Research Article

One-Pot Synthesis of 1,8-Dioxo-octahydroxanthenes using Ni – Mg Ferrite as Novel, Magnetically Separable and Efficient Reusable Heterogeneous Catalyst

Santosh Khillare, Aashish Dhokte, Machhindra Lande, Balasaheb Arbad*

Department of Chemistry, Dr. Babasaheb Ambedkar Marathwada University, Aurangabad (M.S.), 431004, India

Abstract

An eco-friendly Ni – Mg Ferrite solid heterogeneous catalyst has been employed for the synthesis of 1,8-Dioxo-octahydroxanthene derivatives. The catalyst was prepared by simple co precipitation method and calcined at 550 °C. The calcined sample was characterized by XRD, FT-IR, SEM and EDS, techniques. The catalytic activity results suggest that, the methodology adopted to offer significant improvements in the synthesis of substituted 1,8-Dioxo-octahydroxanthene derivatives with regards to short reaction times, high yields and the catalyst was successfully reused for four cycles without significant loss of activity.

Keywords: loss Aromatic aldehyde; Ferrite, One pot synthesis; Heterogeneous catalysis; Metal oxide
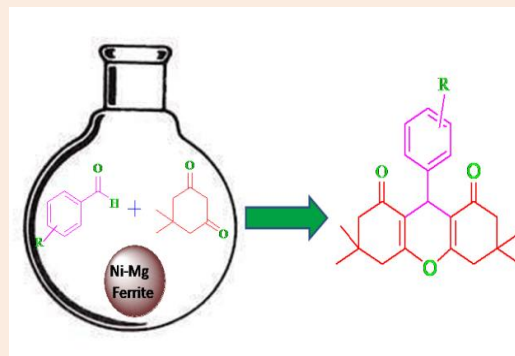
*Correspondence
Balasaheb Arbad,
Email: abrchem9@yahoo.co.in

Introduction

In the past few decades, the synthesis of new heterocyclic compounds has been a subject of great interest due to the wide applicability of them. The importance of multi-component reactions in organic synthesis has been recognized, and considerable efforts have been focused on the design and development of one-pot procedures for the generation oflibraries of heterocyclic compounds [1]. Xanthene derivatives are important due to their various synthetic and industrial applications. For example, they possess a large array of pharmacological activities such as anti-inflammatory [2], anti-bacterial [3] and antiviral properties [4]. Besides, some of them are served as leuco-dyes [5], intracellular pH indicators and as fluorescent materials [6]. Moreover, application of such compounds in photodynamic therapy as well as in laser technologies has also been reported [7, 8].

Various methods for the synthesis of xanthenes are described in the literature including condensation of aromatic aldehydes and dimedone using DABCO [1], Silica-Supported Preyssler Nano Particles [9], Cellulose Sulfonic Acid [10], Selectfluor[TM] [1- (chloromethyl)-4-fluoro-1,4-diazoniabicyclo[2.2.2]octane bis (tetrafluoroborate)] [11], MCM-41 functionalized sulfonic acid [12], However, most catalysts are difficult to remove, and some of them are corrosive and volatile and often cause environmental problems. Hence, there is increased interest in the development of environmentally benign reactions and atom-economical catalytic processes. Heterogeneous solid acid catalysts for the synthesis of fine chemicals have attracted considerable attention from both environmental and economical perspectives. Recently, more emphasis is made on metal oxides containing both acidic and basic sites. These heterogeneous catalysts find increased advantages such as easy separation from the reaction medium; reactions are usually clean and selective, procedures are usually cost-effective, and the catalyst is stable and hence can be recycled, which leads to high turn-over numbers.

Present work is a part of our earlier efforts in the synthesis, characterization and applications of mixed metal oxides of transition metals in organic synthesis reactions. In recent past, metal and mixed metal oxides specially ferrites have attracted much attention because of their many significant applications in various areas such as catalysis [13], to supports of catalysts [14], and can be used in biomedicine [15]. Especially, the magnetic properties of these materials make possible the complete recovery by means of an external magnetic field. In this paper, we had the opportunity to further explore the catalytic activity of Ni – Mg Ferrite in the synthesis of 1,8-dioxo-octahydroxanthenes.

Experimental

Materials and Reagents

The entire chemicals used were of synthesis grade reagents (Merck) and used as received.

Preparation of Catalyst

In a typical reaction, stoichiometric amounts of iron (III), nickel (II) and magnesium (II) nitrates were dissolved in deionized water. The pH of the solution was adjusted to 9 by the addition of aqueous ammonia, and then the solution was stirred vigorously for 4 h at 80°C and the precipitate so appeared was filtered, washed, and dried. Thus, the composite hydroxide of mixed metals so formed is calcined at 550°C for 5 hrs. After calcination $Ni_xMg_{1-x}Fe_2O_4$ (Ni – Mg Ferrite) is formed. The catalytic material was synthesized by varying composition of Ni (II) and Mg (II) such as

(a) x = 0.8, (b) x = 0.6, (c) x = 0.4 and (d) x = 0.2.

General procedure for the synthesis of 1,8-dioxo-octahydroxanthenes

A mixture of arylaldehyde 1(10 mmol), dimedone 2(20 mmol) and Ni – Mg Ferrite (0.2g) in ethanol (20 ml) was stirred at 120 °C for 3 hrs (scheme 1). Completion of the reaction was monitored by TLC, the catalyst was separated by magnet and dried for its next use and the reaction mixture was filtered. The material was poured on ice cold water and the mixture was stirred for 5 min. The solid so obtained was filtered off and recrystallized from ethanol to give the corresponding pure compound 3. The pure products were characterized by IR, ^{1}H- NMR and physical data (M.P.) and compound with those reported in the literature.

3a: white solid IR (KBr) - 3028, 2959, 1719, 1589, 1368, 1224, 1069, 1010 cm^{-1}. 1HNMR (in DMSO): 7.08-7.31 (m, 5H), 5.07 (s, 1H), 2.40 (s, 4H), 2.20 (s, 4H), 1.23 (s, 6H), 1.07 (s, 6H).

3b: white solid IR (KBr)-3028, 2958, 1586, 1485, 1367, 1223, 1068, 1041 cm^{-1}. 1HNMR (in DMSO): 6.94-7.38 (dd, 4H), 5.46 (s, 1H), 2.42 (s, 4H), 2.33 (s, 4H), 1.20 (s, 6H), 1.09 (s, 6H).

Results and Discussion

Characterization of synthesized ferrite

The X-ray diffraction (XRD) patterns of the catalysts were recorded on a Bruker D8 advance X-ray diffractometer using Cu Kα radiation with a wavelength of 0.154056 nm. To study the surface morphology of synthesized ferrite scanning electron microscopy (SEM) analyses were carried out with a JEOL JSM-6330 LA operated at 20.0kV and 1.0nA. The elemental composition of the metals in the synthesized Ni – Mg ferrite was examined using an energy dispersive spectrophotometer (EDS). BET surface area has been measured by means of N_2 adsorption at 77.68 K performed on a micromeritics ASAP 2010 and temperature programmed desorption of ammonia (NH_3-TPD) measurements were carried out on a micromeritics chemisoft TPx V1.02.

XRD analysis

The powder X-ray diffraction pattern of Ni - Mg ferrite calcined at 550 ^{o}C for 5 hrs is shown in Figure 1. While analyzing XRD pattern, it is observed that there are slight differences between the relative intensities and width of reflexes, which indicates the differences of crystallite size. The sharp peaks represents that all Ni-Mg ferrites are crystalline in nature.

The highly intense and sharp peaks are present at 2Θ =38, 41, 44.20, 50.68, 66.39 from the reflection planes indexed as (220) (311) (431) (400) (620) respectively indicates the cubic structure of Ni-Mg ferrites. The X-ray diffraction pattern were material with standard data (ICPDS PDF card no 00-008-0234) also confirms the formation of cubic Ni - Mg ferrite.

The lattice parameter 'a' of Ni-Mg ferrites are given in Table 1 which are in close agreement with standard data (8.34A^o) [16]. The size of crystallite was evaluated by measuring the FWHM of the most intense peak (311) mentioned in Table 1. Using the Debye Scherrer's formula [17] the mean crystalline size of the sample was calculated and that lies in the range of 28-45 nm.
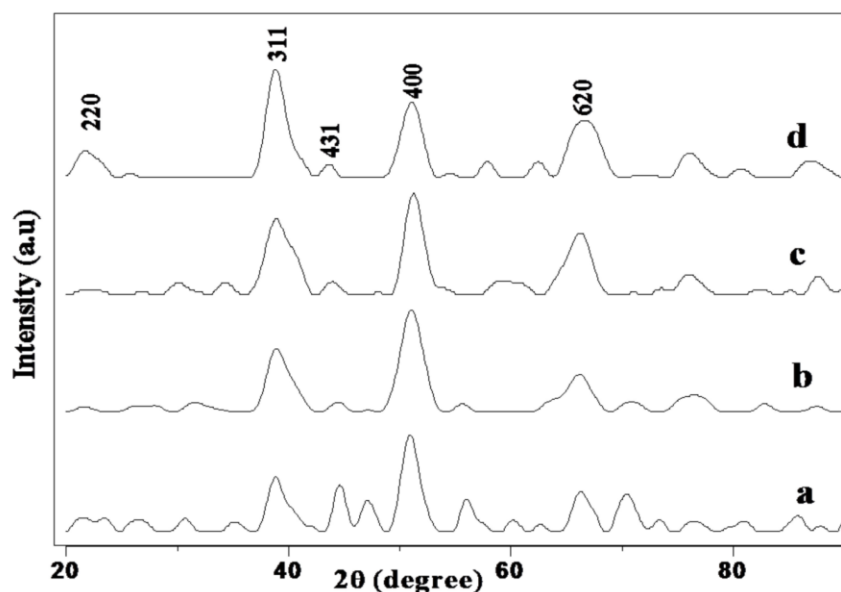

Figure 1 XRD pattern of series of Ni – Mg Ferrite ($Ni_xMg_{1-x}Fe_2O_4$) where, (a) x=0.8, (b) x=0.6, (c) x=0.4 and (d) x=0.2 at 550°C

Table 1 XRD analysis of Ni-Mg Ferrite ($Ni_xMg_{1-x}Fe_2O_4$) samples

Sample	Crystallite size (nm)	Lattice constant (A^o)
x = 0.8	45.13	8.4412
x = 0.6	36.38	8.4412
x = 0.4	28.05	8.4412
x = 0.2	40.19	8.4412

FT-IR analysis

The FT –IR spectra of series of Ni-Mg ferrites using dry KBr as a standard reference lies in the range of 4000-500 cm^{-1} are shown in Figure 2. From the IR spectrum, it is observed that in each sample (a-d) the broad peak is present in the range 3200-3500cm^{-1} which is due to the hydroxyl group adsorbed on the surface of catalyst, similarly in all the cases the peak in the range of 1500-1600 and 1380- 1460 cm^{-1} is due to the deformation of the surface hydroxyl groups [18]. In the range from 1000-400, two main metal-oxygen bands are seen in IR spectra of all samples. The higher one generally observed in the range 600-550cm^{-1} is caused by the stretching vibrations of the tetrahedral metal-oxygen bond (M_{tetra}-O) and the lowest band usually observed in the range 450-400cm^{-1} is caused by the metal oxygen vibrations in the octahedral sites.(M_{octa}-O) [19].
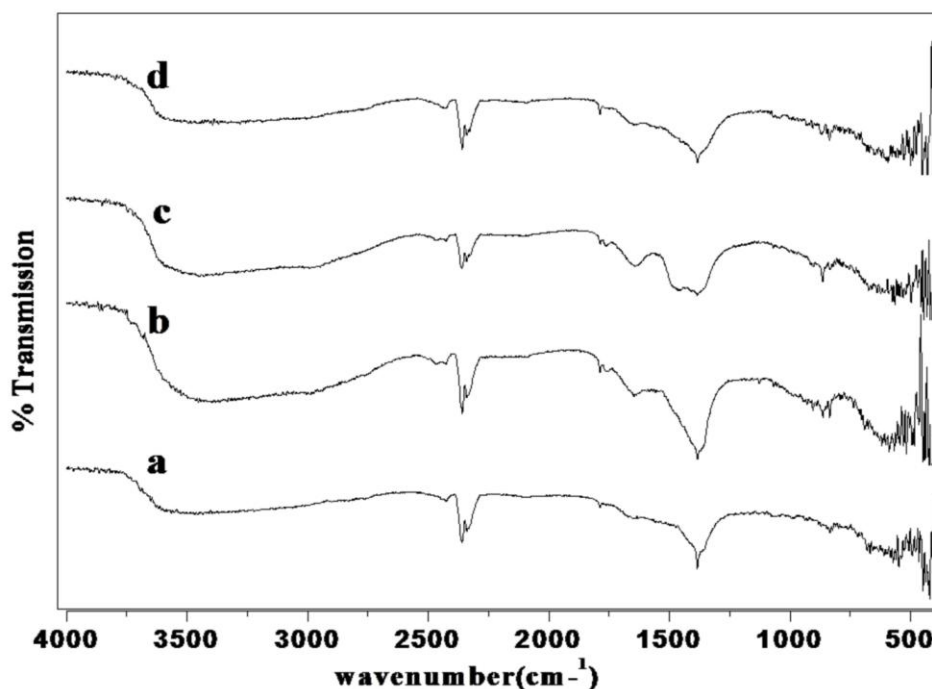

Figure 2 FT-IR spectra of Ni-mg ferrite ($Ni_xMg_{1-x}Fe_2O_4$) where, (a) x = 0.8, (b) x = 0.6, (c) x = 0.4, (d) x=0.2 calcined at 550 ^{o}C

SEM and EDS analysis

The surface morphology of the synthesized Ni - Mg Ferrite is studied by scanning electron micrograph and are shown in Figure 3. The SEM micrograph of Ni-Mg ferrite catalyst shows agglomeration of particles and irregular in shape. The as prepared samples have spongy and fragile network structure with voids and pores.

Energy dispersive X-ray spectroscopy (EDS) is an analytical technique used for elemental analysis. EDS pattern obtained for all the samples which gives the elemental composition in the samples. Table 1 shows the elemental composition of Ni - Mg Ferrite samples. The compound shows the presence of Ni, Mg, Fe and O.
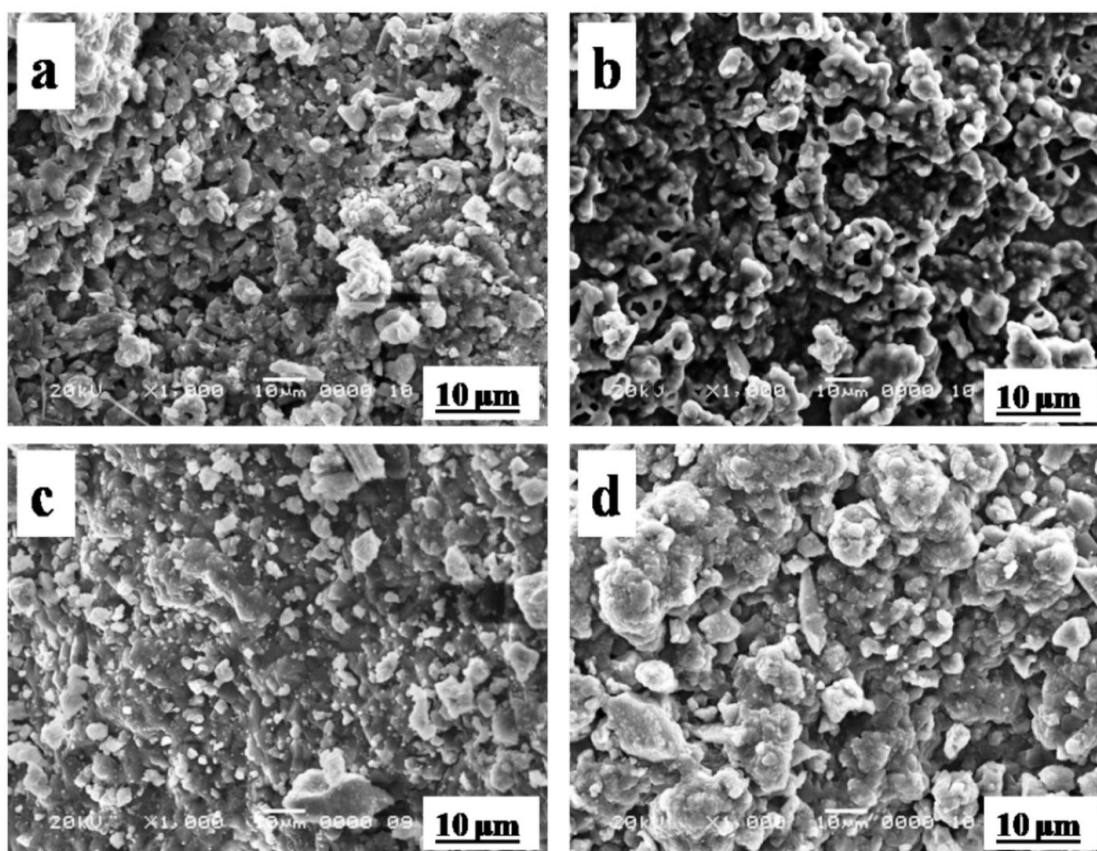
Figure 3 SEM images of $Ni_xMg_{1-x}Fe_2O_4$ (a) x = 0.8 (b) x = 0.6 (c) x = 0.4 (d) x=0.2

Table 2 Elemental composition of Ni-Mg Ferrite ($Ni_xMg_{1-x}Fe_2O_4$) samples

Catalyst	Mass %				Total
	Ni	Mg	Fe	O	
X = 0.8	18.31	2.01	47.09	32.59	100
X = 0.6	13.96	3.65	49.53	32.86	100
X = 0.4	9.87	6.95	51.25	31.93	100
X = 0.2	4.93	9.03	54.19	31.85	100

BET and NH_3-TPD analysis

NH_3-TPD measurements were carried out by i) preheating 200 mg sample to 500^oC/min heating rate in helium with flow rate $20cm^3$/min. ii) adsorption of NH_3 at room temperature. iii) desorption of adsorbed NH_3 with an heating rate

70°C/min from room temperature to 550°C. The acidity of sample $Ni_{0.2}Mg_{0.8}Fe_2O_4$ was detected by temperature programmed desorption of ammonia. Total acidity of Ni-Mg ferrite is found to be 0.3763 mmol/g. BET theory aims to explain the physical adsorption of gas molecules on solid surface and serves as the basis for the measurement of the specific surface area of a catalytic material. The calculated BET surface area of Ni-Mg ferrite is 1.6665 m^2/g.
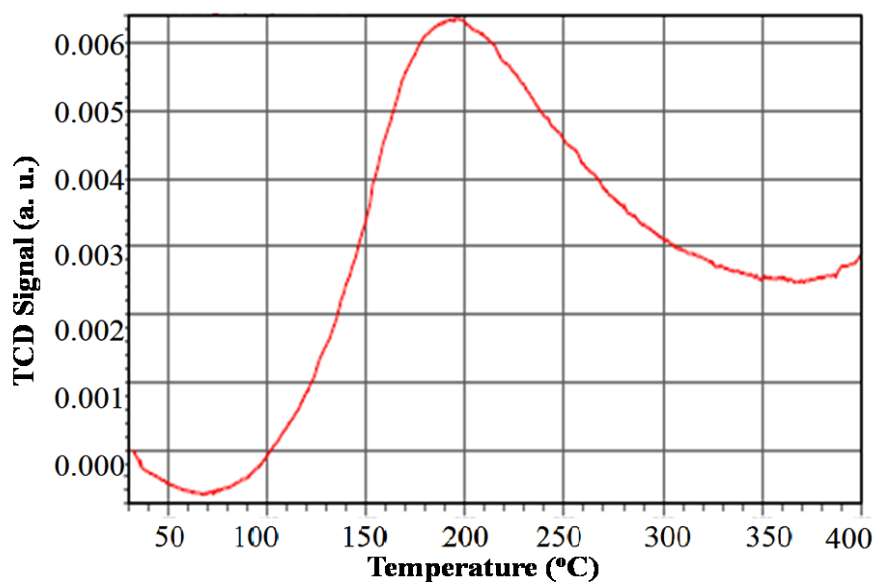

Figure 4 NH$_3$-TPD curve $Ni_{0.8}Mg_{0.2}Fe_2O_4$ calcined at 550^0C

Catalytic activity results

In this study the use of Ni – Mg Ferrite as catalyst in organic reactions, we synthesized 1,8-dioxo-octahydroxanthenes derivatives (3a-i) *via* a one-pot reaction of aromatic aldehyde (1) and dimedone (2) in presence of Ni - Mg Ferrite catalyst and reflux conditions in excellent yields in this work (Scheme 1).
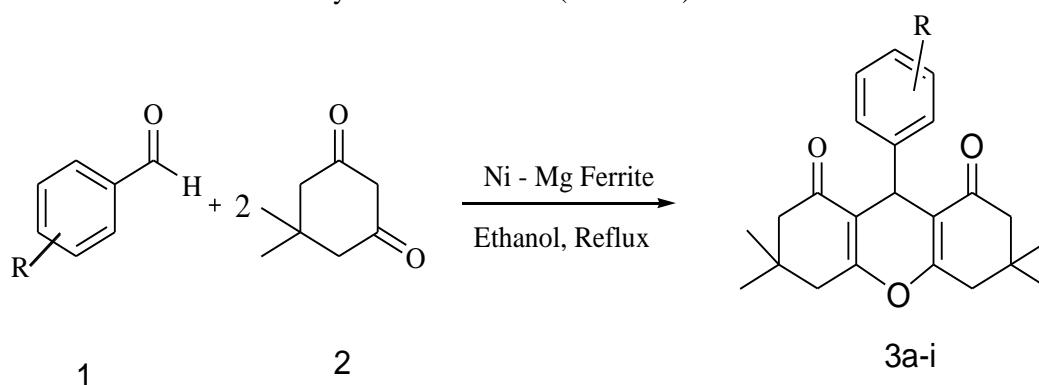
Scheme 1 Synthesis of 1,8-Dioxo-octahydroxanthene catalyzed by Ni-Mg Ferrite solid heterogeneous catalyst

Also, the effect of various solvents on the rate of the reaction was studied (Table 3). These results shows that the reaction in aprotic solvents such as CH$_2$Cl$_2$, THF and CH$_3$CN gives only 30-45% conversion after 3 h while the reaction in H$_2$O gives moderate yield Table 3. However, in EtOH enhanced the rate of reaction with excellent yield. The reaction gives maximum yield i.e. up to 90%, thus solvent played vital role in the Ni-Mg Ferrite catalyzed Knoevenagel condensation reaction.

Table 3 Synthesized Ni – Mg Ferrite catalyzed synthesis of 1,8-Dioxo-octahydroxanthene in different solvents[a]

Entry	Solvent	Isolated Yield[b] %
1	EtOH	90
2	CH_3CN	40
3	THF	45
4	CH_2Cl_2	35
5	H_2O	56

[a]Reaction condition: benzaldehyde (10mmol) and dimedone (20mmol), Ni-Mg Ferrite 0.2 gm, 20 ml solvent, refluxed 180 min. [b] Isolated Yield

The catalyst can be quantitatively recovered by applying external magnetic field and reused. The possibility of recycling the catalyst was examined using the reaction of 4-Cl benzaldehyde and dimedone under the optimized conditions. After completion of reaction, the catalyst was separated by putting external magnet, washed with ethyl acetate, dried at 60°C and activated at 120°C for 1hr before the next catalytic run. During washing with the solvent, it was clearly observed that there was no loss of catalyst. In present work, it is observed that Ni-Mg Ferrite catalyst shows excellent to good reactivity with better yield even after four cycles for the same reaction. The results are listed in table 4.

Table 4 Recycle and reusability of $Ni_{0.8}Mg_{0.2}Fe_2O_4$[a]

Entry	Ni-Mg Ferrite	Time (min)	Isolated Yield[b] %
1	$Ni_{0.8}Mg_{0.2}Fe_2O_4$	180	90
2	$Ni_{0.8}Mg_{0.2}Fe_2O_4$	180	90
3	$Ni_{0.8}Mg_{0.2}Fe_2O_4$	180	88
4	$Ni_{0.8}Mg_{0.2}Fe_2O_4$	180	86
5	$Ni_{0.8}Mg_{0.2}Fe_2O_4$	180	86

[a]Reaction condition: 4-Cl benzaldehyde (10mmol) and Dimedone (20mmol), Ni-Mg Ferrite 0.2 gm, EtOH as solvent 20 ml, stirred 180 min. [b] Isolated Yield

The reaction of structurally diverse aldehydes with dimedone under similar conditions was investigated. By this method, the reactions were carried out easily and very cleanly in the presence of Ni – Mg Ferrite to produce xanthene derivatives in good yields and no undesirable by-products are observed. The experimental procedure is very simple,

convenient and has the ability to tolerate a variety of other functional groups such as NO_2, Me, Cl, OMe, and OH under the reaction conditions. It was indicated that both electron rich and electron deficient aldehydes worked well, mostly leading to high yields of products.

Table 5 Synthesized Ni-Mg Ferrite catalyzed synthesis of 1,8-Dioxo-octahydroxanthene derivatives[a]

Entry	R	Time (min)	Isolated Yield[b] (%)	M. P. (°C)	
				Found	Reported
3a	H	180	90	204-206	203-205 [9]
3b	4-Cl	180	90	226-228	231-233 [9]
3c	4-NO$_2$	180	92	225-227	228-230 [9]
3d	4-OCH$_3$	200	89	245-247	248-250 [9]
3e	4-CH$_3$	190	88	220-222	219-221 [9]
3f	4-OH	180	85	242-244	243-245 [12]
3g	3-NO$_2$	180	90	171-173	168-170 [12]
3h	2-OH	210	82	202-204	202-205 [12]
3i	2-Cl	180	87	226-227	228-230 [12]

[a]Reaction condition: aromatic aldehyde (10mmol) and Dimedone (10mmol), Ni-Mg Ferrite 0.2 gm, 20 ml EtOH as solvent, stirred. [b]Isolated Yield,

Conclusions

Ni – Mg Ferrite is a highly efficient, reusable and green solid acid catalyst for the synthesis of 1,8-dioxo-octahydroxanthenes *via* a one-pot condensation reaction of aromatic aldehydes and dimedone in reflux conditions. Moreover, we have also shown that the catalyst can be reused at least 4 times without loss of activity. Among the synthesized ferrites $Ni_{0.8}Mg_{0.2}Fe_2O_4$, shows better catalytic activity for the synthesis of 51,8-dioxo-octahydroxanthenes. Excellent yields, enhanced reaction rates and short reaction times, simplicity of operation and easy work-up are some advantages of this protocol.

Acknowledgement

References

[1] Paliwal Pradeep, Jetti Srinivasa Rao and Jain Shubha, *Research Journal of Chemical Sciences,* **2012**, 2, 21.
[2] J. P. Poupelin, Saint-G. Rut, Blapin O Foussard, G. Narcisse, Ernouf G Uchida, and R. Lacroix, *Eur J Med Chem.,* **1978,** 13, 67.
[3] R. W. Lambert, J. A. Martin, J. H. Merrett, K. E. B. Parkes, G. J. Thomas, *Chem Abstr.,* **1997**, 126.
[4] T. Hideo and Jpn Tokk Koho, *Chem Abstr* **1981**, 95, 80922.
[5] J. A. Baner and A. K. Mukherjee, *Stain Technol*., **1981**, 56, 83.

[6]   C. G. Knight and T. Stephens, *Biochem J*., **1989**, 258, 683.
[7]   R. M. Ion, D. Frackowiak, A. Palnner and K. Wiktorowicz, *Acta Biochim Pol.,* **1998**, 45, 833.
[8]   M. Ahmed, T. A. King, D. K. Ko, B. H. Cho and J. Lee, *J Phys D: Appl phys.,* **2002**, 35(13), 1473.
[9]   Ali Javid, Majid M. Heravi and Fatemeh F. Bamoharram, *E-Journal of Chemistry*, **2011**. 8(2)**,** 910.
[10] H. A. Oskooie, L. Tahershamsi, M. M.Heravi and B. Baghernejad, *E-Journal of Chemistry*, **2010** 7(3), 717.
[11] M.R. Poor Heravi, *J. Iran. Chem. Soc.,* **2009**, 6(3), 483.
[12] G. H. Mahdavinia, M. M. Ghanbari, H. Sepehrian, F. Kooti, *J. Iran. Chem. Res* **2010**. 3 117.
[13] S. R. Borhade, S. B. Waghmode, *Beilstein J. of Org. Chem* **2011**. 7, 310.
[14] Jianming Liu, Xingao Peng, Wei Sun, Yongwei Zhao, Chungu Xia, *OrganicLetters* **2008** 10, 2933.
[15] A. Ito, M. Shinkai, H. Honda and T. Kobayashi, *J. Biosci.and Bioeng.,* **2005** 100, 1.
[16] J. smit, HPJ wijn, *ferrite* Philips technical library The Netherlands **1959** p137.
[17] B. D. Cullity, *Elements of X-ray diffraction*. Addison-Wesley, California **1978** p102.
[18] A. Lagashetty, V. havanoor, S. Basavaraja, *sci Technol. Adv .mater.* **2007** 8**,** 484.
[19] R. D. Waldron, *phys.Rev*. **1955** 99, 1727.