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(MS)



Microwave Assisted Green Synthesis of 1,8-Dioxo-Octahydroxanthenes Using Lemon Juice

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Abstract:-

The natural acid lemon juice catalyzed an efficient synthesis of 1,8-dioxo-octahydroxanthene via condensation of aromatic aldehydes and dimedone under microwave-irradiation. This method provides several advantages such as environment benign, high yields and simple work-up procedure.

Keywords:- 1,8-dioxo-octahydroxanthenes, Dimedone, Microwave, Lemon Juice.

Introduction:-

Heterocycles plays an important role in the designing of new pharmacologically active compound [1]. Chemically 1,8-dioxo-octahydroxanthenes are heterocyclic compound with the Xanthene framework. These derivatives are parent compounds of a large number of naturally occurring and synthetic derivatives and occupy a prominent position in medicinal chemistry [2]. Xanthenes are an important class of organic compounds that find use as dyes [3], fluorescent materials for visualization of biomolecules [4]. In particular, xanthenedione constitute a structural unit in a number of natural products [5] and have been used as versatile synthones because of inherent reactivity of the inbuilt pyran ring [6]. The synthesis of these heterocyclic compounds is of great interest for both organic and heterocyclic chemistry. These compounds have also been investigated for agricultural anti-bacterial activity [7], anti-inflammatory activity [8] and anti-viral activity [9]. The synthesis of xanthenedione usually carried out by condensation of active methylene carbonyl compounds with aldehydes catalyzed by sulphuric acid or HCl [10]. Recently, many procedures have been reported for the synthesis of 1,8-dioxo-octahydroxanthenes by condensation of dimedone and aldehydes using silica supported sulphuric acid [11], Dowex-50W [12], HClO₄-SiO₂ and PPA-SiO₂ [13], silica chloride and NaHSO₄-SiO₂ [14], p-dodecylbenzenesulphonic acid [15], Fe³⁺-montmorillonite [16], Amberlite-25 [17], diammonium hydrogen phosphate [18], TMSCl [19], tetrabutylammonium hydrogen sulphate [20], Ferric hydrogen sulphate [21], InCl₃.4H₂O [22], triethylbenzylammonium chloride [23] and Bismuth trichloride [24] as a catalyst. Each of these methods have their own advantages but most of the reactions suffer from one or more disadvantages such as prolonged reaction time [14], [15], [17], [19], tedious work-up processes, low yield [13] and harsh reaction condition [18]. The major disadvantage of some of the method is that the reaction does not give the cyclized compound [18]. Consequently, there is still need to develop a more efficient, milder, simple and high yield protocol for the synthesis of Xanthene derivatives.

Citrus aurantium, Citrus indica, Citrus limonium are some important species of citrus family commonly known as lemon. The lemon is indigenous to the north-west regions of India. It is now widely grown in all tropical and subtropical countries. In India it is also cultivated in home gardens. The main constituent of lemon juice are moisture (85%), carbohydrates (11.2%), citric acid (5-7%), protein (1%), vitamin-C (0.5%), fat (0.9%), minerals (0.3%), fibers (1.6%) and some other organic acids. As lemon juice is acidic in nature (pH ≈ 2-3) and percentage of citric acid (5-7%) is more than other acids, it worked as acid catalyst for various reactions



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such as Biginelli reaction^[25], synthesis of Schiff Base^[26], synthesis of Big-, Tri-, Tetrahydro^[27], synthesis of 3,4-dihydropyrimidine-2(1H)-one^[28], Synthesis of Bisindolylmethanes^[29] etc.

Microwave irradiation is a rapid means of material heating for domestic, industrial and medical purposes. Microwaves offer a number of advantages over conventional heating such as non-contact heating, energy transfer instead of heat transfer, material selective and volumetric heating, fast start-up and stopping. Moreover, the reduced time of processing under microwave conditions found for a great number of chemical reactions was the main reason that microwave techniques became so attractive for chemists, who, in the last two decades, have begun to apply this technique as a routine in their everyday practice. Overview of application of microwaves in polymer synthesis can be found in the review articles and in the comprehensive review with over 600 references cited in the recently published book and chapter.

In continuation of our previous work, we have developed the cheap and eco-friendly materials as catalysts for development of new synthetic methodologies^[30]. In this paper, we would like to report a mild and high yielding method for the synthesis of 1,8-dioxo-octahydroxanthenes via cyclo-condensation of various aldehydes and 1,3-cyclohexenedione using Lemon Juice under microwave-irradiation.

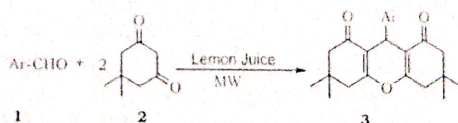
Experimental:-

The materials were obtained from commercial suppliers. The uncorrected melting points of compounds were taken in an open capillary in a paraffin bath. Microwave oven (LG Smart Chef MS-255R operating at 2450 MHz having maximum output power of 960 W) was used for microwave irradiation. The progress of the reactions was monitored by TLC (Thin Layer Chromatography). ¹H NMR spectra were recorded on an 400 MHz FT-NMR spectrometer in CDCl₃ as a solvent and chemical shift values are recorded in units δ (ppm) relative to tetramethylsilane (Me₄Si) as an internal standard.

General procedure: The mixture of aldehyde (1 mmol), dimedone (2 mmol) and Lemon Juice (1ml) were irradiated under microwave as the time indicated in Table 1. The completion of reaction was monitored by TLC (Hexane: EtOAc 8:2). The reaction mixture was cooled at room temperature and the solid product was extracted with dichloromethane. The organic layer was evaporated under reduced pressure and the crude product was obtained. The crude products were purified by recrystallization from ethanol.

Result and Discussion:-

Herein, we would like to report a mild and high yielding method for the synthesis of 1,8-dioxo-octahydroxanthene derivatives in excellent yield using Lemon Juice as a natural catalyst.



Scheme-1

We have carried out the model reaction by taking; the 4-chlorobenzaldehyde and dimedone under Microwave-irradiation

using Lemon Juice as a catalyst.



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We observed that, the model reaction was carried out in presence of 0.5 ml of Lemon Juice catalyst to give the product (3b) in modest 75% yield but when the concentration of catalyst have been increased to 1ml which results in accelerating the reaction yields to 91%. Use of 2 ml of catalyst is sufficient to push the reaction forward. Higher amount of the catalyst did not improve catalyst for this reaction, as shown in (Table 1).

Table 1: Optimization of catalyst(ml) for model reaction (3b).

Entry	Catalyst (ml)	Yield (%) ^a
1	0.5	75
2	1	91
3	2	91

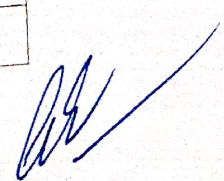
^a Isolated yields.

We have also observed that the aldehydes both with electron donating groups electron and withdrawing groups afforded the corresponding product in good yields. Para and meta substituted substrates reacted almost well. However aldehydes bearing substituent at ortho position turned out to be reluctant to undergo the condensation reaction, the longer reaction time is required for this substrate to get the corresponding product in high yield (Table 2, entries 3e, 3i).

Table 2: Microwave assisted synthesis of 1,8-dioxo-octahydroxanthenes using Lemon Juice as a catalyst.

Entry	Ar	Product	Time (Min)	Yield (%) ^a	M.P (°C)
1	C ₆ H ₅	3a	15	89	202-203
2	4-ClC ₆ H ₄	3b	10	91	228-230
3	4-OCH ₃ C ₆ H ₄	3c	10	88	238-240
4	4-OH,3-OCH ₃ C ₆ H ₃	3d	10	89	227-228
5	2-NO ₂ C ₆ H ₄	3e	25	83	244-246
6	4-BrC ₆ H ₄	3f	15	83	238-240
7	4-OHC ₆ H ₄	3g	10	88	247-248
8	4-FC ₆ H ₄	3h	15	83	224-226
9	2-ClC ₆ H ₄	3i	25	85	227-229
10	3-NO ₂ C ₆ H ₄	3j	25	83	169-170

^a Isolated yields.


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Conclusion:-In conclusion this method presents a mild and 'green' protocol for obtaining 1,8-dioxo-octahydroxanyhene under Microwave-irradiation. The Lemon Juice has been shown to be an efficient catalyst and no additional cocatalysts were necessary to promote the reaction. It is expected that the present methodology will find application in organic synthesis

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