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Review Article

Transition metal oxides nanoparticles catalysis for sustainable organic synthesis under solvent free conditions

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Abstract: Organic reactions are typically carried out in the presence of solvents. Isolation of the pure products requires separation and purification steps, which result in a substantial decrease in yield and can be environmentally hazardous processes. A simple and efficient way to increase yields and reduce environmental impact is to conduct the reaction in the absence of solvent, which includes solvent free or solid-state reactions. Solvent-free organic reactions have drawn great interest, particularly from the viewpoint of green chemistry, and environmentally friendly solvent-free reactions have been investigated widely. Due to enormous advantages of solvent free reactions, various solvent free approaches are being discovered for ecofriendly synthesis of many compounds. Metal oxide nanoparticles in the form of nanocatalyst have emerged as viable alternatives to conventional materials in various fields of chemistry and attracted marvelous interest of chemists. This is because the activity of the catalyst resides in the exposed portion of the particles by decreasing the size of the catalyst, advantages such as more surface area would be exposed to the reactant, only negligible amount would be required to give the significant result and selectivity could be achieved, thereby, eliminating the undesired products. The nanocatalyst is inexpensive, stable, can be easily recycled and reused for several cycles with consistent activity. The current review enlists the various types of transition metal oxide nanoparticles involved in catalysis of the organic synthesis.

Keywords: Green chemistry, Solvent free synthesis, Nanoparticles, Metal oxides.

Introduction

Organic reactions are typically carried out in the presence of solvent. Isolation of the pure products requires separation and purification steps, which result in a substantial decrease in yield and can be environmentally hazardous processes. In solvent-based reactions, the weight ratio of waste to product, which is known as the E factor is inevitably high. A simple and efficient way to increase yields and reduce environmental impact is to conduct the reaction in the absence of solvent, which includes solvent free or solid-state reactions. Compared to conventional organic reaction, solvent free reactions have several advantages that include high reaction rate, cost savings, considerable process reduction, and minimal impact on the environment. Byeongno L *et.al*. [1]. To minimize the environmental pollution caused by solvents, the chemists have been showing more concern for developing environment-friendly synthetic procedures. This initiative, aided with the recent development of new strategies in solid-solid reactions has prompted them to develop sufficiently valuable methodologies to achieve organic synthesis under solvent-free condition. Working without solvents gives the potential for a simpler process, smaller plants, and eliminates the energy costs of removal, recycling and eventual disposal of waste solvents. So, several techniques and protocols for the efficient use of solvent-free reactions have been reported in organic synthesis Davood et al [2].

Recently, some chemists found that many reactions proceed efficiently in the solid state. Indeed, in many cases, solid state organic reaction occurs more efficiently and more selectively than does its solution counterpart. Solvent-free reactions lead to new environmentally benign procedures that save resources and energy. These kinds of reactions promise to be an essential facet of 'Green Chemistry" and are of high interest from both the economical and synthetic point of view. Solvent-free reactions possess some advantages over traditional reactions in organic solvents, for example they not only reduce the burden of organic solvent disposal, but also enhance the rate of many organic reactions reduced pollution, have low costs, simplicity in process, and easier work-up Sara. M and Reza.N [3]. Intensive studies have been focused on the development of catalytic systems owing to their importance in synthetic organic chemistry. One of the most attractive synthetic strategies favored by organic

chemists is the use of heterogeneous catalyst in increasing the efficiency of a wide range of organic synthesis vinay kumar. B et al [4]. Since the end of the 1990s, and with the development of nanosciences, nanocatalysis has clearly emerged as a domain at the interface between homogeneous and heterogeneous catalysis, which offer unique solutions to answer the demanding conditions for catalyst improvement. The main focus was to develop well defined catalysts, which may include both metal nanoparticles and a nanomaterial as support. These nanocatalysts should be able to display the ensuing benefits of both homogenous and heterogeneous catalysts, namely high efficiency and selectivity, stability and easy recovery/recycling. Specific reactivity can be anticipated due to the nanodimension that can afford specific properties which cannot be achieved with regular non-nanomaterials Dighore N.R.et al [5].

Development of new catalysts by nanoscale design has emerged as a fertile field for research and innovation. In recent years, nanostructured materials have generated intense research interest in many scientific and technological fields specifically; nanoparticles have drawn attention from the heterogeneous catalysis community, due to the high catalytic activities that can be generated over nanomaterial. The catalytic properties of nanoparticles can be directly associated with the increase of the surface to volume (A/V) ratio at the nanoscale level, which increases both available surface area and active site density for catalytic reaction. Moreover, non-linear evolution of the surface properties could be observed with crystal size reduction, resulting in even higher surface reactivity (‘‘quantum effect’’) characterized by an increased turnover frequency over active sites Said. L et.al [6]. The ability of the nanotechnology to enhance catalytic activity opens the potential to replace expensive catalysts with lower amounts of inexpensive nanocatalysts. In particular, nanocrystalline oxides have proved to be useful to chemists in the laboratory and industry due to the good activation of adsorbed compounds and reaction rate enhancement, selectivity, easier work-up, recyclability of the supports and the eco-friendly reaction conditions Jelale.A et.al [7].

Metal Oxide Nanoparticles

The metal elements can form a large diversity of oxide compounds, which can adopt structural geometry with an electronic structure that can exhibit metallic, semiconductor, or insulator character Rodriguez, J.A. and Fernandez-Garcia,M. [8]. Most of the catalysts used in industrial applications involve an oxide as active phase, promoter, or support. At the nanoscales, these compounds can exhibit unique physical and chemical properties due to their limited size and a high density of defect sites such as edges, corners and point defects Fern_andez-García [9]. The nanoparticle size is also related to the transport properties of the oxide, since, as already stated, the nanostructure produces the so-called quantum size or confinement effects, which essentially arise from the presence of discrete, molecular-like electronic states. Additional general electronic effects of quantum confinement experimentally probed on oxides are related to the energy shift of exciton levels and optical bandgap. Balashov, E.M et.al [10]. Oxide materials can present ionic or mixed ionic/electronic conductivity and it is experimentally well established that both can be influenced by the nanostructure of the solid. Chiang, Y.M et.al [11] structural and electronic properties obviously drive the physical and chemical properties of the solid, and this properties is influenced by size in a simple classification. In their bulk state, many oxides have wide band gaps and a low reactivity. A decrease in the average size of an oxide particle does in fact change the magnitude of the band gap with strong influence on the conductivity and chemical reactivity. Wang, C et.al [12], Bochenkov, V.E[13]. and Sergeev, G.B. [14] and Colon Ibanez, G.et.al [15]. The use of transition-metal nanoparticles in catalysis is crucial as they mimic metal surface activation and catalysis at the nanoscale and thereby bring selectivity and efficiency to heterogeneous catalysis. Metal oxide nanoparticles in the form of nanocatalyst have emerged as viable alternatives to conventional materials in various fields of chemistry and attracted marvelous interest of chemists. Metal oxide nanoparticles are known to be promising heterogeneous catalysts in a variety of organic transformations. In general, the nanoparticle is considered to be more reactive because it offers higher surface area and low coordinating sites. The surface area of the catalyst increases tremendously when size decreases to nano levels which are responsible for the higher catalytic activity and have the potential for improving the efficiency, selectivity and yield of catalytic processes Mohanraj V. J. and Chen Y [16], Astruc. D [17], Moreno.M and Pleixats .R, Djakovitch.L et.al [18]

Solvent free reactions catalyzed by ZnO naonparticles

Solvent-free organic reactions have drawn great interest, particularly from the viewpoint of green chemistry, and environmentally friendly solvent-free reactions have been investigated widely. Solvent-free reactions have some unique advantages, such as the elimination of harmful organic solvents, which account for a great proportion of the waste material generated in syntheses and impose health and environmental risks. Solvent-free reactions also reduce pollution, reduce handling costs due to the simplification of the experimental procedure and work-up technique, and have high selectivity in some cases. Nowadays, the restrictions imposed by the waste-minimization laws and economic considerations driven to the development of new catalytic technologies. Modern processes are in fact, based on solid catalysts. Different researcher groups have been reported that ZnO exhibit one of the best performance in the Friedel-Crafts acylation of

various benzene derivatives in solvent free conditions, (Hosseini-Sarvari & Sharghi, [19]; Wang et al., [20].

In a comparative study the catalytic efficiency of ZnO with other catalysts was examined and it was observed that ZnO exhibited high activity and the corresponding product was performed in high yield. The higher catalytic activity of ZnO may be attributed to the surface area which is available for greater adsorption of the reactants on its surface. The result encouraged them to use ZnO nanoparticles instead of bulk ZnO in reactions. As result the experiment indicated that ZnO nanoparticles decreased the reaction time considerably. It might seem that high surface area and better dispersion of nanoparticles in the reaction mixture are reasons for better activities of ZnO nanoparticles. Optimization of catalyst amounts was carried out in the model study by using different amounts of the ZnO nanoparticles. The higher yield was obtained with increasing the amount of catalyst from 10 mol% to 12 mol%. However, further increase of the molar amount of the catalyst from 12 mol% to 20 mol% did not significantly increase the yield of the product. According Javad S.G et.al [21] to improve the yield of the target product, work was carried out in the presence of various solvents and the results are presented in Table 1. As can be seen from the table, solvent-free conditions accelerated the rate of reaction and also high yields were obtained for all products.

A convenient method was reported for the effective conversion of benzyl alcohol and its derivatives to their corresponding aldehydes in the presence of nano structured ZnO as the catalyst. The results showed that increasing the amount of nano catalyst in solvent free condition and at 30 minutes would increase the reaction yield. The optimum concentration of nano catalyst was found to be 0.5 mmol and after that has no more increasing in yield of the reaction. Effect of solvents was also carried out by using several solvents, the obtained results showed that the optimum oxidation was at solvent free condition (90 % at 30 minutes).

According to Bvinzy et al [22] in the synthesis of ethyl 2-oxo-2*H*-chromene-3-carboxylate a mixture of *o*-hydroxy benzaldehyde (2 mmol), ZnO (10 mol %) and diethyl malonate (2.5 mmol) was irradiated in microwave oven or heated in an oil bath in different solvents. A control experiment was conducted in the absence of zinc oxide nanoparticle catalyst; for ethyl 2-oxo- 2*H*-chromene-3-carboxylate the reaction did not proceed and the substrate remained unchanged, while good results were obtained in the presence of ZnO nanoparticles. On the optimized amount of catalyst 10 mol% of ZnO nanoparticles could effectively catalyze the reaction for synthesis of the desired product. With the inclusion of 5 mol% of ZnO nanoparticles the reaction took longer time. Using more than 20 mol% ZnO nanoparticles has less effect on the yield and time of the reaction. It is remarkable that the reaction carried out by changing the size of the particles from nanoparticles to bulk resulted in a drop in the catalytic activity. It is interesting to note that the ZnO nanoparticle catalyst catalyses the reaction in excellent yield within a shorter reaction time than the bulk. The efficiency of the solvent-free versus solution, reaction was examined in several solvents under microwave and thermal conditions. As mixture of 2-hydroxy benzaldehyde (2 mmol), ZnO (0.4 mmol) and *β*-dicarbonyl compound (2.5 mmol) were irradiated in microwave oven (300 W, max. 120◦C) or heated in an oil bath (100◦C) in different solvents, lower yields and longer reaction times were observed in solution conditions. Therefore, the solvent-free method is more efficient B Vinay Kumar et al. [4]] Hashem Sharghi and Hosseini described a solventless reaction protocol for synthesizing aldoximes from corresponding aldehydes using ZnO as catalyst at 80°C. Interestingly, they obtained Beckmann rearrangement product at higher temperatures (140-170°C. Effect of solvents was carried out by using several solvents the obtained results showed the optimum oxidation were at solvent free condition (90 % at 30 minutes). We have conducted the oxidation of structurally different derivatives of this alcohol with this oxidation system under solvent- free conditions using only 0.5 mmol of the ZnO nanocatalyst. Oxidations of benzyl alcohol and its derivatives performed on nano ZnO as catalyst into corresponding aldehydes proceeded at high conversion (99% in some cases) in lower than 30 minutes, and selectively in solvent free condition Sorror. S and Fariba. M [23].

Recycling efficiency of ZnO nanoparticles

According to Javad S.G et.al [21] in the synthesis of 1,8-dioxo-decahydroacridine and 1,8-dioxooctahydro-xanthene derivatives the result indicated that the catalyst nanozinc oxide was reused and recycled without any loss of activity and product yield. The catalyst can be recycled by a simple protocol that after the completion of reaction, ZnO was removed by filtration, washed with methanol and dried at the pump. The recovered catalyst was reused for second and third consecutive cycles without any significant loss in catalytic activity.In another study the reusability of the catalyst was examined by repeating of the model reaction using ZnO nanoparticles under optimized reactions. The results of the experiments showed that the catalytic activity of nano ZnO did not decrease significantly even after five catalytic cycles.

Solvent free reactions catalyzed by TiO_2 nanoparticles

Currently, TiO_2 nanoparticles have emerged as an attractive multi-functional material. TiO_2 nanoparticles have unique properties such as high stability, long lasting, safe and broad-spectrum anti-biosis. TiO_2 nanoparticles have been used as a green catalyst in many organic reactions. Quinazolin-4(1H)-

ones are important N-heterocyclic compounds having various biological activities. However, methods for the selective synthesis of 2, 3-dihydroquinazolin- 4(1H)-ones have not been explored before. Thus, developing versatile approaches to synthesize 2,3-dihydroquinazolin-4(1H)- ones still remains a highly desired goal in organic synthesis. According to Siva Prasad.S [24] in the solvent free synthesis of quinazolinone, TiO_2 nanoparticles were used as catalyst. When the reaction optimized with various amount (mol %) of TiO_2 nanoparticles catalyst concentration plays a major role in the product yields. It was observed that increasing the loading of the catalyst from 2 to 5 mol% gave an improved yield of of the product. Further increase of catalyst loading leads to lower reaction yields as indicated in table 2.

To elucidate the role of the solvents, various solvents were used to evaluate the scope and limitation of the reaction. After screening different solvents, it was found that TiO_2 nanoparticles catalyzed syntheses of quinazolinone were not only faster, but also resulted in better yields under solvent free conditions as mentioned in table 3, Siva Prasad.S 2014[24]

Synthesis of 14-aryl or alkyl-14*H*-dibenzo[*a,j*]xanthenes using nano-TiO_2 as eco-friendly and efficient catalyst was reported by B.F. Mirjalili et al [25]. Catalytic activity for the synthesis of 14-aryl and alkyl-14*H*-dibenzo [*a,j*] xanthenes in the presence of nano- TiO_2 under heating conditions were investiga ted. Nano- TiO_2 was found to be an efficient and reusable catalyst for the synthesis of 14-aryl or alkyl-14*H*-dibenzo [*a,j*]xanthenes derivatives and is comparable with some other applied catalysts. The reaction of benzaldehyde (1 mmol) with 2-naphthol (2mol) was also investigated for optimization of the reaction conditions. Reaction at different temperatures and various molar ratios of substrates in the presence of nano- TiO_2 revealed that the best conditions were solvent-free at 90 ºC. The utility of bulk TiO_2 in synthesis of dibenzoxanthenes showed that its efficiency is lower than nano TiO_2. The study indicated that 15 mol% amount of nano TiO_2 catalyses the reaction in 12 min with higher yield and cleaner workup than bulk TiO_2.

A research work done by Javad Safari [26] to prepare 3,4-dihydropyrimidin-2(1H)-one scaffolds with the solvent-free condensation of acetophenone, aromatic aldehydes and urea in the Biginelli-like reaction was used as model reaction. After the success of the reaction, the condensation reaction was carried out under solvent-free conditions at 90 ^oC and also in various solvents with varying polarity and protic nature such as ethanol, dioxane, propanol, acetonitrile, toluene and cyclohexane. The polar solvents such as ethanol, methanol and acetonitrile were much better than non-polar solvents. The results could be explained with the much better solubility of the reagents and the much better dispersion of the catalyst in the polar solvents. It also carried out the model reaction under solvent-free conditions and obtained an excellent yield.

Recycling efficiency of TiO_2 nanoparticles

The reusability of the catalyst TiO_2 nanoparticles was recovered from the reaction of indole with benzaldehyde by centrifugation and washed with ethylacetate. It was then used without further purification for the next reaction. There were no significant decreases in efficiency of the recovered catalyst compared to the fresh material. The reusability of the nano- TiO_2 catalyst was also examined and it became reusable at least up to four times. After each run, the product was filtered, the solvent was evaporated and the catalyst residue was washed with $CHCl_3$ and reused. Treatment with $CHCl_3$ removes tars more efficiently from the catalyst surface and the reaction gave 90% and 87% for second and third run at 90^0C respectively. The catalyst was reusable, although a gradual decline in activity was observed Mirjalili B.F. et.al [25]. To explore the potentiality of the present catalytic approach and to fulfill the requirements of green chemistry, the work concentrated on reusability of the catalyst. After completion of reaction as indicated by TLC with first time use of the catalyst, the mixture is dissolved in DCM and filtered to recover the catalyst. Thus obtained catalyst was washed with DCM twice to eliminate tars on catalyst surface, dried and reused successfully for four cycles and the isolated yields obtained for four successive cycles respectively are 92, 91, 90 and 88 %. The data suggested that the catalyst has not lost its activity and could be reused for four times.

Solvent free reactions catalyzed by CeO_2 nanoparticles

Nano catalysts showed very valuable role in organic synthesis because of obtaining high yield, simple preparation and isolation, low expense, high recovery, reusability and green properties, therefore, a lot of interest in various chemical transformations using catalysts under heterogeneous conditions has been increased. For unusual physico chemical properties of nano sized metal oxides, they can exist with numerous surface sites and enhanced surface reactivity such as crystal corners, edges or ion vacancies. Cerium oxide is a prominent material for various kinds of industrial applications related to catalysis The small size and large specific surface area of nano sized CeO_2 allow for certain unique and unusual physico chemical properties Lietti L et.al [27].

According to Shahram. B [28] the synthesis of 1,8-dioxo-dodecahydroxanthenes was reported using the methods in literature with some modifications. A mixture of 5,5-dimethyl-1,3-cyclohexanedione (2 mmol), aldehyde (1 mmol) and Nano CeO_2 (0.15 g) was heated at 110 oC for 12 h. The solvent was evaporated and the crude product was recrystallized from ethanol to

obtain the pure product. All products were known and characterized by comparison of their physical data with those reported in literatures. To study the effect of catalyst in the reaction of 5,5-dimethyl- 1,3-cyclohexanedion (2 mmol) and benzaldehyde (1 mmol) nano sized CeO_2 (0.15 g) was selected as model reaction under thermal and solvent free conditions. The aromatic aldehydes containing electron realizing and withdrawing groups were also employed. In all cases the reaction gave the products in good yields and prevents problems associated with solvent utilizing such as toxicity, cost, handling, safety and pollution Naeimi. H and Nazifi. Z. S. [29].

To elucidate the role of the cerium oxide nanoparticle as catalyst, a control reaction was conducted using benzaldehyde (1 mmol), ethylacetoacetate (1 mmol) , demidone (1 mmol) and ammonium acetate (1mmol) in methanol in the absence of cerium oxide nanoparticles. The reaction resulted in the formation of a fused product with low yield after 8h at 90°C. However, reaction carried out with the same reactants in methanol using 10 mol% of Cerium oxide nanoparticles under microwave irradiation afforded the products in quantitative yield. Thus in the absence of cerium nanoparticles the reaction was slow with unsatisfactory yields. To compare the efficiency of the solvent free conditions the reactions were examined in several solvents under microwave condition. The obtained results as mentioned in table 4 clearly showed the lower yield and longer reaction time was observed in the solution conditions while the solvent free method was more efficient. Suresh. P et al [30].

Recycling efficiency of CeO2 nanoparticles

The reusability of cerium oxide nanoparticles catalyst system was examined by condensation consecutively in four cycles. The data showed Table 5 a gradual loss of the activity of the catalyst used in the experiment with the increasing number of cycles indicating that it is indeed a recyclable catalyst, Due to limited stability and slow oxidation of cerium nanoparticles results in progressively slower rate of catalytic activity Khazaei A,et.al [31].

Solvent free reactions catalyzed by Fe_3O_4 nanoparticles

Fe_3O_4 nanoparticles are arguably the most extensively studied. The main characteristic of these nanoparticles is the simple and convenient separation from a reaction media by magnetic separation Rossi L. M et.al [32]. Recently magnetite nanoparticles were used as an efficient catalyst in many organic transformations. It was thought that there is scope for further innovation towards milder reaction conditions, short reaction time and improvement of yield in the synthesis of xanthene derivatives. A highly efficient and clean method for the synthesis of 14-aryl-14*H*-dibenzo[*a*,*j*]-xanthene and 1,8-dioxooctahydroxanthene derivatives using Fe_3O_4 nanoparticles as a green and robust catalyst under thermal and solvent-free conditions was reported. The experimental research was continued using different amounts of nanocatalyst in the reaction involving 4-nitrobenzaldehyde (1 mmol) and 2-naphthol (2 mmol) to afford the product 14-(4-nitrophenyl)-14*H*-dibenzo[*a*,*j*]xanthenes under solvent-free conditions at 100 °C. From these experiments, the optimum amount of this catalyst was found to be 10 mol %. The effect of solvent was investigated. Thus, the model reaction in the presence of magnetite nanoparticles was run using different solvents and under solvent-free conditions. It was noteworthy that the solvent free conditions afforded the product in excellent yield and shorter reaction time than under solvent conditions Mohammad ALI .G et.al [33]

According to Masoud N.E et.al 2011[34] in the synthesis of 3,4-dihydropyrimidin-2(1H)-ones (thiones) upon catalysis by Fe3O4 nanoparticles three types of catalysts were examined, *i.e.*, Fe_3O_4, Fe_3O_4 nanoparticles and recovered Fe_3O_4 nanoparticles. The highest yield of the product was obtained using Fe3O4 nanoparticles, which may be due to the better diffusion of nano Fe_3O_4 in the reaction mixture. The effect of solvent was investigated. Thus, the model reaction in the presence of magnetite nanoparticles was run using different solvents and under solvent-free conditions. As shown in table 6 it is noteworthy that the solvent free conditions afforded the product in excellent yield and shorter reaction time than under solvent conditions.

Recycling efficiency of Fe_3O_4 nanoparticles

The reusability of the catalyst is important for large scale operations and an industrial point of view. Therefore, according to Masoud N.E et.al [34] the reusability of the catalysts Fe_3O_4 nanoparticle was examined in the reaction between ethylacetoacetate, urea, and benzaldehyde. Since the catalyst can be separated from the reaction mixture using an external magnetic field it was recovered with a simple magnet after the dilution of the reaction mixture with ethanol. The recovered catalysts were dried and weighed. Afterwards, according to the amount of catalyst the required amount of fresh ethylacetoacetate, urea, and benzaldehyde were added. The results showed in table 7 that the catalyst can be reused four consecutive times without a noticeable loss in activity

Solvent free reactions catalyzed by CuO nanoparticles

Metal oxide nanoparticles are known to generate a very high catalytic activity toward a wide range of catalytic based applications. In recent years, methods have been developed for the preparation of novel nanostructures of oxides. Recently, nano ctystalline Al_2O_3 and γ-Fe_2O_3 nanoparticles have been used for Freindlander reaction Alarreca G et.al [35]. In another hand, CuO nanoparticles have been previously used as heterogeneous and recyclable catalyst for α-aminophosphonate synthesis and cross coupling

reactions. The major benefits of the CuO nanoparticles as a heterogeneous catalytic process are the fast reactions, solvent-free environment, and improved yields. Zhong L.S, neet.al [36] studied the catalytic activity of CuO nanoparticles. Model reaction was carried out by taking the mixture of 2-aminobenzophenone, ethyl acetoacetate and 5 mol % of catalyst in solvent free condition at 60 °C. TiO_2, SiO_2, Al_2O_3, ZnO, MgO, CuO bulk and nano CuO have been used. The study indicated that CuO nanoparticle was the best. This would be a novel application of CuO nano catalyst for the Friedlander quinoline synthesis. Various reaction parameters were optimized for this reaction. The reaction was carried out with and without solvents keeping the catalyst amount constant. It was observed that solvent-free condition gave the excellent yield of product than that in the presence of solvents.

According to Dighore N.R et.al [5] a mild and high yielding solvent free method for the synthesis of 5-arylidene barbiturates by a condensation reaction between aromatic aldehyde and barbituric acid catalyzed efficiently by CuO nanoparticles was reported. The catalytic activity of the synthesized CuO nanoparticles was investigated in the synthesis of arylidene barbituric acid derivatives at room temperature. To study the efficiency of the CuO nanocatalyst, 4-chlorobenzaldehyde and barbituric acid were used as the model substrate. The reaction was carried out without any catalyst, but the product isolated gave poor yield (25%). In optimizing the reaction conditions, the amount of catalyst was the major factor. The model reaction was studied using 25, 50, 75, 100 and 125 mg of a reaction of 4- chlorobenzaldehyde. The results revealed that best yield was obtained by using 100mg catalyst. With increase in the catalyst concentration, the yield of the desired product was found to be constant. Therefore, the catalyst plays a crucial role in the success of the reaction in terms of yields of the product.

According Zhong L.S, et.al [36] a comparative studys of CuO nanoparticles catalysis with other catalysts reported in the literature were investigated, the results of the synthesis of arylidene barbituric acid derivatives in the presence of different reported catalysts with respect to time and yield of the product indicated CuO nanoparticles gave 5-arylidene barbituric acids as the desired products in short time span and in quantitative yields by a simple high speed stirring at room temperature. The catalyst CuO nanoparticles was recovered by simple work-up using centrifugation method, washed with ethanol and reused for three successive reactions. The isolated yields obtained for the three successive cycles respectively were 94, 91 and 85%.

Conclusion

In conclusion, the use of metal oxide nanoparticles as a green, mild and effective catalyst satisfactorily catalyzed the synthesis of most organic compounds. Metal oxide nanoparticles are known to be promising heterogeneous catalysts in a variety of organic transformations Working without solvents gives the potential for a simpler process, smaller plants, and eliminates the energy costs of removal, recycling and eventual disposal of waste solvents. The catalyst was recyclable and could be reused for consecutive cycles with little loss of the catalytic activities. The simplicity together with the use of inexpensive, non-toxic and environmentally benign catalyst are remarkable features of organic reactions.

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Appendix

Table 1: The model study for the one-pot synthesis of acridine in the presence of various solvents

Entry	Solvent	Time (min)	Yield (%)
1	Ethanol	30	62
2	Methanol	30	59
3	CH3CN	30	57
4	CHCl3	30	53
5	Toluene	30	45
6[b]	Solvent-free condition	**7**	95,94,94,93

[b] Catalyst was reused four times

Table 2: Optimization of the amount of TiO_2 nanoparticles in the synthesis of 2,3-dihydro-3-methyl-2- (4-(dimethylamino) phenyl) quinazolin-4(1H)one.

Catalyst (mol%)	2	3	4	5	6
Yield GC–MS (%)	49.68	54.53	76.42	91.86	89.47

Table 3: Effect of solvent for the synthesis of 2, 3-dihydro-3-methyl-2-(4-(dimethylamino)- phenyl)quinazolin-4(1H)one. Catalytic activity TiO_2

Solvent	Time (min)	Yield GC–MS (%)
DCM	90	36.76
$CHCl_3$	60	40.54
EtOH	45	73.64
H_2O	30	76.05
Solvent free	30	91.86

Table 4. Synthesis of Polyhydroquinolines using various solutions versus the solvent-free conditions

Solvent	Time (min)	Yield GC–MS (%)
No solvent	8	90
DMF	25	36
Dioxane	20	30
Methanol	12	72
Ethanol	10	88

Table 5. Reusability of nano sized CeO_2 as a heterogeneous catalyst for synthesis of 1,8-dioxo-octahydroxanthenes

Cycle	Time (min)	Isolated Yield (%)
1	20	93
2	20	92
3	20	91
4	20	90
5	20	88

Table 6. Synthesis of 3,4-dihydropyrimidin-2(1H)-ones in various solvents catalyzed by Fe_3O_4 nanoparticles;

Entry	Solvent	Time (min)	Yield (%)
1	CH_2Cl_2	180	60
2	THF	120	70
3	toluene	210	45
4	ethanol	90	75
5	No solvent	20	92

Table 7. Reusability of Fe_3O_4 NPs for the reaction between benzaldehyde,ethylacetoacetate, and urea in Synthesis of 3,4-dihydropyrimidin-2(1H)-ones

Run	Time (min)	Yield (%)
1	16	90
2	18	88
3	18	86
4	20	85