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Ultrasound Assisted One-Pot Synthesis of 12-Aryl -8, 9, 10, 12-tetrahydrobenzo[a]xanthen-11-one Derivatives Using Chlorosulphonic Acid as a Catalyst under Solvent-free Conditions

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ABSTRACT

A multi component condensation of β-naphthol, aromatic aldehydes and cyclic 1,3-dicarbonyl compounds in presence of Chlorosulphonic acid ($ClSO_3H$) as a catalyst to furnish 12-Aryl -8,9,10,12-tetrahydrobenzo [a]xanthen-11-ones derivatives in good to excellent yields under ultrasound and solvent free conditions at ambient temperature is described. This is an efficient and environmentally benign methodology.

Keywords: Xanthenes; multi component reaction; $ClSO_3H$ catalyst; Sonochemistry.

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INTRODUCTION

Multi component reactions play an important role in modern synthetic organic chemistry, since they are since they are generally one pot reaction and exhibit a high atom-economy and selectivity [1]. They also deliver fewer byproducts compared to classical stepwise synthetic routes. This reduces time and saves energy and raw materials [2]. Xanthene derivatives have been received special attention due to aryl functionality which is a key structural unit of many biological activities such as anti-inflammatory, antibacterial, antiviral [3-5] and in photodynamic therapy [6]. Xanthene-based compounds have also been investigated for agricultural bactericide activity [7] and some other benzoxanthenes find application in industries such as dyes [8], in laser technology [9] and as pH sensitive fluorescent materials for visualization of biomolecules [10]. Earlier tetrahydrobenzo [a] xanthenes have been synthesized under reflux for 4-5h in dichloromethane and 1,2 dichloroethane in the presence of acid catalysts such as $BF_3.Et_2O$, [11] silica supported $NaHSO_4$,[12] $Sr(OTf)_2$ [13] and TBAF[14]. However, all these methods have many disadvantages such as low yields, the need for a prolonged reaction time, the use of toxic organic solvents, excess reagents, often expensive catalysts and harsh reaction conditions. Moreover, the synthesis has been usually carried out in solvent leading to complex isolation and recovery procedures. Over the past decade, various advanced sequentially multicomponent reactions, have been developed, where 1, 3-dicarbonyl derivatives are important synthetic intermediates due to its multiple functionalities that can be involved either as nucleophilic or electrophilic species in a large variety of synthetic transformations [15]. In continuation of our ongoing project on the application of cheap and ecofriendly materials as catalysts for developing of new synthetic methodology, we herein describe an Ultrasound-assisted one-pot three-component condensation reaction to synthesize 12-aryl-8, 9, 10, 12-tetrahydrobenzo[*a*]xanthen-11-one derivatives by using Chlorosulphonic acid as a catalyst under solvent-free conditions (Scheme 1).

MATERIALS AND METHODS

All melting points were measured in open capillaries. IR spectra were recorded on a Shimadzu-IR 408 spectrometer with KBr plates. ^{1}H NMR Spectra were recorded on **MSL**-300 instrument. All spectra were recorded in $CDCl_3$/DMSO and chemical shifts are reported in ppm down field from tetra methyl silane (TMS) as the internal standard. For ultrasound assisted organic reactions, the ultrasonicator was used having the following specifications.

Electric supply:	230 v A.C. 50 Hz, 1phase.
Ultrasonic frequency:	36 ±3 KHz.
Ultrasonic power:	100 watts.

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Preparation of 12-Aryl -8, 9, 10, 12-tetrahydrobenzo[a]xanthen-11-one 5a-l: general procedure

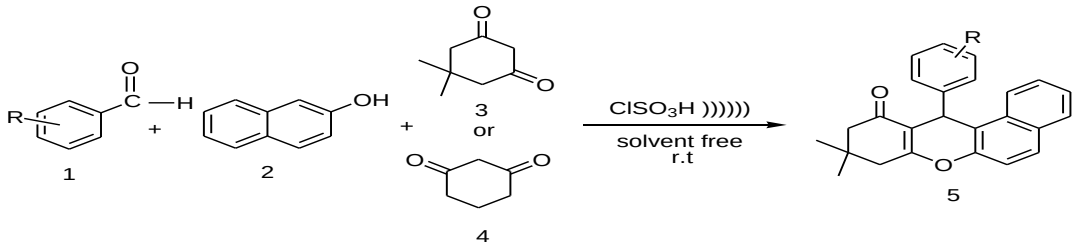
A mixture of 2-naphthol (1mmol), aromatic aldehyde (1mmol), cyclic 1, 3-dicarbonyl compound (1.2mmol) and Chlorosulphonic acid (0.02mmol) was taken in 25 ml round bottom flask fitted with reflux condenser and this was kept in sonicator bath and irradiated at ambient temperature and maintained for the appropriate time (Table 1). After the completion of the reaction {indicated by TLC), the reaction mixture was poured into ice water and the precipitated solid was collected by filtration, washed with water and dried. The resulting solid products were recrystallized from ethanol. The physical and spectral data of the known compounds were in agreement with those reported in literature. The spectral and analytical data for the new compounds are given below.

12-(4-Hydroxy-3-methylphenyl)-9, 9-dimethyl-8, 9, 10, 12-tetrahydrobenzo[α]xanthen-11-one (5i): White solid; Rf¼ 0.56(1:4 EtOAc/Hexane), mp 230-232 ^{o}C. IR (KBr): 3406, 2956, 1665, 1325, 1286, 1100, 900, 577 cm^{-1}. **^{1}H NMR** (**DMSO**-d6, 200 MHz**,** δ ppm): 8.80 (s,1H), 6.68-6.55 (m, 3H), 4.43 (s,1H), 3.69 (s,3H), 2.32 (d, 1H), 2.23 (d, 1H), 1.04 (s, 3H), 0.92 (s, 3H). Anal. Calcd. for $C_{26}H_{24}O_4$: C, 78.0, H, 6.0, found: C, 78.12, H, 5.93.

12-(2-Hydroxyphenyl) 8, 9, 10, 12-tetrahydrobenzo[α]xanthen-11-one (5j): White solid; Rf¼ 0.45 (1:4 EtOAc/Hexane), mp 222-224^{o}C. IR (KBr): 3340, 2924, 1629, 1590, 1481, 1377, 1229, 1187, 1127, 817, 755 cm^{-1}. **^{1}H NMR** (**DMSO**-d6, 200 MHz**,** δ ppm): 9.59 (s,1H), d 8.21(d, 1H), 7.84–7.80 (t, 2H), 7.7–7.35 (m, 5H), 6.90 (t, 2H), 6.74-6.63 (m, 5H), 5.78 (s, 1H) ,2.77 (d,1H), 2.37 (d, 1H), 2.03 (d, 1H). Anal. Calcd for $C_{23}H_{18}O_3$: C, 80.70, H, 5.26, found: C, 80.67, H, 5.31.

RESULTS AND DISCUSSION

We investigated the activity of Chlorosulphonic acid as a catalyst in the synthesis of xanthene derivatives by condensation of aromatic aldehydes **1**, β-naphthol **2**, 5, 5-dimethyl-1, 3-cyclohexanedione **3** and 1, 3-cyclohexanedione **4** (scheme1).under ultrasound and solvent free conditions. The results are summarized in table **1**. To optimize the reaction condition, the condensation of benzaldehyde, β-naphthol, 5, 5-dimethyl-1, 3-cyclohexanedione was carried out under different solvent and ultrasound irradiation using chlorosulphonic acid as catalyst. The results are shown in table **2**. It is found that optimum results are obtained under solvent free condition



Scheme1.

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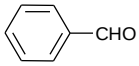
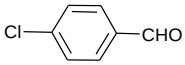
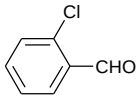
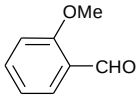
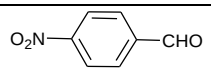
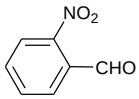
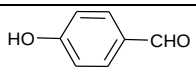
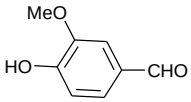
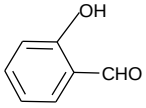
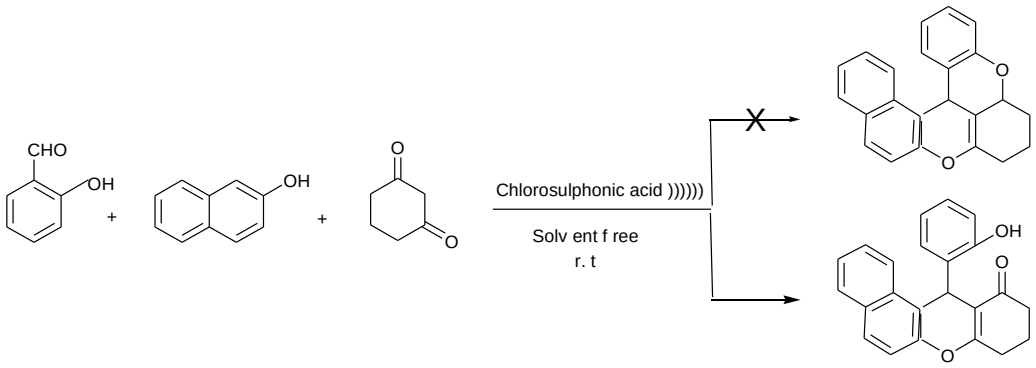
Table1.Synthesis of 12-Aryl -8, 9, 10, 12-tetrahydrobenzo*[a]*xanthen-11-one 5

Entry	Aldehydes	Time (min)	Product	Yield (%)[a]	Found	M.P (^{0}C) Lit. [Ref.]
1		20	5a	98	148-150	149-150 [16]
2		20	5b	98	180-182	180-182 [17]
3		15	5c	90	178-180	179-180 [17]
4		20	5d	85	202-204	204-205 [17]
5		35	5e	92	162-164	163-165 [17]
6		30	5f	83	174-176	174-175 [16]
7		40	5g	88	222-224	223-235 [17]
8		30	5h	95	220-224	223-225 [17]
9		40	5i	94	186-188	-
10		40	5j	90	222-224	-

[a] isolated yield

Further, it is intersecting to note that when salicyaldehyde, β-naphthol and 1,3 cyclohexadione are condensed under the similar experimental condition (Scheme 2)as mentioned above there is no epoxide formation this is confirmed by spectral data and elemental analysis .



Scheme 2. No epoxide Formation

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Table 2 Optimization of conditions for the condensation reaction of aldehyde, β -naphthol, and dimedone [a]

Entry	Solvent	Time (mins)	Yields (%) [b]
1	Water	90	45
2	Acetonitrile	120	30
3	ethanol	75	60
4	Neat	20	98

[a]Reaction conditions: benzaldehyde 1a (1mmol), β-naphthol 2 (1mmol), 5, 5-dimethyl- cyclohexane-1, 3- dione 3 (1.2mmol), Chlorosulphonic acid (0.02mmol), solvent (3mL),
[b] isolated yield

CONCLUSION

In conclusion, we have developed an efficient and simple process for the synthesis of 12-Aryl -8, 9, 10, 12-tetrahydrobenzo[a]xanthen-11-one derivatives via three-component reaction catalyzed by Chlorosulphonic acid under ultrasound and solvent-free conditions. The simple experimental procedure, short reaction times, solvent- free conditions, and excellent yields are the advantage of the present method.

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