An Efficient One-Pot Synthesis of Polyhydroquinolines at Room Temperature Using MCM-41 catalyst under solvent-free conditions

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An efficient Hantzsch condensation of polyhydroquinoline derivatives was reported via a four component coupling reaction of aldehydes, dimedone, ethyl acetoacetate and ammonium acetate in the presence of MCM-41 under solvent-free condition.
Keyword 1,4-Dihydropyridines, MCM 41,Solvent free, Room Temperature Hantzsch condensation

Introduction

A major emerging and challenging area of heterogeneous catalysis is that of environmental pollution control, with tightening legislation on the release of waste and toxic emissions having serious implications for the chemical industry. While heterogeneously catalyzed processes were developed at the turn of the century, and focused on product yield, disregarding the environmental impact of inorganic waste and toxic by-products formed during the reaction [1].Tightening legislation on the emission of hazardous pollutants is driving the industry toward the implementation of innovative "clean technology" including the use of alternative heterogeneously catalyzed processes [2]. The recently developed family of mesoporous materials [3] with their tunable large pore sizes displayed the exposition of the inherently present acid [4] and base catalytic properties [5] will find and enlarge their possible applications as novel catalysts in the fine chemical synthesis. Brunel and his co-workers [6] were the first to report the covalent attachment of organoamino groups on MCM-41. The modified mesoporous materials/silica anchored with organic basic moieties are found to be excellent catalysts for Knoevenagel, aldol and Michael reactions [6-8].

1, 4-Dihydropyridines exhibit a variety of biological properties. They can cure the disordered heart ratio as a chain cutting agent of factor IV channel and also possess the calcium channel agonist-antagonist modulation activities [9-11]. These compounds also behave as neuroprotectants, cerebral antiischaemic agents and chemosensitizers [12, 13].

In the past, many methods for synthesis of polyhydroquinoline derivatives have been reported, such as conventional heating [14] refluxing in acetic acid [15] and microwave irradiation and ultrasound [16]. Ionic liquids [17], have also been used to promote the reaction. Different other heating approaches for the syntheses of polyhydroquinoline derivatives have subsequently been reported [18-20] recently, some other method for the preparation of 1,4-dihydropyridines and the progress in this field is remarkable including recently the promotion of microwave [21], TMSCl [22], ionic liquids [23, 24], polymers [25,26], Yb(OTf)3.[27], $HClO_4$-SiO [28] and HY-zeolite [29] mont. K10.[30]. However in spite of there potential utility some of the reported methods suffer drawbacks, these methods are associated with several shortcomings such as long reaction times, expensive reagents, harsh conditions, low-product yields, occurrence of several side products.

Recently, polyhydroquinoline derivatives have been reported by heterogeneous catalyst such as HY-zeolite [29] using acetonitrile as a solvent The possibility of performing multicomponent reactions under solvent-free conditions with a heterogeneous catalyst could enhance their efficiency from an economic as well as an ecological point of view. In recent years heterogeneous catalysts are gaining more importance due to environmental-economic factors. The catalyst is generally of low cost and can be easily handled or removed. In recent times, the progress in the field of solid-state organic reactions is gaining significance both

from the mechanistic and synthetic point of view [31-33]. Number of articles are available reporting solid-state reactions by grinding such as, Grignard reaction[34], Reformatsky reaction [35], Aldol condensation [36], Dickhmann condensation [37], phenol coupling reaction [38], reduction reaction [39], Wittig reaction [40], Grignard and McMurry reaction [41]. Most of these reactions are carried out at room temperature, absolutely solvent-free and use only a mortar and pestle. In addition to economical and green procedures are efficient as well. Therefore, we focus on developing the novel procedure involving a solid-state reaction performed by grinding.

Herein, we would like to report a convenient and efficient procedure for one-pot synthesis of polyhydroquinolines by four-component coupling reactions of aldehydes, ethyl acetoacetate, dimedone and ammonium acetate in the presence of MCM-41 as a catalyst by grinding in mortar and pestle in excellent yield.

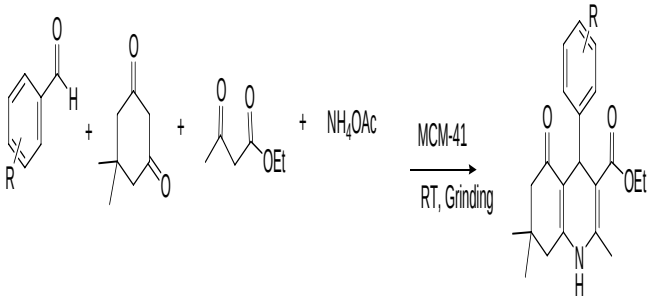
Experimental

Melting points were determined in open capillaries and are uncorrected. IR spectra were recorded on a FTIR 8201,spectrometer, ^{1}H NMR spectra were measured on Varian 300 MHz spectrophotometer in $CDCl_3$ as a solvent and TMS as an internal standard Mass Spectra were determined on Jeol SX-102(FAB) massspectrometers.

Typical experimental procedure. A mixture of aldehyde (1 mmol), dimedone (1mmol), ethylacetoacetate (1 mmol), ammonium acetate (1.5 mmol) and MCM-41 (50 mg) were added to a mortar. The mixture was ground by mortar and pestle at room temperature for 15 min, the reactant was disappeared (TLC). After completion, 10mL dichloromethane was added to the reaction mixture; the catalyst was removed by filtration and washed with dichloromethane. The solvent was evaporated under reduced pressure on a rotary evaporator to give crude products were obtained. The crude products were purified by recrystallization from ethanol. The authenticity of the products was established by comparing their melting points and the spectral data for selected compounds are presented in the subsequent section under results.

Result and discussion

Scheme 1. An Efficient One-Pot Synthesis of Polyhydroquinolines at Room Temperature Using MCM-41 catalyst under solvent-free conditions



Ethyl-1,4,7,8-tetrahydro-2,7,7-trimethyl-4-aryl-5(6H)- oxoquinolin-3-carboxylate (4a).

IR (KBr): 3050, 2940, 1715, 1630, 1605, 1460, 1375, 1215, cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.94 (s, 3H, CH_3), 1.07 (s, 3H, CH_3), 1.14 (t, 3H CH_2CH_3), 2.20 (m, 4H, $2CH_2$), 2.36 (s, 3H, CH_3), 4.09 (q, 2H, CH_2CH_3), 5.02 (s, 1H, CH), 6.0 (s, 1H, NH), 7.05–7.26 (m, 5H,Ar).

Mass (ES/MS): m/z 339

Ethyl-1,4,7,8-tetrahydro-2,7,7-trimethyl-4-(2-chlorolphenyl)-5(6H)-oxoquinolin-3-carboxylate(4c).

IR (KBr): 3065, 2957, 1725, 1644, 1614, 1467, 1386, 1227, cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.97 (s, 3H, CH_3), 1.06 (s, 3H, CH_3), 1.22 (t, 3H, CH_3), 2.03-2.22 (m, 4H, 2 CH2), 2.40 (s, 3H, CH_3), 4.07 (q 2H, CH_2), 4.63 (s, 1H, CH), 7.12-7.29 (m 4,ArH), 7.60 (s, 1H, NH). Mass (ES/MS): m/z 373

The results are summarized in Table 1. It can be seen that the one pot condensation of series of aldehyde with dimedone, ethylacetoacetate and ammonium acetate leading to 4H-pyrimidine derivatives gives 90-95% yield under the grinding by use of mortar and pestle.

We also performed the model reaction of benzaldehyde with dimedone, ethylacetoacetate and ammonium acetate catalyzed by MCM-41 used ethanol as a solvent with stirring at room temperature and conventional method. The condensation was carried out 4 hrs. and 3 hrs. with 60% and 70% yield respectively. It is clear that the grinding method can accelerate the one pot reaction. We also examine the reactions using donating and withdrawing substituted aryl aldehyde such as halogen, methoxy and nitro group were tolerated. In all cases the corresponding to 4H-pyrimidine derivatives were obtained in excellent yields. The results are given in Table 1.

Conclusion

In summary, we have we have developed a simple and efficient method for the synthesis of polyhydroquinoline derivatives via Hantzsch condensation using a heterogeneous catalyst (MCM-41) in the absence of solvent at room temperature by using a grinding method. Compared with the conventional heating and stirring method, the main advantages of the procedure are milder reaction condition, better yield, and easier work-up.

Table 1 Synthesis of of polyhydroquinoline by using MCM 41 at room temperature.

Sr. No.	Ar	Time (min)	Yield %	M. P. ^{o}C
4 a	C_6H_5	2	95	225-227
4 b	4-Me.C_6H_4	4	94	265-268
4 c	2-Cl. C_6H_4	3	93	208-210
4 d	3-Cl. C_6H_4	2	94	230-232
4 e	4-Cl. C_6H_4	3	92	245-246
4 f	4-OH. C_6H_4	4	91	238-240
4 g	4-OMe. C_6H_4	5	92	258-260
4 h	4-NO_2. C_6H_4	2	96	240-242
4 i	4-OH, 3-OMe.C_6H_3	5	92	208-210
4 j	2-OMe	5	91	248-250

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