



Synthesis of 9,10-dihydro-9,9-dimethyl-12-phenyl-8H-benzo[a]xanthen-11(12H)-one derivatives promoted by Tartaric acid under ultrasound irradiation

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Abstract: A proficient and simplified procedure for the synthesis 9,10-dihydro-9,9-dimethyl-12-phenyl-8H-benzo[a]xanthen-11(12H)-one derivatives in the presence of tartaric acid as a organocatalyst under ultrasound irradiation is demonstrated. A series of functionalized derivatives have been synthesized in shorter reaction times with moderate to good yields by means of sustainability means.

Keywords: Benzoanthenones, simplified procedure, ultrasound irradiation, Organocatalysis.

Introduction

In the list of different oxygen containing heterocyclic ring system such as Xanthenes and benzoxanthenes possesses wide range of medicinal and pharmaceutical properties¹⁻⁹ such as anti-viral, anti-inflammatory, anti-bacterial, antagonists, anti-fungal, anti-cancer, and anti-inflammatory. Beside this it has also been tasted against therapeutic effects more particularly on diabetes and Alzheimer.

In the literature there are few moieties consist of xanthene nucleus shows applications against the action of doxylamine chemical and in therapeutic functions of photodynamic mechanism. Nevertheless, few reports have been revealed the non-medicinal applications specifically in fluorescent dyes, imagining of photo activated biomass and in laser therapies etc.¹⁰⁻¹³

With this prodigious significance cited above the synthesis of xanthene derivatives attracted much of our consideration. Therefore, our interest is enhanced in this oxygen containing heterocyclic compounds as these possesses implication in the various aspects of medicinal chemistry, alongside they propose the challenges to design and develop environmentally sustainable methods for the synthesis of these bioactive xanthene heterocycles.

Current environmental global scenario needs user friendly and ecofriendly laboratory protocols, because day by day imbalance in nature is mainly due to different types of pollutions.¹⁴ That affects considerably on living things. Nevertheless, we are not that much aware about environmental consequences.

As a part of society we have to think about such chemical protocols that consumes less energy or power.¹⁵ Wherever possible use of hazardous chemicals /organic solvents is to be avoided and need to keep control on reaction conditions that will not generate side products.¹⁶ In concern with this such practices have been found in the literature.¹⁷⁻²⁰ Nevertheless effort has to be taken for research methodology development that covers green chemistry aspects. This can be achieved by application of organic acids as a catalysts.

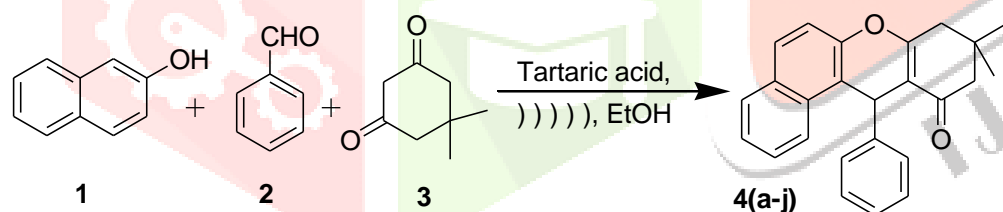
Herein, we have developed ultrasound assisted tartaric acid catalyzed synthesis of tetra hydro xanthenes. Tartaric acid occurs in nature in citrus fruits with stronger, sharper taste than citric acid. More specifically natural it occurrence in grapes, apples, tamarind, in some quantity tomato, cherries, guava, pineapple, strawberries, mangos, and other citrus fruits. Itself tartaric acid having antimicrobial activity and some other medicinal importance.²¹⁻²³

Tartaric acid has been used as an organocatalyst for several one-pot synthesis as well as multicomponent reactions with substituted aliphatic, aromatic, heteroaromatic, core nucleus containing various functional groups.²⁴⁻²⁶

Here it has been observed that the most suitable method for the synthesis of xanthene-11-ones is the condensation of aldehyde, beta-naphthol and dimedone.

Result and Discussion

In continuation of our research to develop sustainable protocols²⁷⁻³⁴ initially, we thought to investigate suitable organic acid as a catalysts because of several advantages of it. Accordingly, we have started checking of catalytic efficiency of some available organic acids such as lactic acid, oxalic acid, uric acid, malic acid and tartaric acid in aqueous and non-aqueous solvents for the one pot multicomponent cyclocondensation of beta-naphthol **1**, aromatic aldehyde **2**, and dimedone **3** (**Scheme 1**).



Scheme 1: Synthesis of tetrahydro-benzo[a]xanthene-11-one derivatives under ultrasound irradiations.

Experimental evaluation study reveals that tartaric acid in ethanol under ultrasound irradiation is considerable protocol for the cyclocondensation of aldehyde, beta-naphthol and dimedone which gives 84% product yield (**Table 1, Sr. No 4**). Other solvents like methanol, isopropanol, ethyl acetate and acetone produces 30 %, 45 %, 60 % and 55 % product yield respectively in stipulated period of time. Hence, under ultrasound irradiation tartaric acid and ethanol at 60-65 °C proved to be promising reaction condition for the proposed moiety.

Herein, it has been found that catalytic competency of malic acid is near to tartaric acid but other acids are not showing remarkable considerations in terms of percent yield of the product, reaction time and easy work up procedure as shown in **table 1**.

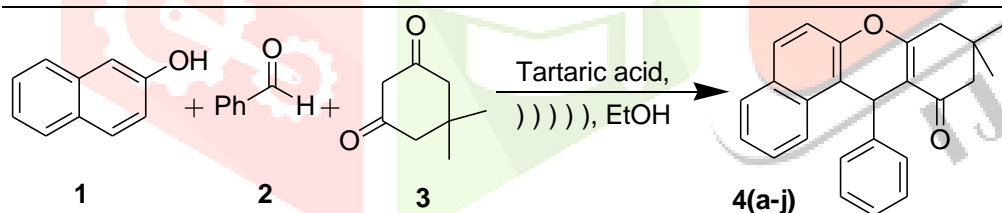
Table 1. Study of catalytic competency of organic acids for the synthesis of 9,10-dihydro-9,9-dimethyl-12-phenyl-8H-benzo[a]xanthen-11(12H)-one.

Sr. No.	Organic Acid	Reaction Time(h)	Yield
1	Lactic acid	8.5	58
2	Oxalic acid	9.0	45
3	Malic acid	7.0	66
4	Tartaric acid	6.5	84
5	Uric acid	8.5	35

To estimate the optimum concentration of the catalyst tartaric acid we have examined the trial and error method, for this the model reaction of cyclocondensation of β -naphthol **1**, benzaldehyde **2**, and dimedone **3** at stoichiometric concentrations of tartaric acid such as 4, 8, 12, 16 and 18 mol %. It has been observed that the products in 35%, 50%,

75%, 84% and 84 % yields, respectively obtained. These results reveals that 16 mol % of tartaric acid formed the better results with respect to yield of the products.

To establish further scope and generalization of optimized protocol we have implemented this route for various precursors of aromatic system with activating (hydroxyl, alkyl, aryl, alkoxy etc.) and deactivating (halides, nitro and nitrile etc.) substituents. Interestingly all the reactants were reacted smoothly with equal response to the established reaction pathway (**Table 2**).

Table 2: Synthesis of tetrahydrobenzo[a]xanthen-11-one derivatives.

Entry	Compound	Ph	Time (h)	^a Yield(%)	M.P.(°C)
1	4a	C ₆ H ₅	6.5	84	150-152
2	4b	4-OH C ₆ H ₄	5.5	88	222-224
3	4c	4-OMe C ₆ H ₄	6.0	85	205-207
4	4d	4-Me C ₆ H ₄	6.5	84	173-175
5	4e	2-Cl C ₆ H ₄	6.5	82	176-77
6	4f	2-NO ₂ C ₆ H ₄	6.5	82	220-221
7	4g	4-Cl C ₆ H ₄	6.5	84	181-183
8	4h	3-NO ₂ C ₆ H ₄	7.0	78	170-171
9	4i	2-Furyl	7.5	74	172-176
10	4j	2-Thienyl	7.5	74	174-176

^aIsolated yield of the product.

Experimental

Experimental Procedure for the synthesis of 9,10-dihydro-9,9-dimethyl-12-phenyl-8H-benzo[a]xanthen-11(12H)-one:

In the hard glass test tube Benzaldehyde (0.221 g, 0.002 mol) and dimedone (0.280 g, 0.002 mol) and tartaric acid (16 Mol%) in 25 mL ethyl alcohol was subjected for ultrasound irradiation for one and half hours. To this solution, β -naphthol (0.288g, 0.002 mol) was added portion wise at same reaction vessel. The progress of the reaction was monitored after interval of each half hour by TLC. The reaction is completed after specified period of time. After completion the reaction mixture was extracted in ethyl acetate and water (65:35) as a solvent system. Organic layer was once washed by brine solution degassed on rotary evaporator. Thus obtained solid was dried and purified by recrystallization in ethanol to yield a pure product. Similar procedure was applied for the synthesis of other derivatives. All compounds were characterized by spectroscopic analysis.

Spectral analysis of representative compound

Compound 4a (Table 2): $^1\text{H NMR}$ (CDCl_3) δ ppm; of 0.98(s,3H, CH_3),1.15(s, 3H, CH_3),2.29 (q, $J=16.5\text{Hz}$, 2H, CH_2),2.55 (s, 2H, CH_2), 5.69 (s, 1H ,CH), 7.11 – 7.39 (m, 8H, Ar-H),7.1–7.75(m, 2H, Ar-H), 7.99 (d, $J=7.2$ Hz, 1H, Ar-H); MS $m/z = 357.15$; IR (KBr); ν cm^{-1} 3065 (N-H Str.), 1721 (C=O Str.), 1461 (C=C Str.).

Conclusions

We have established an organic acid as a green catalyst for user friendly mild and clean synthetic protocol for tetrahydrobenzo[a]xanthen-11-one derivatives. For this methodology, application of tartaric acid has been utilized for one pot multicomponent cyclocondensation reaction. Actually reaction temperature is ambient under ultrasound irradiation which is noteworthy for this protocol. This synthetic strategy also covers the advantages of one-pot multicomponent transformations which will make this research work practical and economically feasible and provides foresight for green chemistry aspects.

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