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Multicomponent synthesis of 4H-pyran derivatives using KOH loaded calcium oxide as catalyst in solvent free condition

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ABSTRACT

A Convenient and green synthesis of 4H-pyran derivatives via one-pot multicomponent reaction of aromatic aldehydes, malononitrile and ethyl acetoacetate using KOH loaded CaO as a catalyst under solvent free condition is reported. The morphology of the catalyst has been characterized by XRD and TEM. This protocol have numerous advantages like lesser reaction time, environment friendly, low cost, easy to separate, and provide higher yield. The synthesized compounds have been characterized and confirmed by different spectroscopic techniques like ¹H NMR, ¹³C NMR, FT- IR, and LC- MS.

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1. Introduction

Multicomponent reactions (MCRs) are based on three or more reactants reacting in one step to form a single product which includes portion of all reactants. Heterocyclic compounds having functionalized nitrogen and oxygen play a significant role in medicinal chemistry and have been frequently utilized as scaffolds for the development of drugs. MCRs play an important role in organic chemistry which have come out as an effective means for delivering the molecular diversity which have an important role in the combinatorial approaches for the preparation of heterocyclic compounds. MCRs, such as the Biginelli, Passerini, Ugi, and Hantzsch reactions provide a wide platform of important heterocyclic compounds¹. The MCRs contain their extensive range of significance in selectivity, synthetic convergence, and atom-economy. MCRs possess other benefits of effortlessness and synthetic effectiveness budding as a powerful means in modern synthesis of 4H-pyran derivatives in organic chemistry². 4H-pyran derivatives are widely used in organic synthesis especially for synthesizing natural products³. It plays a significant role in the medicinal chemistry field owing to different biological and pharmacological activities of its derived substitutes⁴ like inhibiting tyrosinase⁵ and acting as anti-influenza virus agents⁶. Also these derivatives can be used as pigments⁷, fluorescent reagents⁸, photoactive materials⁹ etc. different catalysts like cetyltrimethylammonium

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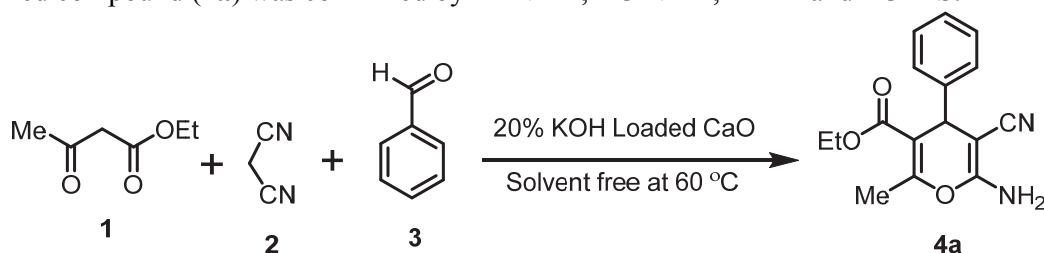
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chloride (CTACl), Baker's yeast, L-proline, sodium bromide (NaBr), phenyl boronic acid, piperidine, KF-montmorillonite, Ru, imidazole, nickel chloride (NiCl), nano-ZnO, S-proline, SiO₂ -NPs, 4-dimethylaminopyridine (DMAP) and triethyl amine (NEt₃) were studied for the synthesis of pyrans via multicomponent reactions¹⁰. These methods were not found to be satisfactory because of the involvement of toxic catalyst, low yield, tedious method, harmful solvent and long reaction time, no reusability of the catalyst and difficulty for separation and purification of reaction mixture from the homogenous catalyst by filtration. In today scenario, tremendous efforts have been made to develop the new processes that minimize pollution in chemical synthesis, due to different types of heterogeneous catalysts are in demand within industry because of easy catalyst removal, recovery, and recycling. In recent years, KOH-loaded metal oxide catalyst has been investigated for biodiesel production.¹¹ However 20% KOH-loaded CaO has not been used as catalyst in the synthesis of 4H-pyran derivatives by multicomponent reactions. So in the present study, we have used KOH-loaded CaO as a catalyst in the multicomponent reactions of 4H-pyran derivatives and found a good yield in lesser time, good catalytic efficiency of recycled catalyst and this catalyst can be separated from reaction mixture by filtration and may be reused.

Initially, MCRs between ethyl acetoacetate (1.0 mmol) (**1**), malononitrile (**2**) (1.0 mmol), benzaldehyde (**3**) (1.0 mmol), in the presence of KOH loaded calcium oxide (10 mmol) as a catalyst was carried out under solvent free condition, at 60°C for 10 min (**Scheme 1**). The completion of the reaction is determined by thin layer chromatography (TLC) on silica gel. The structure of the synthesized compound (**4a**) was confirmed by ¹H NMR, ¹³C NMR, FT-IR and LC-MS.



Scheme 1.

2. Results and Discussion

Initially, the reaction of ethyl acetoacetate (**1**), malononitrile (**2**) and benzaldehyde (**3**) has been carried out in a one pot under solvent free condition in the presence of a catalytic amount of Al₂O₃ at 60°C, after 3 h the product (**4a**) was formed in 50% yield (**Entry 4, Table 1**). The product (**4a**) was characterized as *2-amino-3-cyano-5-ethoxycarbonyl-4-phenyl-6-methyl-4H-pyran*, on the basis of spectral analysis and analytical data. Now same reaction was carried out in the presence of Fe₂O₃ as catalyst and the product (**4a**) was obtained in 35% yield after 3 h (**Entry 5, Table 1**). When the reaction was carried out in the presence of CaO (**Entry 6, Table 1**) as catalyst, the reaction takes place within 3 h and product (**4a**) is formed with 45% yield but when KOH is used as a catalyst reaction proceed and product (**4a**) formed in 1 h in 50% yield. In the next reaction 20% KOH loaded CaO was used as a catalyst and reaction completed within 10 minutes with 92% yield of product (**4a**) (**Entry 10, Table 1**) was obtained. It seems that, the basic medium plays an important role to provide high yield in lesser time. This result encouraged us to study the reaction in detail. Various catalysts have been studied under solvent free condition at 60°C for product yield and reaction time (**Table 1**). 20% KOH loaded CaO was found to be the most advantageous catalyst, In the presence of 20% KOH loaded CaO as catalyst, the reaction was completed after stirring for 10 minutes at 60°C. By increasing the quantity of KOH loading after 20% there was decreasing in the yield of product (**4a**). That needs for the optimization of KOH loading. However we also studied the effect of NaOH loaded catalyst on product yield, we found no equivalent changes (**Entry 9, Table 1**). The effect of catalyst loading and temperature has been given in Tables 2 and 3. The catalytic activity increased by increasing the concentration of KOH loading over CaO up to 20% due to the presence of high number of basic sites. However, loading of KOH

exceeds from 20-25 wt%, this excess KOH covered basic sites hence there is no increase in basic strength and surface areas so the catalytic activity were lower¹¹. When 20% KOH loading over CaO (**Table 2**) yield of 4H-Pyran derivatives increased upto 92%, however when the amount of loaded KOH exceeds 20% the yield of product decreased. This could be attributed to the agglomeration of KOH phase.

We studied the effect of various solvent on the product yield and reaction time where we found that solvent like CH₂Cl₂ or CHCl₃ did not give the preferred product (**4a**) in proper yield. Even though ethanol didn't give the desire yield (**Table 4**). The reaction in ethanol could proceed smoothly under the same reaction conditions to afford the corresponding product (**4a**) in 70% yield (**Entry 5, Table 4**). When water used as a solvent then no product was formed, because of poor solubility of reaction mixture in water (**Entry 7, Table 4**). But when reaction was carried out in solvent free condition than product (**4a**) gives 92% yield (**Entry 8, Table 4**).

Table 1. Effect of catalysts on yield of 4H-pyran derivative (**4a**) under solvent free condition at 60°C

Entry	Catalyst	Reaction Time (Min)	Product Yield (%)
1.	KOH	60	50
2.	K ₂ CO ₃	180	Trace
3.	Na ₂ CO ₃	120	20
4.	Al ₂ O ₃	180	50
5.	Fe ₂ O ₃	180	35
6.	CaO	180	45
7.	20% KOH loaded Al ₂ O ₃	55	30
8.	20% KOH loaded Fe ₂ O ₃	60	40
9.	20% NaOH loaded CaO	15	90
10.	20% KOH loaded CaO	10	92

Table 2. Effect of KOH loading on CaO

Entry	KOH Loading (%)	Product Yield (%)
1.	5	75
2.	10	80
3.	15	85
4.	20	92
5.	25	90

Table 3. Effect of temperature on yield of 4H-pyran derivative (**4a**) under solvent free condition using 20% KOH loaded CaO as catalyst

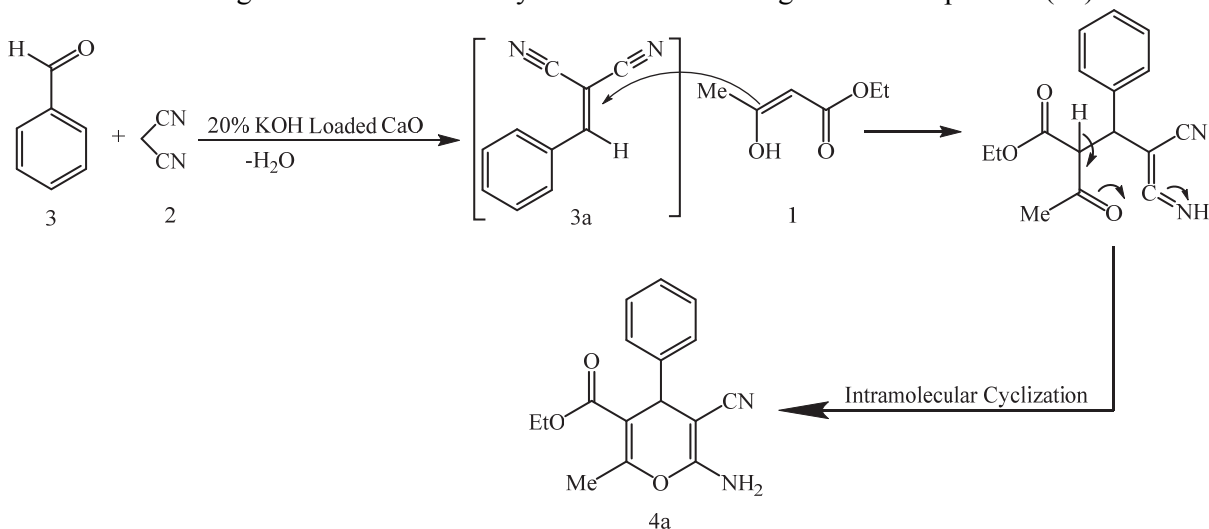
Entry	Temperature	Yield (%)
1.	RT	35
2.	40°C	52
3.	60°C	92
4.	70°C	80
5.	100°C	No reaction

RT = Room Temperature

Table 4. Effect of solvent on yield of 4H-pyran derivative (**4a**)

Entry	Solvent	Catalyst	Time	Yield (%)
1.	Ethanol	CaO	5 h	62
2.	Ethanol	KOH	6 h	45
3.	CH ₂ Cl ₂	20%KOH loaded CaO	10 h	30
4.	CHCl ₃	20%KOH loaded CaO	7 h	25
5.	Methanol	20%KOH loaded CaO	10 h	70
6.	Ethanol	20% KOH loaded CaO	5 h	70
7.	Water	20% KOH loaded CaO	10 h	No reaction
8.	Solvent free	20%KOH loaded CaO	10 min	92

On the basis of the literature, , the reaction for one-pot reaction of 4H- pyrans was performed in two ways. The overall mechanism is given in **Scheme 2**. When ethyl acetoacetate (**1**) was reacted with aromatic aldehyde (**3**) or malononitrile (**2**) under solvent free condition in the presence of catalytic amount of 20% KOH loaded CaO at 60°C, signifying that the one-pot reaction should be initiated from malononitrile (**2**) and aromatic aldehyde (**3**) via Knoevenagel condensation reaction. In order to confirm our hypothesis, a step-wise reaction was performed¹². First benzylidene malononitrile intermediate was formed that was followed by Michael addition reaction of ethyl acetoacetate (**1**) with benzylidene malononitrile intermediate, catalyzed by 20% KOH loaded CaO, therefore, the intermediate was formed which undergo the intramolecular cyclization reaction to give the final product (**4a**).



Scheme 2.

The recyclability of the catalyst was studied using the residue after filtering off the reaction product in the model reaction. The catalyst was regenerated by washing sequentially with ethanol thrice and drying at 80°C for 3 h. It was observed that the effectiveness of the catalyst did not change significantly even after five cycles.

The production of 4H-pyran derivatives under given reaction conditions by stirring a mixture of ethyl acetoacetate, aromatic aldehyde and malononitrile in the presence of catalytic amount of KOH loaded CaO (10 mmol), under solvent free condition. It generated the desired 2-amino 4H-pyran derivative (**4a**) in very good yield (92%). The procedure was extended to synthesize other 2-amino 4H-pyran derivatives (**Table 5**) by changing aromatic aldehydes, a very good yield of desired products (**4a-k**) were obtained. It seems that there was no effect on yield of products (**4a-k**) by using different aromatic aldehydes bearing both electron-withdrawing groups and electron donating groups. The structures of the synthesized compounds (**4a-k**) were confirmed by ¹H NMR, and ¹³C NMR spectroscopy. Molecular mass of compounds (**4a-k**) were confirmed by liquid chromatography mass spectrometry (LC-MS). Functional groups in compounds (**4a-k**) were confirmed by Infra-red spectroscopy. Also, almost the same results were obtained for methyl acetoacetate upon stirring with aromatic aldehydes and malononitrile in the presence of catalytic amount of KOH loaded CaO (10 mmol) under similar reaction conditions. By optimizing the reaction parameters such as catalyst, catalyst loading, temperature and solvent, the suitability of the optimized protocol was observed for kinds of aromatic aldehydes. The synthesized products were successfully isolated and purified by recrystallization from warm ethanol without the use of chromatography.

2.1 Pretreatment of the catalyst, KOH loaded CaO

The catalyst was synthesized by using the grinding method. In this method, the measured ratio of KOH pellets and oxides were taken and grinded at room temperature using a mortar pestle till thick

slurry was obtained, after that the slurry was transferred from mortar pestle to a crucible and calcinated at 350°C for 180 minutes. After calcination the catalyst was taken out and stored in vacuum desiccator and used as such in multicomponent reactions. KOH was loaded over three oxides such as: Al_2O_3 , CaO , and Fe_2O_3 .

2.2 Characterization of KOH loaded CaO

The X-ray diffraction spectrum of the powdered KOH loaded CaO catalyst is shown in the **Fig. 1** and FT-IR of 20% KOH loaded CaO is shown in the **Fig. 2**. **Fig. 1** shows the XRD pattern of various concentration of KOH loaded CaO. There are three crystal phase: $\text{Ca}(\text{OH})_2$ observed at $2\theta = 28.70, 34.10$, CaO observed at $2\theta = 33.49, 37.40, 47.62, 54.12, 61.12$ and K_2O observed at $2\theta = 29.50, 31.40$. New peak of CaO at 33.49 and K_2O at 31.40 were observed in XRD pattern and there is also increasing in intensity of peak (33.49, 31.40) when amount of KOH loading increased from 5% to 20%. The peaks (29.50, 33.49 and 31.40) disappeared when KOH loading is increased from 20% to 25%. This determines that the phase of K_2O is probably the cause of high catalytic activity. From **Fig. 2** typical characteristic peaks of IR (KBr) at λ_{max} 1438.62, 2849.31, 2918.44, 3643.76 cm^{-1} were confirmed loading of KOH at CaO.

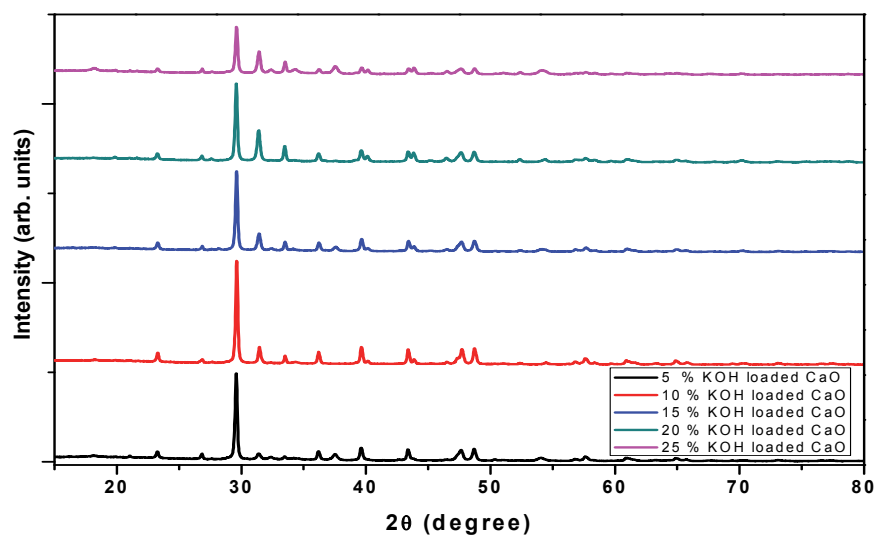


Fig. 1. XRD of various concentration of KOH loaded CaO

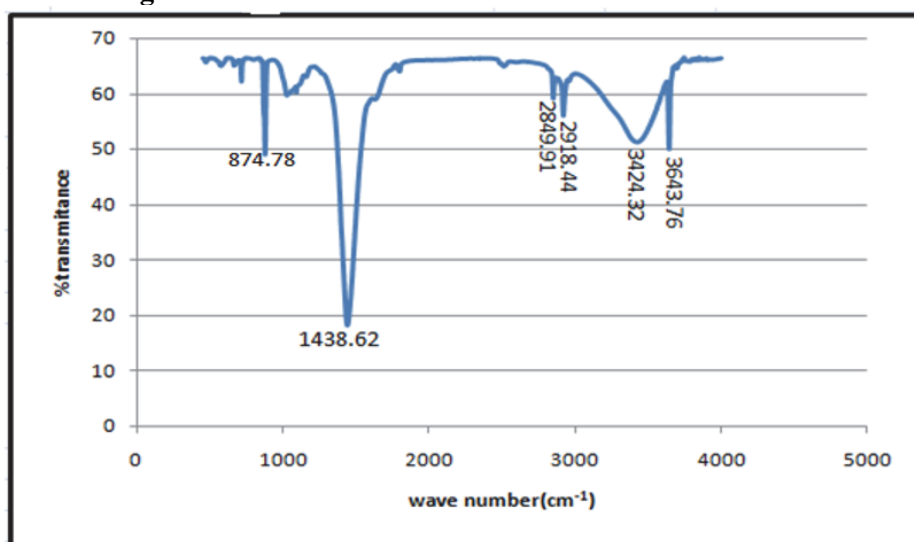


Fig. 2. FT-IR of 20% KOH loaded CaO

2.3 Transmission electron microscope analysis (TEM)

TEM images of 20% KOH loaded CaO are shown in **Fig. 3(a)** for fresh catalyst and **Fig. 3(b)** for recovered catalyst. The 20% KOH loaded CaO consist of rhombohedral structures. TEM images of 20% KOH loaded CaO indicated that particles have rhombohedral morphology that have varied size from 50 nm to 100 nm of fresh and 200 nm of recovered catalyst. The dark surface in the given images indicated the loading of KOH onto CaO surface.

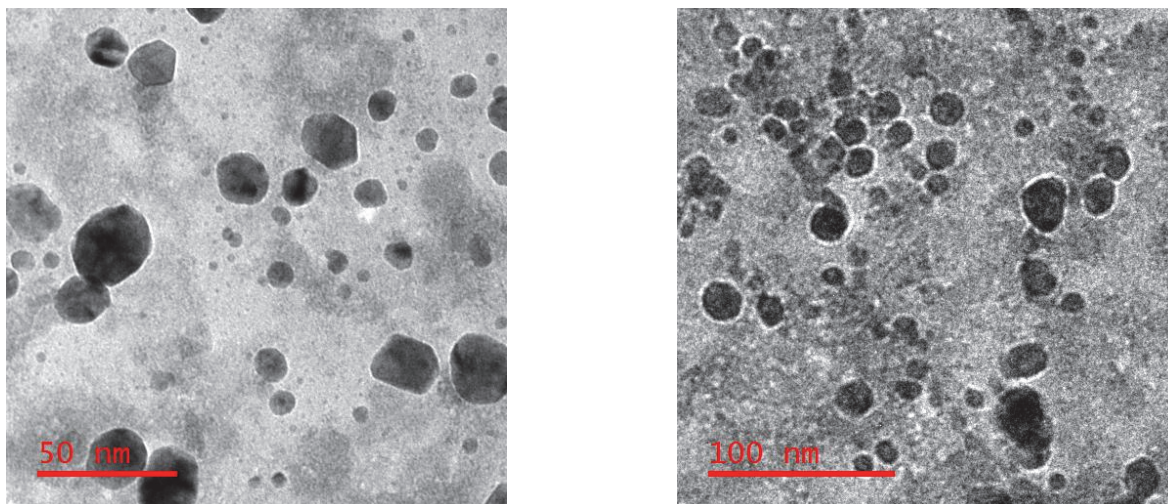


Fig. 3 (a). TEM images of fresh 20% KOH loaded CaO

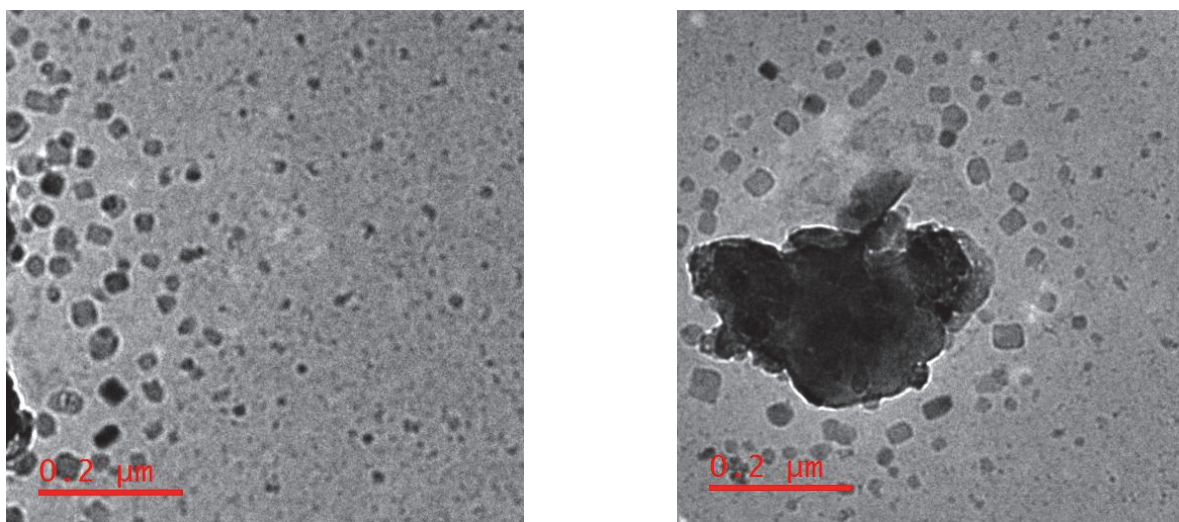
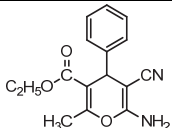
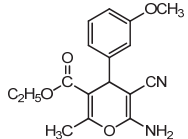
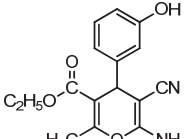
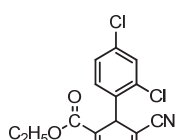
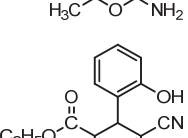
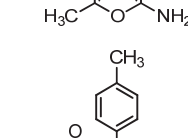
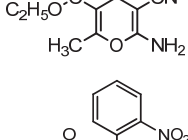
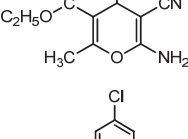
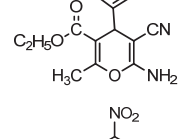
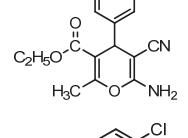
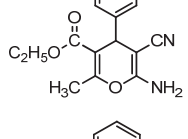


Fig. 3. (b). TEM images of recovered 20% KOH loaded CaO

Table 5. Synthesis of 4H-Pyran Derivatives Using KOH loaded Calcium Oxide as Catalyst

Compounds	Time (min)	Yield (%)	Melting Points in °C	
			Observed	Reported
4a 	10	92	191-193	190-193 ^[16]

4b		60	90	146-148	-
4c		30	89	166-168	163-165 ^[19]
4d		20	88	164-166	-
4e		90	95	167-169	-
4f		120	91	177-179	177-179 ^[16]
4g		10	90	177-179	181-182 ^[16]
4h		55	93	172-174	173-175 ^[16]
4i		10	88	175-177	172-175 ^[16]
4j		20	93	156-158	154-156 ^[19]
4k		30	89	178-180	176-178 ^[19]

Reaction condition: Ethyl acetoacetate (1.0 mmol), benzaldehyde (1.0 mmol) and malononitrile (1.0 mmol) in the presence of 20% KOH loaded calcium oxide (10 mmol) as a catalyst was carried out under solvent free condition at 60°C.

Table 6. Comparative study of effect of catalyst for synthesizing 4H-Pyran derivatives

Entry	Catalyst	Reaction time	Yield (%)
1	SiO ₂ -NPs	2h	85 ¹³
2	DMAP	3h	78 ¹⁴
3	KF.Al ₂ O ₃	3h	90 ¹⁵
4	NaOH	8h	75 ¹²
5	NbCl ₅	72h	80 ²
6	Sodium alginate	170 min	88 ¹⁶
7	CsF	3.5 h	79 ¹⁷
8	Potassium Phthalimide	35 min	89 ¹⁸
9	Thiourea dioxide	40 min	90 ¹⁹
10	20% KOH loaded CaO	10 min	92

From the above tabulated data it can be concluded that 20% KOH loaded CaO catalyst has got the amazing features in comparison to other catalyst already reported in the literature. The reactions carried out by using the other catalyst have been employed in different types of solvents, while as in our study we have carried out our reaction in solvent free condition. Most of the reported catalysts are hazardous to environment and difficult to separate from reaction mixture but KOH loaded CaO is ecofriendly and easy to separate by filtration from reaction mixture and gives better yield in short reaction time.

3. Experimental section

All the reactants and the catalysts were purchased from Sigma-Aldrich Company, and used without any further purification. Synthesized compounds were recrystallized with warm ethanol. IR spectra were recorded on a Perkin–Elmer FT-IR spectrometer. ¹H NMR and ¹³C NMR spectra were recorded on a VARIAN 400 MHz spectrometer. Mass spectra were obtained from SHIMADZU 8030 mass spectrometer by the ESI method. The X-ray diffraction (XRD) patterns were recorded on a RIGAKU MINIFLEX 600 diffractometer with F.F.tube operated at 40 kV and 15 mA detector. The TEM analyses were performed on JEOL JEM- 1230 electron microscope. Melting points were determined in an open capillary. TLC experiments were carried out using MERCK TLC aluminum sheets (silica gel) and chromatograms were visualized by exposing in iodine chamber or using UV-lamp.

3.1. General procedure for synthesis of benzylidene malononitrile intermediate.

A mixture of benzaldehyde (1 mmol) and malononitrile (1 mmol) were taken into a round-bottom flask (100 ml), catalytic amount of 20% KOH loaded over CaO (10 mmol) was added with slow stirring and was heated at 60°C, after sometime benzylidene malononitrile intermediate was formed. The steps of the reaction were monitored by TLC and spectral analysis.

White powder, mp 82°C, IR (KBr) λ_{\max} 2192, 1581 cm⁻¹; ¹H NMR (400 MHz, DMSO-*d*₆) δ 7.47 (t, 2H, J 8.44 Hz), 7.53 (t, 1H, J 8.24), 7.84 (d, 2H, J 8.3 Hz), 8.46 (s, 1H, CH); ¹³C NMR (DMSO-*d*₆) δ 168.1, 133.5, 130.1, 131.6, 128.9, 112.5, 111.4, 81.5. MS (ESI) for C₁₀H₆N₂ found 154.16.

3.2. General procedure for synthesis of 4H-pyran derivatives.

A mixture of benzylidene malononitrile intermediate and ethyl acetoacetate (1 mmol) were taken into a round-bottom flask (100 ml) and catalytic amount of 20% KOH loaded over CaO (10 mmol) was added while stirring mildly and was heated at 60°C. The steps of the reaction were monitored by TLC. After completion of the reaction, ethanol was added to the reaction mixture to dissolve the solid product and was filtered. The residue of KOH loaded CaO was washed thoroughly with warm ethanol until no compound was detected in the residue. The combined ethanolic solution was concentrated under vacuum and allowed to stand in the refrigerator to get pure crystalline product.

3.2.1. 2-amino-3-cyano-5-ethoxycarbonyl-4-phenyl-6-methyl-4H-pyran derivative (4a)

Yellowish solid, mp 191-193°C; IR (KBr) λ_{\max} 3403, 2190, 1692 cm⁻¹; ¹H NMR (400 MHz, DMSO-*d*₆) δ 1.33 (t, 3H, J = 6.0 Hz, OCH₂CH₃), 2.51 (s, 3H, CH₃), 4.32 (q, 2H, J = 7.2 Hz, OCH₂CH₃), 4.73 (s, 1H), 6.36 (br s, 2H, NH₂), 7.25-7.94 (m, 5H, C₆H₄); ¹³C NMR (400 MHz, DMSO-*d*₆) δ 13.12,

18.51, 36.85, 54.45, 65.13, 127.5, 128.4, 129.0, 132.2, 143.03, 164.0, 164.1, 168.5. MS (ESI) for $C_{16}H_{16}N_2O_3$ found 284.11.

3.2.2. 2-amino-3-cyano-5-ethoxycarbonyl-4-(3-methoxyphenyl)-6-methyl-4H-pyran derivative (**4b**)

Yellow solid, mp 146–148°C, IR (KBr) λ_{max} 3328, 2192, 1602 cm^{-1} ; 1H NMR (400 MHz, DMSO- d_6) δ 1.36 (t, 3H, $J = 7.0$ Hz, OCH_2CH_3), 2.25 (s, 3H, CH_3), 2.5–2.7 (s, 3H, OCH_3), 3.63 (q, 2H, $J = 7.1$ Hz, OCH_2CH_3), 4.38 (s, 1H), 6.43 (s, 2H, NH_2), 6.51–6.69 (m, 4H, C_6H_4); ^{13}C NMR (400 MHz, DMSO- d_6) δ 31.3, 37.3, 37.1, 47.1, 65.2, 106.4, 117.1, 137.1, 143.4, 149.2, 149.3, 152.1, 153.7. MS (ESI) for $C_{17}H_{18}N_2O_4$ found 314.11.

3.2.3. 2-amino-3-cyano-2-ethoxy-5-ethoxycarbonyl-4-(3-hydroxyphenyl)-6-methyl-4H-pyran derivative (**4c**)

Yellow solid, mp 166–168°C; IR (KBr) λ_{max} 3478, 2202, 1692 cm^{-1} ; 1H NMR (400 MHz, DMSO- d_6) δ 1.13 (t, 3H, $J = 7.0$ Hz, OCH_2CH_3), 3.31 (s, 3H, CH_3), 3.38 (s, 1H), 3.98 (q, 3H, $J = 7.0$ Hz, OCH_2CH_3), 4.4–5.4 (s, 1H, OH), 6.93 (s, 2H, NH_2), 7.10 (m, 3H, C_6H_4), 7.35 (s, 1H, C_6H_4); ^{13}C NMR (400 MHz, DMSO- d_6) δ 15.14, 19.52, 37.1, 55.03, 55.64, 106.4, 120.1, 128.4, 139.2, 143.4, 157.2, 164.1, 168.7. MS (ESI) for $C_{16}H_{16}N_2O_4$ found 300.46.

3.2.4. 2-amino-3-cyano-5-ethoxycarbonyl-4-(2,4-dichlorophenyl)-6-methyl-4H-pyran derivative (**4d**)

Yellow solid, mp 164–166°C, IR (KBr) λ_{max} 3476, 2203, 1685 cm^{-1} ; 1H NMR (400 MHz, DMSO- d_6) δ 1.58 (t, 3H, $J = 7.0$ Hz, OCH_2CH_3), 3.4 (s, 3H, CH_3), 2.48 (s, 3H, CH_3), 3.42 (q, 2H, $J = 7.0$ Hz, OCH_2CH_3), 4.38 (s, 1H), 5.88 (s, 2H, NH_2), 7.34 (dd, 2H, C_6H_4), 7.94–7.21 (s, 1H, C_6H_4); ^{13}C NMR (400 MHz, DMSO- d_6) δ 18.4, 19.4, 37.3, 57.1, 58.2, 106.4, 120.1, 127.4, 128.4, 141.2, 157.2, 160.1, 165.7. MS (ESI) for $C_{16}H_{14}N_2O_3Cl_2$ found 353.90.

3.2.5. 2-amino-3-cyano-2-ethoxy-5-ethoxycarbonyl-4-(2-hydroxyphenyl)-6-methyl-4H-pyran derivative (**4e**)

Yellow solid, mp 167–169°C; IR (KBr) λ_{max} 3329, 2190, 1693 cm^{-1} ; 1H NMR (400 MHz, DMSO- d_6) δ 1.17 (t, 3H, $J = 7.0$ Hz, OCH_2CH_3), 2.16 (s, 3H, CH_3), 4.04 (q, 2H, $J = 7.0$ Hz, OCH_2CH_3), 4.38 (s, 1H), 4.3–5.2 (s, 1H, OH), 6.68 (s, 2H, NH_2), 7.03–7.6 (m, 4H, C_6H_4); ^{13}C NMR (400 MHz, DMSO- d_6) δ 16.7, 35.6, 37.3, 57.3, 61.4, 113.6, 114.3, 123.4, 131.2, 143.4, 154.4, 162.2, 163.7. MS (ESI) for $C_{16}H_{16}N_2O_4$ found 300.45.

3.2.6. 2-amino-3-cyano-5-ethoxycarbonyl-4-(4-methylphenyl)-6-methyl-4H-pyran derivative (**4f**)

Yellow solid, mp 177–179°C, IR (KBr) λ_{max} 3410, 2197, 1696 cm^{-1} ; 1H NMR (400 MHz, DMSO- d_6) δ 2.38 (t, 3H, $J = 7.0$ Hz, OCH_2CH_3), 2.4–3.6 (s, 3H, CH_3), 2.43 (s, 3H, CH_3), 4.00 (s, 1H), 4.5 (q, 2H, $J = 7.0$ Hz, OCH_2CH_3), 5.87 (s, 2H, NH_2), 6.93–7.12 (dd, 2H, C_6H_4), 7.16–7.85 (dd, 2H, C_6H_4); ^{13}C NMR (400 MHz, DMSO- d_6) δ 13.7, 18.3, 38.1, 58.2, 61.2, 106.4, 114.1, 120.5, 130.0, 141.2, 157.2, 162.1, 162.7. MS (ESI) for $C_{17}H_{18}N_2O_3$ found 298.45.

3.2.7. 2-amino-3-cyano-5-ethoxycarbonyl-4-(2-nitrophenyl)-6-methyl-4H-pyran derivative (**4g**)

Yellow solid, mp 177–179°C, IR (KBr) λ_{max} 3454, 2208, 1692 cm^{-1} ; 1H NMR (400 MHz, DMSO- d_6) δ 1.10 (t, 3H, $J = 7.0$ Hz, OCH_2CH_3), 2.4 (s, 3H, CH_3), 3.04 (q, 2H, $J = 7.0$ Hz, OCH_2CH_3), 3.37 (s, 1H), 5.79 (s, 2H, NH_2), 7.34–7.61 (m, 4H, C_6H_4); ^{13}C NMR (400 MHz, DMSO- d_6) δ 13.7, 17.4, 38.1, 58.2, 60.2, 108.5, 116.2, 117.5, 129.2, 147.4, 157.4, 162.1, 167.7. MS (ESI) for $C_{16}H_{15}N_3O_5$ found 329.45.

3.2.8. 2-amino-3-cyano-5-ethoxycarbonyl-4-(4-chlorophenyl)-6-methyl-4H-pyran derivative (**4h**)

Yellow solid, mp 172–174°C, IR (KBr) λ_{max} 3403, 2209, 1691 cm^{-1} ; ^1H NMR (400 MHz, DMSO- d_6) δ 1.12 (t, 3H, $J = 7.0$ Hz, OCH_2CH_3), 2.35 (s, 3H, CH_3), 3.05 (q, 2H, $J = 7.0$ Hz, OCH_2CH_3), 3.38 (s, 1H), 5.17 (s, 2H, NH_2), 6.91-7.26 (dd, 2H, C_6H_4), 7.3-7.34 (dd, 2H, C_6H_4); ^{13}C NMR (400 MHz, DMSO- d_6) δ 13.7, 18.3, 38.1, 59.4, 60.4, 107.4, 115.4, 119.6, 129.1, 140.2, 158.2, 161.2, 167.7. MS (ESI) for $\text{C}_{16}\text{H}_{15}\text{N}_2\text{O}_3\text{Cl}$ found 318.45.

3.2.8. 2-amino-3-cyano-5-ethoxycarbonyl-4-(4-nitrophenyl)-6-methyl-4H-pyran derivative (**4i**)

White solid, mp 175–177°C, IR (KBr) λ_{max} 3404, 2200, 1691 cm^{-1} ; ^1H NMR (400 MHz, DMSO- d_6) δ 1.54 (t, 3H, $J = 7.0$ Hz, OCH_2CH_3), 2.37 (s, 3H, CH_3), 3.54 (q, 2H, $J = 7.0$ Hz, OCH_2CH_3), 4.38 (s, 1H), 6.18 (s, 2H, NH_2), 6.93-7.22 (m, 4H, C_6H_4); ^{13}C NMR (400 MHz, DMSO- d_6) δ 13.9, 18.5, 38.3, 59.1, 60.4, 107.6, 115.3, 116.6, 129.1, 144.4, 158.4, 161.1, 163.9. MS (ESI) for $\text{C}_{16}\text{H}_{15}\text{N}_3\text{O}_5$ found 329.14.

3.2.9. 2-amino-3-cyano-5-ethoxycarbonyl-4-(3-chlorophenyl)-6-methyl-4H-pyran derivative (**4j**)

Yellow solid, mp 156–158°C, IR (KBr) λ_{max} 3399, 2184, 1698 cm^{-1} ; ^1H NMR (400 MHz, DMSO- d_6) δ 1.12 (t, 3H, $J = 7.0$ Hz, OCH_2CH_3), 2.34 (s, 3H, CH_3), 3.46 (q, 2H, $J = 7.1$ Hz, OCH_2CH_3), 4.39 (s, 1H), 5.89 (s, 2H, NH_2), 7.1-7.82 (m, 4H, C_6H_4); ^{13}C NMR (400 MHz, DMSO- d_6) δ 13.7, 18.5, 38.7, 59.4, 60.5, 107.7, 115.8, 119.7, 129.3, 141.3, 157.3, 162.0, 168.8. MS (ESI) for $\text{C}_{16}\text{H}_{15}\text{N}_2\text{O}_3\text{Cl}$ found 318.45.

3.2.10. 2-amino-3-cyano-5-ethoxycarbonyl-4-(2-chlorophenyl)-6-methyl-4H-pyran derivative (**4k**)

Yellow solid, mp 178–180°C, IR (KBr) λ_{max} 3430, 2195, 1688 cm^{-1} ; ^1H NMR (400 MHz, DMSO- d_6) δ 1.09 (t, 3H, $J = 7.0$ Hz, OCH_2CH_3), 2.4-3.6 (s, 3H, CH_3), 2.34 (s, 3H, CH_3), 3.35 (q, 2H, $J = 7.0$ Hz, OCH_2CH_3), 4.36 (s, 1H), 5.87 (s, 2H, NH_2), 7.0-7.73 (m, 4H, C_6H_4); ^{13}C NMR (400 MHz, DMSO- d_6) δ 13.6, 18.7, 38.7, 59.3, 60.6, 107.3, 115.2, 120.5, 129.8, 140.7, 158.6, 161.5, 167.3. MS (ESI) for $\text{C}_{16}\text{H}_{15}\text{N}_2\text{O}_3\text{Cl}$ found 318.45.

4. Conclusion

Here in this present work, we have developed a new catalyst for the synthesis of 4H-pyran derivatives via multicomponent reaction in solvent free condition and we suggested a mechanism for the synthesis of 4H-pyran derivatives. This protocol provides a new platform for the synthesis of medicinal important compounds.

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