

Nanosized MoO₃ as a reusable heterogeneous catalyst for the synthesis of 2,6-bis(benzylidene)cyclohexanones

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Crystalline MoO₃ nanoparticles were obtained by electrochemical synthesis process using tetrapropylammonium bromide as a stabilizer and structure-directing agent in ACN:THF(4:1) solvent. Formation of MoO₃ nanoparticles took place at a constant supply current of 14 mA/cm². These synthesized MoO₃ nanoparticles were characterized by UV-Vis spectroscopy, FT-IR spectroscopy, powder X-ray diffraction (XRD), scanning electron microscopy (SEM). So prepared MoO₃ nanoparticles were used as a heterogeneous catalyst for the synthesis of 2,6-bis(benzylidene)cyclohexanone derivatives. This protocol offers several advantages, such as simple work-up procedure, recyclability of the catalyst, excellent product yield in a short reaction time and purification of products with a non-chromatographic method.

Keywords: *electrochemical synthesis; MoO₃ nanoparticles; heterogeneous catalyst; 2,6-bis(benzylidene)cyclohexanone*

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1. Introduction

The α,α' -unsaturated ketones have been attracting much attention particularly the α,α' -unsaturated derivatives of cyclohexanone, such as 2,6-bis(benzylidene)cyclohexanone [1], not only due to their intriguing biological activities, such as antiangiogenic [2], cytotoxic [3], cholesterol-lowering activity [4], but also their potential for nonlinear optical materials [5]. Arylidene cycloalkanones are also useful intermediates for synthesis of bioactive pyrimidine [6], perfumes [7], bis-spiroisoxazolines [8], liquid crystalline polymers [9] and in pharmaceutical applications, especially as HIV-1 integrase inhibitors [10].

Owing to the importance of these compounds, various methods for synthesis of this type of compound have been developed. The typical methods for the preparation of 2,6-bis(benzylidene)cyclohexanone generally involve cross-aldol condensation of cyclohexanone with aldehydes in presence of strong acids or bases [11], however, the acid or base catalyzed reactions result in low yield of product due to reverse and side

reactions [12]. Coordination complexes with a variety of metals have been introduced to replace acid or base, but no satisfactory effect on the yield of the product has been achieved in most cases [13]. Continuing efforts to find a new catalyst resulted in the introduction of various reagents, such as RuCl₃ [14], KF/Al₂O₃ [15], KOH [16], NaOH [17], I₂ [18], SSA [19], Yb(OTf)₃ [20], Cu(OTf)₂ [21], CH₃CO₂Na/CH₃CO₂H [22], PEG/AlCl₃ [23] and Fe₂O₃ nanoparticles [24]. The other synthetic methods for preparation of these compounds involve microwave radiation [25] and ultrasound irradiation [26]. However, these methods suffer from one or more disadvantages, such as the use of toxic organic solvents or toxic catalyst and, in many cases, after the completion of the reaction, the catalyst system cannot be recycled. Considering the importance of the preparation of 2,6-bis(benzylidene)cyclohexanone and disadvantages of the currently reported methods, it is important to exploit a simple, efficient and clean procedure for the synthesis of this compound without using hazardous solvents, using less toxic, inexpensive and reusable catalysts.

Nanoparticles have been successfully used to enhance the immobilization and activity of

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a catalyst as the nanocrystalline metal oxide or metal particles have a large surface to volume ratio and increased surface reactivity as compared to that of the bulk material. Molybdenum oxide is a potential material because of its wide range of stoichiometry and interesting behavior, which includes structural [27], chemical [28], electrical and optical [29] properties. MoO₃ has received considerable attention in many technological applications, such as erasable optical storage media, optical switching coatings, high density memory devices, gas and chemical sensors [30] catalysis [31, 32] photography, future display materials [33], energy efficient window technology, photochromic and electrochromic devices [34].

In the framework of our studies on electrochemical synthesis of nanoparticles, characterization and their applications in catalytic organic reactions [35–37], we would like to report herein an efficient protocol for aldol condensation of cyclohexanone with various aromatic aldehydes using MoO₃ NPs as catalysts.

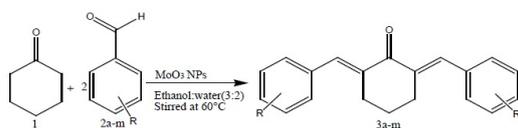


Fig. 1. Scheme 1.

2. Experimental

The AR grade tetrapropylammonium bromide (TPAB), tetrahydrofuran (THF) and acetonitrile (ACN) were delivered from Aldrich and S.D. Fine Chemical Supplier and used without any additional preparation. The sacrificial anode in the form of molybdenum sheet and platinum sheet as the inert cathode having thickness of 0.25 mm and purity of 99.9 % were purchased from Alfa Aesar. The specially designed electrolysis cell with a volume capacity of 30 ml was used.

2.1. Catalyst preparation

In the initial experiment we have used a molybdenum metal sheet (1 × 1 cm) as the anode and a

platinum sheet (1 × 1 cm) as the cathode. These two electrodes were placed parallel to one another and separated by 1.0 cm in 0.01 M solution of TPAB prepared in ACN/THF (4:1), which also served as the supporting electrolyte (Fig. 1). The electrolysis process was then carried out at 14 mA/cm² current density for 2.0 h. The colloidal solution thus obtained was kept in air-tight glass bottle to settle for a day. The agglomerated solid sample was separated from the solution by decantation and washed three to four times with THF to remove TPAB. The washed samples were then dried under vacuum desiccators and stored in air-tight containers.

2.2. Characterization

The prepared molybdenum oxide nanoparticles were characterized by UV-Vis, FT-IR, XRD, TEM and SEM-EDS techniques. The UV-Vis studies were recorded with JASCO 503 spectrophotometer using a quartz cuvette with ACN/THF (4:1) as a reference solvent. The IR spectra were recorded on FT-IR spectrophotometer (JASCO, FT-IR/4100, Japan), using dry KBr as a standard reference in the range of 400 to 4000 cm⁻¹. The X-ray powder diffraction patterns of the molybdenum oxide nanoparticles were recorded on Bruker 8D advance X-ray diffractometer using CuK α radiation of the wavelength = 1.54056 Å. The morphology and elemental composition of molybdenum oxide nanoparticles were examined using energy dispersive spectrophotometer (EDS). The SEM analysis was carried out with JEOL, JSM-6330 LA operated at 20.0 kV and 1.0000 nA. ¹H NMR and ¹³C NMR spectra were recorded on a Bruker AvIII HD-300 MHz FT-NMR spectrometer with CDCl₃ as a solvent. The chemical shift values were recorded as δ (ppm units) relative to tetramethylsilane (Me₄Si) as an internal standard. Mass spectra were recorded on an Agilent 6520 Q-TOF mass spectrometer for ESI scan.

2.3. Procedure of the synthesis of 2,6-bis(benzylidene)cyclohexanone

A mixture of aromatic aldehyde (10 mmol), cyclohexanone (5 mmol) and MoO₃ nanoparticles (60 mg) in 5 mL ethanol:water (3:2) was stirred at

60 °C till the completion of reaction (monitored by TLC). After cooling, the obtained solid product was filtered, washed with water and recrystallized with ethanol to obtain pure product. The hot reaction mixture was centrifuged for recovery of catalyst. The recovered catalyst was washed with ethanol, dried and reused three times in same reaction.

2.4. Spectral data of the compounds

2,6-bis(benzylidene)cyclohexanone (3a) Color-yellow crystals MP: 115 to 116°C.

IR(KBr) V_{max}/cm^{-1} : 3020, 2902, 1658, 1607, 1573, 1486, 970, 750, ¹H-NMR (300.13 MHz, CDCl₃, δ ppm): 1.73 to 1.81(m, 2H, CH₂), 2.90 to 2.93(t, 4H, 2CH₂), 7.24 to 7.55(m, 10H, Ar-H), 7.80(s, 2H, 2=CH). ¹³C-NMR (75.46 MHz, CDCl₃, δ ppm): 23.19(CH₂), 28.62 to 29.09(2CH₂), 128.08(4CH of Ar), 128.55(4CH of Ar-H), 135.80(2CH), 136.17(2C-Ar), 136.38(2C=C), 190.50(C=O). MS (EI) m/z 275(M⁺).

2,6-bis(p-chlorobenzylidene)cyclohexanone (3b) Color-brown solid; MP: 149 to 151°C.

IR(KBr) V_{max}/cm^{-1} : 2930, 1665, 1606, 1576, 1350, 810 cm^{-1} . ¹H-NMR (300.13 MHz, CDCl₃, δ ppm): 1.82 to 1.88(m, 2H, CH₂), 2.96(t, 4H, 2CH₂), 7.60 to 8.22(m, 8H Ar-H), 8.30(s, 2H, 2=CH). ¹³C-NMR 26.72(CH₂), 27.46(2CH₂), 126.4(4 CH-Ar), 128.70(4 CH of Ar), 135.20(2C-Ar), 137.20(2C=C), 145.40(2CH=C), 187.20(C=O).

2,6-bis(p-nitrobenzylidene)cyclohexanone (3d) Color-yellow solid; MP: 158 to 160°C.

IR(KBr) V_{max}/cm^{-1} : 3081, 2925, 1660, 1606, 1575, 1260, 828 cm^{-1} . ¹H-NMR (300.13 MHz, CDCl₃, δ ppm): 1.75 to 1.82(m, 2H, CH₂), 2.92(t, 4H, 2CH₂), 7.35 to 7.44(m, 8H Ar-H), 7.72(s, 2H, 2=CH). ¹³C-NMR 26.72(CH₂), 27.46(2CH₂), 121.10(4 CH-Ar), 127.30(4 CH of Ar), 137.20(2C-Ar), 141.30(2C=C), 145.40(2CH=C), 181.20(C=O).

3. Results and discussion

The UV-Vis absorption spectrum recorded for MoO₃ nanoparticles exhibits maximum absorption at 634 nm, which can be attributed to the Surface Plasmon Resonance (SPR) peak of molybdenum oxide nanoparticles. A broad peak around 634 nm can be attributed to a wide size distribution of particles in the solution. The broadening of SPR peak was due to the agglomeration of the nanoparticles in the sample and high width of these particles distribution.

In IR spectrum of MoO₃ nanoparticles, broad peaks appear at 3432 cm^{-1} and 1633 cm^{-1} due to the stretching and bending vibrations of hydroxyl groups adsorbed on molybdenum oxide nanoparticles. The peak at 949 cm^{-1} is due to the terminal Mo=O bonds, which indicate the layered orthorhombic phase [38] and absorption at 848 cm^{-1} and 597 cm^{-1} are of the stretching and bending mode of Mo–O–Mo vibrations. The spectrum also contains distinct peaks at 496 cm^{-1} and 669 cm^{-1} , which correspond to the mixed phase that contains molybdenum and molybdenum oxide.

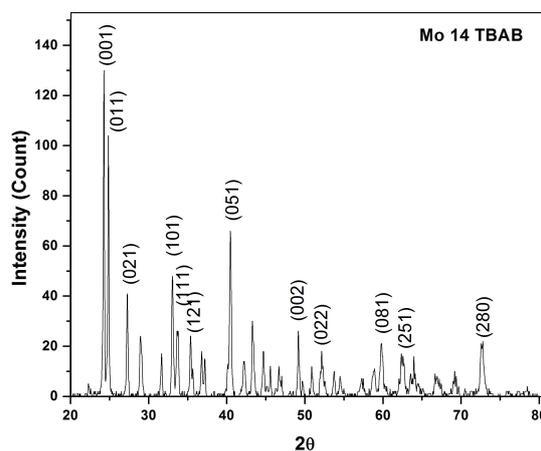


Fig. 2. XRD pattern of MoO₃ nanoparticles.

The X-ray diffraction pattern shown in Fig. 2 explains the crystal structure and phase composition of MoO₃ nanocrystalline materials. The sharp diffraction peaks at (021), (101), (001), (011), (111), (121), (051) and (002) indicate crystalline nature of MoO₃ nanomaterials with orthorhombic lattice system, having lattice

parameters $a = 3.966 \text{ \AA}$, $b = 13.82 \text{ \AA}$, $c = 3.703 \text{ \AA}$ (JCPDS: 05-0506) and strong peaks show crystalline nature of MoO_3 nanoparticles.

The morphology of the product was examined by scanning electron microscope. Fig. 3a reveals that the sample has ununiform crystals, which show square- and cubic-like structures. The quantitative and qualitative analysis was carried out on the basis of EDS spectra and the elemental composition of MoO_3 nanoparticles is shown in Fig. 3b. The Mo and O peaks can be obviously found in the spectra but lack of any other peaks indicates that the sample is composed of pure MoO_3 nanoparticles.

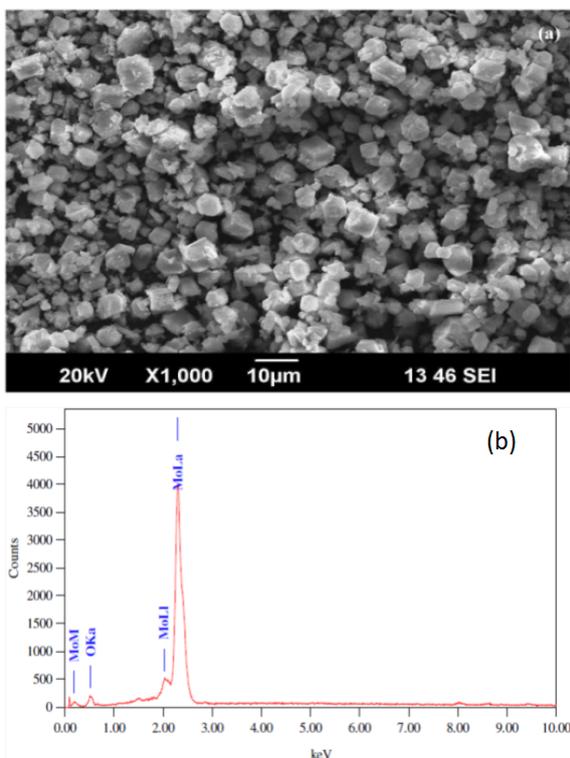


Fig. 3. (a) SEM micrograph; (b) EDS plot of MoO_3 nanoparticles.

3.1. Catalytic activity of MoO_3 nanoparticles

We have revealed herein for the first time, that the MoO_3 nanoparticles catalyzed aldol condensation of cyclohexanone with a variety of aldehydes by simple stirring at $60 \text{ }^\circ\text{C}$. In the present work, an attempt has been made to optimize the

reaction conditions by using 4-nitro-benzaldehyde and cyclohexanone as a model reaction at different solvents and amounts of catalyst used. From Table 1 it can be seen that the best amount of MoO_3 nanoparticles in the starting material is 60 mg. There is a considerable increase in the yield of product when the concentration of MoO_3 nanoparticles increases from 10 mg to 60 mg. But when we increased catalyst quantity to 70 mg there was no considerable change in reaction time and yield of the product.

Table 1. Screening of catalyst (MoO_3) concentration for the synthesis of 3d.

Entry	Catalyst amount (mg)	Time (min)	Yield ^a (%)
1	10	240	Trace
2	20	160	36
3	40	120	66
4	50	90	92
5	60	90	94
6	70	90	95

^aisolated yield

Table 2. Optimization of solvent in the aldol condensation of cyclohexanone and 4-nitrobenzaldehyde with 60 mg MoO_3 nanoparticles as catalyst.

Entry	Solvent	Time (h)	Yield ^a (%)
1	ACN	3	54
1	Toluene	3	32
2	THF	3	35
4	Methanol	3	62
5	Ethanol	3	76
6	Ethanol:water (3:2)	2	94

^aisolated yield

In this study, the effect of different solvents was investigated and given in Table 2. The choice of a solvent proved critical. We observed that polar solvents, such as methanol, ethanol, acetonitrile, offered better yield than nonpolar ones and the mixture of water (2 mL) and ethanol (3 mL) was most effective solvent offering maximum yield of the product.

Table 3. Synthesis of 2,6-bis(benzylidene)cyclohexanone using MoO₃NPs catalyst under ethanol:water ratio (3:2).

Products ^a	R	Time (min)	Yield ^b (%)	Melting point (°C)	
				Found	Reported
3a	H	120	91	115 – 116	115 – 118 [14]
3b	4-Cl	95	95	145 – 147	147 – 148 [14]
3c	2-Cl	130	92	103 – 105	102 – 106 [23]
3d	4-NO ₂	90	94 ^b , 91 ^c , 89 ^c , 84 ^c	158 – 160	160 – 163 [14]
3e	3-NO ₂	130	95	191 – 192	188 – 190 [21]
3f	4-CH ₃	100	90	160 – 162	170 – 171 [14]
3g	2,4-Cl ₂	140	89	166 – 167	163 – 164 [16]
3h	4-OMe	95	93	160 – 161	161 – 163 [20]
3i	4-OH	100	94	172 – 174	–
3j	4-F	105	94	156 – 157	156 – 158 [17]
3k	4-Br	110	92	162 – 163	163 – 165 [23]
3l	2-furfuralde	145	85	140 – 142	140 – 142 [21]
3m	Cinnamalde	130	88	180 – 181	180 [14]

^aReaction condition: aldehyde (2 mmol), cyclohexanone (1 mmol), and 60 mg of MoO₃ nanoparticles stirred at 60 °C, ^bisolated yield, ^cisolated yield reused of catalyst 1st, 2nd and 3rd cycle, respectively.

Table 4. Comparison of the results for MoO₃ nanoparticles with other catalysts reported in the literature.

Sr. No.	Catalyst	Reaction condition/time in h	Yield (%)	Literature
1	RuCl ₃	120 °C sealed/12	94	14
2	KOH	0 °C ethanol RT/4	90	16
3	I ₂	CH ₂ Cl ₂ RT/4.5	92	18
4	Yb(OTf) ₃	Fluorous solvent 120 °C/12	95	20
5	Cu(OTf) ₂	Solvent free 80 °C/6	94	21
6	NaOAc/HOAc	120 °C/7	86	22
7	MoO ₃ nanoparticles	Ethanol:water(3:2) 60 °C/ 1.5	94	Present work

After optimizing the conditions, the generality of this method was examined by the reaction of cyclohexanone with several aldehydes bearing electron withdrawing groups (such as nitro, chloro, bromo, fluoro, and hydroxyl) and electron donating groups (such as methyl, methoxy). The entire product reacted in a similar manner producing moderate to good yield of expected product. The para-substituted aromatic aldehyde reacted in a shorter reaction time as compared with ortho and meta substituted aromatic aldehyde in Table 3.

In this study, the catalyst was recovered and reused. The catalyst was recovered by a simple work-up using centrifugation, and then it was

washed with ethanol and reused. The catalyst was removed in excellent yields and was used in mentioned reaction for three times; the observation revealed that as the number of recycling of the catalyst increases the activity decreases (Table 4).

Table 4 shows a comparison of the results of our work with the other reported procedures. There are the results of the synthesis of 2,6-bis(benzylidene)cyclohexanone derivatives in the presence of different reported catalyst with respect to time and yield of the product. These results show that our catalyst, MoO₃ nanoparticles, is more stable in air and nontoxic. It ensures good yield in a short reaction time.

4. Conclusions

MoO₃ nanoparticles are inexpensive and efficient reusable catalyst for the synthesis of 2,6-bis(benzylidene)cyclohexanone derivatives. The advantages offered by this method are simple workup, short reaction times, ease of product isolation and high yields. We believe that this method is a useful addition to the present methodology for the synthesis of 2,6-bis(benzylidene)cyclohexanone.

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