Heterocyclic Letters
Vol. 6| No.4 |623-630|Aug-Oct| 2016
ISSN : (print) 2231–3087 / (online) 2230-9632
CODEN: HLEEAI
http://heteroletters.org

Ag-TiO_2NANO COMPOSITE AS AN EFFICIENT AND RECYCLABLE CATALYST FOR THE HANTZSCH SYNTHESIS OF POLYHYDROQUINOLINES

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ABSTRACT

TheHantzsch four-component reaction between various aldehyde, 1,3-dione, *β*-ketoester and ammonium acetate to provide corresponding polyhydroquinolineshave been studiedin the presence ofAg-TiO_2nano compositeas an efficient and recyclable catalyst under solvent-free conditions at room temperature. The isolation of the desired products could be attained*via* simple filtration and Ag-TiO_2nano composite could be recycled and reused continuously.

KEYWORDS

Ag-TiO_2nano composite, Hantzsch reaction, Polyhydroquinolines, Solvent-free conditions.

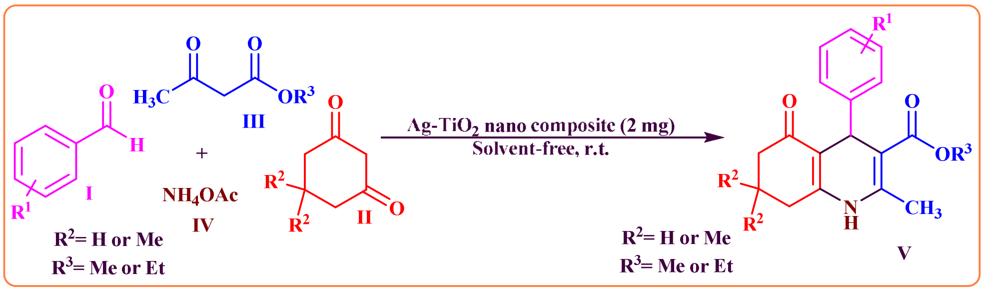
INTRODUCTION

Compared with pure semiconductor, metal-semiconductor nanocompositesdisplaypreferable catalytic, gas sensing, luminescent,[1] and nonlinear optical[2] properties. Coating of the metal or semiconductor with a suitable semiconductor or metal produces the core materials more stable at some extreme conditions. Ag clusters supported on titania (TiO_2) are of practical significance since Ag-TiO_2nano composites are favorable photo catalysts for areas for example disinfecting, self-cleaning and water splitting also air and water purification. Since other noble metals for instance Pd, Rh, Pt and Au are very expensive, Ag nanoparticles may serve as a much more cost-efficient solution. Furthermore, Ag nanoparticles dispersed on metal oxide supports are of interest because they are worthy catalysts for the oxidative dehydrogenation of methanol to formaldehyde[3, 4] and are efficient epoxidation catalysts.[5-7] As for the Ag-TiO_2nano composite, due to its interaction between the metal nanoparticle and dielectric matrix, the surface effect or quantum size effect, it has unique electric, optical and photoelectric transforming properties. Stimulation with a femtosecond laser pulse, the Ag-TiO_2nano composite shows large nonlinear optical properties resulting from itsoptical temporary rapid and relaxation response to time.[8-11]

The synthesis of complex biologically active scaffolds *via* the one-pot multicomponent reactions (MCRs) has engrossed considerable attention.[12] Designing eco-friendly and simple mild reactions for the synthesis of medicinal structures is an attractive aspect of chemical studies. Multi-component reaction (MCR) mainly environmentally friendly conditions, is one of the most appropriate routs which can helps chemists to adapt their reaction processes to the requirements of “green chemistry” as well as to develop libraries of medicinal scaffolds.[13]

Because of the general stability and versatility of the 1,4-dihydropyridine (DHP), Hantzsch process has continued the most common process for the synthesis of DHPs.[14]The synthesis of DHPs is of great significance in chemistry because of its pharmacological and biological activities.[15]While DHPs were primarily developed as cardiovascular agents, but they are antihypertensive, hepatoprotective, vasodilator, antimutagenic, antiatherosclerotic, geroprotective, bronchodilator, antitumor and antidiabetic agents.[16]Numerous methods have been reported for the synthesis of these compounds usingseveral homogeneous or heterogeneous catalysts such as {[HMIM]$C(NO_2)_3$},[17]MCM-41,[18]polymer,[19] TMSCl,[20] hafnium(IV)bis(perfluorooctanesulfonyl)imide,[21]fluoro alcohols,[22] silica sulfuric acid[23] and [2-MPyH]OTf.[24]

In this study, we investigate an efficient and benign four-component synthesis of polyhydroquinolines*via*theHantzsch condensation reaction between numerous aldehyde, 1,3-dione, *β*-ketoester and ammonium acetate in the presence ofAg-TiO_2nanocomposite as a recyclable catalyst under solvent-free conditions at room temperature (Scheme I).



Scheme I. Synthesis of polyhydroquinolinesusingAg-TiO_2nanocompositeas a recyclable catalyst.

EXPERIMENTAL

General.

All of the chemical materials applied in this study were purchased from Merck and Fluka and used without further purification. Melting points were determined with an Electro thermal 9100 apparatus and were uncorrected. FTIR spectra were attained on a Perkin-Elmer spectrometer. ^{1}H NMR and ^{13}C NMR spectra were recorded on a Bruker DRX-400 AVANCE at 400 and 100 MHz (respectively) using TMS as internal standard and DMSO-d_6 as solvent. Mass spectra data were achieved using a MS Model: 5975C VL MSD with Tripe-Axis Detector.

General procedure for the synthesis of Ag-TiO_2 nano composite.

Ag-TiO_2 nano composite as a catalyst was produced according to previous literature.[25] Titanium tetrachloride was used as the starting material to synthesize pure TiO_2 by sol-gel process and the preparation procedure and characterization methods were reported in previous study. Silver nitrate was used as a silver source. The Ag immobilization onto the TiO_2 nano particles was gave based on the earlier investigate.

General procedure for the Hantzsch synthesis of polyhydroquinolines.

Ag-TiO_2nano composite as a catalyst (2 mg) was added and mixed to a mixture of various aldehyde (1 mmol), 1,3-diones (1 mmol), *β*-ketoester (1 mmol) and ammonium acetate(1 mmol; 77mg) under solvent-free conditions at room temperature for the suitable time. After completion of the reaction which was monitored by TLC (*n*-hexane/ethyl acetate: 5/2), for the recycle of Ag-TiO_2nano composite, hot ethyl acetate was added to the reaction mixture and centrifuged to separate product and starting materials from the catalyst (Ag-TiO_2nano composite as a catalyst is insoluble in ethyl acetate). The solvent of organic layer was removed and the crude product was purified by recrystallization from ethanol to yield pure products. All of the attained products are identified and were known by comparison of their physical data with those of reported in the paper.

RESULTS AND DISCUSSION

Numerous synthetic processes for the preparation of polyhydroquinolines have been reported; of these processes, we describe a rapid preparation of a series of eighteen polyhydroquinolineswith good to excellent overall yields (90-98%) based on the use of 2 mg of Ag-TiO_2nano composite as a catalyst optimized procedureusing commercially available numerous aldehyde, 1,3-dione, *β*-ketoester and ammonium acetate under solvent-free conditions at room temperature (Scheme I).

Atomic force microscopy (AFM) is a method that lets us find and analyze surfaces with high resolution and accuracy. AFM affordsvarious advantages; for instance hard surfaces like the surface of a ceramic material, or the dispersal of metallic nano composite; or very soft ones, for example molecules of proteins or plastic materials. Fig. Idisplays the two- and three-dimensional AFM images of Ag-TiO_2nano composite as a catalyst. No significant partition area in size is known in the illustrations. By achieving the three-dimensional 2.1 $\mu m^2 \times 2.1\ \mu m^2$ frameworks, we can identify that the attainedAg-TiO_2nano composite confirms an interrupted structure with a desirable outside planarity. The surface of the coat on the Ag-TiO_2nano composite was clearly exposed to be less than 25 nm.

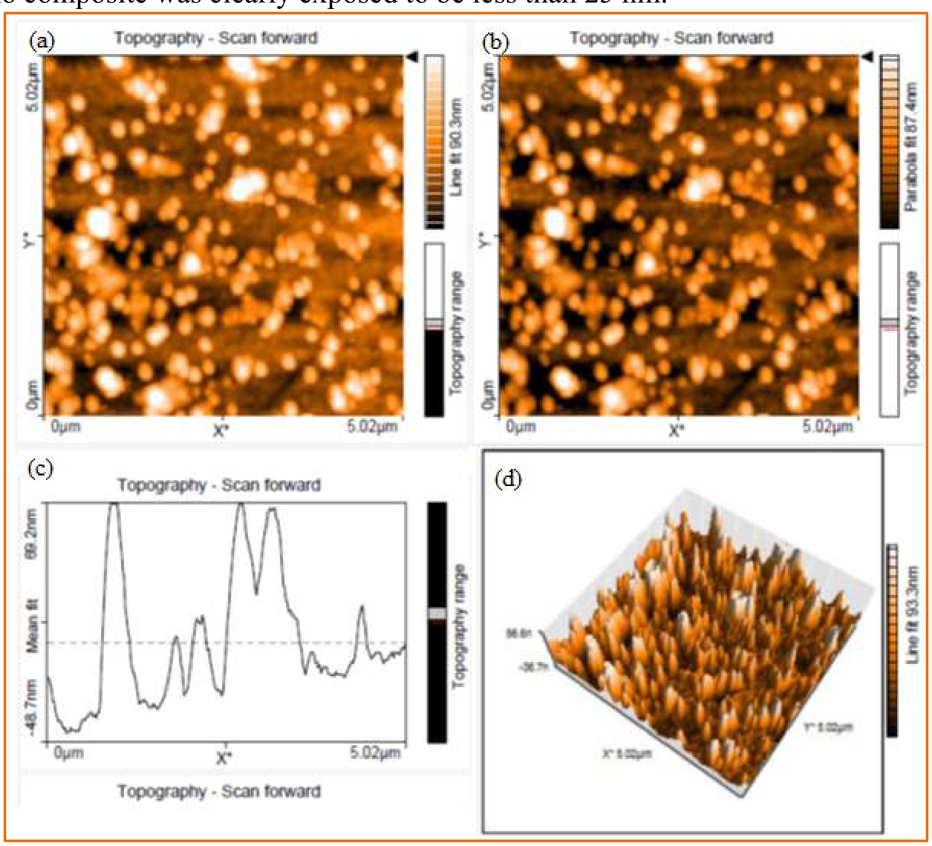


Fig. I. Two-dimensional (a and b), topography(c) and three-dimensional (d) of AFM images of the Ag-TiO_2nano composite.

To choice a suitable amount of catalyst required to synthesize superb yield of products, the reaction of investigation substrates was performed in the presence of different amounts of Ag-TiO_2nano composite. It was found that 2 mg of Ag-TiO_2nano composite as a catalyst was enough to carry out the reaction in lesser time with high yield of products. There was no important change in the yield of products when large amounts of Ag-TiO_2nano composite were applied instead of 2 mg. The results are summarized in the Table I. Further, to create the reaction conditions even more effective for the synthesis of polyhydroquinolinesin less time with high yields, the study reaction was also attempted at various temperatures for exampleroom temperature, 50°C, 75°C and 100°C and it has been found that the reaction was fast at room temperatures, whereas at higher temperatures, it becomes low reactive but loses its selectivity and provided multiple products. Thus, room temperature was chosen as the optimum reaction temperature at which the reaction proceeded efficiently to afford a better yield of products. At room temperature optimized reaction temperature, 98% yield was detected during the reaction of the test substrates, as shown in Table I.

Table I. Effect of different amounts ofAg-TiO_2nano composite and temperature in the synthesis of polyhydroquinolines under solvent-free conditions.[a]

Entry	Amounts of catalyst (mg)	Temperature (°C)	Time (min)	Yield[b] (%)
1	Catalyst-free	r.t.	30	27
2	Catalyst-free	100	30	25
3	1	r.t.	10	71
4	1	50	10	71
5	1	100	10	67
6	2	r.t.	5	98
7	2	50	5	98
8	2	75	5	98
9	2	100	5	96
10	5	r.t.	5	97
11	5	100	5	94

Reaction conditions: [a]Dimedone (1 mmol), biphenyl-4-carbaldehyde (1 mmol),methyl acetoacetate (1 mmol), ammonium acetate (1 mmol); [b]Isolated yield.

The reaction of investigation substrates was also performed using polar and non-polar solvents like ethanol, water, acetonitrile, CH_2Cl_2, ethyl acetate, toluene, *n*-hexane and also under solvent-free condition. It was detected that the reaction carried out under solvent-free condition provided the best results in terms of yield and reaction time. Thus, solvent-free condition was chosen as the solvent system for the synthesis of polyhydroquinolines. The results are revealed in Table II.

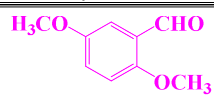
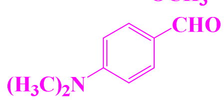
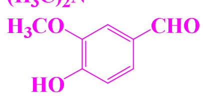
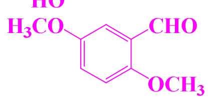
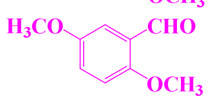
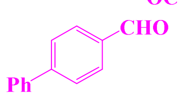
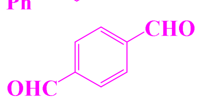
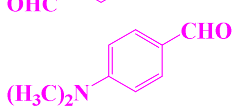
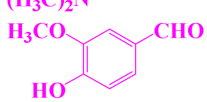
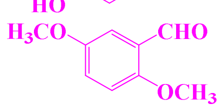
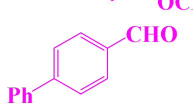
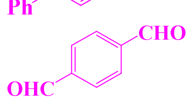
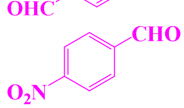
Table II. The effect of solvents/solvent-free condition in the synthesis of polyhydroquinolines at room temperature using 2 mg of Ag-TiO_2 nano composite as a catalyst.[a]

Entry	Solvent	Time (min)	Yield[b] (%)
1	Solvent-free	5	98
2	H_2O	30	51
3	C_2H_5OH	10	95
4	CH_3CN	15	93
5	CH_3CO_2Et	20	91
6	CH_2Cl_2	20	89
7	Toluene	30	78
8	*n*-Hexane	30	71

Reaction conditions: [a]Dimedone (1mmol), biphenyl-4-carbaldehyde (1 mmol),methyl acetoacetate (1 mmol), ammonium acetate (1 mmol); [b]Isolated yield.

To generalize the application of the Ag-TiO_2nano composite as a catalyst, the Hantzschreaction of various aldehyde, 1,3-dione, β-ketoester and ammonium acetate were performedin the presence of2 mgAg-TiO_2nano composite as a catalyst under solvent-free conditions at room temperature (Table III). The reactions proceeded well with a variety of aldehyde, 1,3-diones and β-ketoesters. For most of the substrates, the reaction could be completed in5-25 min with good to excellent yields, with the substrates having either electron-withdrawing groups or electron-donating groups. As it is seen, both electron-withdrawing and releasing groupson aromatic ringprovided the corresponding products in high to excellent yields. It was found that the yield of reaction ortho-position aldehyde is lower than those of para- or meta-substituted aldehyde. Also, in this reaction conditions dimedone reacted faster than 1,3-cyclohexanedione and methyl acetoacetate reacted faster than ethyl acetoacetate.Furthermore, In the presence of terephthalaldehyde as an aldehyde derivative, bispolyhydroquinoline products were produced (Table III, entries 7 and 12).

Table III. The four-component Hantzsch synthesis of polyhydroquinolines in the presence of 2 mg of Ag-TiO_2nano composite as a catalyst.[a]

Entry	Aldehyde	R^2	R^3	Time (min)	Yield[b] (%)	M.p (°C)[Ref.]
1		H	CH_3	20	92	235-237[17]
2		H	CH_3	15	92	251-253[17]
3		H	CH_3	20	90	225-227[17]
4		H	CH_2CH_3	25	90	201-203[17]
5		CH_3	CH_3	15	94	197-199[17]
6		CH_3	CH_3	5	98	253-255[17]
7		CH_3	CH_3	10	93	341-343[17]
8		CH_3	CH_3	10	94	225-227[17]
9		CH_3	CH_3	15	92	269-271[17]
10		CH_3	CH_2CH_3	20	92	195-197[17]
11		CH_3	CH_2CH_3	10	96	197-199[17]
12		CH_3	CH_2CH_3	15	91	365-367[17]
13		CH_3	CH_2CH_3	10	97	241-243[24]

14	CH_3	CH_2CH_3	10	96	235-237[24]

Reaction conditions: [a]Aldehyde (1 mmol), 1,3-diones (1mmol), *β*-ketoesters(1mmol), ammonium acetate (1 mmol); [b]Isolated yield.

In order to study the recycling of the catalyst, the Hantzsch reaction between biphenyl-4-carbaldehyde, methyl acetoacetate, dimedone and ammonium acetate catalyzed by 2 mg of Ag-TiO_2nano composite was selected as a typical reaction. The results displayed that Ag-TiO_2nano composite can be reused six times without important loss of catalytic activity (Fig. II).

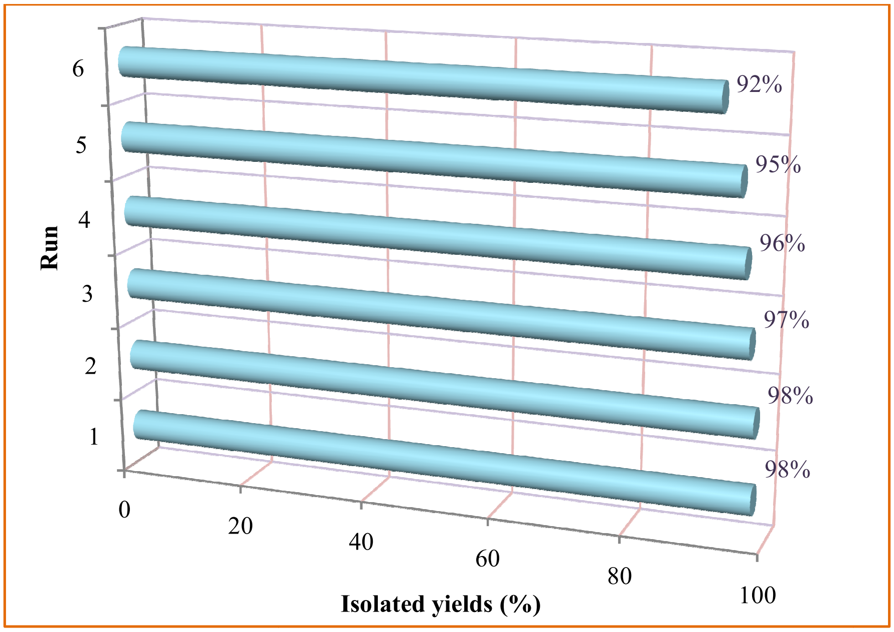


Fig.II. The recycling of the Ag-TiO_2nano composite for the Hantzsch reaction after 5 min.

CONCLUSION

In summary, the Ag-TiO_2nano composite as a recyclable and efficient catalyst have been demonstrated to be a Hantzcsh four-component condensation reaction between various aldehyde, 1,3-dione, *β*-ketoester and ammonium acetate under solvent-free conditions at room temperature. While the reaction was accomplished in heterogeneous model, isolation of the desired products as well as Ag-TiO_2nano composite as a catalyst could be attained*via* a simple centrifuged and the Ag-TiO_2nano composite could be reused continually.

ACKNOWLEDGEMENTS

This study was financially supported by Islamic Azad University, Hamedan Branch, Iran.

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Received on August 17, 2016.