

Microwave-Assisted Synthesis of Nano-Sized Cadmium Oxide As a New and Highly Efficient Catalyst for Solvent Free Acylation of Amines and Alcohols

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In present studies, a new and efficient method for synthesis of cadmium oxide nanoparticles by using microwave (MW) activation is reported. To ensure the specific efficiency of microwave irradiation *versus* conventional heating, the synthesis of Cd(OH)₂ as precursor of CdO was carried out under similar temperature (80 °C), time and reaction conditions without microwave irradiation. The formation of CdO was characterized by XRD, TEM, FT-IR analysis. Catalytic activity of CdO nanopowder for acylation of alcohols, phenols and amines has been investigated. The results show that the reaction times and yields of desired products were improved by using CdO.

Key Words: Microwave, Nano-Sized cadmium oxide, Catalyst.

INTRODUCTION

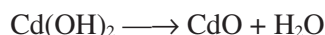
The acylation of alcohols and amines is one of the most basic and frequently used transformations in organic synthesis, as it provides a useful and efficient protection protocol in multistep synthetic processes. Especially in the synthesis of complicated natural products and glycosylation of sugars, acyl moiety plays a pivotal role as protecting group of hydroxy group. Amide compounds because of their extensive application in pharmaceutical industry have also attracted much attention. Acetylation of alcohols and amines is commonly carried out by reaction of alcohols with acetic anhydride or acid chloride in the presence of basic or acidic catalyst in a suitable organic solvent. The most efficient basic catalysts are triethylamine or pyridine¹ together with 4-(dimethyl amino)pyridine (DMAP)² were used for acylation of alcohols with acetic anhydride. Tributylphosphine (Bu₃P)³ as a less basic catalyst particularly for base sensitive substrates and KF/Al₂O₃⁴ as a solid supported reagent were also used in the acylation of alcohols and amines respectively with acetic anhydride. Various metal salts including CoCl₂⁵, ZrCl₄⁶, InCl₃⁷, Mg(ClO₄)₂⁸, Cu(BF₄)·xH₂O⁹, RuCl₃¹⁰, P₂O₅/SiO₂¹¹, ZrOCl₂·8H₂O¹², triflates such as Sc(OTf)₃¹³, Cu(OTf)₂¹⁴, indium¹⁵, ZrO₂⁻ pillared clay composite¹⁶, ionic liquids *p*-toluenesulfonate¹⁷, I₂ under solvent-free condition¹⁸ and NiCl₂ under microwave irradiation¹⁹ have also been reported to promote the acylation reactions. Although, all of the above mentioned methods has some degree of generality and can be applied for the

acylation of various acid/base sensitive substrates. Most of them have one or more practical drawback associated with hazardous reagents, long reaction times, toxic organic solvents, tedious experimental procedures, harsh reaction conditions, use of expensive and moisture sensitive toxic catalysts, formation of side products and poor yields of the desired products. Also, generally the reported methods work well on only primary or secondary alcohols and failed to protected tertiary alcohols or less reactive phenols and amines. A few of these methods also suffer from side reactions such as dehydration and rearrangement and might not be fully compatible for the acylation reactions with substrates bearing acid-sensitive groups. Therefore, a great demand for a practical, efficient and greener alternative for this important transformation prompted us to disclose here a simple procedure for acylation of alcohols and amines under solvent-free conditions and using an easily available, economical and safe catalyst.

EXPERIMENTAL

The microwave-assisted reaction were performed in a domestic microwave cavity (2.45 GHz, maximum power 1000 W, butane) equipped with a condenser and reaction temperature (*ca.* 80 °C) was controlled *via* the on-line sensor. Transition electron microscopy (TEM) was done on a LEO instrument (model 912 AB) operating at 120 KV. Powder X-ray diffraction patterns (XRD) were measured by D8 Avance Bruker system using CuK α ($\lambda = 0.154056$ nm) radiation with 2θ in range 20-70°. Fourier transform infrared spectroscopy (FT-IR) was performed using Perkin-Elmer (RX 1) with KBr. Absorption spectra were obtained using a Shimadzu UV-vis spectrophotometer. All chemicals used were of analytical grade or of the highest purity available, which were obtained from Sigma-Aldrich and used as received.

General experimental procedure for synthesis of CdO nanoparticles: In a typical procedure 266 mg (1 mmol) of Cd(CH₃COO)₂·2H₂O was introduced in a flask and suspended in 120 mL of 2-propanol under vigorous stirring at 50 °C. An alcoholic solution of sodium hydroxide was prepared by adding 80 mg (2 mmol) NaOH to 30 mL of 2-propanol under vigorous stirring at 50 °C. The flask containing Cd(CH₃COO)₂·2H₂O and alcoholic solution of NaOH was cooled in an ice-water bath. The sodium hydroxide solution was then added drop-wise to cadmium acetate solution under vigorous stirring to give a total volume of 150 mL. The final solution was heated under microwave irradiation at *ca.* 80 °C for 5 min. A white colloidal solution was obtained, then centrifugated and washed the solution two times with methanol to remove impurities, filtered and dried at 80 °C for 2 h in electrically heated laboratory (oven). A white precipitate product was thus prepared. During the calcinations of Cd(OH)₂ at 400 °C for 1 h, a dark yellow precipitate CdO was prepared as follows:



Structure of the calcinated powder was investigated by X-ray diffraction (XRD), TEM, FT-IR and UV.

Characterization of the catalysts: The XRD pattern of calcinated powder at 400 °C for 2 h is shown in Fig. 1. The average particle size (t) was estimated from the width at half-maximum (FWHM) as the diffraction peak of CdO, (111), (200) and (220) at 2θ values of 33.25, 38.45 and 55.43° using Debye-Scherrer's formula.

$$t = \frac{k\lambda}{\beta \cos \theta}$$

where λ is the wavelength of X-ray, θ the Bragg's angle (in radian), k a constant which depends on the grain shape (0.89 for circular grains) and $\beta_{1/2}$ the width at half maximum, It is observed that the average particle size of the different samples lies in the range 25-30 nm. Transition electron microscopic micrograph of the powder is shown in Fig. 2. It was used to determine the particle size and morphology of the nano-sized powder is *ca.* 25nm. This result is in good agreement with the crystallite size calculated using the XRD data.

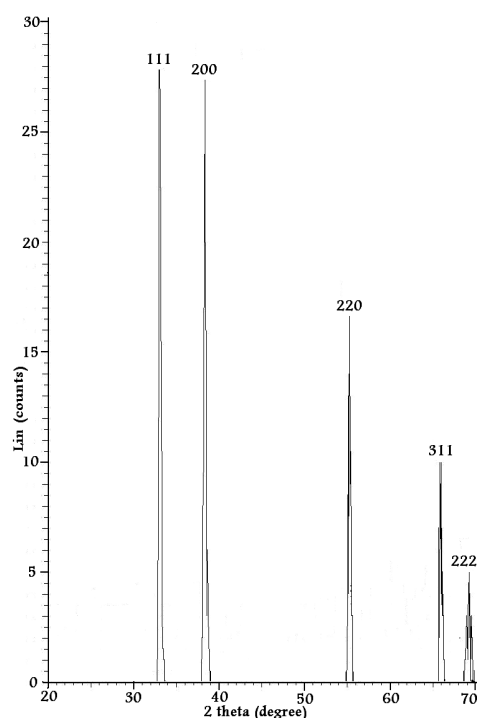


Fig. 1. XRD pattern of nano-sized CdO calcinated at 400 °C for 2 h

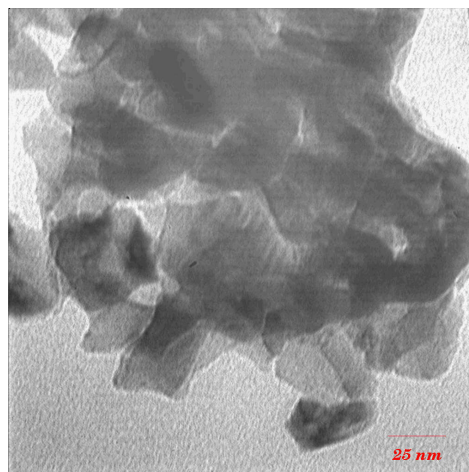


Fig. 2. TEM pattern of the CdO

The FT-IR spectroscopy could be useful in understanding the bonding between the Cd-O atoms. The formed CdO is characterized by an intense and very broad IR band with poor resolved as shoulders at about 1400 cm^{-1} (Fig. 3). UV-Vis spectra of CdO had a maximum absorbance at 350 nm.

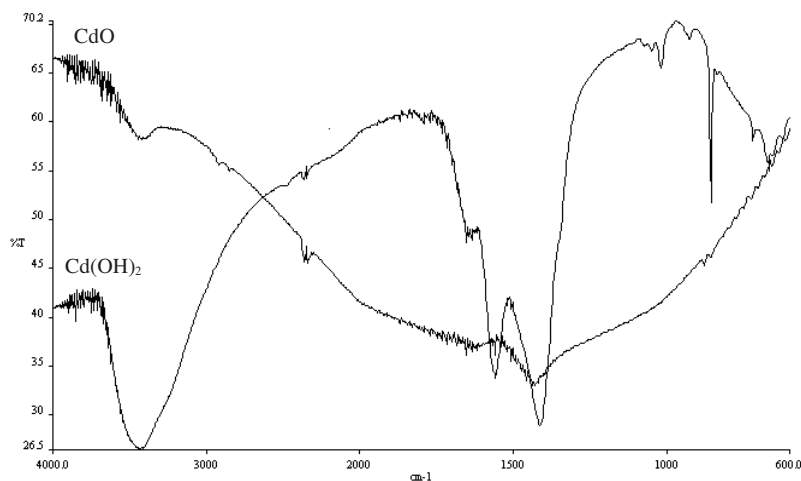


Fig. 3. FT-IR spectra of Cd(OH)₂ and CdO

To check the specific efficiency of microwave irradiation with when compared to conventional heating, the reaction of Cd(CH₃COO)₂·2H₂O and NaOH was carried out in 2-propanol at the same temperature (80 °C) for 5 min without microwave irradiation. Cd(OH)₂ as precursor of CdO calcinated at 400 °C for 2h. The XRD pattern of CdO, displayed average particle size about 100 nm (data not shown).

Typical experimental procedure for solvent-free acylation of alcohols or phenols and amines: CdO nano particles (10 mol %) were added to a mixture of alcohol or phenol and amine (1 mmol) and acetic anhydride (1.2 mmol) in pyrex glass and irradiated in a microwave oven at 300 w power for 5-30 min. The reaction progress was monitored by TLC (EtOAc:*n*-hexane) (2:3). The mixtures were quenched with saturated hydrogen carbonate solution (2 mL) and extracted with ether (2 × 10 mL). The ether layer was separated dried over anhydrous Na₂SO₄. The solvent evaporated *in vacuo* to give almost pure product. Further purification by column chromatography over silica gel using petroleum ether:ether (8:2) provided the desired pure acetate.

RESULTS AND DISCUSSION

Microwave irradiation of organic reactions has gained in popularity in the recent years since it was found to accelerate a wide variety of transformation. Especially, microwave- promoted reactions in conjunction with environmentally benign solventless conditions has attracted fast growing interest as time and energy saving protocol throughout the organic synthesis²⁰⁻²².

Cadmium oxide is an interesting multifunctional material for its promising applications in semiconductor and has found various uses in transparent electrodes, photodiodes, solar cells, photo transistors and in sensors²³⁻²⁶. This material reveals also potential properties as catalyst. The intensity of optical, electrical and catalytic effects of CdO depend on the deviation from the CdO stoichiometry, as well as the

size and shape of the particles. Several methods have been used for the preparation of nanoparticles of CdO including solvothermal²⁷, sonochemical²⁸ and irradiation techniques using γ and ultraviolet energy^{29,30}, but most of these methods describe only the thin film formation of CdO³¹⁻³⁴. There are only very few papers describing the synthesis of the particles as free-standing powder. The formation of CdO nanoparticles by thermal treatment of cadmium acetate³⁵ with dimethyl cadmium in DMF³⁶ preparation of Cd(OH)₂ as precursor to CdO by solvo and hydro-thermal methods³⁷⁻⁴⁰ which have also been developed for the fabrication of CdO with various morphologies and size. A few studies have also been reported on the preparation of nano-crystalline and bulk CdO powder under microwave irradiation⁴¹.

As a continuation of our investigation on organic reactions performed under solvent-free microwave irradiation conditions⁴²⁻⁴⁶, we employ this technology in the synthesis of nanoparticle size of CdO and investigated its catalytic activity in the acylation of alcohols and amines.

One of the simplest methods to synthesize CdO nanoparticle powders is a chemical co-precipitation method. In most cases this technique involves nucleation and growth from a homogeneous solution. Processes, such as coarsening and aggregation can compete with nucleation and growth in modifying the particle size distribution in these methods.

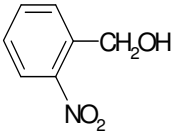
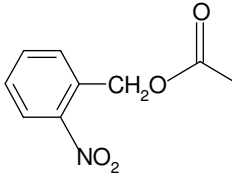
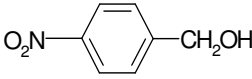
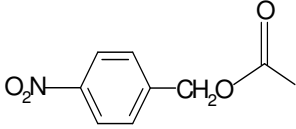
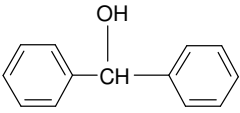
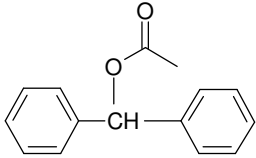
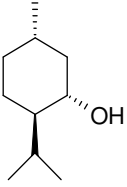
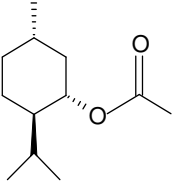
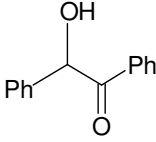
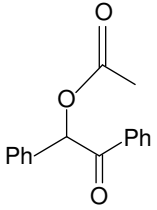
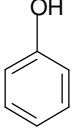
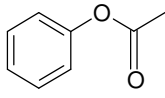
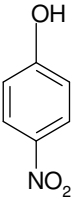
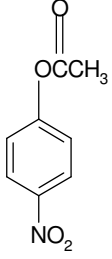
In this paper, three strategies for the synthesis of CdO nanoparticle powders have been used: (a) Using non aqueous solvent such as 2-propanol, because in aqueous solution growth usually proceeds rapidly with formation of relatively large particles. (b) Using cadmium acetate as the precursor, since acetate ion can act as capping agent. (c) Using controlled microwave activation during a short time because in most cases nucleation and growth of nanoparticles are allowed to take place over an extended period of time at a moderate temperature yielding a wide range size.

Therefore for the synthesis of narrow distribution sizes of CdO, we investigated the potential ability of microwave irradiation as an energy source by using cadmium acetate and sodium hydroxide as a carrier. The microwave irradiation method comparing with the other procedures is very fast and doesn't need high temperatures during the reaction. Furthermore, the use of the surfactants is not necessary for this method and another advantage of using microwave irradiation is that it yields smaller particles. The catalytic activity of CdO nanoparticles for acylation of alcohol, phenol and amines using acetic anhydride without other solvents under microwave irradiation has also been studied (Table-1).

In a second part, the results of acylation of a range of alcohols and amines under optimal conditions, phenol or amine (1 equiv) with acetic anhydride (1.2 equiv) in the presence of 10 wt % CdO without use of any solvents in domestic microwave oven for 10-20 min provided the corresponding acetate esters and amides in high yields. The experimental results of acylation of alcohols are shown in Table-2. Both primary and secondary alcohols react very well (entries 1-5) and tertiary alcohol (entry 6) is also acylated easily without any side products. No selectivity between primary and secondary hydroxyl groups was observed. Phenolic compounds containing both electron-withdrawing and donating groups were also satisfactorily acylated.

TABLE-1
 ACYLATION OF ALCOHOLS OR PHENOLS WITH Ac₂O/CdO UNDER MICROWAVE
 IRRADIATION (TEMPERATURE = 80 °C, POWER = 400 W)

Entry	Alcohol / phenol	Product	Time (min)	Yield* (%)
1	CH ₃ CH ₂ OH		20	90
2			10	91
3			10	87
4			20	85
5			20	80
6			20	65
7			15	96
8			10	98
9			10	95
10			10	97

11			20	90
12			10	96
13			10	90
14			10	98
15			10	85
16			10	96
17			15	90

*Isolated yields.

TABLE-2
 ACYLATION OF PRIMARY AROMATIC AMINES WITH Ac₂O/CdO UNDER
 MICROWAVE IRRADIATION (TEMPERATURE = 80 °C, POWER = 200 W)

Entry	Substrate	Time (min)	Product	m.p. (°C) (literature)	Yield* (%)
1		5		129-131 (130-132)	98
2		5		–	97
3		10		91-93 (93-94)	98
4		10		149-150 (149-151)	98
5		10		63-64 (65-67)	97
6		10		108 (109-110)	96
7		10		–	98
8		20		113 (111-115)	60
9		5 10		–	98 100
10		5 10		178 (177-179)	70 98
11		10		80-82 (78-80)	98

12		30		–	80
13		10		214-215 (215-217)	98
14		20		–	60
15		10		–	96
16		10		–	87

*Isolated yields.

Under similar reaction conditions, the acylation of amines was also investigated. The results of the preparation of a series of amides of substrates possessing a variety of potentially labile groups and their melting points are shown in Table-2. When aniline was used as a substrate, a different type of substituted group on the phenyl ring would influence the yield. If the aniline contained an electron-withdrawing group on the phenyl ring, (such as chloro, nitro or cyano group) the yields of N-acetylation reached 60-98 % within 10-20 min. These groups in *para*-position led to higher yields than in the *ortho*-position because of the '*ortho* effect'. In contrast the aniline bearing an electron-donating group on the phenyl ring (methyl, methoxy) group reacted very rapidly within 5-10 min with high yield (96-98 %), whereas the conversion of aniline into acetanilide (entry 8) afforded 60 % yield in 20 min.

Under such conditions, reaction of amines with Ac_2O was so fast in comparison to those aliphatic alcohols. Selective protection of an amine in the presence of hydroxyl group appeared to be a distinct possibility, for example amino group in aminophenol was selectively acylated (entry 16). Other functional groups such as cyano remained unaffected during the acylation reaction (entry 12). A comparison show the catalytic efficiency of CdO , the similar reaction condition was carried out in the absence of catalyst under microwave irradiation (Table-3). Acylation of amines with withdrawing substituents and aniline in the absence of catalyst was obtained lower yields (entries 5-10).

Conclusion

We have demonstrated a new, efficient procedure and catalyst for the green acetylation of a variety of alcohols, phenols and amines. Acetylation reactions using acetic anhydride (Ac_2O) as the reagent proceeded in excellent yields in the presence of catalytic amounts of CdO nanopowder under microwave irradiation. CdO nanoparticles were successfully synthesized in propanol by an efficient and simple controlled microwave-assisted approach by using $\text{Cd}(\text{CH}_3\text{COO})_2 \cdot 2\text{H}_2\text{O}$ and NaOH and characterized by powder XRD, TEM, FT-IR spectroscopy and UV-Vis. The XRD peaks revealed the nanoparticles with the average mean particle size 25 nm. TEM image show the morphology of CdO nanopowder. To show the specific effects of microwave irradiation, we also compare microwave irradiation and classical heating (CH) for the preparation of CdO under similar conditions. The significant features of this method provided a mild and effective catalyst for a wide variety of substrates, which may prove widely useful in organic synthesis with good yields in short times. The N-Ac protection of amine was so fast in comparison to hydroxyl group that the selective protection of an amine in the presence on OH group appeared to be a distinct possibility. The primary and secondary alcohols are acylated faster than tertiary alcohols. Secondary and tertiary alcohols did not experience any competitive dehydration. Also, the main advantages of the new method include an easy to handle method, an available, economical and environmentally friendly catalyst and the absence of organic solvents, a large scale treatment, clean and rapid reactions, high yields and excellent chemoselectivity.

In the absence of CdO, under the standard reaction condition was obtained in longer reaction time with lower yield.

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