# Green protocol for the synthesis of 1,8-dioxo-decahydroacridines *via* Hantzsch condensation using citric acid as organocatalyst

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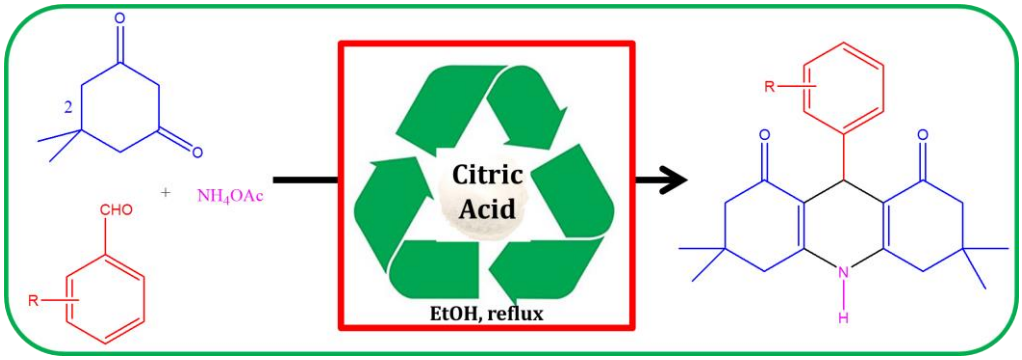
**Graphical Abstract:**




**Abstract:**

Herein we describe a clean and sustainable, one-pot, multi-component protocol for the synthesis of 1, 8-dioxo-decahydroacridines *via* Hantzsch condensation of cyclic 1, 3-dicarbonyl compound and $NH_4OAc$ with diverse aryl aldehydes using citric acid as an inexpensive green additive in ecological safe solvent. The utilization of cheaper, and safer catalyst, cleaner reaction profile, straightforward work-up procedure and good to excellent yields of the desired product are the noteworthy aspects of this method.

**Keywords:** Citric Acid, Organocatalysts, MCRs, 1,8-dioxo-decahydroacridines.

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**Introduction:**

As our environment is endowed by nature, needs to be protected from growing production of large amounts of waste and toxic by-products that sequentially leads to chemical pollution. Therefore, synthetic chemists have earned tremendous interest to develop relatively safer technologies which play a vital role in green chemistry. By concerning above fact, establishing newer chemical transformations should satisfy green principles such as non-toxic, non-flammability, eco-friendly medium, and separation as well as recycling of the catalysts. Since, from the last decade, desperate efforts were made towards the design and synthesis of an environmental friendly method with respect to reagents, catalysts and solvents that could be easily biodegradable [1, 2]. Multi-component reactions (MCRs) strategies have been widely used in the convergent synthesis of complex organic entities. The MCRs uses simple and easily available starting materials and provides high atom economy and high selectivity. It is one of the important synthetic tool available to achieve both economic and environmental friendly goals. Therefore, the synthesis of heterocyclic compounds using significant bioactivities with MCR support is an immensely important pursuit in organic synthesis.

Synthesis of acridines is an enormous area of interest due to polyfunctionalized groups with a wide range of biological activities [3]. Among them, 1,8-dioxo-decahydroacridines is an important class of aza-heterocycles in which a phenyl substituted pyridine ring is fused with two cyclohexanone rings. These structures contain 1, 4-dihydropyridine (1,4-DHP) as a parent core which acts as fluorescent probes in Bioanalytical Chemistry [4] and also used as potential drug candidates for the treatment of cardiovascular diseases. Some of these compounds are used in dye sensitized solar cells and in the preparation of blue light-emitting devices [5-6]. In addition, 1,8-dioxo-decahydroacridines have been widely employed as DNA intercalator, SIRT1 inhibitors, calcium and potassium channel modulators [7-8]. Several studies reveal that these heterocycles exhibits numerous medicinal applications which include antitumor, calcium channel blockers, antileukimic, antifungal, anticancer, anti-atherosclerotic, and bronchodilator [9-13]. These are also used as laser dyes, chemosensors and initiators in the photo polymerization process. These derivatives are highly important due to their structural similarities with coenzyme nicotinamide adenine dinucleotide (NADH), which play an important role in biological systems.

The most common route for the synthesis of 1,8-dioxo-decahydroacridines includes condensation of diverse range of aryl aldehydes, dimedone or cyclic 1, 3-dicarbonyl compounds with various nitrogen sources such as ammonium acetate, urea, ammonium hydroxide, ammonium bicarbonate, and hydroxylamine [14-18]. A variety of catalysts such as sulfonated polyethylene glycol (PEG-$OSO_3H$), Silzic ($SiO_2$-$ZnCl_2$), silica boron-

sulfuric acid, Proline, $Zn(OAc)_2$, nano nickel cobalt ferrite ($Ni_{0.5}Co_{0.5}Fe_2O_4$), Carbon based solid acid, Bronsted acidic imidazolium salts, Ascorbic acid, Acetic acid, Tris(pentafluorophenyl)borane/$B(C_6F_5)_3$, Silica-Supported polyphosphoric acid, ammonium chloride, Silica-supported preyssler nanoparticles [19-32] have been employed to accomplish this reaction. However, most of these reported methods have certain drawbacks such as use of toxic and corrosive solvent, use of expensive reagents, tedious preparation of catalyst, prolonged reaction times, complicated work-up procedure, harsh reaction condition and low yields of the anticipated product. Therefore, a great demand still exists for utilization of an efficient, simple and eco-friendly process especially by using chiefly available organocatalysts.

The citric acid is a weak organic acid with the formula $C_6H_8O_7$ and was initially isolated and crystallized from the lemon juice in 1784. It has been found as a natural preservative and antioxidant in a variety of citrus fruits like orange, lemon, pineapple, peach and pear. This organic acid is almost widespread intermediate product of metabolism. Furthermore, citric acid is also used for the preparation of salt and form complex with many metals such as magnesium, iron, manganese, calcium and copper. Due to its widespread presence, non-toxic nature and chemical stability, it has been mostly used as sequestering in industrial process, as a softener in detergent, as an anticoagulant blood preservative and as a complexing agent in metal treatment. Other industrial and pharmaceutical applications of citric acid include an antioxidant in cosmetics, cleaning, buffering. Despite its huge industrial and pharmaceutical importance, only a few reports exemplify its catalytic application in organic synthesis.

Herein, in continuouation of our research for the development of green and sustainable methodologies for the synthesis of bioactive heterocyclic scaffolds [33-37], herein we wish to report green protocol for the synthesis of 1,8-dioxo-decahydroacridines from one-pot, multi-component reaction of dimedone and $NH_4OAc$ with range of aryl aldehydes in the presence of readily available citric acid as organocatalyst in ethanol at reflux.

**Results and Discussion:**

In order to optimize the various reaction conditions, such as effect of solvents and catalyst, the reaction of benzaldehyde (1 mmol), dimedone (2 mmol), and $NH_4OAc$ (1.2 mmol) was selected as a template reaction in presence of citric acid (2 mmol) as organocatalyst (**Scheme 1**).

In preliminary experiment, the reaction was carried out in various solvents such as water, ethanol, ethanol:water, methanol, acetonitrile, dichloroethane and toluene at reflux and the results are depicted in **Table 1**. The best result was obtained in ethanol providing an excellent yield (89 %) of the expected product in 150 min. (**Table 1, entry 2**). Though the reaction proceeded in water (**Table 1, entry 1**) ethanol:water (1:1),

methanol, acetonitrile, dichloroethane or toluene, the yield of the desired product was moderate in these solvents with prolonged reaction time (**Table 1, entries 3-7**).

Next, we optimized the amount of by varying the amount of citric acid and the results are documented in **Table 2**. It was found that the quantity of catalyst shows crucial role in yield of the desired product. No product was formed without catalyst (**Table 2**, **entry 1**). When the quantity of citric was increased, the yield of desired product was significantly increased (**Table 2**, **entries 1-3**). It was observed that the maximum yield was obtained in the presence of 2.0 mmol catalyst (**Table 2, entries 1-4**). Further increase in the amount of citric acid, did not have profound influence on the yield as well as reaction time of anticipated product (**Table 2**, **entry 5**).

After optimization of the reaction conditions, we evaluated the scope and generality of present protocol by reacting the variety of substituted aryl aldehydes, dimedone and $NH_4OAc$ in the presence of catalyst (2.0 mmol) in ethanol at reflux, and results are demonstrated in **Table 3**. Gratifyingly, aromatic aldehydes with varied structural and electronic nature undergo smooth conversion affording the expected 1,8-dioxodecahydroacridines in good to excellent yields. It was observed that, the electronic nature of the substituents on aldehyde had slender influence on the yield of the anticipated 1,8-dioxo-decahydroacridines. Furthermore, aromatic hetrocyclic aldehyde also showed good conversion with 81 % yield **(Table 2, entry 10)**. However, the reaction of aliphatic aldehyde showed low yield with prolonged reaction time (**Table 3**, **entry 11**).

The recyclability of the catalyst was checked for model reactions and the results are depicted in Fig. 1. After completion of reaction, the product was recovered by filtration and the filtrate was extensively extracted with chloroform. The catalyst present in aqueous layer was then dried under vacuum before performing the reusability test. The recovered citric acid could be used in the next reaction cycle. The results indicated that the catalyst could be reused for at least three runs with a modest change in the yield of product.

The plausible mechanism of the formation 1,8-dioxodecahydroacridines is conceptualized in **Fig. 2**. First the citric acid promotes enolization of 1, 3-diketone **(2)**, which reacts with aldehyde (**1**) to form the Knoevengel adduct (**5**). The adduct (**5**), underwent Michael addition with second molecule of dimedone to yield intermediate **(6)**. The intermediate **(6)** then reacts with ammonium acetate to yield amine **(7)** *via* imine intermediate. The resulting imine **(7)** undergo intramolecular cyclization followed by dehydration to yield the desired product **(4)**.

In order to compare the efficiency and the advantages of citric acid with reported catalysts, we have tabulated several results in the synthesis of 1,8-dioxo-decahydroacridines in **Table 4**. It demonstate that, citric acid is effective in terms of yield as well as reaction times than reported catalysts.

**Experimental:**

All the chemicals were obtained from local supplier and used without further purification. The melting points were determined by the open capillary method and are uncorrected. FT-IR spectra were measured on Bruker ALPHA FT-IR spectrometer. The NMR spectra were recorded on Bruker AC (400 MHz for $^{1}$H NMR and 75 MHz for $^{13}$C NMR) spectrometer using TMS as an internal standard. The chemical shifts (δ) are expressed in parts per million.

**General procedure for the synthesis of 1, 8-dioxo-decahydroacridine derivatives (4a-k)**:

A mixture of aromatic aldehyde (1 mmol), dimedone (2 mmol), $NH_4OAc$ (1.2 mmol) and citric acid (2 mmol) was stirred in ethanol (4 mL) at reflux. After completion of the reactions as monitored by TLC, the reaction mixture was allowed to cool at room temperature, poured into ice-cold water (20 ml) and stirred continuously for 10 minutes. The resultant solid was filtered, washed with cold water and then dried. The crude solid was recrystallized in ethanol, and characterized by spectroscopic techniques.

**Spectral data:**

**3, 3, 6, 6-Tetramethyl-9-(phenyl)-1,8-dioxo-decahydroacridine (Table 3, entry 1):** Yield 89%, Mp: 193-195°C, (192-194°C)[27]; $^{1}$H NMR (400 MHz, $CDCl_3$) δ (ppm): 7.45 (s, 1H, NH), 7.65-7.10 (m, 5H, Ar-H), 5.15 (s, 1H, CH), 2.42-2.17 (m, 8H, $CH_2$), 1.12 (s, 6H, $CH_3$), 0.98 (s, 6H, $CH_3$); $^{13}$C NMR (75 MHz, $CDCl_3$) δ: 193.8, 148.3, 136.4, 126.8, 128.1, 126.8, 114.3, 51.1, 41.3, 34.2, 33.6, 29.9, 27.6; IR (KBr, $cm^{-1}$): 3275, 2959, 1631, 1368.

**3, 3, 6, 6-Tetramethyl-9-(4-chlorophenyl)-1,8-dioxo-decahydroacridine (Table 3, entry 3):** Yield 87%, Mp: 294-296 °C, (295-297°C)[27]; $^{1}$H NMR (400 MHz, $CDCl_3$) δ (ppm): 7.66 (s, 1H, NH), 7.48 (d, *J* = 9 Hz, 2H, Ar-H), 7.38 (d, *J* = 9 Hz, 2H, Ar-H), 5.16 (s, 1H, CH), 2.30-2.13 (m, 8H, $CH_2$), 1.17 (s, 6H, $CH_3$), 0.95 (s, 6H, $CH_3$); $^{13}$C NMR (75 MHz, $CDCl_3$) δ: 196.1, 150.1, 144.9, 132.0, 130.1, 127.9, 113.2, 51.5, 41.1, 34.4, 33.6, 30.5, 26.8; IR (KBr, $cm^{-1}$): 3436, 2954, 1647, 1612, 1365.

**3, 3, 6, 6-Tetramethyl-9-(4-cynophenyl)-1, 8-dioxo-decahydroacridine (Table 3, entry 5):** Yield 74%, Mp: <300°C, (<300°C)[35]; $^{1}$H NMR (400 MHz, $CDCl_3$) δ (ppm): 7.52 (d, *J* = 8.3 Hz, 2H, Ar-H), 7.46 (d, *J* = 8.3 Hz,

2H, Ar-H), 5.11 (s, 1H, CH), 5.91 (s, 1H, NH), 2.43 (d, $J$ = 16.5 Hz, 2H), 2.26 (d, $J$ = 16.5 Hz, 2H), 2.28 (d, $J$ = 16.5 Hz, 2H), 2.19 (d, $J$ = 16.5 Hz, 2H), 1.13 (s, 6H, $CH_3$), 0.96 (s, 6H, $CH_3$); $^{13}$C NMR (75 MHz, $CDCl_3$) δ: 194.8, 148.7, 146.1, 130.2, 129.5, 120.7, 112.9, 50.4, 32.9, 32.0, 30.5, 29.1, 26.6; ); IR (KBr, $cm^{-1}$): 3321, 2955, 2233, 1631, 1491

**3, 3, 6, 6-Tetramethyl-9-(4-methoxyphenyl)-1,8-dioxo-decahydroacridine (Table 3, entry 7):** Yield 90%, Mp: 270-272°C, (270-272°C)[27]; $^1$H NMR (400 MHz, $CDCl_3$) δ (ppm): 8.82 (s, 1H, NH), 7.12 (d, $J$ = 8.6 Hz, 2H, Ar-H), 6.64 (d, $J$ = 8.6 Hz, 2H, Ar-H), 4.83(s, 1H, CH), 3.65 (s, 3H, O-$CH_3$), 2.35 (d, $J$ = 17.0 Hz, 2H), 2.24 (d, $J$ = 16.3 Hz, 2H), 2.10 (d, $J$ =15.9 Hz, 2H), 1.98 (d, $J$ = 16.2 Hz, 2H), 1.01 (s, 6H, $CH_3$), 0.98 (s, 6H, $CH_3$); $^{13}$C NMR (75 MHz, $CDCl_3$) δ: 192.4, 154.6, 149.1, 138.9, 128.6, 112.8, 111.8, 54.6, 51.8, 32.2, 30.3, 28.9, 26.5.; IR (KBr, $cm^{-1}$): 3448, 2954, 1643, 1612, 1365, 1141.

**3, 3, 6, 6-Tetramethyl-9-(4-methylphenyl)-1,8-dioxo-decahydroacridine (Table 3, entry 8):** Yield 79%, Mp: 272-274°C, (271-273°C)[27]; $^1$H NMR (400 MHz, $CDCl_3$) δ (ppm): 11.9 (s, 1H, NH), 7.09 (d, $J$ = 9 Hz, 2H, Ar-H), 6.98 (d, $J$ = 9 Hz, 2H, Ar-H), 5.50 (s, 1H, CH), 2.29 (s, 3H, $CH_3$), 2.19-2.47 (m, 8H, $CH_2$), 1.22 (s, 6H, $CH_3$), 1.09 (s, 6H, $CH_3$); $^{13}$C NMR (75 MHz, $CDCl_3$) δ: 190.6, 135.5, 135.1, 129.3, 128.9, 126.5, 117.7, 47.2, 46.6, 32.5, 31.3, 29.8, 27.4; 20.9; IR (KBr, $cm^{-1}$) : 2958, 2877, 1569, 1369.

**Conclusion:**

In summary, we reported simple and economically viable one-pot method for the synthesis of 1,8-dioxo-decahydroacridine derivatives *via* Hantzsch condensation of dimedone, $NH_4OAc$ with various aromatic aldehydes using commercially available, inexpensive citric acid as a greenorgano catalyst. Some important advantages of this method are use of inexpensive reagents, absence of toxic effluents, use of green solvent, easy work-up. In addition, the catalyst could be reused for at least three runs with a modest change in the product yield.

**References:**


[1] Liu, P., Hao, J. W., Mo, L. P. and Zhang, Z. H., Recent advances in the application of deep eutectic solvents as sustainable media as well as catalysts in organic reactions. *RSC Adv.*, 2015, **5**, 48675-48704.

[2] Vladu, M. I., "Green" electronics: biodegradable and biocompatible materials and devices for sustainable future. *Chem. Soc. Rev.*, 2014, 43, 588-610.

[3] Khedkar, S. A. and Auti, P. B., 1, 4-Dihydropyridines: A class of pharmacologically important molecules. *Mini. Rev. Med. Chem.*, 2014, **14**, 282-290.

[4] Huang, C., Yan, S. J., Li, Y. M., Huang, R. and Lin, J., Synthesis of polyhalo acridones as pH-sensitive fluorescence probes. *Bioorg. Med. Chem. Lett.*, 2010, *20*, 4665-4669.

[5] Anandan, S., Madhavan, J., Maruthamuthu, P., Raghukumar, V. and Ramakrishnan, V. T., Synthesis and characterization of naphthyridine and acridinedione ligands coordinated ruthenium (II) complexes and their applications in dye-sensitized solar cells. *Sol. Energy Mater. Sol. Cells*, 2004, **81**, 419-428.

[6] Islam, A., Murugan, P., Hwang, K. C. and Cheng, C. H., Blue light-emitting devices based on 1,8-acridinedione derivatives. *Synth. Met.*, 2003, 139, 347-353.

[7] Rajendran, A. and Nair, B. U., Unprecedented dual binding behaviour of acridine group of dye: A combined experimental and theoretical investigation for the development of anticancer chemotherapeutic agents. *Biochim. Biophys. Acta. Gen. Subj.*, 2006, **1760**, 1794-1801.

[8] Alvala, M., Bhatnagar, S., Ravi, A., Jeankumar, V. U., Manjashetty, T. H., Yogeeswari, P. and Sriram, D., Novel acridinedione derivatives: Design, synthesis, SIRT1 enzyme and tumor cell growth inhibition studies. *Bioorg. Med. Chem. Lett.*, 2012, **22**, 3256-3260.

[9] Cholody, W. M., Horowska, B., Paradziej-Lukowicz, J., Martelli, S. and Konopa, J., Structure-activity relationship for antineoplastic imidazoacridinones: Synthesis and antileukemic activity in *Vivo. J. Med. Chem.*, 1996, **39**, 1028-1032.

[10] Mikata, Y., Yokoyama, M., Mogami, K., Kato, M., Okura, I., Chikira, M. and Yano, S., Intercalator-linked cisplatin: synthesis and antitumor activity of *cis*-dichloroplatinum(II) complexes connected to acridine and phenylquinolines by one methylene chain. *Inorg. Chem. Acta.*, 1998, **279**, 51-57.

[11] Lacasagne, A., Buu-Ho, N. P., Daudel, R. and Zajdela, F., The relation between carcinogenic activity and the physical and chemical properties of angular benzacridines. *Adv. Cancer Res.*, 1956, **4**, 315-369.

[12] Berkan, O., Sarac, B., Simsek, R., Yildirim, S., Sariogli, Y. and Safak, C., Vasorelaxing properties of some phenylacridine type potassium channel openers in isolated rabbit thoracic arteries. *Eur. J. Med.*, 2002, **37**, 519-523.

[13] Wainwright, M. J. J., Acridine-a neglected antibacterial chromophore. *Antimicrob. Chemother.*, 2001, **47**, 1-13.

[14] Suarez, M., Loupy, A., Salfran, E., Moran, L. and Rolando, E., Synthesis of decahydroacridines under microwaves using ammonium acetate supported on alumina. *Heterocycles*, 1999, **51**, 21-27.

[15] Bakibaev, A. A., Fillimonov, V. D. and Nevgodova, E. S., Ureas in the organic synthesis. Part 6. reactions of 1, 3-dicarbonyls with azomethines and urea in DMSO as a method for the synthesis of arylacridines. *Zh. Org. Khim.*, 1991, **27**, 1512-1519.

[16] Martin, N., Quinteiro, M., Seoane, C., Soto, J. L., Mora, A., Suarez, M., Ochoa, E. and Morales, A., Synthesis and conformational study of acridine derivatives related to 1,4-dihydropyridines. *J. Heterocyclic Chem.*, 1995, **32**, 235-238

[17] Tu, S. J., Lu, Z., Shi, D., Yao, C., Gao, Y. and Guo, C., A convenient synthesis Of 9-aryl-3,3,6,6-tetramethyl-1,2,3,4,5,6,7,8,9,10-decahydroacridine-1,8-diones under microwave irradiation without solvent. *Synth. Commun.*, 2002, **32**, 2181-2185.

[18] Tu, S., Fang, F., Zhu, S., Li, T., Zhang, X. and Zhuang, Q., One-Pot synthesis of a novel compound *N*-hydroxydecahydroacridine under microwave irradiation. *J. Heterocyclic Chem.*, 2004, **41**, 767-770.

[19] Vekariya, R. H. and Patel, H. D., Sulfonated polyethylene glycol (PEG-$OSO_3H$) as a polymer supported biodegradable and recyclable catalyst in green organic synthesis: recent advances. *RSC Adv.*, 2015, **5**, 49006-49030.

[20] Soliman, H. A., Mubarak, A. Y., EL-Mekabati, A. and Elmorsy, S. S., $SiO_2/ZnCl_2$-catalyzed heterocyclic synthesis: Green, rapid and efficient one-pot synthesis of 14-*H*-dibenzo [*a, j*]xanthenes, 1,8-dioxo-octahydroxanthenes and 1,8-dioxo-decahydroacridines under solvent-free conditions *Chem. Sci. Trans.*, 2014, **3**, 819-825.

[21] Khalafi-Nezhad, A., Panahi, F., Mohammadi, S. and Foroughi, H. O., A green and efficient procedure for one-pot synthesis of xanthenes and acridines using silica boron-sulfuric acid nanoparticles (SBSANs) as a solid Lewis-protic acid. *J. Iran. Chem. Soc.*, 2013, **10**, 189-200.

[22] Venkatesan, K., Pujari, S. S. and Srinivasan, K. V., Proline-catalyzed simple and efficient synthesis of 1,8-dioxo-decahydroacridines in aqueous ethanol medium. *Synth. Commun.*, 2009, **1**, 228-241.

[23] Saeed, B., Fatemeh, C., Fatemeh, D. and Hamid Reza, B., One-pot synthesis of 1,8-dioxo-decahydroacridine derivatives in aqueous media. *Chin. J. Chem.*, 2009, **27**, 1953-1956.

[24] Maripi, S., Korupolu, R. B. and Madasu, S. B., Nano nickel-cobalt ferrite catalysed one-pot multi-component synthesis of xanthenediones and acridinediones. *Green and Sustainable Chemistry*, 2017, **7**, 70-84.

[25] Davoodnia, A., Khojastehnezhad, A. and Tavakoli-Hoseini, N., Carbon-based solid acid as an efficient and reusable catalyst for the synthesis of 1,8-dioxodecahydroacridines under solvent-free conditions. *Bull. Korean. Chem. Soc.*, 2011, **32**, 2243-2248.

[26] Shen, W., Wang, L. M., Tian, H., Tang, J. and Yu, J. J., Brønsted acidic imidazolium salts containing perfluoroalkyl tails catalyzed one-pot synthesis of 1,8-dioxo-decahydroacridines in water. *J. Fluorine Chem.,* 2009, **130**, 522-527.

[27] Sehout, I., Boulcina, R., Boumoud, B., Boumoud, T. and Debache, A., Solvent-free synthesis of polyhydroquinoline and 1,8-dioxodecahydroacridine derivatives through the Hantzsch reaction catalyzed by a natural organic acid: A green method. *Synth. Commun.*, 2017, **47**, 1185-1191.

[28] Gomez, S. M. M., Alzate-Sanchez, D. M., Rodriguez-Cordoba, W., Sierra, C. A. and Ochoa-Puentes, C., Competitive one-pot reactions: simultaneous synthesis of decahydroacridine-1,8-diones and 1,8-dioxo-octahydroxanthenes and photophysical characterization. *Synth. Commun.*, 2014, **44**, 648-659.

[29] Chandrasekhar, S., Rao, Y. S., Sreelakshmi, L., Mahipal, B. and Reddy, C. R., Tris(pentafluorophenyl)borane-catalyzed three-component reaction for the synthesis of 1,8-dioxodecahydroacridines under solvent-free conditions. *Synthesis.*, 2008, **11**, 1737-1740.

[30] Moeinpour, F. and Khojastehnezhad, A., An efficient one-pot synthesis of 1,8-dioxodecahydroacridines using silica-supported polyphosphoric acid(PPA-$SiO_2$) under solvent-free conditions. *E-J. Chem.*, 2012, **9**, 504-509.

[31] Banerjee, B. and Brahmachari, G., Ammonium chloride catalysed one-pot multicomponent synthesis of 1,8-dioxo-octahydroxanthenes and *N*-aryl-1,8-dioxodecahydroacridines under solvent free conditions. *J. Chem. Res.*, 2014, **38**, 745-764.

[32] Javid, A., Khojastehnezhad, A., Heravi, M. and Bamoharram, F. F., Silica-supported preyssler nanoparticles catalyzed simple and efficient One-Pot synthesis of 1,8-dioxodecahydroacridines in aqueous media. *Synth. React. Inorg. Met. Org. Chem.*, 2012, **42**, 14-17.

[33] Karhale, S., Patil, K., Bhenki, C., Rashinkar, G. and Helavi, V., Zirconocene catalyzed synthesis of 2-substituted benzimidazole derivatives. *Res. Chem. Intermed.*, 2016, **42**, 7257-7268.

[34] Karhale, S., Survase, D., Bhat, R., Ubale, P. and Helavi, V., A practical and green protocol for the synthesis of 2,3-dihydroquinazolin-4(*1H*)-ones using oxalic acid as organocatalyst. *Res. Chem. Intermed.*, 2017, **43**, 3915-3924.

[35] Karhale, S., Patil, M., Rashinkar, G. and Helavi, V., Green and cost effective protocol for the synthesis of 1,8-dioxo-octahydroxanthenes and 1,8-dioxo-decahydroacridines by using sawdust sulphonic acid. *Res. Chem. Intermed.*, 2017, **43**, 7073-7086.

[36] Karhale, S., Bhenki, C., Rashinkar, G. and Helavi, V., Covalently anchored sulfamic acid on cellulose as heterogeneous solid acid catalyst for the synthesis of structurally symmetrical and unsymmetrical 1,4-dihydropyridine derivatives. *New J. Chem.*, 2017, **41**, 5133- 5141.

[37] Patil, M. A., Ubale, P. A., Karhale, S. S. and Helavi, V. B., Lemon Juice: an Environmentally benign catalyst for synthesis of benzothiazoles and benzoxazole derivatives in aqueous medium. *Der Chemica Sinica*, 2017, **8**, 198-205.

**Scheme1.** Citric acid catalyzed multi-component synthesis of 1, 8-dioxo-decahydroacridines.

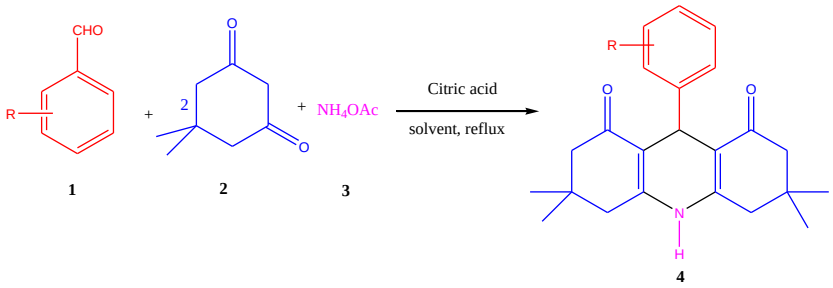



**Table 1:** Optimization of solvent for synthesis of 1, 8-dioxo-decahydroacridine.[a]

| Entry | Solvent | Time (min) | Yield[b] (%) |
|---|---|---|---|
| 1 | Water | 240 | 70 |
| 2 | Ethanol | 150 | 89 |
| 3 | Ethanol:Water | 200 | 80 |
| 4 | Methanol | 300 | 72 |
| 5 | Acetonitrile | 360 | 68 |
| 6 | Dichloroethane | 400 | 55 |
| 7 | Toulene | 390 | 65 |

[a]**Reaction conditions:** Benzaldehyde (1 mmol), dimedone (2 mmol), $NH_4OAc$ (1.5 mmol) and citric acid monohydrate (2 mmol), solvent (4 mL) at reflux.
[b]Isolated yields.

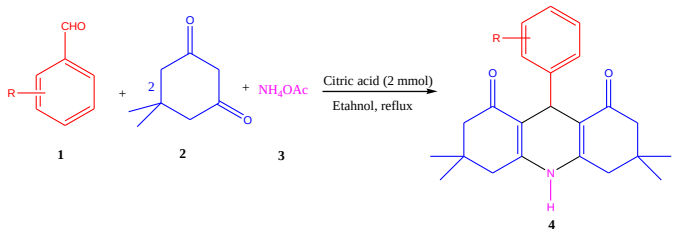
**Table 2:** Optimization of the amount catalyst for the synthesis of 1, 8-dioxo-decahydroacridine.[a]

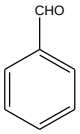
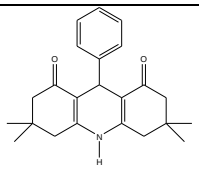
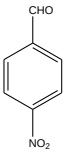
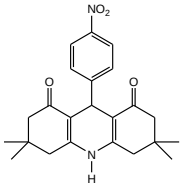
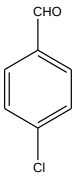
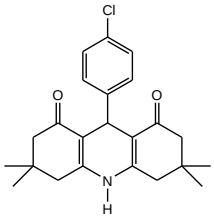
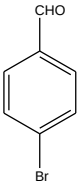
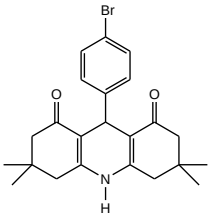
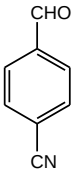
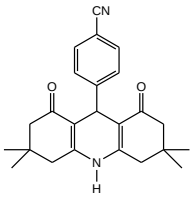
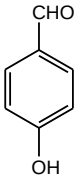
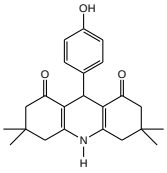
| Entry | Catalyst (mmol) | Time (min) | Yield[b] (%) |
|---|---|---|---|
| 1 | - | 150 | - |
| 2 | 1 | 150 | 68 |
| 3 | 1.5 | 150 | 78 |
| 4 | 2.0 | 150 | 89 |
| 5 | 3.0 | 150 | 89 |

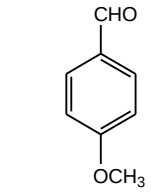
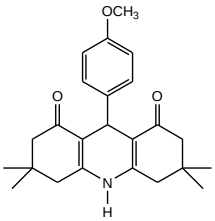
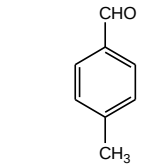
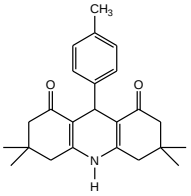
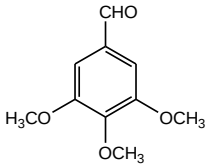
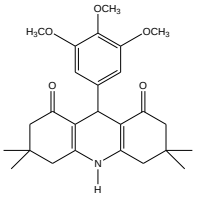
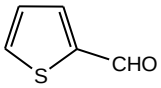
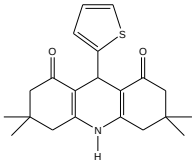
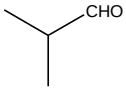
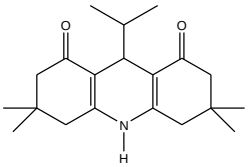
[a]**Reaction conditions:** Benzaldehyde (1 mmol), dimedone (2 mmol), $NH_4OAc$ (1.5 mmol) and citric acid monohydrate (1-3 mmol), ethanol (4 mL) at reflux.

[b]Isolated yields.

**Table 3:** Synthesis of 1, 8-dioxo-decahydroacridine derivatives.[a]




| Entry | Aromatic aldehyde | Product | Time (min) | Yield[b] (%) |
|---|---|---|---|---|
| 1 |  |  | 150 | 89 |
| 2 |  |  | 100 | 90 |
| 3 |  |  | 160 | 87 |
| 4 |  |  | 180 | 85 |
| 5 |  |  | 200 | 74 |
| 6 |  |  | 160 | 83 |

| | | | | |
|---|---|---|---|---|
| 7 |  |  | 210 | 90 |
| 8 |  |  | 130 | 79 |
| 9 |  |  | 230 | 80 |
| 10 |  |  | 240 | 81 |
| 11 |  |  | 300 | 45 |

[a]**Reaction conditions:** Dimedone (2 mmol), aryl aldehyde (1 mmol), $NH_4OAc$ (1.5 mmol) and citric acid monohydrate (2 mmol) in ethanol (4 mL) at reflux.

[b]Isolated yields.

**Table 4:** Effect of various catalysts on synthesis of 1, 8-dioxo-decahydroacridines.

| Entry | Catalyst | Reaction Condition | Time (min) | Yield (%) | Ref. |
|---|---|---|---|---|---|
| 1 | Citric acid (2 mmol) | Ethanol/Reflux | 150 | 89 | Present work |
| 2 | $Ni_{0.5}Co_{0.5}Fe_2O_4$ (20 mol %) | EtOH:$H_2O$ (1:1), Reflux | 40 | 92 | 24 |
| 3 | $SiO_2$-$ZnCl_2$ (0.2 g mol %) | Solvent free/100° C | 30 | 70 | 20 |
| 4 | B $(C_6F_5)_3$ (3 mol %) | Solvent free/RT | 168 | 80 | 29 |
| 5 | PPA-$SiO_2$ (0.02 gm) | Solvent free/100°C | 10 | 93 | 30 |
| 6 | Ammonium chloride | Solvent free/120°C | 60 | 87 | 31 |
| 7 | SPNP (0.03 mmol) | $H_2O$, reflux | 120 | 91 | 32 |

**Fig 1.** Reusability of citric acid for synthesis of 1, 8-dioxo-decahydroacridines.

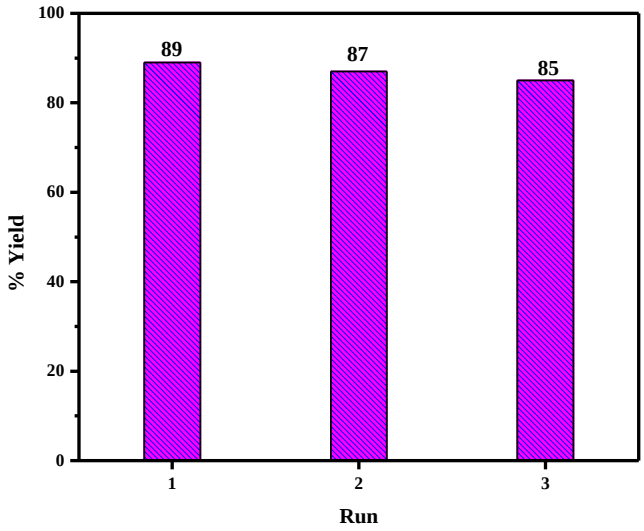


**Fig. 2:** Proposed reaction mechanism for the synthesis of 1,8-dioxo-decahydroacridines