



**A GREEN SOLVENT-FREE PROTOCOL FOR KNOEVENAGEL CONDENSATION
USING HETEROGENEOUS REUSABLE 5% of MgO/La₂O₃ CATALYT**

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Abstract: When newly prepared 5% of MgO/La₂O₃ heterogeneous catalyst was used for the Knoevenagel condensation reactions, the catalyst accelerate the reactions time with high percentage of yield under solvent-free conditions. The condensation reactions were optimized using various reaction conditions. The catalyst was characterized by various techniques, including X-ray powder diffraction (XRD), Fourier transform infrared spectroscopy (FT-IR), Scanning electron microscopy (SEM), Brunauer-Emmett-Teller (BET) Surface Area, Energy Dispersive X-ray Spectrometry (EDS) and UV-Visible DRS, and the Knoevenagel condensation derivatives evaluated using IR, ¹H NMR and mass spectroscopy.

Keywords: Knoevenagel condensation, 5% of MgO/La₂O₃, heterogeneous catalyst, solvent-free.

Introduction:

Knoevenagel condensation is most widely used reaction for the formation of carbon-carbon double bond in many organic syntheses^I including Coumarin derivatives^{II-III}, fragrances^{IV}, UV filters in cosmetics^V and in many drugs & therapeutic substances^{VI}. The new double bond have been developed between carbonyl compounds and active methylene group when the reaction was catalyzed by bases, Lewis acids, ionic liquids and metal compounds etc. The earlier reported catalysts were sodiumhydroxide^{VI}, potassiumcarbonate^{VII}, piperidine^{VIII} and di-*n*-propylamine^{IX}, ZnCl₂^X, silica gel^{XI} and ammonium acetate (NH₄OAc)-basic alumina^{XII} Mg(ClO₄)₂^{XIII}, LaCl₃^{VIX}, NbCl₅^{XV}, TiCl₄^{XVI}, ZnCl₂^{XVII}, MgBr₂^{XVIII}, CuCl₂^{XIX} ionic liquid^{XX}, clay^{XXI}, zeolite^{XXII}, *Bacillus licheniformis* (BLAP)^{XXIII}, and Baker's yeast^{XXIV}. Moreover, the reactions were commonly carried out in organic solvents and the most recent report shows new approach to this reaction was to use water as inert solvent^{XXV-XXIX} and the reaction was carried out under solvent-free methods^{XXX}. These two methods are more environmental friendly and step forward to green chemistry.

However, many of the previous catalytic systems suffer from long reaction time with low to moderate yields, economically and environmentally not benign. The heterogeneous metal catalyst has attracted significant attention due to their high selectivity with mild reaction

conditions and the reusable nature. The heterogeneous catalyst promiscuity provides a new green tool for organic synthesis, and thus largely extends the application. The chemical industry has been looking towards more environmentally acceptable processes, involving green chemistry methods in order to eliminate/reduce chemical waste at the source and reducing use of hazardous reagents in the synthesis. The key technologies utilized in green chemistry are solvent-free synthesis and heterogeneous catalytic synthesis. In the view of importance of Knoevenagel condensation reaction and green chemistry synthesis, we carried out Knoevenagel condensation reaction in the presence of 5% of MgO/La₂O₃ catalyst **scheme-1** under various conditions to optimize the reaction conditions (**Table-1**). It was found that the maximum yield was obtained in the presence of 5% of MgO/La₂O₃ catalyst under solvent-free condition.

Scheme-1: Synthesis of Knoevenagel condensation reactions (IIIa-p)

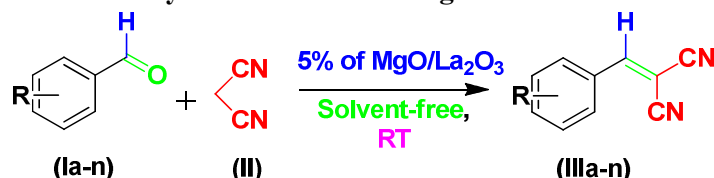


Table-1: Optimization of catalysts and reaction condition

Entry	Reagent	solvent	Reaction time (hr)	Yield ^a
1	MgO/La ₂ O ₃	Acetonitrile	2	<85%
2	MgO/La ₂ O ₃	Chloroform	3	80%
3	MgO/La ₂ O ₃	DMF	1	85%
4	MgO/La ₂ O ₃	Ethanol	1.5	80%
5	MgO/La ₂ O ₃	t-butanol	2	80%
6	MgO/La₂O₃	Neat	0.33	95%
7	MgO/La ₂ O ₃	water	1	90%
8	La(NO ₃) ₃ .6 H ₂ O	Neat	6	<60%
9	La ₂ O ₃	Neat	6	60%
10	MgO	Neat	3	75%

^a isolated yield

Table-2: Physical data of Knoevenagel condensation reactions (IIIa-p)

Compound ®	M.P (°C)	Reaction time (min)	Yield	Compound ®	M.P (°C)	Reaction time (min)	Yield (%)
IIIa) hydrogen	80-82	20	95	IIIh) 3,4-dichloro	172-174	15	90
IIIb) 3-methoxy	92-94	15	92	IIIi) 2,6-difloro	173-175	15	93
IIIc) 4-hydroxy	186-188	20	90	IIIj) 4-methoxy	112-114	15	95
IIId) 4-nitro	159-161	20	91	IIIk) 3-hydroxy-4-methoxy	135-138	20	92
IIIe) 4-methyl	134-135	20	94	IIIl) 2-furfuryl	63-65	20	94
IIIf) 2-chloro	94-96	20	90	IIIm) 2-thiophenyl	93-95	15	92
IIIg) 4-chloro	160-162	35	95	IIIn) naphthyl	157-159	30	92

Experimental:

FTIR (KBr) spectra were recorded on a Shimadzu FT-IR-8400s spectrophotometer. The powder X-ray diffraction pattern has been recorded on a Siemens D-5000 diffract meter by using Cu K radiation source and a Scintillation counter detector. The XRD phases present

in the samples were identified with the help of JCPDS data files. The BET surface area was determined by Nitrogen physisorption at liquid Nitrogen temperature on a Micromeritics Gemini 2360 instrument. Prior to measurements, samples were oven-dried at 393°K for 10 hr and flushed with Argon gas for 1 hr. Melting points were determined in open capillary tubes and are uncorrected. The purity of the compounds was checked by TLC using precoated silica gel plates 60₂₅₄(Merck). ¹H NMR and ¹³C NMR spectra were recorded on Bruker Avance II 400 MHz spectrometer using tetramethylsilane as an internal standard. Mass spectra were recorded on a GCMS-QP 1000 EX mass spectrometer.

Preparative method for 5% of MgO/La₂O₃:

5% of MgO/La₂O₃ prepared from pulverised Lanthanum (III) hydroxide with Mg(NO₃)₂.6H₂O. Initially, When 0.1M ammonium hydroxide was added too lanthanum nitrate heexahydrate (50 gm) in distilled water, wwhite precipitate of Lanthanum hydroxide was formed. The hydroxyl white precipitate was filtered using Buchner funnel and washed with ammonium hydroxide then dried under oven at 150°C for 12 hr. Finally, The pulverised Lanthanum (III) hydroxide (25 gm) was dissolved in distilled water and added Mg(NO₃)₂.6H₂O, then heated the mixture on water bath up to precipitate formation, after formation of precipitate the compound was dried under oven at 150°C for overnight and further calcinations at 650°C for 4 hours to obtain pure pulverised 5% of MgO/La₂O₃.

Result and Discussion:

Catalyst characterization:

The FT-IR spectrums of La₂O₃ and MgO/La₂O₃ were shown two characteristic stretching frequency peaks around 1462 and 854 cm⁻¹ (**Figure-1**). The peak around 1462 cm⁻¹ is representing to presence of oxide and the peak found at 854 cm⁻¹ is characterizing the crystalline La₂O₃. Based on FT-IR data it concludes that the crystalline of La₂O₃ do not changes with Magnesia.

The X-ray diffraction of the compounds La₂O₃ and MgO/La₂O₃ calcined at 650°C showed in **Figure-2**. The strongest three intense peaks appeared at 2θ values 25.42, 30.08 and 44.1 are associated with (111) (200) (201) h, k, l planes respectively, which indicates Magnesia doped La₂O₃ is in hexagonal phase. The average particle size was calculated using the Scherer equation $D=0.9 \lambda/\beta \cos\theta$ (where D is the average crystalline size, λ is x-ray wavelength, β is (FWHM) diffraction line and θ is the diffraction angle). The average crystalline size of both La₂O₃ and MgO/La₂O₃ is below 50 nm.

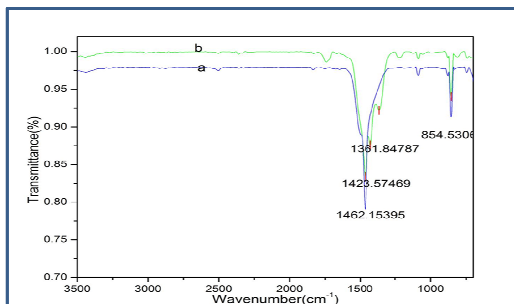


Fig-1: FTIR image of MgO/La₂O₃(a) and La₂O₃ (b)

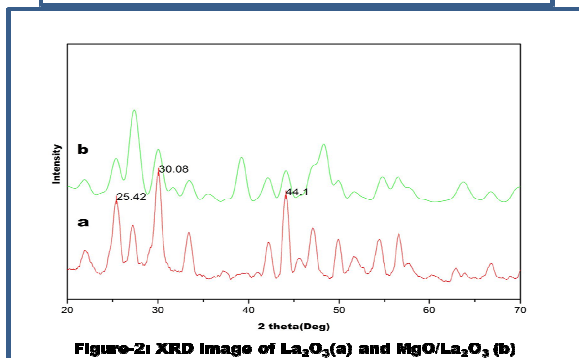


Figure-2: XRD image of La₂O₃(a) and MgO/La₂O₃ (b)

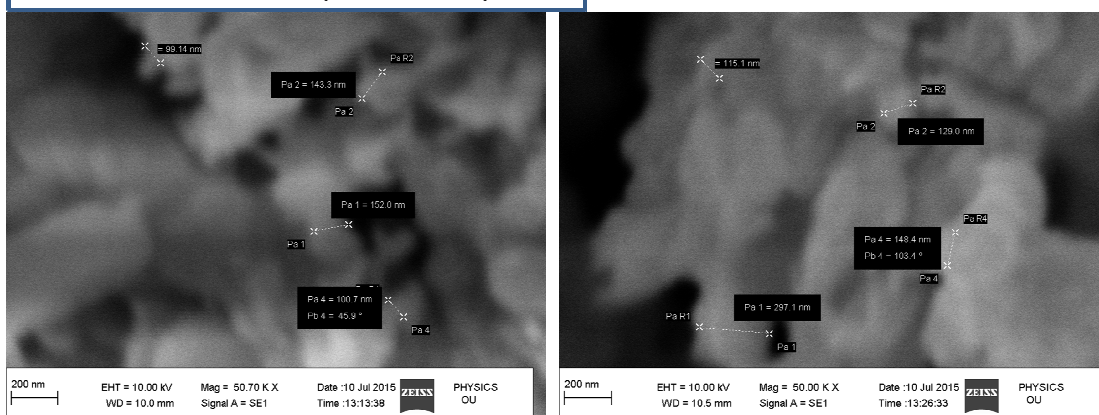


Figure-3: SEM images of La₂O₃ (image-1) and MgO/La₂O₃ (image-2)

SEM images of La₂O₃ and MgO/La₂O₃ (Figure-3) are similar to each other. The average crystalline size of the particles was also found to be same in both images. It indicates that the particles were uniformly distributed all over the surface and spherical in shape and this result was in agreement with XRD results with same crystallite size.

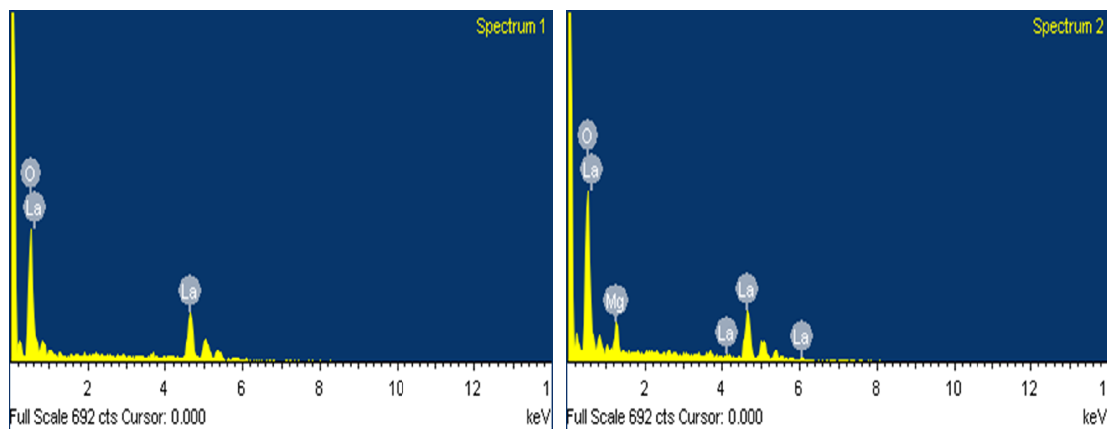
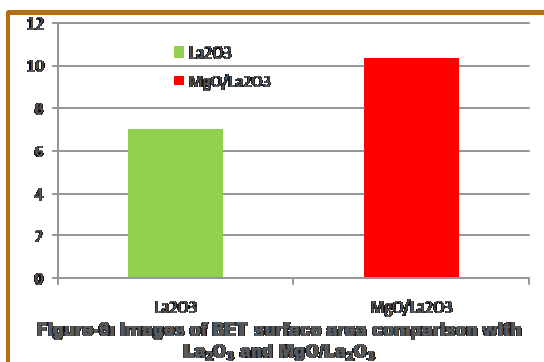
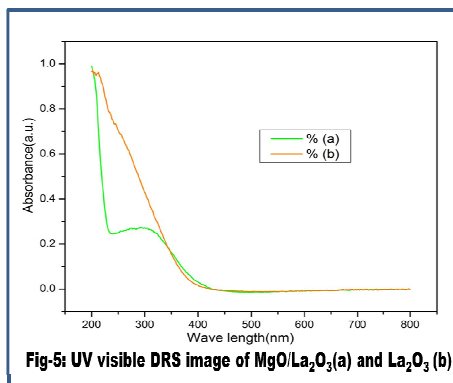


Figure-4: EDX Images of La_2O_3 (Spectrum-1) and $\text{MgO}/\text{La}_2\text{O}_3$ (Spectrum-2)

In EDX spectrum (**Figure-4**) of La_2O_3 shows two characteristic signals which corresponds to La and O (Oxygen) it the indicate the compound La_2O_3 present without any impurity, spectrum-2 of $\text{MgO}/\text{La}_2\text{O}_3$ shows La, Mg and O (Oxygen) characteristic signals which represent Mg incorporation on La_2O_3 .

The UV-Visible DRS spectrums of La_2O_3 and $\text{MgO}/\text{La}_2\text{O}_3$ were presented in **Figure 5**. The absorption edges obtained from the plots of absorbance vs. wavelength. (The interception of the tangent on the descending part of the absorption peak of the wavelength axis gives the value of diffuse absorption edge in nm). The UV-visible DRS spectrum of La_2O_3 shows absorption peak in visible region, wavelength observed at 380 nm with band gap 3.26 eV (The band gap measured using $E_g=1240/\lambda$ formula, where E_g is the band gap energy and λ is the wavelength of the absorption edge). The UV-visible DRS spectrum of $\text{MgO}/\text{La}_2\text{O}_3$ shows a red shift when compared to La_2O_3 and observed at 420 nm with band gap of 2.95 eV. The red shift in UV-visible DRS spectrum clearly indicates incorporation of Magnesia on La_2O_3 .

The specific surface area of Lanthanum was found to be 7.0157 m^2/g and the Magnesia promoted La_2O_3 was found 10.3239 m^2/g (**Figure-6**). The specific surface area of $\text{MgO}/\text{La}_2\text{O}_3$ was bigger than that of pure La_2O_3 . The bigger surface area may due to impression of Magnesia on surface of the Lanthanum. It clearly represent the MgO compounds strongly influences the surface area of pure La_2O_3 .



General procedure for the synthesis of Tetrahydropyrimidine (IVa-n):.

A mixture of aromatic aldehydes (**Ia-n**) (1 mmol), melanonitrile (**II**) (1mmol) and 5% of MgO/La₂O₃ (30 mg) was stirred for 20-30 min at room temperature. The progress of the reaction was monitored by TLC. After completion of the reaction the reaction mixture poured into ice cold water and the compound extracted with ethyl acetate, purified by Colum chromatography using ethyl acetate: hexane to afford pure condensation product (**IIIa-n**).

Spectral data:

IIIa) 2-Benzylidenemalononitrile: IR spectrum, ν , cm⁻¹: 675, 754, 1562, 1589 and 2222; ¹H NMR spectrum, δ , ppm: 7.52-7.56 (m, 2H), 7.62-7.66 (m, 1H), 7.88 (s, 1H), 7.90-7.92 (d, 2H); *M* 155 [*M*+H]⁺.

IIIb) 2-(3-methoxybenzylidene)malononitrile: IR spectrum, ν , cm⁻¹: 779, 1276, 1494, 1568 and 2227; ¹H NMR spectrum, δ , ppm: 3.86 (s, 3H) 7.16-7.18 (m, 1H), 7.42-7.48 (m, 3H), 7.74 (s, 1H); *M* 185 [*M*+H]⁺.

IIIc) 2-(4-hydroxybenzylidene)malononitrile: IR spectrum, ν , cm⁻¹: 829, 1178, 1269, 1504, 1562 and 2218; ¹H NMR spectrum, δ , ppm: 6.99-7.01 (d, 2H), 7.65 (s, 1H), 7.89-7.91 (d, 2H); *M* 171 [*M*+H]⁺.

IIId) 2-(4-nitrobenzylidene)malononitrile: IR spectrum, ν , cm⁻¹: 846, 1244, 1518, 1577 and 2202; ¹H NMR spectrum, δ , ppm: 7.88 (s, 1H), 8.06-8.08 (d, 2H), 8.38-8.40 (d, 2H); *M* 200 [*M*+H]⁺.

IIIe) 2-(4-methylbenzylidene)malononitrile: IR spectrum, ν , cm⁻¹: 833, 1259, 1573 and 2225; ¹H NMR spectrum, δ , ppm: 2.35 (s, 3H) 7.30-7.32 (d, 2H), 7.72 (s, 1H), 7.79-7.81 (d, 2H); *M* 169 [*M*+H]⁺.

IIIff) 2-(2-chlorobenzylidene)malononitrile: IR spectrum, ν , cm⁻¹: 760, 1225, 1587 and 2219; ¹H NMR spectrum, δ , ppm: 7.43-7.46 (m, 1H), 7.55-7.56 (m, 2H), 8.12-8.15 (m, 2H); *M* 189 [*M*+H]⁺.

IIIg) 2-(4-chlorobenzylidene)malononitrile: IR spectrum, ν , cm^{-1} : 827, 1222, 1487, 1570 and 2227; ^1H NMR spectrum, δ , ppm: 7.50-7.52 (d, 2H), 7.72 (s, 2H), 7.85-7.87 (d, 2H); M 189 $[M+H]^+$.

IIIh) 2-(3,4-dichlorobenzylidene)malononitrile: IR spectrum, ν , cm^{-1} : 789, 1197, 1511, 1586 and 2217; ^1H NMR spectrum, δ , ppm: 7.35 (s, 1H), 7.63-7.64 (d, 1H), 7.68 (s, 1H), 7.80-7.81 (d, 1H); M 189 $[M+H]^+$.

IIIi) 2-(2,6-difluorobenzylidene)malononitrile: IR spectrum, ν , cm^{-1} : 871, 1275, 1601 and 2227; ^1H NMR spectrum, δ , ppm: 7.96-7.01 (m, 1H), 7.06-7.10 (m, 1H), 8.01 (s, 1H), 8.32-8.38 (m, 1H); M 191 $[M+H]^+$.

IIIj) 2-(4-methoxybenzylidene)malononitrile: IR spectrum, ν , cm^{-1} : 831, 1179, 1275, 1504, 1562 and 2221; ^1H NMR spectrum, δ , ppm: 3.90 (s, 3H), 7.00-7.02 (d, 2H), 7.65 (s, 1H), 7.89-7.91 (d, 2H); M 191 $[M+H]^+$.

IIIk) 2-(3-hydroxy-4-methoxybenzylidene)malononitrile

IIIl) 2-(furan-2-ylmethylene)malononitrile: IR spectrum, ν , cm^{-1} : 758, 1208, 1481, 1642 and 2225; ^1H NMR spectrum, δ , ppm: 6.73-6.75 (dd, 1H), 7.34-7.36 (dd, 1H), 7.54 (s, 1H), 7.80-7.82 (dd, 1H); M 145 $[M+H]^+$.

IIIm) 2-(thiophen-2-ylmethylene)malononitrile: IR spectrum, ν , cm^{-1} : 764, 1214, 1495, 1626 and 2218; ^1H NMR spectrum, δ , ppm: 7.30-7.33 (dd, 1H), 7.85-7.86 (dd, 1H), 7.92-7.94 (m, 2H); M 161 $[M+H]^+$.

III n) 2-(naphthalen-1-ylmethylene)malononitrile: IR spectrum, ν , cm^{-1} : 833, 1214, 1504, 1569 and 2221; ^1H NMR spectrum, δ , ppm: 7.58-7.71 (m, 3H), 7.93-7.96 (m, 2H), 8.10-8.11 (d, 1H), 8.27-8.28 (m, 2H); M 205 $[M+H]^+$.

Conclusion:

The heterogeneous metal catalyst was successfully prepared by using Lanthanum nitrate hexahydrate and $\text{Mg}(\text{NO}_3)_2 \cdot 6\text{H}_2\text{O}$ and characterized on the basis of FTIR, XRD, SEM, and UV-DRS spectrums. It's proved similarities of the pure La_2O_3 and the Magnesia doped Lanthanum, and the EDX spectrum confirms presence of La and Mg in the Magnesia doped Lanthanum. The 2-Arylidenemalononitrile has been synthesized with excellent yields in lesser reaction time using heterogeneous $\text{MgO}/\text{La}_2\text{O}_3$ catalyst under solvent-free condition. The compound structures were established on the basis of IR, NMR and mass Spectroscopy.

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