

THIAMINE HYDROCHLORIDE AS EFFICIENT CATALYST FOR ONE-POT SYNTHESIS OF 14-ARYL -14H DIBENZO [a, j] XANTHENES UNDER GREENERY CONDITIONS

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ABSTRACT

Thiamine hydrochloride (THC) is a biodegradable, readily available and inexpensive eco-friendly metal free biocatalyst, which is efficiently used in the condensation of 2-naphthol and aromatic aldehydes under thermal and microwave conditions without using toxic solvents. Developed methods herein afforded 14-aryl 14H-dibenzo [a, j] xanthenes in very good yields and offered several advantages such as shorter reaction time, comparable yield, neat practice, easy work-up and mild organo Lewis acid catalyst.

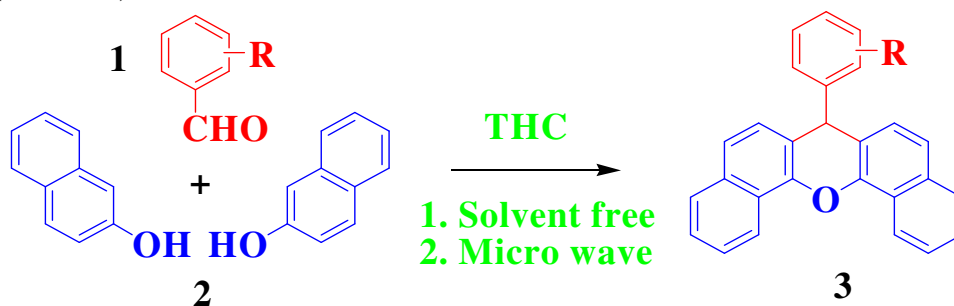
Keywords: Thiamine hydrochloride (THC), Biodegradable mild organo Lewis acid catalyst, Solvent Free and Micro wave condition, One-pot synthesis of 14-aryl 14H-dibenzo [a, j] xanthenes, High Yields, Easy workup.

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INTRODUCTION

Benzoxanthenes fall under a special category of xanthenes, which are known to exhibit antiviral and antibacterial properties¹⁻³. Some of the benzoxanthenes find their applications in the preparation of dyes³, fluorescent compounds⁴, photodynamic therapy, and also in laser technologies⁵⁻⁹. In a recent publication¹Ganeshet *al* revealed that benzoxanthenes can be prepared by the condensation of β -naphthol with varieties of aldehydes using different types of catalysts like mineral acids, Lewis acids, carboxylic acids, sulfonic acids, molecular iodine and ionic liquids, NaHSO₄ and aluminum bisulfate. In addition to a helpful review of literature in this publication, Singh and coworkers¹ developed an eco-friendly solvent-free condensation method to obtain 14- aryl- or alkyl-14H-dibenzo [a, j] xanthenes using P₂O₅ or InCl₃ as catalysts. For the synthesis of 14-aryl-14H-dibenzo [a, j] xanthene derivatives, Geng-Chen Li, has used aryl aldehydes, and freshly prepared expanded graphite as a catalyst¹⁰, while Hamid Reza Shaterian et al., reported the use of ferric hydrogen sulfate and aluminum hydrogen sulfate as catalysts^{11,12}. Carbon tetra bromide (CBr₄)¹³, and polyvinyl poly pyrrolidine-supported boron trifluoride (PVPP-BF₃)¹⁴ were the other important catalysts used for the synthesis of dibenzo xanthenes. FarhadShirini et al illustrated the synthesis of benzoxanthenes compounds through the condensation of 2-naphthol and 1,3 cyclohexanedione with and without succinimide N- sulfonic acid as catalyst¹⁵. In another MCR protocol, Javad Safaei-Ghomi and Mohammad Ali¹⁶ used recoverable AgI nano particles as a catalyst to achieve 14-aryl-14H-dibenzo [a, j] xanthenes via the reaction of 2-naphthol with different aldehydes. In another publication Davinder Prasad and fellow researchers used *p*- dodecylbenzenesulfonic acid as a catalyst in MW assisted green synthesis of dibenzo [a, j] xanthenes to achieve good product yields¹⁷. As a matter of fact efforts several workers focused their attention on improving the greenery in the synthesis of 14-Aryl -14H Dibenzo [a, j] xanthenes by using large varieties of catalysts such as, [H-NMP][HSO₄]¹⁸, (SiO₂-Pr-SO₃H)¹⁹, N-sulfonic acid poly(4-vinyl pyridinium) chloride (NSPVP)²⁰, 1-methyl-3-propane sulfonic-imidazolium hydrosulfate ([MIMPS] HSO₄)²¹ and many more²². Many of these protocols are conducted either under solvent-free conditions and/or under the MW irradiation; because MW assisted reactions to accelerate the reactions through bulk activation of molecules and give product yields²³. Enthused by these factors, we want to explore readily available and inexpensive thiamine hydrochloride (THC) as a

biodegradable and ecofriendly catalyst in the one-pot synthesis of 14-aryl-14H-dibenzo [a, j] xanthene derivatives using condensation of aromatic aldehydes with β -naphthol under solvent-free and MW conditions (Scheme-1).



Scheme-1: THC accelerated One-pot Synthesis of 14-Aryl-14H-Dibenzo [a, j] Xanthenes

EXPERIMENTAL

Solvent Free Method for Synthesis of Xanthene Derivatives

Round bottomed reaction flask containing β -naphthol (2mmol), benzaldehyde (1mmol) and THC (100 mg) was placed in the mantle and refluxed at about 120 °C. After the reaction is completed (as indicated by TLC), the reaction mixture was kept aside for cooling to room temperature. The reaction mixture was neutralized with 15% Na₂CO₃; ethyl acetate was added to the flask to extract organic components. Finally, the resultant organic layer was run through the column containing silica gel (60-120 mesh size). Separated product was again recrystallized with 15% aqueous EtOH.

Microwave Irradiation for Synthesis of Xanthene Derivatives

After preparing the reaction mixture as mentioned in the preceding section, the reaction flask was placed in a laboratory microwave oven (BPL, 800T model) on a silica gel solid support and allowed to heat at 300 W for the appropriate time. After completion, the product was isolated and purified using the above workup.

RESULTS AND DISCUSSION

Initially, the reaction conditions are optimized using β -naphthol (2mmol), benzaldehyde (1mmol), and varied amounts of biodegradable thiamine hydrochloride (THC) catalyst in different reaction media, under also solvent-free conditions. Obtained results are presented in Table-1.

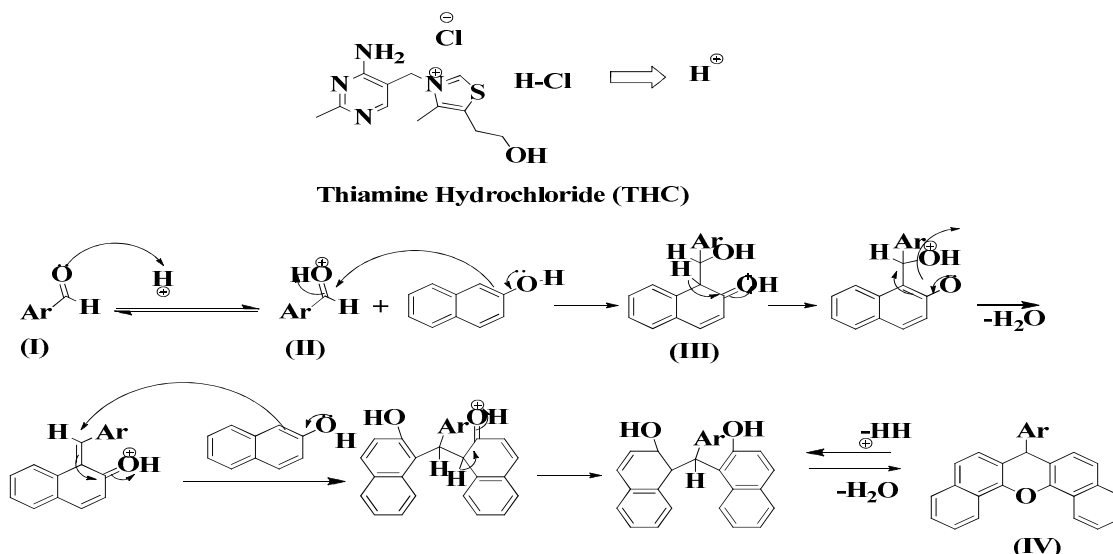
Table-1: Optimization of Catalyst Thiamine Hydrochloride (THC):

S. No.	Reaction Media	THC (mg)	Temp. (0C)	Time	3a Yield (%)
1	Acetonitrile	100	Reflux	4.0 hours	20
2	Dichloro Ethane	100	Reflux	4.0 hours	35
3	Ethanol	100	Reflux	3.0 hours	60
4	Methanol	100	Reflux	3.0 hours	50
5	Chloroform	100	Reflux	3.5 hours	43
6	Water	100	Reflux	5.0 hours	12
7	None	0	0	3.0 hours	0
8	None	40	120	3.0 hours	53
9	None	60	120	120 minutes	66
10	None	80	120	75 minutes	79
11	None	100	120	45 minutes	92
12	None	120	120	50 minutes	92
13	None	120	MW assistance	4-5 min	92

Under solvent-free conditions and using 100 mg THC the reaction afforded excellent product (3a) yield at 120°C. This reaction required 45 minutes for completion in solvent-free conditions. But MW assisted reaction under otherwise similar conditions took only 4 to 5 and gave desirable yields. Under optimized conditions, a large array of aldehydes were used to get corresponding 14-aryl-14H-dibenzo [a, j] xanthene derivatives (3a–3p). Products were characterized by physical spectroscopic (mass, IR, NMR and C-13NMR data). Reaction times and product yields are presented in table-2. The most plausible mechanism is proposed as shown in Scheme-2, which shows that THC acts as an acid catalyst to produce (H⁺) ions with internal rearrangement of THC salt. First step, proton is abstracted by the aryl aldehyde leads to the formation of aryl oxocarbenium ion intermediate (II), which in turn reacts with β-naphthol in a condensation step to generate naphthyl oxonium intermediate (III) by the elimination of water molecule as shown Scheme-1, which is further reacted with one more β-naphthol molecule to form target compound (IV) by the removal of H₂O molecule. Total progress of the reaction parameters such as time and yields are tabulated in Table-2 for their respective derivatives.

Table -2: One-pot Synthesis of 14-aryl -14H Dibenzo [a, j] Xanthene Derivatives.

S. No.	Aldehydes	Products (3)	¹ Solvent Free		² Micro Wave	
			R.T (min)	Yield (%)	R.T (min)	Yield (%)
1	C ₆ H ₅ -CHO	3a	43	92	4	96
2	2-NO ₂ -C ₆ H ₄ -CHO	3b	45	86	5	92
3	4-Et-C ₆ H ₄ -CHO	3c	44	90	4	95
4	4-Me-C ₆ H ₄ -CHO	3d	42	92	4	96
5	4-MeO-C ₆ H ₄ -CHO	3e	42	93	4	96
6	4-OH-C ₆ H ₄ -CHO	3f	42	93	4	97
7	2-Cl-C ₆ H ₄ -CHO	3g	43	91	4	95
8	4-Cl-C ₆ H ₄ -CHO	3h	42	93	4	96
9	CH ₃ -CH ₂ -CHO	3i	44	90	5	95
10	C ₆ H ₄ -CHO	3j	45	90	5	95
11	4-Br-C ₆ H ₄ -CHO	3k	44	92	5	96
12	3-OH-C ₆ H ₄ -CHO	3l	43	92	4	96
13	4-NO ₂ -C ₆ H ₄ -CHO	3m	45	89	5	93
14	3-MeO-C ₆ H ₄ -CHO	3n	43	91	4	94
15	4-CN-C ₆ H ₄ -CHO	3o	44	92	4	95
16	3-F-C ₆ H ₄ -CHO	3p	45	92	4	96



Scheme-2: Plausible Mechanism for the Formation of 14-Aryl -14H Dibenzo [a, j] Xanthenes

In MW assisted reactions all the molecules acquire energy directly from the source without any time lapse from MW irradiation, which causes bulk activation of molecules. The fraction of activated molecules grows exponentially under MW irradiation when compared to the thermal reactions which occur due to thermal collisions. Due to this bulk activation of molecules reaction, times reduce enormously, accelerate the reactions and afford higher product yields, as explained by several workers²³⁻²⁸.

Characterization of Products

The spectral (¹HNMR, ¹³CNMR, IR, and m/z) data of few representative compounds are as follows:

14-Phenyl-14H-dibenzo [a,j] Xanthene (3a)

White solid; MP. 184–186 °C; ¹HNMR (400 MHz, CDCl₃): δ=6.48 (s, 1H), 6.79 (t, *J* = 8.4 Hz, 2H), 7.37-7.46 (m, 6H), 7.56 (t, *J* = 8.0 Hz, 2H), 7.78 (, *J* = 8.4 Hz, 2H); ¹³CNMR (100 MHz, CDCl₃): δ = 38.2, 117.4, 118.1, 122.5, 124.3, 126.4, 126.8, 128.3, 128.3, 128.8, 128.9, 131.1, 131.3, 148.8; IR (KBr, Cm⁻¹): 3075, 1582, 1444, 1252, 1081, 966; m/z (%) = 358 (M⁺), 281, 268.

14-(2-Nitrophenyl)-14H-dibenzo [a, j] Xanthene (3b)

Yellow solid; MP. 293 °C; ¹HNMR (300 MHz, CDCl₃): δ = 6.45 (s, 1H), 6.98-7.17 (m, 3H), 7.40-7.85 (m, 12H), 8.38 (d, *J* = 8.4 Hz, 2H); ¹³CNMR (75 MHz, CDCl₃): δ 32.9, 118.4, 124.6, 125.3, 128.0, 129.5, 130.8, 132.6, 134.5, 141.3, 147.5, 149.8; IR (KBr Cm⁻¹): 3400, 3058, 1593, 1523, 1350, 1240, 1142, 810, 748; m/z: 403(M⁺), 281, 268.

14-(4-methylphenyl)-14H-dibenzo [a, j] Xanthene (3d)

Yellow Solid; MP. 224-226 °C; ¹HNMR (400 MHz, CDCl₃): δ = 2.13 (s, 3H), 6.44 (s, 1H), 6.96 (d, *J* = 8.0 Hz, 2H), 7.39 -7.43 (m, 4H), 7.47 (d, *J* = 8.8 Hz, 2H), 7.54-7.58 (m, 2H), 7.78–8.39 (m, 6H); ¹³CNMR (100 MHz, CDCl₃): δ = 20.8, 37.6, 117.4, 118.0, 122.7, 124.2, 126.7, 128.7, 129.1, 131.4, 135.8, 142.1, 148.7; IR (KBr Cm⁻¹): 3074, 1623, 1515, 1258, 1123, 1086, 966, 841, 744; m/z (%) = 372 (M⁺).

CONCLUSION

In brief the authors explored a simple and greenery method for one-pot synthesis of 14-aryl-14H dibenzo [a, j] xanthene derivatives by the cyclocondensation of β-naphthol and aryl aldehydes with biodegradable THC as a bio catalyst under solvent-free and micro wave conditions with several compensation such as high yields, very low reaction times and cost-effective ecofriendly catalyst with simple work-procedure.

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