel and also has higher applications in industry as well as electroplating. In organic industry, it is used in the hydrogenation of C=C bond formation [15]. Moreover, the complexes of nickel such as nickel sulphate provide the highest source of Ni<sup>+2</sup> ions.

Addition of ammonium sulphate to aqueous solutions of nickel sulphate precipitates ammonium nickel sulphate, commonly termed as Mohr's salt. Mohr's salt (Ammonium nickel sulphate) has been used in several organic reactions [16, 17]. We have studied the transesterification reactions with this ammonium nickel sulphate as a comparative study to ferrous ammonium sulphate catalysed transesterification reactions. Transesterification using  $\beta$ -keto esters is a well-known transformation [18].  $\beta$ -Keto esters are prepared by the condensation reaction between two esters or one ester and one carbonyl group [19, 20].

Transesterification of  $\beta$ -keto esters is one of the most important classes of synthetic procedures. Besides, transesterification is more advantageous than the ester synthesis from carboxylic acid and alcohol, due to poor solubility of some of acids in organic solvents, where the esters are commonly soluble in most of the solvents [21]. Some esters, especially methyl and ethyl esters are readily or commercially available and thus serve conveniently as starting materials in transesterification. A survey of literature shows that  $\beta$ -keto esters are versatile organic intermediates that are extensively used in agrochemical, pharmaceutical, and dyestuff industries [22]. Besides,  $\beta$ -keto esters are also useful organic building blocks for the synthesis of complex natural products [23].

Encouraged by the earlier investigations on transesterification reactions [24], in the present work, we want to explore the catalytic activity of transition metal complexes for the transesterification of  $\beta$ -keto esters with variety of alcohols under reflux conditions. And we have also explored the same reactions under microwave condition. Obtained results are presented in Table 1 and 2. The products are characterized by IR, NMR and mass spectroscopic studies.

## Experimental

### *Materials and methods*

All the chemicals were purchased from Aldrich or Arcos Organics and used without further purification. Analytical TLC was carried out using Merck aluminium-backed 0.2 mm silica gel 60 F-254 plates. Column chromatography was conducted using Merck silica gel 60 (230–400 mesh). For ultrasonically assisted reactions, a sonicated bath (KQ-250B, China) was used. A flat transducer with a frequency of 40 kHz and voltage of 220V (with an output of 100 watt electric power rating) was mounted at the bottom of the Sonication bath. The reaction vessel was placed inside the ultrasonic bath containing water. CEM laboratory microwave oven was used in this study for microwave assisted reactions.

### *General procedure for the transesterification under conventional condition*

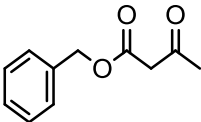
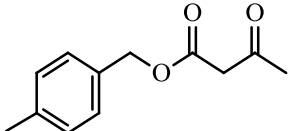
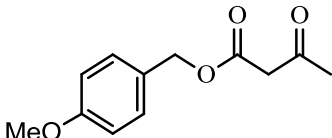
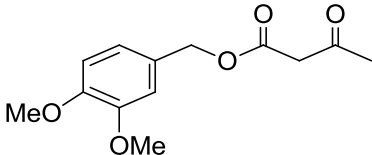
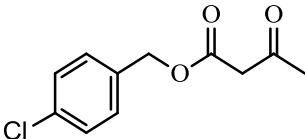
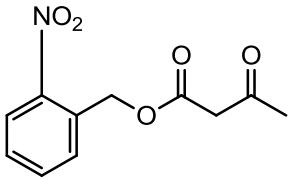
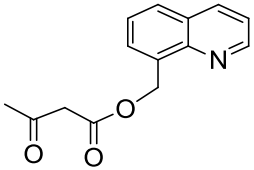
For condensation, the contents such as benzyl alcohol (10 mmol), ethyl acetoacetate (10 mmol), catalytic amount of FAS or ANS (5 mmol) and solvent (Toluene, 20 mL) were taken in a previously cleaned round bottom flask and were subjected to reflux at 100–1100 °C for about 10–14 h (For ANS reflux at 100–1200 °C for about 12–16 h). After the complete conversion, as indicated by TLC, the reaction mixture was quenched with water and treated with dilute NaHCO<sub>3</sub> solution which was in turn followed by the addition of ethyl acetate. The organic layer was separated, dried over Na<sub>2</sub>SO<sub>4</sub>, evaporated under vacuum, and purified with column chromatography using *n*-hexane/ethyl acetate as eluent to get pure product. Obtained product is characterized by NMR Spectroscopy studies. The spectral data of the obtained products are demonstrated as supplementary information in a separate document.

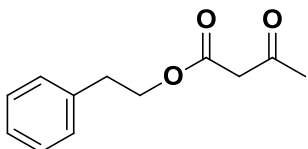
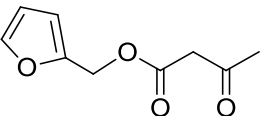
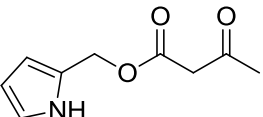
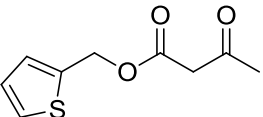
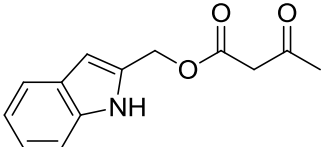
### *Procedure for ultrasonically assisted method*

For ultrasonically assisted reaction, the contents of the reaction such as benzyl alcohol (10 mmol), ethyl acetoacetate (10 mmol), catalytic amount of FAS or ANS (5 mmol) and solvent (Toluene, 20 mL) were taken in a boiling tube placed in a sonication bath. A high energy sound wave of about 40 kHz

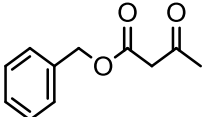
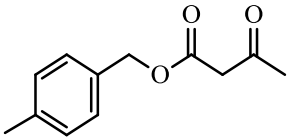
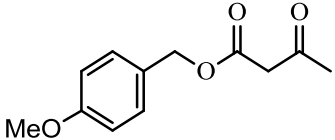
frequency and voltage of 220 v (With an output of 100 watt electric power rating) was mounted at the bottom of the sonication bath. The mechanism of the reaction is discussed in the above section.

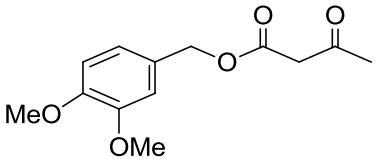
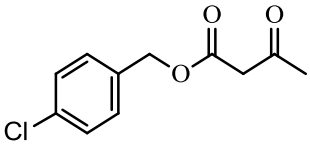
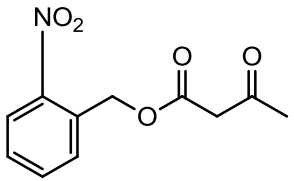
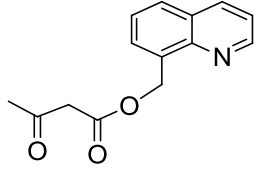
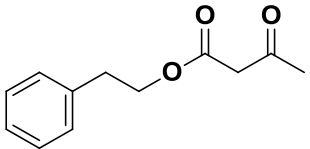
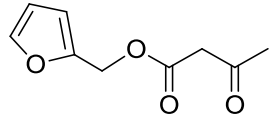
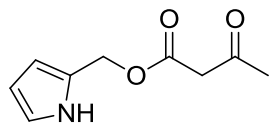
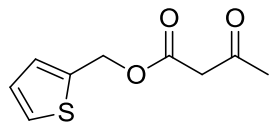
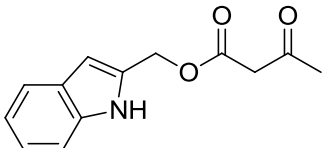
**Table 1.** Ferrous ammonium sulphate catalysed transesterification of  $\beta$ -ketoesters

Entry	Product	Conventional		Sonication		Microwave	
		Time (h)	Yield (%)	Time (min)	Yield (%)	Time (min)	Yield (%)
1		10	86	45	87	5	90
2		12	84	48	85	6	88
3		14	81	50	84	8	86
4		14	80	52	81	9	83
5		13	80	50	80	7	81
6		14	77	53	79	9	80
7		13	78	55	78	8	79

8		10	85	46	86	6	88
9		13	80	53	81	8	83
10		14	78	56	79	9	81
11		14	76	58	78	10	80
12		12	77	55	80	9	83

**Table 2.** Ammonium nickel sulphate catalysed transesterification of  $\beta$ -ketoesters

Entry	Product	Conventional		Sonication		Microwave	
		Time (h)	Yield (%)	Time (min)	Yield (%)	Time (min)	Yield (%)
1		12	85	46	86	5	88
2		14	82	50	83	7	86
3		15	80	54	81	8	83

4	 <chem>CC(=O)CCOCc1cc(OC)c(OC)cc1</chem>	16	77	56	79	9	80
5	 <chem>CC(=O)CCOCc1ccc(Cl)cc1</chem>	14	78	53	80	7	81
6	 <chem>CC(=O)CCOCc1ccccc1[N+](=O)[O-]</chem>	15	77	58	79	9	80
7	 <chem>CC(=O)CCOCc1cccc2ncn12</chem>	14	79	55	78	8	79
8	 <chem>CC(=O)CCOCc1ccccc1</chem>	12	85	46	86	6	88
9	 <chem>CC(=O)CCOCc1ccoc1</chem>	15	78	55	82	8	83
10	 <chem>CC(=O)CCOCc1c[nH]c1</chem>	16	76	60	79	10	81
11	 <chem>CC(=O)CCOCc1ccsc1</chem>	16	74	60	78	10	79
12	 <chem>CC(=O)CCOCc1c[nH]c2ccccc12</chem>	13	75	56	81	9	82

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The progress of the reaction is monitored by TLC. The work up procedure and characterization is same as discussed in conventional method.

#### *Procedure for microwave assisted reaction*

This is a solvent-free technique in which the contents of the reaction such as benzyl alcohol (10 mmol), ethyl acetoacetate (10 mmol), and catalytic amount of FAS or ANS (5 mmol) are taken in a 50 mL beaker and mixed thoroughly. About 500 mg of silica-gel was added to the mixture and heated (320 watt) in a controlled microwave synthesizer. The progress of the reaction is monitored by TLC. The work up procedure and characterization is the same as discussed in conventional method.

### **Results and Discussion**

In this manuscript, we have performed the transesterification reactions using beta keto esters and various alcohols in the presence of transition metal complex catalysts in toluene media as well as solvent-free microwave assisted conditions.

Initially, we wanted to optimize the catalyst (FAS and ANS) quantity for transesterification reaction. In order to identify the optimum amount of catalyst, we under took benzyl alcohol as a model substrate. In order to improve the yields, we performed the reactions using different quantities of FAS and ANS catalysts. Data compiled in [Table 3](#) revealed that optimum quantity of ANS catalyst for transesterification reaction is 0.3 g whereas for FAS catalyst is 0.4 g. Further increase of catalyst amount did not appreciably affect the yield of the product. The conversion yields of the transesterification of benzyl alcohol presented in [Table 3](#) also indicates that best results can be obtained with FAS over ANS catalyst. This is because of the fact that both of the catalysts exhibit different oxidation states and also Ni catalyst becomes slowly oxidized when compared to that of FAS. It is important to point out that no transesterification product was observed in the absence of the catalyst.

**Table 3.** Catalyst optimization for transesterification of benzyl alcohol

Entry	FAS		ANS	
	Catalyst (g)	Yield (%)	Catalyst (g)	Yield (%)
1	0.01	58	0.1	56
2	0.15	64	0.15	61
3	0.20	77	0.20	74
4	0.3	85	0.3	79
5	0.4	85	0.35	79
6	-	-	0.4	82

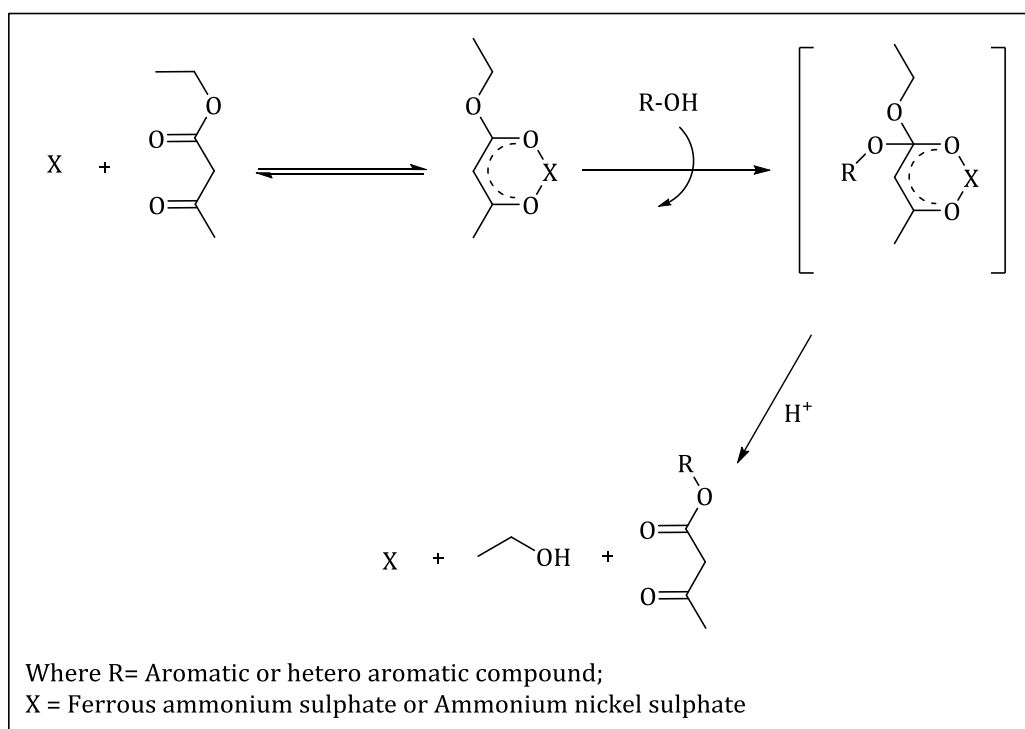


With optimum amount of the catalyst, both of the reactions were conducted under conventional reflux as well as sonication condition in toluene media. For FAS catalysed transesterification, the conventional reflux temperature was set to be 100–1100 °C which resulted in the formation of product in 10–14 hours. However, for ANS, the reaction time was increased for about 2 hrs ie. 12–16 h at 100–1200 °C, as Ni complexes become active only at higher temperatures and get slowly oxidised. For ultrasonically assisted method the reaction time was found to be 45–60 min approximately.

However to reduce the reaction times and for better yields, we thought of conducting the same reactions under solvent-free microwave assisted synthesis using a microwave using both of the catalysts. Fortunately, the reaction time was dramatically reduced to manifold that is from 5–10 min. The yields produced in microwave irradiation synthesis were also good to excellent compared to the traditional conventional reflux conditions, showing the catalytic effect of non-conventional energy. The observations are in accordance with the literature reports that the chemical reactions are accelerated because of selective absorption of microwave energy by polar molecules, nonpolar molecules being inert to the MW dielectric loss. Rate enhancements under microwave could be attributed due to bulk instigation phenomenon [25] which is achieved due to rapid heating and pressure effects.

It is interesting to note that the nature and size of the alcohol involved in the reaction significantly affect the rate of transesterification. Small alcohols with higher nucleophilic character generally facilitate transesterification faster than large alcohols. Reaction times were reduced by almost five to six times from conventional to ultrasonically assisted conditions to microwave conditions.

Iron is an adaptable element like other transition metals with (Atomic number 26) and electronic configuration [Ar] 3d<sup>6</sup> 4s<sup>2</sup>. Nickel, too, belongs to the transition metals bearing atomic number 28 and electronic configuration [Ar] 3d<sup>8</sup> 4s<sup>2</sup>. Both Iron and nickel, belonging to d-block elements in the periodic table, exhibit different oxidation states which are more stable at +2 oxidation state. Nickel along with Iron and other transition metals like cobalt are ferromagnetic. Many literature reports have claimed the catalytic properties of these metals and their complexes [26, 27]. They are softer acids with sufficient number of vacant orbitals that can form loosely bound adducts with ethyl acetoacetate and hydroxyl compounds (Hard bases) through weak soft-hard interactions according to Hard and soft acid base theory [28, 29]. Ethyl acetoacetate, a harder base than hydroxyl compound, interact between soft acids (FAS & ANS) and hard base (Ethyl acetoacetate) through two carbonyl oxygen atoms to form a loosely bound cyclic intermediate. The loosely bound cyclic intermediate probably reacts with hydroxyl compound and affords the product with the elimination of ethyl alcohol and catalyst (FAS & ANS). Reaction sequence of the proposed mechanism is shown in [Scheme 1](#).



**Scheme 1.** Mechanism of FAS and ANS catalysed transesterification of  $\beta$ -ketoester

## Conclusion

In this manuscript, we have clearly demonstrated the transesterification of  $\beta$ -keto esters with aromatic and hetero aromatic alcohols using FAS and ANS catalysts in toluene mediated conventional reflux and sonication conditions as well as solvent-free microwave conditions. However reduced reaction rates and higher yields are observed in solvent-free microwave assisted synthesis as compared to conventional reflux and sonication conditions. The time taken for FAS catalyst is also less when compared to that of ANS catalyst. Higher yields and shorter reaction times are the advantages of the mentioned protocols.

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## Disclosure statement

No potential conflict of interest was reported by the authors.

## Supporting Information

Additional supporting information related to this article can be found, in the online version, at [http://www.ajgreenchem.com/article\\_57304.html](http://www.ajgreenchem.com/article_57304.html).

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