Journal of Saudi Chemical Society (2020) **24**, 636–641

King Saud University

Journal of Saudi Chemical Society

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ORIGINAL ARTICLE

Visible light irradiation promoted catalyst-free and solvent-free synthesis of pyrano[2,3-*d*]pyrimidine scaffolds at room temperature

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Received 9 May 2020; revised 19 June 2020; accepted 27 June 2020
Available online 4 July 2020

KEYWORDS

Catalyst-free;
Solvent-free;
Pyrano[2,3-*d*]pyrimidine scaffolds;
Visible light irradiation;
Green procedure

Abstract A catalyst-free and solvent-free synthetic route for convenient one-pot synthesizing pyrano[2,3-*d*] pyrimidine scaffolds *through* Knoevenagel-Michael cyclocondensation is reported using visible light irradiation as a green promoter at room temperature based on green chemistry principles. Completing the reactions takes thoroughly less time while obtaining the products in outstanding yields. This green method includes the application of non-hazardous reaction circumstances, direct work-up without column chromatographic separation, catalyst-free, solvent-free, cost effective, simple synthesis, one-pot procedure, and high atom-economy.

1. Introduction

Over the previous years by increased demand for sustainable, environmentally friendly, and effective synthesis approaches in green chemistry, catalyst-free and solvent-free for preparing the organic mixtures has arisen as a key approach considering their low cost, simple workup, decreased pollution, and preventing the catalysts and solvents influence on sensitive substrates. In recent years, the development of the use of visible light irradiation due to its low cost, abundant reserves of this type of energy and its renewable capability as a powerful energy source in environmentally friendly synthesis of organic compounds has attracted the attention of green chemists [1]. Generally compact fluorescent lights (CFLs) and light emitting diodes (LEDs) are used as visible light source for different transformations.

Structures containing the pyran derivatives with various pharmacological features like Chk1 kinase inhibitory activity [2], anticancer [3], cardiotonic [4], anti-leukemic [5,6] and antitumor activities [7]. There are numerous approaches for synthesizing these compounds using various catalysts such as DABCO-based ionic liquids [8], L-proline [9], iron ore pellet [10], nano-sawdust-OSO_3H [11], Al-HMS-20 [12], TSA/$B(OH)_3$ [13], Mn/ZrO_2 [14], cellulose-based nanocomposite [15], DBA [16], TBAB [17], Fe_3O_4@SiO_2@$(CH_2)_3$-Urea-SO_3H/HCl [18], Et_3N-Ultrasonic [19], $ZnFe_2O_4$ nanoparticles [20], microwave [21], nickel nanoparticles [22], $CaHPO_4$ [23], Zn[(L)proline]$_2$ [24] and theophylline [25]. Each of the these methods has its own merits but some of these methods are limited in terms of the use of expensive catalysts, long reaction periods, low yields, harsh reaction conditions, tedious

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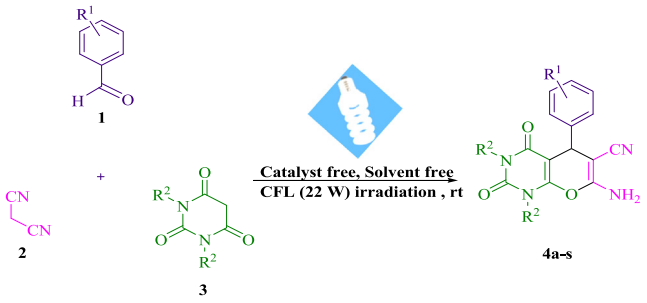
Peer review under responsibility of King Saud University.

Production and hosting by Elsevier

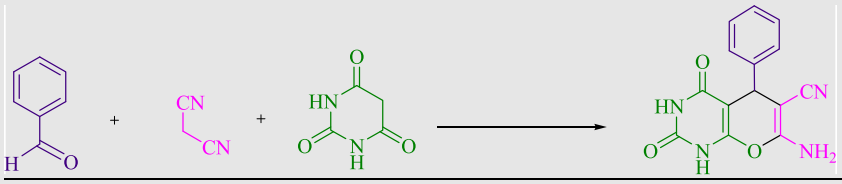
https://doi.org/10.1016/j.jscs.2020.06.006



Scheme 1 Synthesis of pyrano[2,3-*d*]pyrimidine scaffolds.

work-up and needing additional quantities of catalysts or reagents and hazardous or toxic catalysts with column chromatographic separation. Hence, finding the environmentally friendly and appropriate approaches for synthesizing this kind of compounds is vital. Since we partly aimed to develop green synthetic processes [26,27] and due to the above considerations, the search for eco-safe, simple and effective strategies capable of promoting organic reactions under green circumstances has attracted a huge deal of interest in producing pyrano[2,3-*d*] pyrimidine scaffolds. Hence, here catalyst-free and solvent-free environmentally friendly synthesis of pyrano [2,3-*d*] pyrimidine scaffolds are reported using aryl aldehyde derivatives (**1**, 1.0 mmol), malononitrile (**2**, 1.0 mmol) and barbituric acid/1,3-dimethylbarbituric acid (**3**, 1.0 mmol) are reported in the presence of CFL (22 W) irradiation as a green promoting media at room temperature *via* tandem Knoevenagel-Michael cyclocondensation provided the anticipated products in outstanding yields and short reaction times which might solve some cost problems in industry.

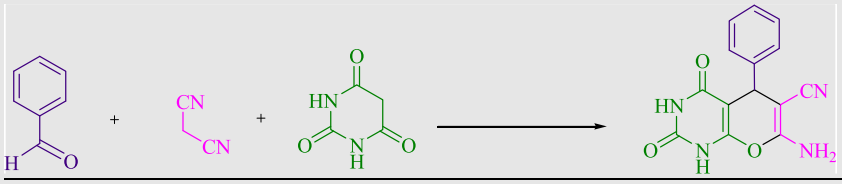
Table 1 Optimizing the reaction circumstance in the existence of various solvents on time and yield of **4a**.[a]



Entry	Solvent (3 mL)	Time (min)	Isolated Yields (%)
1	EtOH	25	63
2	H_2O	20	71
3	MeOH	35	56
4	H_2O/EtOH (1:1)	25	67
5	H_2O/EtOH (1:2)	30	59
6	DMF	55	40
7	**Solvent free**	**20**	**93**
8	DMSO	50	37
9	EtOAc	45	19
10	CH_3CN	55	45
11	THF	60	35
12	DCM	75	18

[a] Reaction conditions: benzaldehyde (1 mmol), malononitrile (1 mmol) and barbituric acid (1 mmol) in the presence of CFL (22 W) irradiation under catalyst-free circumstances at rt.

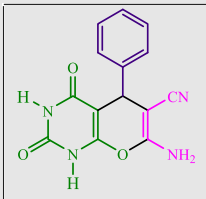
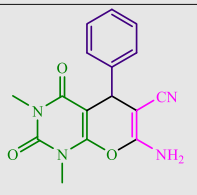
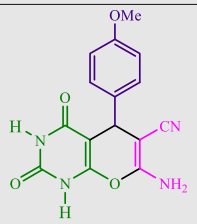
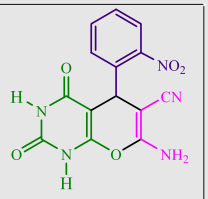
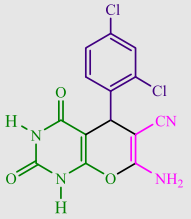
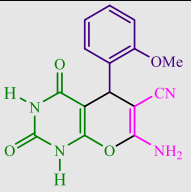
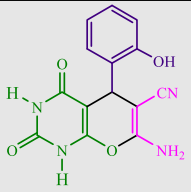
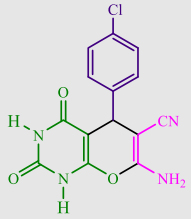
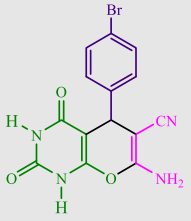
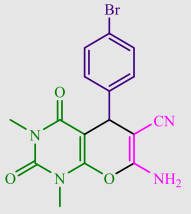
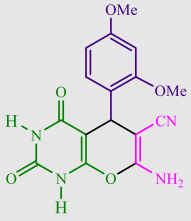
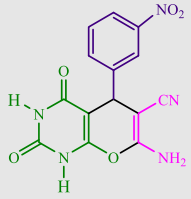
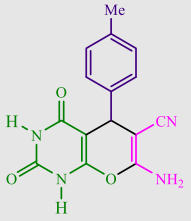
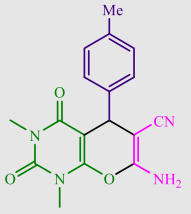
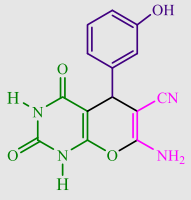
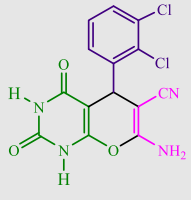
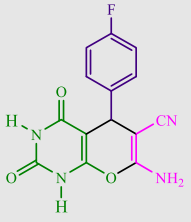
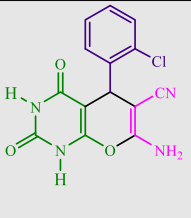
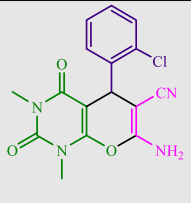
Table 2 Optimization of the CFL on the synthesis of **4a**.[a]



Entry	Reaction conditions	Time (min)	Isolated Yields (%)
1	CFL (18 W)	20	81
2	CFL (20 W)	20	89
3	**CFL (22 W)**	**20**	**93**
4	CFL (23 W)	20	93
5	CFL (32 W)	20	93

[a] Reaction conditions: benzaldehyde (1 mmol), malononitrile (1 mmol) and barbituric acid (1 mmol) in the presence of CFL irradiation under catalyst and solvent free conditions at rt.

Table 3 Catalyst and solvent free synthesis of pyrano[2,3-*d*]pyrimidine scaffolds.

 **4a** (20 min, 93%) Mp. 225-227 °C Lit. 224-225 °C [8]	 **4b** (25 min, 91%) Mp. 236-238 °C Lit. 237-238 °C [13]	 **4c** (25 min, 86%) Mp. 274-276 °C Lit. 272-274 °C [11]	 **4d** (20 min, 94%) Mp. 252-254 °C Lit. 254-256 °C [8]
 **4e** (35 min, 83%) Mp. 239-241 °C Lit. 241-242 °C [9]	 **4f** (20 min, 91%) Mp. 228-230 °C Lit. 230 °C [24]	 **4g** (30 min, 86%) Mp. 170-172 °C Lit. 169-170 °C [10]	 **4h** (35 min, 85%) Mp. 235-237 °C Lit. 235-237 °C [13]
 **4i** (35 min, 81%) Mp. 241-243 °C Lit. 240-245 °C [10]	 **4j** (35 min, 84%) Mp. 208-210 °C Lit. 210-211 °C [14]	 **4k** (25 min, 88%) Mp. 226-228 °C Lit. 227-228 °C [10]	 **4l** (20 min, 90%) Mp. 260-262 °C Lit. 259-261 °C [11]
 **4m** (20 min, 95%) Mp. 224-226 °C Lit. 226 °C [13]	 **4n** (25 min, 93%) Mp. 207-208 °C Lit. 205-207 °C [13]	 **4o** (30 min, 84%) Mp. 159-161 °C Lit. 158-160 °C [9]	 **4p** (35 min, 87%) Mp. 242-244 °C Lit. 243-245 °C [17]
 **4q** (20 min, 94%) Mp. 257-259 °C Lit. 256-260 °C [8]	 **4r** (25 min, 86%) Mp. 213-215 °C Lit. 211-214 °C [13]	 **4s** (30 min, 89%) Mp. 244-246 °C Lit. 243-244 °C [20]	

2. Experimental

2.1. General

Utilizing an Electro thermal 9100 device, all compounds' melting points were found. Moreover, recording nuclear magnetic resonance, ^{1}H NMR spectra was carried out on a Bruker DRX-400 and Bruker DRX-300 Avance tool with DMSO d_6 as solvent. All solvents and reagents were bought from Acros, Merck, and Fluka chemical companies and were utilized with no additional purification.

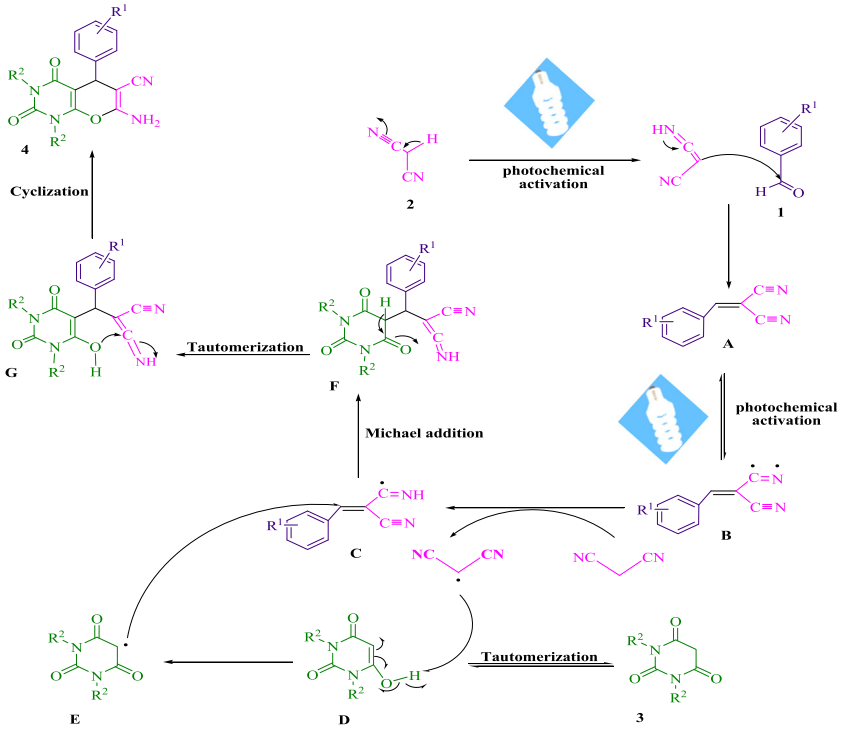
2.2. Overall process of preparing (*4a-s*)

A mixture of aryl aldehyde derivatives (**1**, 1.0 mmol), malononitrile (**2**, 1.0 mmol) and barbituric acid/1,3-dimethylbarbituric acid (**3**, 1.0 mmol) was reacted in the presence of CFL (22 W) irradiation as a green promoter under catalyst and solvent free conditions at room temperature (Scheme 1). The reaction progress was monitored by TLC utilizing ethyl acetate–*n*-hexane (2:7) as an eluent. After completing the reaction, the achieved solid was filtered, rinsed with water and the crude solid was recrystallized from ethanol to provide the pure material without requiring more purification. Comparing the spectroscopic information, the products were categorized (^{1}HNMR). Supporting Information associated with this article can be found, in the online version.

3. Results and discussion

Initially, the reaction between benzaldehyde (1 mmol), malononitrile (1 mmol) and barbituric acid (1 mmol) was studied in various solvents under catalyst-free circumstances in the presence of compact florescent lamp (CFL) (22 W) irradiation at room temperature and the outcomes are provided in Table 1. Based on Table 1, only a small quantity of products was found in EtOH, H_2O, MeOH, H_2O/EtOH (1:1), H_2O/EtOH (1:2), DMF, DMSO, EtOAc, CH_3CN, THF and DCM. A great enhancement was found under solvent-free conditions (Table 1, entry 7). An outstanding yield of 93% was created by using of CFL (22 W) irradiation with no further catalyst under solvent-free circumstances for 20 min (Table 1, entry 7). Also, the optimized conditions were determined by varying the intensities of CFL (18 W, 20 W, 22 W, 23 W and 32 W) irradiation. Based on Table 2, the best outcomes were found in the presence of compact florescent lamp (CFL) (22 W) irradiation (Table 2, entry 3). As observed in Table 3 and Scheme 1, it was indicated that this technique can work with various substrates.

Scheme 2 shows the suggested mechanism for synthesizing pyrano[2,3-*d*]pyrimidine scaffolds. The reaction was encouraged by creating an inclusion the radical intermediate ylidenemalononitrile (cyano olefin) **B** was readily created in situ from Knoevenagel condensation between arylaldehyde **1** and active methylene compound **2** in the presence of visible light irradiation. This can be demonstrated by the arylaldehydes' steric influences on the reaction effectiveness (Table 3). Intermediate **B** absorbs one hydrogen from methylene malononitrile, thereby converting malononitrile to a radical malononitrile, consequently, it consists of intermediate **C**. Then, malononitrile radical absorbs one hydrogen from form **3** and converts it to form intermediate **E**. Intermediate **E** attacks to intermediate **C** as Michael acceptor to give **F** that after tautomerizing and cyclizing affords the target products **4**.



Scheme 2 Proposed mechanism for synthesizing pyrano[2,3-*d*]pyrimidine scaffolds.

4. Conclusion

In conclusion, in the present work, it was demonstrated that visible light irradiation, can be used as a green promoter for catalyst-free and solvent-free one-pot synthesizing pyrano [2,3-*d*]pyrimidine scaffolds. Use of inexpensive initiating substances, catalyst-free, solvent-free, time-saving aspects of the reaction, excellent yields, the application of non-hazardous reaction circumstances, direct work-up without column chromatographic separation, convenient and expedient procedure are the notable advantages of this green and simple protocol. However, the use of CFL irradiation as a green and low-cost promoting media makes this procedure greatly advantageous in addressing the industrial requirements and environmental worries.

Conflict of interest

There is no conflict of interest.

Acknowledgements

We gratefully acknowledge financial support from the Research council of the Apadana Institute of Higher Education.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.jscs.2020.06.006.

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