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Molybdenum Oxide Nanoparticles as Recyclable Heterogeneous Catalyst for Synthesis of Arylidene Ethyl Cyanoacetates

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This work reports an adapted route to the highly efficient synthesis of arylidene ethyl cyanoacetate derivatives in the presence of catalytic amounts of molybdenum oxide nanoparticles (MoO_3 NPs) under green conditions at ambient temperature. From the reaction, a wide range of novel arylidene ethyl cyanoacetates was successfully synthesized with high yields from the Knoevenagel condensation reaction between various aryl aldehydes and ethyl cyanoacetate in the presence of MoO_3 nanoparticles. The capability of catalyst to separate from the reaction mixture and then reuse is another advantage of this reaction. Furthermore, obtained products belong to analogous of organic compounds that have shown biological activity, and can be used pharmaceutics.

Keywords: Nano-MoO_3, Knoevenagel Condensation, Arylidene Ethyl Cyanoacetate, Green Procedure, Recyclable Catalyst.

1. INTRODUCTION

One of the most familiar and important routes to the formation of carbon–carbon double bond is obtaining from the condensation reaction between carbonyl compounds and activated methylene compounds that is well known as Knoevenagel condensation.[1–2] Up to date this reaction widely used to the synthesis of a broad range of organic and biologically active compounds.[3,4] Also, this reaction occasionally has been used to examine the activity of various solid basic catalysts with considering the fact that pKa value of CH-acidic compounds in β-dicarbonyl compounds are in the range of 9–11.[5]

Because of the importance of this reaction in organic synthesis and chemical industries, so far numerous methods for Knoevenagel condensations with various techniques have been reported. For instance, running reaction in the presence of Lewis acids or bases,[6,7] Brönsted acids,[8] ionic liquids,[9] green medium,[10] microwave assistance,[11] ultrasound irradiation,[12] solid-phase reactions,[13] grinding methods,[14] solvent-free microwave assisted conditions,[15] and using biocatalysts,[10] organocatalysts[16] or polyoxometalates[17] can be countered. Furthermore, there are reports that Knoevenagel condensation was performed under continuous flow synthesis[18] or fluorous biphasic system.[19] Because of all above mentioned techniques tolerate some drawbacks such as use of expensive and non-recyclable catalysts, harsh thermal conditions, use of toxic solvents and catalysts, non-compatible with green chemistry aspects, not economically viable, and long reaction times, the attempts to develop and modify new and efficient protocols to Knoevenagel condensation reaction have been continued by chemists.[2]

Arylidene ethyl cyanoacetate derivatives are one of important α, β-unsaturated compounds which obtain via the Knoevenagel condensation reaction between ethyl cyanoacetate and aryl aldehydes. So far a broad range of works on biological and pharmaceutical activities of arylidene ethyl cyanoacetate and its derivatives is published. For example they have been recognized as antinociceptive agents modulating the TREK-1 channel,[20] inhibitors of 12-Lipoxygenase,[21] new group of fungicidal and acaricidal agents,[22] a new class of antagonists at the glycine site of the NMDA receptor,[23] an ingredient in sunscreens and cosmetics,[24] herbicidally active compounds,[25] and also a therapeutic agent for diseases of the circulatory system.[26] Also these molecules have seen

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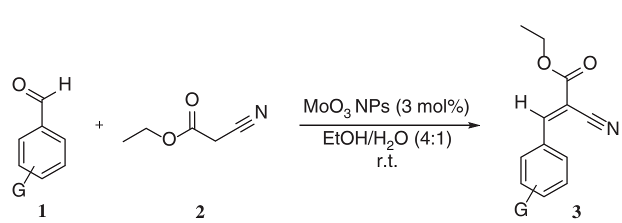
in molecular rotors motifs.[27] These revealed properties encourage chemists and pharmacologists designing synthetic protocols to synthesize newly prepared molecules exhibiting pharmacological and biological activities which may be applied in the treatment of human disease as new medicine in the future.[28,29]

Considering the green chemistry principles, using recyclable green catalysts and replacement of toxic organic solvents by safe and clean ones have increasingly attracted the interest of chemists and industrialists to avoid waste production in chemical reactions.[30,31]

Nanoscience and nanotechnology are very important topics in the word and have been applied in a wide range spanning from science to engineering to medicine.[32] Nowadays, nanocatalysts have also attracted much attention from chemists because of their specific, considerable, and efficient role in chemical reactions. For instance, nano-sized catalysts dramatically increase the contact between functional groups of reactants with the surface of the catalyst.[33] Among efficient and green nanocatalysts, molybdenum oxide nanoparticles (MoO_3 NPs) have emerged as green, highly efficient, and recyclable catalyst in chemical reactions.[34] Furthermore, MoO_3 NPs in the orthorhombic phase has been successfully applied as the efficient catalyst for condensation reaction between aryl aldehydes and cyclohexanone as a CH-acidic precursor.[34]

Based on above, and in connection with our recent works to the catalytic synthesis of newly prepared potentially interesting biological active organic compounds,[35–42] herein we wish to report a green one-pot catalytic reaction between a broad range of aryl aldehydes **1**, and ethyl cyanoacetate (**2**) in the presence of catalytic amounts of molybdenum oxide nanoparticle (MoO_3 NPs) (Scheme 1).

By this reaction, we found that MoO_3 NPs plays a significant role as a key factor in the synthesis of arylidene ethyl cyanoacetate derivatives via a convenient and environmentally friendly work-up. The structures of all products **3** were deduced from their FT-IR, FT-^{1}H and FT-^{13}C NMR spectroscopies and (C, H, N, S) analyses. Also, herein, preparation, high activation, and regeneration of MoO_3 NPs as an environmentally benign and reusable catalyst in the synthesis of some medicinally important arylidene ethyl cyanoacetate derivatives have been explained. As well as, the efficiency of catalyst on reaction progress with others to the synthesis of a model reaction was compared.



Scheme 1. Knoevenagel condensation reaction between aryl aldehydes with ethyl cyanoacetate by the use of MoO_3 NPs in aqueous medium.

2. EXPERIMENTAL DETAILS

Chemicals were purchased from Merck and Sigma-Aldrich chemical companies. Melting points were measured on an electrothermal IA9100 melting point apparatus fixed at 1 °C/min. IR spectra were recorded by Brucker FT-IR Tensor 27 infrared spectrophotometer with KBr as the matrix. ^{1}H NMR and ^{13}C NMR spectra were recorded on an FT-NMR Bruker Avance Ultra Shield Spectrometer at frequencies of 300 and 75 MHz respectively in $CHCl_3$ as the solvent. Elemental analyses (C, H, N, S) were performed on a Heraeus Rapid analyzer and the results were found in good agreement (±0.3%) with the calculated values. Scanning electron microscopy (SEM) evaluations of the nano-catalyst were performed on a JEOL JEM 3010 instrument operating at an accelerating voltage of 300 kV. An X-ray diffraction pattern to the characterization of the heterogeneous nano-catalyst was studied with XRD, D8, Advance, Bruker, AXS. Transmission electron microscopy (TEM) investigations of the nano-catalyst were performed on a JEOL JEM 3010 instrument operating at an accelerating voltage of 300 kV. TLC was performed on TLC-Grade silica gel-G/UV 254 nm plates EtOAc/*n*-hexane (1:1) as eluent. All products were isolated, purified and deduced from their FT-IR, ^{1}H NMR, and ^{13}C NMR spectral data along with elemental analyses (C, H, N).

2.1. Typical Procedure for the Preparation MoO_3 NPs

For the synthesize of MoO_3 NPs, to the stirred mixture of ammonium heptamolybdate tetrahydrate ($(NH_4)_6Mo_7O_{24} \times 4H_2O$) (2 g, 1.6 mmol) dissolved in 5 mL ethanol, and 15 mL of deionized water, at room temperature for 20 min, HNO_3 (2 M) was added dropwise until the pH of the mixture achieved to 1. Then, formed clear solution was stirred under reflux conditions at 90 °C for 5 h. Afterwards, obtained light-blue precipitates were separated by filtration, washed several times with deionized water until the washing solution being neutral, and dried in an oven at 90 °C for 12 h. In the final step, the catalyst was calcined at 450 °C for 6 h in an electric furnace.

2.2. General Procedure for the Preparation of Corresponding Aldehydes 1

Corresponding aldehydes containing alkylamine ethers was synthesized according to the procedure reported in the literature,[43] and all their structures were confirmed by the comparison of their physical and chemical properties with those reported in the literature.[43] Also, 4-(benzyloxy)benzaldehyde derivatives were prepared by treating with 4-hydroxybenzaldehyde with appropriate benzyl chloride/bromide derivatives in the presence of K_2CO_3 as the catalyst. The physical and chemical properties of all obtained substrates were compared with the ones reported in the literature and all of their structures were confirmed.[43]

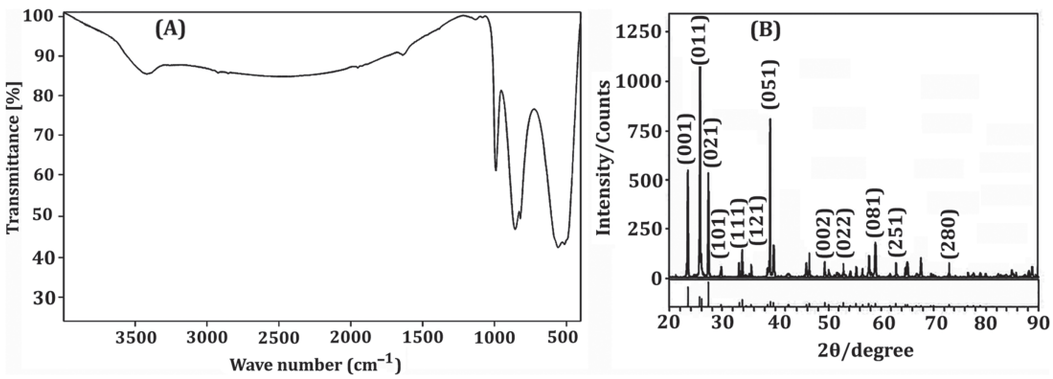


Figure 1. (A) FT-IR spectrum of MoO_3 NPs; (B) X-ray diffraction pattern of the MoO_3 NPs.

2.3. Typical Procedure for the Synthesis of 3l

4-(morpholinoethoxy)benzaldehyde (1 mmol, 0.235 g) was added to a stirring mixture of ethyl cyanoacetate (1.5 mmol, 0.170 g), and the catalytic amount of MoO_3 NPs (0.004 g, 3 mol%) in EtOH/H_2O (4:1). It was allowed to the mixture to stir at room temperature for the time indicated in Table II. After compilation of the reaction (the reaction progress was controlled by TLC EtOAc/*n*-hexane (1:1) as eluent), the reaction mixture was filtered to separate precipitate. Next, the precipitate was dissolved in boiling ethanol and filtrated to separate catalyst. In the end, formed crystalline product was filtrated to obtain the crystalline pure product.

2.4. Representative Spectral Data

2.4.1. Ethyl (E)-2-Cyano-3-(4-(2-morpholinoethoxy) phenyl)acrylate (3l)

White powder; FT-IR spectrum, ν, cm^{-1}: 3033, 2996, 2938, 2217, 1718, 1588, 1514, 1263, 1185, 940, 834, 517; ^{1}H NMR spectrum (300 MHz, DMSO-d_6), δ, ppm (J, Hz): 8.32 (s, 1H, $CH_{vinylic}$), 8.09 (d, $J = 9.0$, 2H, CH_{Ar}), 7.18 (d, $J = 9.0$, 2H, CH_{Ar}), 4.31 (q, $J = 6.0$, 2H, OCH_2), 4.30 (brs, 2H, CH_2), 3.66 (brs, 4H, $2CH_2$), 2.92 (brs, 2H, CH_2), 2.68 (brs, 4H, $2CH_2$), 1.32 (3H, t, $J = 6.0$, CH_3); ^{13}C NMR spectrum (75 MHz, DMSO-d_6), δ, ppm: 163.0, 162.8, 154.9, 133.9, 124.6, 116.7, 115.9, 99.2, 65.9, 65.6, 62.6, 56.7, 53.5, 14.5; Anal. calcd for $C_{18}H_{22}N_2O_4$: C, 65.44; H, 6.71; N, 8.48; Found: C, 65.49; H, 6.68; N, 8.50%.

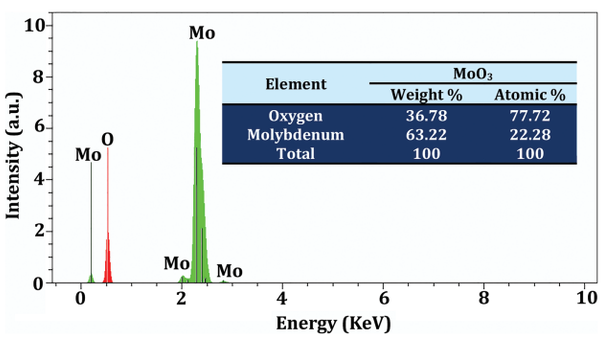


Figure 2. X-ray analysis spectrum of MoO_3 NPs.

2.4.2. Ethyl (E)-3-(4-(4-benzylpiperidin-1-yl)phenyl)-2-Cyanoacrylate (3m)

Orange crystals; FT-IR spectrum, ν, cm^{-1}: 3021, 2992, 2933, 2208, 1727, 1609, 1563, 1510, 1274, 1226, 1172, 964, 812, 751, 705, 517; ^{1}H NMR spectrum (300 MHz, DMSO-d_6), δ, ppm (J, Hz): 8.10 (s, 1H, $CH_{Vinylic}$), 7.96 (d, 2H, $J = 9.0$, CH_{Ar}), 7.36–7.18 (m, 5H, CH_{Ph}), 6.89 (d, $J = 9.0$, 2H, CH_{Ar}), 4.38 (q, $J = 6.0$, 2H, OCH_2), 3.99 (d, $J = 9.0$, 2H, CH_{Ar}), 2.93 (d.t, 2H, $^1J = 9.0$, $^2J = 3.0$, 2CH), 2.61 (d, $J = 6.0$, 2H, CH_2) 1.92–1.86 (m, 1H, CH), 1.81 (d, $J = 12.0$, 2H, 2CH), 1.41 (t, $J = 6.0$, 3H, CH_3), 1.35 (d, $J = 3.0$, 2H, 2CH); ^{13}C NMR spectrum (75 MHz, DMSO-d_6), δ, ppm: 164.2, 154.3, 153.9, 139.9, 134.1, 129.1, 128.4, 126.1, 120.3, 117.4, 113.4, 94.9, 81.9, 47.5, 42.9, 38.1. 31.5, 14.3; Anal. calcd for $C_{24}H_{26}N_2O_2$: C, 76.98; H, 7.00; N, 7.48; Found: C, 77.01; H, 7.13; N, 7.51%.

2.4.3. Ethyl (E)-3-(4-((4-chlorobenzyl)oxy)phenyl)-2-Cyanoacrylate (3o)

White crystals; FT-IR spectrum, ν, cm^{-1}: 3028, 2951, 2925, 2219, 1725, 1590, 1515, 1433, 1387, 1311, 1267, 1214, 1184, 1093, 1005, 831, 760, 563, 515; ^{1}H NMR spectrum (300 MHz, $CDCl_3$), δ, ppm (J, Hz): 8.20 (s, 1H, $CH_{Vinylic}$), 8.04 (d, $J = 9.0$, 2H, CH_{Ar}), 7.41 (brs, 4H,

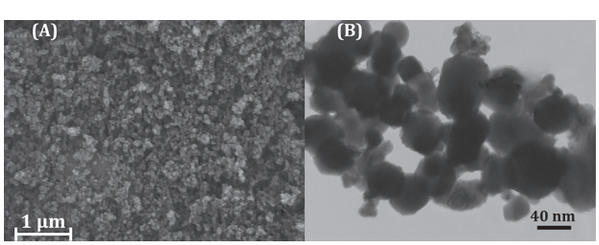


Figure 3. (A) Scanning electron microscopy of MoO_3 NPs; (B) TEM image of MoO_3 NPs.

CH_{Ph}), 7.08 (*d*, $J = 9.0$, 2H, CH_{Ar}), 5.15 (*s*, 2H, OCH_2), 4.40 (*q*, 2H, $J = 6.0$, OCH_2), 1.43 (*t*, $J = 6.0$, 3H, CH_3); ^{13}C NMR spectrum (75 MHz, DMSO-d_6), δ, ppm: 163.0, 162.5, 154.2, 134.3, 134.2, 133.6, 128.9, 128.8, 124.7, 116.1, 115.5, 99.8, 69.5, 62.5, 14.2; Anal. calcd for $C_{19}H_{16}ClNO_3$: C, 66.77; H, 4.72; N, 4.10; Found: C, 66.81; H, 4.69; N, 4.16%.

2.4.4. Ethyl (E)-3-(3-((4-chlorobenzyl)oxy)phenyl)-2-Cyanoacrylate (3p)

White powder; FT-IR spectrum, ν, cm^{-1}: 3061, 2949, 2220, 1726, 1609, 1577, 1491, 1440, 1397, 1258, 1171, 1085, 1044, 851, 777, 682; ^{1}H NMR spectrum (300 MHz, $CDCl_3$), δ, ppm (*J*, Hz): 8.24 (*s*, 1H, $CH_{Vinylic}$), 7.70 (*s*, 1H, CH_{Ar}), 7.54 (*d*, $J = 6.0$, 1H, CH_{Ar}), 7.47–7.38 (*m*, 5H, CH_{Ar}), 7.19 (*dd*, $^1J = 6.0$, $^2J = 3.0$, CH_{Ar}), 5.13 (*s*, 2H, OCH_2), 4.43 (*q*, $J = 6.0$, 2H, OCH_2), 1.44 (*t*, $J = 6.0$, 3H, CH_3); ^{13}C NMR spectrum (75 MHz, DMSO-d_6), δ, ppm: 162.4, 158.8, 154.8, 134.7, 134.0, 132.7, 130.3, 128.9, 128.8, 124.8, 120.9, 115.5, 115.2, 103.2, 69.4, 62.8, 14.1; Anal. calcd for $C_{19}H_{16}ClNO_3$: C, 66.77; H, 4.72; N, 4.10; Found: C, 66.81; H, 4.65; N, 4.13%.

2.4.5. Ehyl (E)-3-(4-((4-bromobenzyl)oxy)phenyl)-2-Cyanoacrylate (3q)

White crystals; FT-IR spectrum, ν, cm^{-1}: 3027, 2948, 2218, 1724, 1590, 1514, 1434, 1381, 1311, 1268, 1214, 1183, 1093, 1069, 1002, 832, 804, 759, 554, 515; ^{1}H NMR spectrum (300 MHz, $CDCl_3$), δ, ppm (*J*, Hz): 8.20 (*s*, 1H, $CH_{Vinylic}$), 8.03 (*d*, $J = 9.0$, 2H, CH_{Ar}), 7.57 (*d*, $J = 9.0$, 2H, CH_{Ar}), 7.34 (*d*, $J = 9.0$, 2H, CH_{Ar}), 7.08 (*d*, $J = 9.0$, 2H, CH_{Ar}), 5.13 (*s*, 2H, OCH_2), 4.40 (*q*, $J = 6.0$, 2H, OCH_2), 1.42 (*t*, $J = 6.0$, 3H, CH_3); ^{13}C NMR spectrum (75 MHz, DMSO-d_6), δ, ppm: 163.0, 162.5, 154.2, 134.8, 133.6, 131.9, 129.1, 124.8, 122.3, 116.1, 115.5, 99.8, 69.5, 62.5, 14.2; Anal. calcd for $C_{19}H_{16}BrNO_3$: C, 59.08; H, 4.18; N, 3.63; Found: C, 59.12; H, 4.11; N, 3.67%.

2.4.6. Ethyl (E)-3-(3-((4-bromobenzyl)oxy)phenyl)-2-Cyanoacrylate (3r)

White powder; FT-IR spectrum, ν, cm^{-1}: 3045, 3028, 2955, 2225, 1732, 1614, 1574, 1486, 1430, 1378, 1254, 1166, 1056, 1011, 980, 871, 798, 776, 680, 476; ^{1}H NMR spectrum (300 MHz, $CDCl_3$), δ, ppm (*J*, Hz): 8.24 (*s*, 1H, $CH_{Vinylic}$), 7.70 (*t*, $J = 3.0$, 1H, CH_{Ar}), 7.57–7.35 (*m*, 6H, CH_{Ar}), 7.21–7.17 (*m*, 1H, CH_{Ar}), 5.12 (*s*, 2H, OCH_2), 4.43 (*q*, $J = 6.0$, 2H, OCH_2), 1.44 (*t*, $J = 6.0$, 3H, CH_3); ^{13}C NMR spectrum (75 MHz, $CDCl_3$), δ, ppm: 162.4, 158.8, 154.8, 135.3, 132.7, 131.8, 130.3, 129.2, 124.8, 122.1, 120.9, 115.5, 115.2, 130.3, 69.4, 62.8, 14.1. Anal. calcd for $C_{19}H_{16}BrNO_3$: C, 59.08; H, 4.18; Br, 20.69; N, 3.63; Found: C, 59.15; H, 4.23; N, 3.65%.

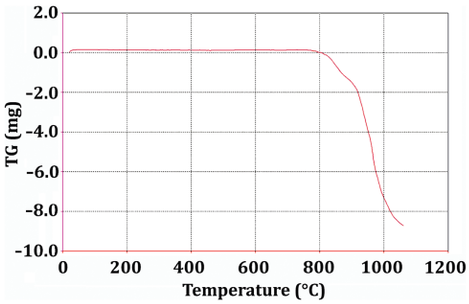


Figure 4. TGA analysis of MoO_3 NPs.

3. RESULTS AND DISCUSSION

Molybdenum (VI) oxide nanoparticles were synthesized by a slight modification of the solvothermal reported method (Iranian Nanomaterials Pioneers Company, Mashhad).[44] The functional groups of the MoO_3 with the best crystalline degree were identified by FT-IR spectrum (Fig. 1(A)). As can be seen from Figure 1, the spectrum shows three strong peaks at 990 cm^{-1} attributed to the stretching vibration of terminal M=O bond with an indicator of the layered orthorhombic MoO_3 lattice, 855 cm^{-1} to the stretching vibration of Mo–O–Mo bonds, and a broad band at 558 cm^{-1} corresponding to the bending-stretching vibration of oxygen atom linked to three Mo atoms.[45] In FT-IR spectrum, not appearing of peaks at 1620 and 1400 cm^{-1} demonstrates that MoO_3 NPs are not in hexagonal phase, and appearing of peaks only at 990, 855, 558 cm^{-1} strongly confirms that MoO_3 NPs are in orthorhombic phase.[44]

X-ray diffraction pattern (XRD) of the MoO_3 NPs was shown in Figure 1(B). In the XRD pattern of MoO_3 NPs, the distinguished diffraction peaks centered at $2\theta \sim 23.7°$, 25.9°, 27.1°, 33.7°, 33.9°, 35.8°, 39.1°, and 49.2° related respectively to the (001), (011), (021), (101), (111), (121), (051) and (002) plane of the MoO_3 with an rutile phase

Table I. Examination of different conditions on model reaction.[a]

Entry	Catalyst	Solvent/temp.	Yield[b]
1	None	EtOH, Reflux	35
2	None	Solvent-free, 80 °C	30
3	Na_2HPO_4 (5 mol%)	CH_2Cl_2, Reflux	43
4	Na_2CO_3 (5 mol%)	CH_3CN, 50 °C	45
5	*p*-TSA (5 mol%)	MeOH, 50 °C	48
6	Piperidine (5 mol%)	H_2O, 50 °C	45
7	Et_3N (5 mol%)	EtOH, 50 °C	51
8	MoO_3 NPs (5 mol%)	H_2O, 50 °C	78
9	MoO_3 NPs (5 mol%)	EtOH, r.t.	85
10	MoO_3 NPs (5 mol%)	EtOH/H_2O (1:1), r.t.	86
11	MoO_3 NPs (5 mol%)	EtOH/H_2O (2:1), r.t.	90
12	MoO_3 NPs (5 mol%)	EtOH/H_2O (3:1), r.t.	91
13	MoO_3 NPs (5 mol%)	EtOH/H_2O (4:1), r.t.	95
14	MoO_3 NPs (4 mol%)	EtOH/H_2O (4:1), r.t.	96
15	MoO_3 NPs (3 mol%)	EtOH/H_2O (4:1), r.t.	96
16	MoO_3 NPs (2 mol%)	EtOH/H_2O (4:1), r.t.	91

Notes: [a]Reaction time: 60 min; [b]isolated yield.

Table II. Highly efficient and green synthesis of arylidene ethyl cyanoacetate derivatives.[a]

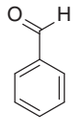
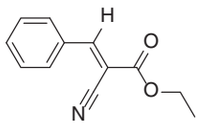
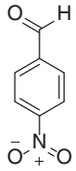
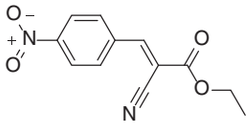
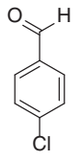
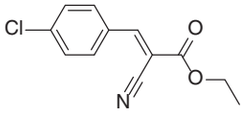
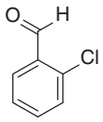
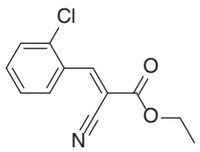
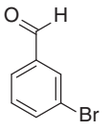
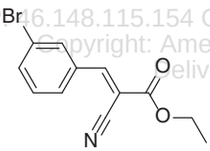
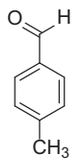
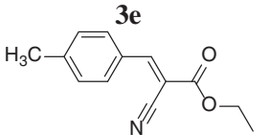
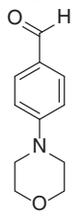
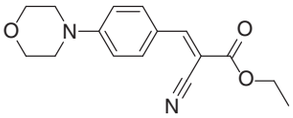
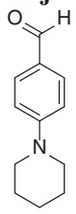
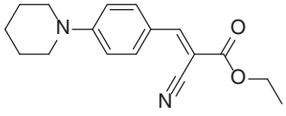
Entry	Aryl aldehyde **1**	Product **3**	Time (min)	Yield[b] (%)/(lit).	m.p. (lit)
1	 **1a**	 **3a**	40	96/86	48–49 (47–48)[46]
2	 **1b**	 **3b**	40	99/94	170–171 (169–170)[46]
3	 **1c**	 **3c**	40	98/91	91–92 (91–92)[46]
4	 **1d**	 **3d**	40	97/99	45–46 (43–45)[47]
5	 **1e**	 **3e**	40	96/95	81–82 (80–81)[48]
6	 **1f**	 **3f**	50	95/90	93–94 (92–93)[46, 49]
7	 **1j**	 **3j**	60	95/86	155–157 (not reported)[50]
8	 **1k**	 **3k**	60	94/90	90–92 (not reported)[50]

Table II. Continued.

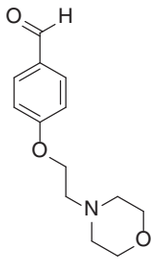
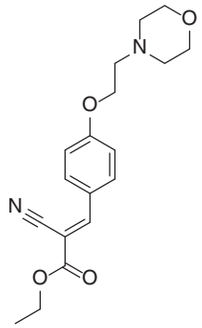
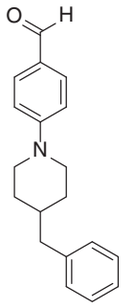
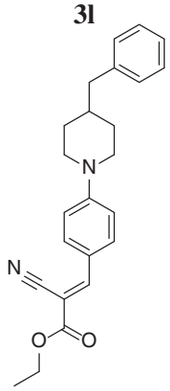
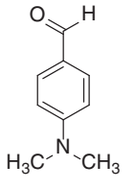
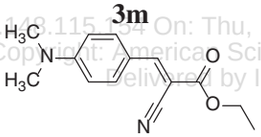
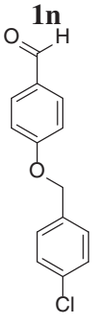
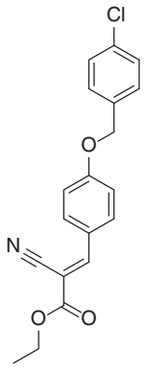
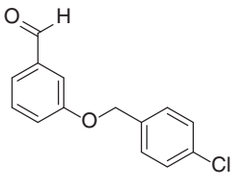
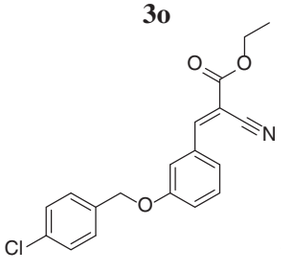
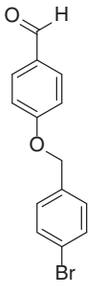
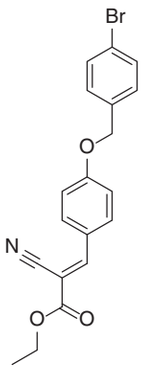
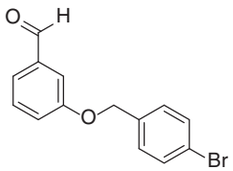
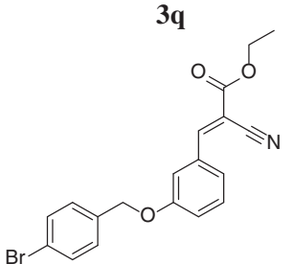
Entry	Aryl aldehyde **1**	Product **3**	Time (min)	Yield[b] (%)/(lit).	m.p. (lit)
9	 **1l**	 **3l**	60	92	217–218[c]
10	 **1m**	 **3m**	60	95	115–116[c]
11	 **1n**	 **3n**	60	97/96	127–129 (123–125)[51]
12	 **1o**	 **3o**	60	98	147–149[c]
13	 **1p**	 **3p**	60	96	88–90[c]

Table II. Continued.

Entry	Aryl aldehyde **1**	Product **3**	Time (min)	Yield[b] (%)/(lit).	m.p. (lit)
14	 **1q**	 **3q**	60	98	140–142[c]
15	 **1r**	 **3r**	60	95	109–111[c]

Notes: [a]Reaction conditions: MoO_3 NPs (3 mol%), EtOH/H_2O (4:1), room temperature; [b]isolated yields; [c]novel product.

which is in agreement with the standard data for the MoO_3 orthorhombic lattice structure (JCPDS: 05-0506).[34] These peaks also strongly confirm the orthorhombic phase of MoO_3 NPs with no impurity detection.[44]

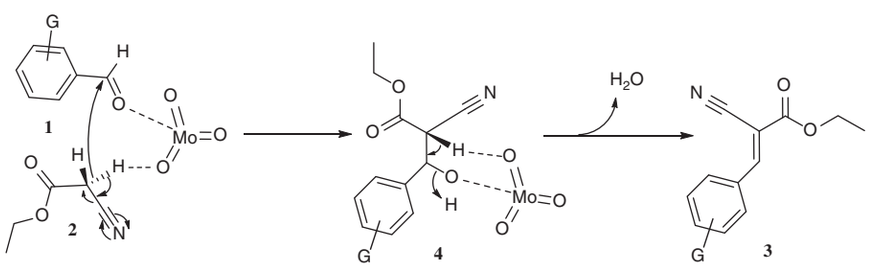
In addition, to determine catalyst purity, energy dispersive X-ray analysis (EDAX) on the molybdenum trioxide nanoparticles (MoO_3 NPs) was performed. The results obtained from taken pattern disclosed peaks correlated to molybdenum and oxygen only that proves the high purity of catalyst (Fig. 2).

The morphology of MoO_3 NPs was studied by scanning electron microscopy (SEM) (Fig. 3(A)). SEM images of MoO_3 NPs show the molybdenum (VI) oxide nanoparticles have a diameter of about 40 nm without any amorphous or other kinds of crystallized phase particles. In addition, the transmission electron microscopy (TEM) image of molybdenum (VI) oxide nanoparticles was studied for more investigation of MoO_3 NPs morphology (Fig. 3(B)). TEM image of MoO_3 NPs clearly demonstrated the MoO_3 NPs have a homogeneous diameter size about 40 nm.

Also, to investigate the thermal stability of catalyst at high temperatures, thermo-gravimetric analysis (TGA) of molybdenum trioxide nanoparticles was taken (Fig. 4). Thermo-gravimetric analysis showed that weight percent of the catalyst remains constant up to about 780 °C. From this investigation, it was concluded that the structure of the catalyst is constant in temperatures downwards 780 °C.

Previous to start loading different reactions to expand and develop of reaction scope, compound **3a** was selected as a model to find the best conditions for running reaction (Table I).

First of all, the reaction was run in catalyst-free conditions. It was observed that no remarkable product was



Scheme 2. Suggested mechanism to MoO_3 NPs-catalyzed synthesis of arylidene ethyl cyanoacetates.

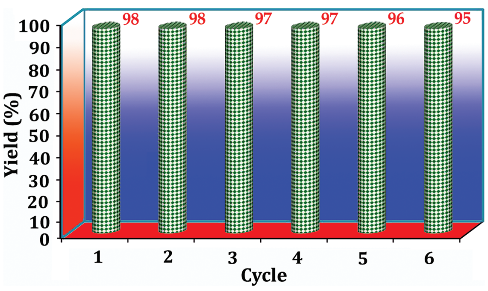


Figure 5. Recyclability results of MoO_3 NPs for the synthesis of compound **3o** over six runs.

obtained. From this experiment, it was understood that among different catalysts and conditions, MoO_3 NPs (3 mol%) in aqueous medium [EtOH/H_2O (4:1)] at room temperature disclosed best efficiency to synthesis of product and under these conditions highest yield of product was obtained in the same reaction times (Table I).

When the optimum conditions for reaction performance were found (see above), it was tried to examine the generality of the reaction by the use of a wide range of aryl aldehydes and in the presence of optimum amounts of MoO_3 NPs as green, highly efficient and recyclable nano-catalyst, and the results were summarized in Table II.[46–51]

As can be seen from Table II, the use of aromatic aldehyde bearing both electron donating/withdrawing groups resulted in the formation of compound **3** with excellent yield, while satisfactory results were not obtained when the reaction was loaded with aliphatic aldehydes under the same reaction conditions.

An admissible mechanism for the synthesis of arylidene ethyl cyanoacetate is expanded in Scheme 2. In this proposed pathway, in the first step, activated ethyl cyanoacetate **2** by MoO_3 NPs is reacted with the carbonyl group of aldehyde **1** which also previously activated by MoO_3 NPs to form intermediate **4**. In the second step, losing water from intermediate **4** by the amphoteric roll of MoO_3 NPs leads to obtain target product **3**. From the illustrated mechanism, it is obviously understood that both Lewis acidic and basic sites of MoO_3 NPs are responsible to activate both electrophile **1** and nucleophile **2** which lead to accelerate reaction progress.

On the other hand, one of the other noteworthy aspects of this protocol is the capability of catalyst to reuse in further cycles which makes it industrially and economically valuable. Therefore, in a furthermore investigation, the recyclability of MoO_3 NPs was also studied for compound **3o** (Fig. 5). The obtained results from this examination showed that MoO_3 NPs remains active in six alternative runs and can dramatically catalyze the reaction without significant loss of activity.

4. CONCLUSION

In conclusion, a green nano-catalytic approach for the synthesis of newly prepared potentially interesting biological active organic compounds was described by the use of MoO_3 NPs as a highly efficient nano-catalyst and also the scope of potentially biologically active compounds was developed. By this procedure some novel products were obtained which can candidate as medicinally important compounds or even important drugs in the future. It is believed that this methodology would attract the interest of chemists, biologists, and pharmacologists in the future. As well as, a new application of MoO_3 NPs as an eco-friendly, highly efficient, recyclable, and easily handled nano-catalyst to the synthesis of organic compounds was introduced. The merit of this protocol is the synthesis of new kind of organic compounds by the use of an efficient nano-Lewis acid catalyst and environmentally benign conditions with good to excellent yields.

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