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ONE POT SYNTHESIS OF 4H-PYRAN DERIVATIVES USING AMBERLITE IR-120 RESIN AS REUSABLE CATALYST IN SOLVENT FREE CONDITION

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Abstract
Amberlite IR-120, an ion-exchanger resin, can catalyze the three component reaction. The newly synthesized series of 4H-Pyran derivatives have been synthesized via one pot three component reaction of malanonitrile, aromatic aldehyde and a ketoester in the presence of Amberlite IR-120 acidic cation exchanger resin catalyst at 80°C in solvent free condition. The newly desired synthesis is environment friendly, simple and economic. This method provides several advantages including easy work-up, good yield, short reaction time and reusability of the catalyst. These compounds have been characterized using IR, NMR and LC-MS.
Keyword: - 4H-pyran derivatives, One-pot reaction, Multi-component reaction, Solvent free condition

1. Introduction

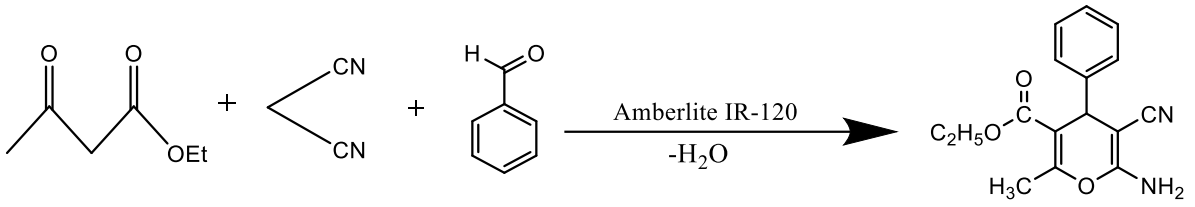
Multicomponent reaction (MCRs) is a powerful tool for drug discovery and has greatly contributed to the convergent synthesis of structurally interesting molecules from simple and readily available starting materials.[i] Multicomponent reactions are useful tool for modern organic synthesis and have advantages of selectivity in atom economic conversions and gives high yield.[ii, iii] In multicomponent reaction three or more reactants formed a single product which includes portion of all reactants in one pot. Multicomponent processes like Biginelli reaction,[iv] passerine,[v] Ugi[vi] and Hantzsch[vii] are the direct conversion of aromatic aldehydes into the corresponding nitriles.[viii] The Fischer indole reaction,[ix] the formation of N-benzylideneanilines[x] and more recently, the molecular rearrangement of perezone into isoperezone.[xi] Another advantage of MCRs in synthesis of 4H-pyran derivatives with synthetic effectiveness and easiness.[xii]

Pyran have an interesting, medicinally, remarkable and unique position in heterocyclic chemistry, 4H-pyran and its derivatives play an important role in synthetic and medicinal chemistry, biological and pharmacological activities,[xiii] such as antibacterial,[xiv-xviii] antitumor,[xix] antiallergic,[xx] 4H-Pyran derivatives are also potential calcium channel antagonists.[xxi]

As far preparation of 4H-pyrans is concerned some novel variety of methods have been used, which include various catalyst such as KF/AlO,[xxii] imidazole,[xxiii] NaBr,[xxiv] DMAP,[xxv] Nano-ZnO,[xxvi, xxvii] S-proline,[xxviii] Phenylboronic acid,[xxix] L-proline,[xxx] CTA-

Cl,[xxxi] piperdine,[xxxii, xxxiii] Baker yeast,[xxxiv] SiO NPs,[xxxv] Ru,[xxxvi] has been utilized for this transformation. However in recent years, when green methods are preferred, many of these methods were not found to be satisfactory as they involve the amine based catalysts, halogenated catalyst, low yield, long reaction time, difficulty for separation and purification of reaction mixture from the homogenous catalyst by filtration and no reusability of catalyst. In today scenario, tremendous efforts have been made to develop the new processes that minimize pollution in chemical synthesis. Due to these different types of catalyst of heterogeneous catalysts, are in demand within industry because of catalyst removal, recovery and recycling.[xxxvii] In recent years, Amberlite IR-120 acidic cation exchanger resin has been investigated more for biodiesel production.

In this article we describe a new green process for synthesizing 4H-pyran derivatives by using ethyl acetoacetate, benzaldehyde and there derivatives and malanonitrile by using Amberlite IR-120 acidic cation exchanger resin in the manner of multicomponent reaction (MCR) (**Scheme 1**).



2 3 1 6a

Scheme 1

Initially, the multicomponent reaction between, ethyl acetoactate (**1**) (1.0 mmol), benzaldehyde (**2**) (1.0 mmol) and malanonitrile (**3**) (1.0 mmol) in the presence of Amberlite IR-120 acidic cation exchanger resin (100 mg) as a catalyst was carried out under solvent free condition, at 80°C for 15 min. The completion of the reaction was determined by thin layer chromatography (TLC) technique. The structure of synthesized compounds was confirmed by ^{1}H NMR, ^{13}C NMR, IR and LC-MS.

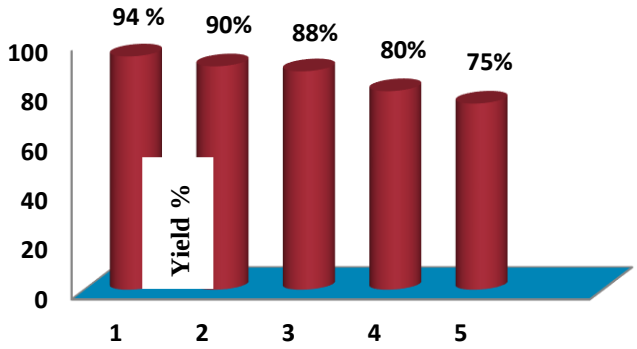
2. Reusability of the catalyst

Amberlite IR-120 acidic cation exchanger resin was recovered over the filter paper after filtration and was used for five consecutive runs. It was observed that catalyst losses activity very slowly or there was no appreciable loss of activity after five runs (**Table-1**).

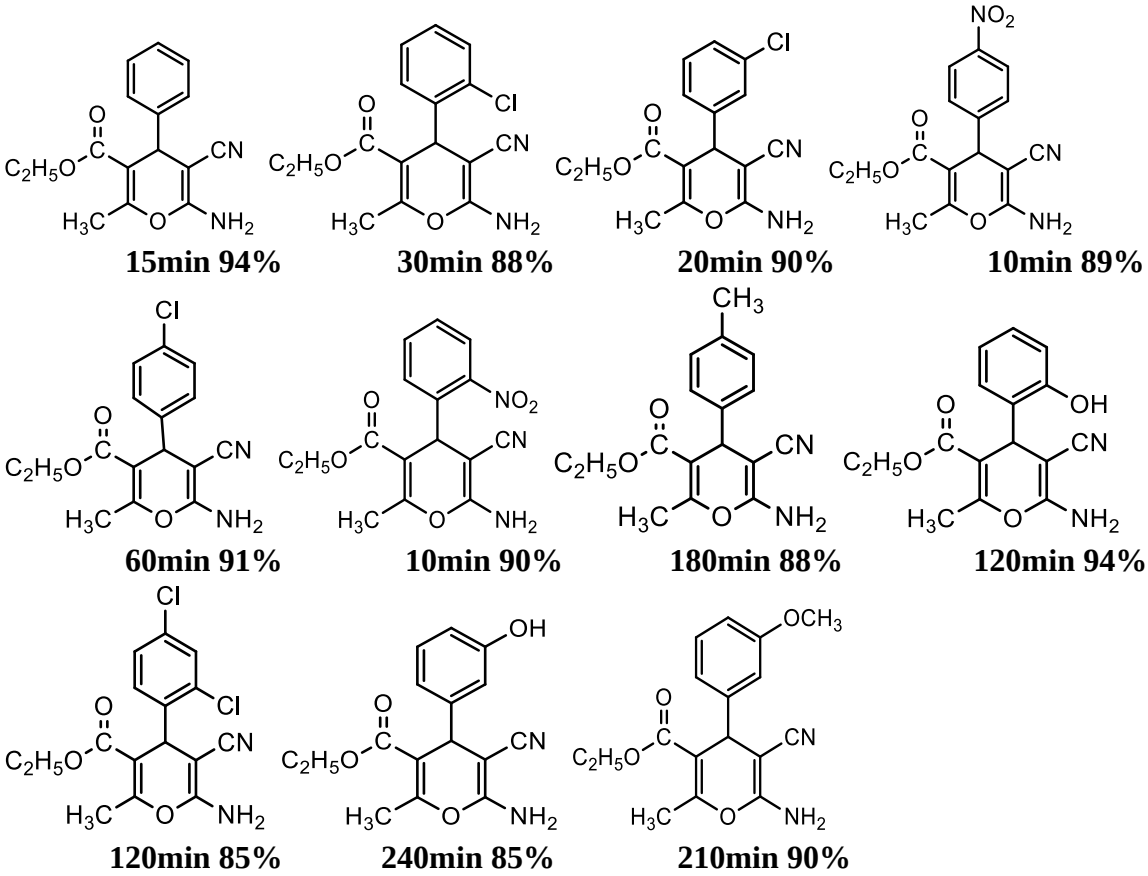
Table 1:- Reusability of the catalyst

Entry	**Runs**	**Yield %**
1	1st	94
2	2nd	90
3	3th	88
4	4th	80
5	5th	75

Reaction conditions: Benzaldehyde (1.0 mmol, 0.106 g), ethylacetoacetate (1.0 mmol, 0.13 g), malanonitrile (1.0 mmol, 0.066 g) and Amberlite IR-120 cation resin solvent free conditions.



Synthesis of *2-amino-4H-pyran* derivatives uses Amberlite IR-120 cation resin as a catalyst at 80ºC



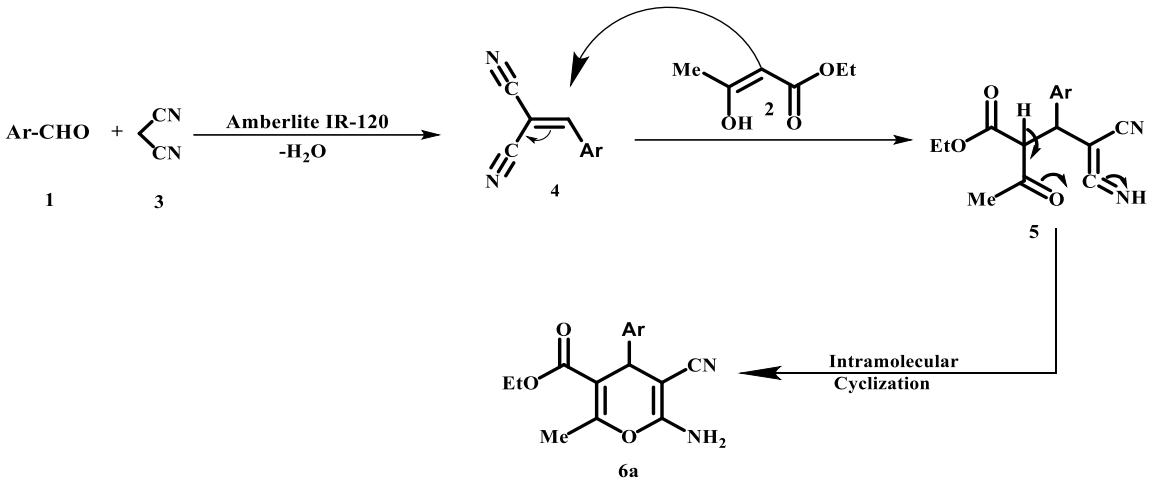
3. Results and discussion

The reaction of mlanonitrile (**1**), benzaldehyde (**2**) and ethylacetoacetate (**3**) has been carried out in (100ml) round bottom flask under solvent free condition in the presence of catalytic amount of acetic acid (0.01 ml) at 80ºC and after 1 hour to check progress of the reaction thin layer chromatography results reveal that no product (**6a)** formation takes place up to two hours hence reaction was continued for 12 hours. After 12 hours only intermediate was formed. The next reaction was carried out in presence of pipredine as catalyst and the product **(6a)** was formed in 40% yield after 2 hour (entry 2, table 2). When reaction was carried out without

catalyst no product was found after 12 hours (entry 4, table 2). However when the reaction was carried out in the presence of various catalysts like Al_2O_3, MgO and CaO, the product **(6a)** was formed in yield 50%, 60%, and 42% respectively in time 8 hour, 10 hour and 7 hour respectively (entry 5, 6, 7, Table 2). When reaction was carried in presence of Amberlite IR 120 acidic cation exchanger resin the reaction proceeded within 15 min. and product **(6a)** was found in 94% yield (entry 8, Table 2). The resin was separated by filtration and washed thoroughly with warm ethanol. The combined filtrate was reduced in rotatory evaporator and allowed to stand overnight to get the pure recrystallized product **(6a)** in 94% yield. It seems that, the Amberlite IR 120 acidic cation exchanger resin play important role in obtaining high yield in short reaction time. The catalyst provided large surface area because its structure is like a round molecule so it provides a whole surface area. Amberlite IR 120 catalyst has another advantage, is its reusability every time it acts as a fresh catalyst. The product *2-amino-3cyano-5-ethoxycarbonyl-4-phenyl-6-methyl-4H-pyran* was characterized on the basis of spectral and analytical data. This result motivated us to elaborate the reaction in detail. To improve the reaction condition like the nature of base, amount of base and also reaction medium was then investigated (Table 2, Scheme 1). Amberlite IR-120 was found to be the most advantageous catalyst; the reaction was completed in 15 minutes at 80 ºC. It has given desired product **(6a)** in 94% yield (entry 8, Table 2). The reactions in solvent such as methanol, ethanol, ethanol plus water, water did not give the preferred product **(6a)**. In order to further investigate the solvent effect, the one-pot reactions were performed in various solvents and results are listed in Table 4. The reaction in ethanol could precede smoothly under the same reaction conditions to afford the corresponding product **(6a)** in 60% (entry 2, Table 4). No desired product **(6a)** was formed when the reaction was performed in water due to the poor solubility (entry 4, Table 4). Without taking any solvent the product **(6a)** yield increases in lesser reaction time (entry 5, Table 4).

The reaction was carried out with different aromatic aldehyde bearing both electron withdrawing groups such as halogen, nitro or electron-donating groups such as ethyl, methyl, methoxy (Table 5). It seems that there was no effect of electron withdrawing group and electron donating group on the yield of product **(6a)**. The structures of synthesized compounds **6a** were confirmed by liquid chromatography mass spectroscopy.

On the basis of the literature, mechanism for one-pot reaction of 4H-pyran, two supporting experiment were performed. No reaction was observed when reaction of aromatic aldehyde (**1**) was treated with ethyl acetoacetate (**2)** and malanonitrile (**3)** under solvent free condition in the presence of catalytic amount of Amberlite IR-120 at 80ºC, signifying that the one-pot reaction should be initiated from the knoevenagel condensation reaction of malanonitrile **3** and aromatic aldehyde **1**. In order to confirm our hypothesis, a stepwise reaction was performed, first benzylidene malanonitrile intermediate was followed by Michal addition reaction of ethylacetoacetate **2** with benzylidene malanonitrile, catalyzed by Amberlite IR-120 acidic cation exchanger resin, therefore, the intermediate was formed which undergo the intermolecular cyclization reaction to give the final product **6a** following mechanism can be suggested. The overall mechanism is given in **Scheme 2**.



Scheme 2

Table 2:- The effects of catalysts amount on the synthesis of methyl 4H-pyran derivatives under solvent free condition 80ºC.

Entry	**Catalyst (mol %)**	**Time**	**Yield %**
1	Acetic acid	12 hour	Intermediate
2	Piperidine	2 hour	40
3	HT (Mg-Al-X)	7 hour	70
4	Catalyst free	12 hour	No reaction
5	Al_2O_3	8 hour	50
6	MgO_3	10 hour	60
7	CaO	7 hour	42
8	Amberlite IR-120	15 min	94

Reaction conditions: Benzaldehyde (1.0 mmol, 0.106 g), ethylacetoacetate (1.0 mmol, 0.13 g), malanonitrile (1.0 mmol, 0.066 g) and Amberlite IR-120 cation resin solvent free conditions.

Table 3:- The effect of Temperature on the yield of 4H-pyran derivatives under solvent free condition using Amberlite IR-120 acidic cation exchanger resin.

Entry	**Temperature (**ºC)	**Yield %**
1	RT	30
2	40	52
3	60	70
4	80	94
5	100	No reaction

Reaction conditions: Benzaldehyde (1.0 mmol, 0.106 g), ethylacetoacetate (1.0 mmol, 0.13 g), malanonitrile (1.0 mmol, 0.066 g) and Amberlite IR-120 cation resin solvent free conditions.

Table 4:- Solvent effect on the synthesis of pyran derivatives

Entry	**Solvent**	**Time**	**Yield %**
1	Methanol	10 hour	50
2	Ethanol	12 hour	60
3	Ethanol + Water	8 hour	75
4	Water	2 hour	76
5	Solvent free	15 min	94

Reaction conditions: Benzaldehyde (1.0 mmol, 0.106 g), ethylacetoacetate (1.0 mmol, 0.13 g), malanonitrile (1.0 mmol, 0.066 g) and Amberlite IR-120 cation resin solvent free conditions.

However, the scope and generality of this three-component one-pot synthesis of 2-amino-4H-pyrans have been illustrated with different aldehydes and the results have been summarized in Table 5. This method has ability to tolerate a variety of other functional groups such as hydroxyl, methyl, nitro and chloro under the reaction conditions. Both, the electron-rich and electron-deficient aldehydes worked well, leading to high yields of products.

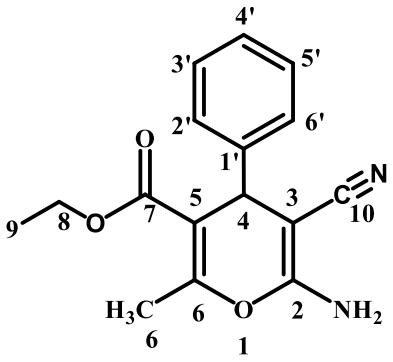
Table 5:- Synthesis of 2-amino-4H-pyran derivatives uses Amberlite IR-120 cation resin as a catalyst at 80ºC.

Entry	**Product**	**Time (min)**	**Yield %**	**Melting Point (ºC)**
				Found
1	6a	15	94	190-192
2	6b	30	88	176-178
3	6c	20	90	158-160
4	6d	10	89	176-178
5	6e	60	91	174-176
6	6f	10	90	176-179
7	6g	180	88	174-179
8	6h	120	94	166-170
9	6i	120	85	170-172
10	6j	240	85	170-172
11	6k	210	90	146-148

Mechanistically, the initial condensation of aromatic aldehyde with malanonitrile in the presence of Amberlite IR-120 acidic cation resin catalyst to formation of arylidenemalanonitrile with the loss of water molecule. The nucleophilic addition of the enolizable ethylacetoacetate to arylidenemalanonitrile followed by intramolecular cyclization of the resulting species produce the 4H-pyran derivatives.

4. Experimental

Melting points were measured by using the capillary tube method with an electro thermal 9200 apparatus. IR spectra obtained from perkin-Elmer FT-IR spectrometer did scanning between 4000-400 cm^{-1}. ^{1}H NMR and ^{13}C NMR spectra were recorded on a Bruker AMX-300 MH/Bruker 400 MHz and 100 MHz AVANCE NMR spectrometer, respectively. LCMS spectra were obtained from SHIMADZU 8030 mass spectrometer by the ESI Method. TLC experiments were carried out using MERCK TLC aluminum sheet (silica gel) and chromatograms were visualized by exposing in iodine chamber or using UV-lamp. In the reaction all the reactants and the catalysts were purchased from Sigma-Aldrich Company, and used without further purification.



6a

The structural explanation of products **6a** was made on the basis of their spectroscopic data. Thus, for instance, infrared (FT-IR) spectra of **6a** exhibited bands at 3329 (NH_2), 2190 (CN) and 1676 (C=O) cm^{-1}. The ^{1}H NMR spectrum of **6a** showed the presence of: (i) five aromatic protons at 7.24-8.017 ppm, (ii) a triplet and quartet at 1.283 and 3.915 ppm integrating for two and three protons of the ethoxycarbonyl group, respectively; (iii) three singlet at 2.50, 4.67 and 6.300 ppm identified as the methine (C-3), methyl (CH3), and NH2 protons. The ^{13}C NMR spectrum displayed: (i) a signal at 166.46 ppm due to the carbonyl group and at 115.90 ppm due to cyano; (ii) four signals for the vinyl carbons at 157.2 (C-2), 154.1 (C-6), 108.3 (C-5), and 57.01 ppm (C-3); and (iii) four signal for aromatic carbons at 157.15-123.01 ppm. The mass spectrum of the same compound show a molecular ion peak [M+H] at m/z 284.09 in agreement with the molecular formula $C_{16}H_{16}N_2O_3$. All the structural analysis of the same compound compare with the same compound reported by Miguel A. Vázquez *et al.*[xxxviii]

4.1. General procedure for synthesis of benzylidene malanonitrile intermediate.

A mixture of benzaldehyde (1 mmol) and malanonitrile (1 mmol) were taken into a round-bottom flask (100 ml), catalytic amount of Amberlite IR-120 cation resin were added with slow stirring and was heated at 80ºC, after sometime benzylidene malanonitrile intermediate was formed. The steps of the reaction were monitored by TLC and spectral analysis.

4.1.1. Benzylidene malanonitrile Intermediate.

Yellowish white powder, mp 84ºC, IR (KBr) λ max 2192, 1581cm^{-1}; ^{1}H NMR (400 MHz, DMSO-d_6) δ 7.48 (t, 2H, J = 8.45 Hz), 7.54 (t, 1H, J = 8.25), 7.85 (d, 2H, J = 8.4 Hz), 8.47 (s, ^{1}H, CH); ^{13}C NMR (100 MHz, DMSO-d_6) δ 169.1, 134.6, 131.0, 130.7, 129.8, 113.6, 112.5, 82.6. LCMS (EI^{+}) for $C_{10}H_6N_2$ found 154.17.

4.2. General procedure for synthesis of *2-amino-3-cyano-5-ethoxycarbonyl-4-phenyl-6-methyl-4H-pyran.*

A mixture of aromatic aldehyde (1.0 mmol, 0.1 ml) and malanonitrile (1.0 mmol, 0.066 g), was taken in to a round bottom flask (100 ml) and then ethyl acetoacetate (1.0 mmol, 0.13 g)

and Amberlite IR-120 cation resin catalyst were added in the reaction while stirring mildly and was heated at 80ºC. After this step, the reaction was monitored by TLC. On completion of the reaction ethanol was added to this reaction in round bottom flask and after filtering from filter paper the crude product was extracted. Yield 94% and mp 190-192ºC. Thus the residue was recrystallized from ethanol. All products formed were in resemblance with those of authentic sample in literature.

4.3. Spectra data

4.3.1. *2-amino-3-cyno-5-ethoxycarbonyl-4-phenyl-6-methyl-4H-pyran* (6a)

White powder, m.p.190-192ºC, Yield: 94%; FT-IR (KBr) νmax, 3404, 3329, 2190, 1676, 1259 cm^{-1}; ^{13}C NMR (100 MHz, DMSO-d_6) δ (ppm) 14.6 ($OCH_2\mathit{C}H_3$), 17.1 ($\mathit{C}H_3$), 38.2 (C-4), 58.3 (C-3), 61.0 ($O\mathit{C}H_2CH_3$), 108.3 (C-5), 116.90 (C≡N), 125.3 (C-4´), 127.1 (C-2´and C-6´), 128.2 (C-3´and C-5´), 144.8 (C- 1´), 154.1 (C-6), 157.2 (C-2), 166.46 (C=O). 1H NMR ($CDCl_3$, 400 MHz) δ 1.283 (t, *J* = 7.0 Hz, 3H, $OCH_2C\mathit{H}_3$), 4.67 (s, 3H, $C\mathit{H}_3$), 3.915 (qd, *J* = 7.0, 1.4 Hz, 2H, OCH_2CH_3), 2.50 (s, 1H, H-4), 6.300 (br s, 2H, NH_2), 7.24-8.017 (m, 5H, H-Ar); LCMS (EI+) for $C_{16}H_{16}N_2O_3$ found (M+) 284.09.

4.3.2. *2-amino-3-cyno-5-ethoxycarbonyl-4-(2-clorophenyl)-6-methyl-4H-pyran* (6b)

Yellow solid, m.p. 176-178ºC; Yield: 88%; FT-IR (KBr) νmax, 3430, 3228, 2195, 1606, 1262 cm^{-1}; ^{13}C NMR (100 MHz, DMSO-d_6) δ 14.07 ($OCH_2\mathit{C}H_3$), 17.52 ($\mathit{C}H_3$), 38.40 (C-4), 42.19 (C-3), 56.92 ($O\mathit{C}H_2CH_3$), 108.01 (C-5), 116.82 (C≡N), 125.24 (C-4´), 127.34 (C-2´and C-6´), 128.32 (C-3´and C-5´), 144.03 (C- 1´), 136.32 (C-6), 157.18 (C-2), 168.01 (C=O). 1H NMR ($CDCl_3$, 400 MHz) δ 1.284 (t, *J* = 7.0 Hz, 3H, $OCH_2C\mathit{H}_3$), 4.63 (s, 3H, $C\mathit{H}_3$), 3.901 (qd, *J* = 7.03, 1.3 Hz, 2H, OCH_2CH_3), 2.54 (s, 1H, H-4), 6.301 (br s, 2H, NH_2), 7.26-8.024 (m, 5H, H-Ar); LCMS (E+) for $C_{16}H_{15}N_2O_3Cl$, found (M+) 318.08.

4.3.3. *2-amino-3-cyno-5-ethoxycarbonyl-4-(3-clorophenyl)-6-methyl-4H-pyran* (6c)

Yellow solid, m.p. 156-158ºC; Yield: 90%; FT-IR (KBr) νmax, 3399, 3218, 2190, 1698, 1270 cm^{-1}; ^{13}C NMR (100 MHz, DMSO-d_6) δ 14.45 ($OCH_2\mathit{C}H_3$), 16.95 ($\mathit{C}H_3$), 38.59 (C-4), 58.03 (C-3), 61.04 ($O\mathit{C}H_2CH_3$), 107.32 (C-5), 118.03 (C≡N), 124.13 (C-4´), 127.31 (C-2´and C-6´), 128.92 (C-3´and C-5´), 144.03 (C- 1´), 156.54 (C-6), 157.15 (C-2), 167.46 (C=O). 1H NMR ($CDCl_3$, 400 MHz) δ 1.30 (t, *J* = 7.0 Hz, 3H, $OCH_2C\mathit{H}_3$), 4.62 (s, 3H, $C\mathit{H}_3$), 3.961 (qd, *J* = 7.01, 1.30 Hz, 2H, OCH_2CH_3), 2.53 (s, 1H, H-4), 6.321 (br s, 2H, NH_2), 7.25-8.031 (m, 5H, H-Ar); LCMS (E+) for $C_{16}H_{15}N_2O_3Cl$, found (M+) 318.09.

4.3.4. *2-amino-3-cyno-5-ethoxycarbonyl-4-(4-nitrophenyl)-6-methyl-4H-pyran* (6d)

White solid, m.p. 175-177ºC; Yield: 89%; FT-IR (KBr) νmax, 3404, 3333, 2176, 1691, 1270 cm^{-1}; ^{13}C NMR (100 MHz, DMSO-d_6) δ 14.43 ($OCH_2\mathit{C}H_3$), 17.32 ($\mathit{C}H_3$), 37.95 (C-4), 58.32 (C-3), 61.57 ($O\mathit{C}H_2CH_3$), 107.32 (C-5), 118.95 (C≡N), 124.13 (C-4´), 127.66 (C-2´and C-6´), 128.03 (C-3´and C-5´), 142.56 (C- 1´), 156.08 (C-6), 157.90 (C-2), 167.10 (C=O). 1H NMR ($CDCl_3$, 400 MHz) δ 1.274 (t, *J* = 7.0 Hz, 3H, $OCH_2C\mathit{H}_3$), 4.62 (s, 3H, $C\mathit{H}_3$), 3.915 (qd, *J* = 7.24, 1.40 Hz, 2H, OCH_2CH_3), 2.50 (s, 1H, H-4), 6.309 (br s, 2H, NH_2), 7.21-8.028 (m, 5H, H-Ar); LCMS (E+) for $C_{16}H_{15}N_3O_5$, found (M+) 329.10.

4.3.5. *2-amino-3-cyno-5-ethoxycarbonyl-4-(4-clorophenyl)-6-methyl-4H-pyran* (6e)

White powder, m.p. 172-176ºC; Yield: 91%; FT-IR (KBr) νmax, 3397, 3219, 2191, 1699, 1270 cm^{-1}; ^{13}C NMR (100 MHz, DMSO-d_6) δ 14.45 ($OCH_2\mathit{C}H_3$), 17.30 ($\mathit{C}H_3$), 37.93 (C-4), 58.37 (C-3), 61.56 ($O\mathit{C}H_2CH_3$), 107.32 (C-5), 118.93 (C≡N), 125.23 (C-4´), 127.18 (C-2´and C-6´), 128.10 (C-3´and C-5´), 144.20 (C- 1´), 156.08 (C-6), 157.90 (C-2), 167.12 (C=O). 1H NMR ($CDCl_3$, 400 MHz) δ 1.271 (t, *J* = 7.0 Hz, 3H, $OCH_2C\mathit{H}_3$), 4.63 (s, 3H, $C\mathit{H}_3$), 3.913 (qd, *J* = 7.01, 1.39 Hz, 2H, OCH_2CH_3), 2.51 (s, 1H, H-4), 6.310 (br s, 2H, NH_2), 7.24-8.017 (m, 5H, H-Ar); LCMS (E+) for $C_{16}H_{15}N_2O_3Cl$, found (M+) 318.10

4.3.6. *2-amino-3-cyno-5-ethoxycarbonyl-4-(2-nitrophenyl)-6-methyl-4H-pyran* (6f)

Yellow solid, m.p. 177-181ºC; Yield: 90%; FT-IR (KBr) νmax, 3454, 33295, 2208, 1683, 1225 cm^{-1}; ^{13}C NMR (100 MHz, DMSO-d_6) δ 14.42 ($OCH_2\mathit{C}H_3$), 17.21 ($\mathit{C}H_3$), 37.95 (C-4), 58.32 (C-3), 61.51 ($O\mathit{C}H_2CH_3$), 107.32 (C-5), 118.90 (C≡N), 125.03 (C-4´), 127.60 (C-2´and C-6´), 128.29 (C-3´and C-5´), 144.24 (C- 1´), 156.08 (C-6), 157.90 (C-2), 167.10 (C=O). 1H NMR ($CDCl_3$, 400 MHz) δ 1.282 (t, *J* = 7.0 Hz, 3H, $OCH_2C\mathit{H}_3$), 4.61 (s, 3H, $C\mathit{H}_3$), 3.911 (qd, *J* = 7.03, 1.45 Hz, 2H, OCH_2CH_3), 2.53 (s, 1H, H-4), 6.305 (br s, 2H, NH_2), 7.25-8.016 (m, 5H, H-Ar); LCMS (E+) for $C_{16}H_{15}N_3O_5$, found (M+) 329.42.

4.3.7. ***2-amino-3-cyno-5-ethoxycarbonyl-4-(4-methylphenyl)-6-methyl-4H-pyran*** **(6g)**

Yellow solid, m.p. 176-179ºC; Yield: 88%; FT-IR (KBr) νmax, 3410, 3331, 2197, 1679, 1263 cm^{-1}; ^{13}C NMR (100 MHz, DMSO-d_6) δ 14.42 ($OCH_2\mathit{C}H_3$), 17.31 ($\mathit{C}H_3$), 37.96 (C-4), 58.32 (C-3), 61.53 ($O\mathit{C}H_2CH_3$), 107.42 (C-5), 118.93 (C≡N), 125.29 (C-4´), 127.14 (C-2´and C-6´), 128.19 (C-3´and C-5´), 142.7 (C- 1´), 156.08 (C-6), 157.91 (C-2), 167.12 (C=O). 1H NMR ($CDCl_3$, 400 MHz) δ 1.284 (t, *J* = 7.0 Hz, 3H, $OCH_2C\mathit{H}_3$), 4.66 (s, 3H, $C\mathit{H}_3$), 3.919 (qd, *J* = 7.1, 1.39 Hz, 2H, OCH_2CH_3), 2.52 (s, 1H, H-4), 6.301 (br s, 2H, NH_2), 7.20-8.013 (m, 5H, H-Ar); LCMS (E+) for $C_{16}H_{15}N_2O_3Cl$, found (M+) 298.14.

4.3.8. ***2-amino-3-cyno-5-ethoxycarbonyl-4-(2-hydroxyphenyl-6-methyl-4H-pyran*** **(6h)**

Yellow solid, m.p. 168-171ºC; Yield: 94%; FT-IR (KBr) νmax, 3452, 3414, 2199, 1651, 1215 cm^{-1}; ^{13}C NMR (100 MHz, DMSO-d_6) δ 14.42 ($OCH_2\mathit{C}H_3$), 17.32 ($\mathit{C}H_3$), 37.92 (C-4), 58.32 (C-3), 61.56 ($O\mathit{C}H_2CH_3$), 107.54 (C-5), 118.94 (C≡N), 125.51 (C-4´), 127.01 (C-2´and C-6´), 128.19 (C-3´and C-5´), 144.2 (C- 1´), 156.07 (C-6), 157.90 (C-2), 167.12 (C=O). 1H NMR ($CDCl_3$, 400 MHz) δ 1.280 (t, *J* = 7.0 Hz, 3H, $OCH_2C\mathit{H}_3$), 4.61 (s, 3H, $C\mathit{H}_3$), 3.905 (qd, *J* = 7.06, 1.29 Hz, 2H, OCH_2CH_3), 2.54 (s, 1H, H-4), 6.320 (br s, 2H, NH_2), 7.25-8.018 (m, 5H, H-Ar); LCMS (E+) for $C_{16}H_{15}N_2O_3Cl$, found (M+) 300.46.

4.3.9. ***2-amino-3-cyno-5-ethoxycarbonyl-4-(2-4-diclorophenyl)-6-methyl-4H-pyran*** **(6i)**

Yellow solid, m.p. 165-167ºC; Yield: 85%; FT-IR (KBr) νmax, 3476, 3324, 2204, 1685, 1227 cm^{-1}; ^{13}C NMR (100 MHz, DMSO-d_6) δ 14.42 ($OCH_2\mathit{C}H_3$), 17.32 ($\mathit{C}H_3$), 37.90 (C-4), 58.32 (C-3), 61.56 ($O\mathit{C}H_2CH_3$), 107.52 (C-5), 118.90 (C≡N), 125.12 (C-4´), 127.34 (C-2´and C-6´), 128.31 (C-3´and C-5´), 144.6 (C- 1´), 156.08 (C-6), 157.92 (C-2), 167.12 (C=O). 1H NMR ($CDCl_3$, 400 MHz) δ 1.280 (t, *J* = 7.0 Hz, 3H, $OCH_2C\mathit{H}_3$), 4.61 (s, 3H, $C\mathit{H}_3$), 3.901 (qd, *J* = 7.01, 1.43 Hz, 2H, OCH_2CH_3), 2.52 (s, 1H, H-4), 6.320 (br s, 2H, NH_2), 7.26-8.026 (m, 5H, H-Ar); LCMS (E+) for $C_{16}H_{14}N_2O_3Cl_2$, found (M+) 353.46.

4.3.10. ***2-amino-3-cyno-5-ethoxycarbonyl-4-(3-hydroxyphenyl)-6-methyl-4H-pyran*** **(6j)**

Yellow solid, m.p. 170-174ºC; Yield: 85%; FT-IR (KBr) νmax, 3478, 3336, 2202, 1692, 1266 cm^{-1}; ^{13}C NMR (100 MHz, DMSO-d_6) δ 14.42 ($OCH_2\mathit{C}H_3$), 17.02 ($\mathit{C}H_3$), 37.93 (C-4), 58.32 (C-3), 61.56 ($O\mathit{C}H_2CH_3$), 107.54 (C-5), 118.93 (C≡N), 125.23 (C-4´), 127.14 (C-2´and C-6´), 128.19 (C-3´and C-5´), 144.6 (C- 1´), 156.08 (C-6), 157.90 (C-2), 167.12 (C=O). 1H NMR ($CDCl_3$, 400 MHz) δ 1.281 (t, *J* = 7.0 Hz, 3H, $OCH_2C\mathit{H}_3$), 4.63 (s, 3H, $C\mathit{H}_3$), 3.912 (qd, *J* = 7.01, 1.39 Hz, 2H, OCH_2CH_3), 2.54 (s, 1H, H-4), 6.310 (br s, 2H, NH_2), 7.25-8.016 (m, 5H, H-Ar); LCMS (E+) for $C_{16}H_{16}N_2O_4$, found (M+) 300.40.

4.3.11. ***2-amino-3-cyno-5-ethoxycarbonyl-4-(3-methoxyphenyl)-6-methyl-4H-pyran*** **(6k)**

Yellow solid, m.p. 145-147ºC; Yield: 90%; FT-IR (KBr) νmax, 3391, 3328, 2192, 1690, 1263; cm^{-1}; ^{13}C NMR (100 MHz, DMSO-d_6) δ 14.45 ($OCH_2\mathit{C}H_3$), 17.32 ($\mathit{C}H_3$), 37.92 (C-4), 58.3 (C-3), 61.56 ($O\mathit{C}H_2CH_3$), 107.54 (C-5), 118.93 (C≡N), 125.24 (C-4´), 127.02 (C-2´and C-6´), 128.19 (C-3´and C-5´), 144.3 (C- 1´), 156.08 (C-6), 157.90 (C-2), 167.12 (C=O). 1H NMR ($CDCl_3$, 400 MHz) δ 1.284 (t, *J* = 7.0 Hz, 3H, $OCH_2C\mathit{H}_3$), 4.62 (s, 3H, $C\mathit{H}_3$), 3.911 (qd, *J* = 7.01, 1.39 Hz, 2H, OCH_2CH_3), 2.53 (s, 1H, H-4), 6.310 (br s, 2H, NH_2), 7.25-8.015 (m, 5H, H-Ar); LCMS (E+) for $C_{17}H_{18}N_2O_4$, found (M+) 314.10.

5. Conclusion

In summary, an efficient catalytic system has been utilized for the synthesis of 4H-pyran derivatives from a one-pot three component condensation of aldehydes, malanonitrile and ethylacetoacetate at 80 ºC. The present method offers significant advantages such as non-toxic, non-corrosive and simple reaction conditions. In addition, simply recovery and reusability of the catalyst makes the reaction successful under environmental friendly conditions.

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