



Vitamin-B₁ An Environmentally Benign Catalyst for the Synthesis of 14-Aryl-4*h*-Dibenzo[*A,J*]Xanthenes Under Solvent-Free Conditions

Somnath Gholap*, Navanath Gunjal and Tushar Kadu

Department of Chemistry and Research Center, Padmshri Vikhe Patil College, Pravaranagar, Tal. Rahata, Dist. Ahmednagar (MS), - 413713 (MS), India.

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ABSTRACT

Thiamine hydrochloride (VB₁) has been used as an environmentally benign catalyst for one pot synthesis of 14-aryl-4*H*-dibenzo[*a, j*]xanthenes derivatives by the three-component reaction of two equivalents of β-naphthol and aldehydes at 110°C under solvent-free conditions. Various type of aldehyde bearing electron donating as well as electron withdrawing substituents underwent smooth reaction under the optimized reaction conditions and products were obtained in good to excellent yield.

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Introduction

Xanthene and its derivatives are present in a large number of compounds with remarkable biological activities like antiviral,¹ antibacterial,² and anti-inflammatory.³ They have application in photodynamic therapy⁴ and antagonists of the paralyzing action of oxazolamine⁵ in laser technologies⁶ and fluorescent material for visualization of biomolecules.⁷ Xanthenes can be found as a core structure of some natural products.⁸ Literature survey revealed that there are list of improved protocols are available for the synthesis of xanthene which includes trapping of benzyne by phenols,⁹ cyclodehydration¹⁰ or cyclocondensation of 2-hydroxy aromatic aldehyde and tetralone,¹¹ alkylation of heteroatom,¹² intermolecular phenyl carbonyl coupling reaction in presence of SmI₂ and hexamethyl phosphoramide,¹³ by reaction of β-naphthol with formamide,¹⁴ 1-hydroxy methyl-naphthalen-2-ol¹⁵ and carbon monoxide.¹⁶ In addition, various methods have been reported for the synthesis of benzoxanthene to minimize shortcomings reported in previous work, such as reaction of β-naphthol with aldehyde in the presence of catalysts as selectfluor TM,¹⁷ Fe(HSO₃)₃,¹⁸ 2,4,6-trichloro-1,3,5-triazine,¹⁹ ceric sulphate,²⁰ expanded graphite,²¹ LiBr,²² PTSA²³ and CoPy₂Cl₂.²⁴

Many procedures have been reported have so far suffered from disadvantages like prolonged reaction time, lack of environment safety, use of organic solvents and lack of catalyst biodegradability. This fact promoted us to develop an alternate procedure for the synthesis of 14-aryl-4*H*-dibenzo[*a, j*]xanthene derivatives with satisfactory improvement yield with dual benefits as environmental safety and economical viability without using hazardous organic solvents.

Metal ion free, environmentally safe and convenient reagents in multicomponent reaction In the view of the conservation of environment combining with economic aspect has always mind blowing attraction for the construction of pharmacologically active heterocyclic compounds in one-pot strategy.²⁵ By considering this fact in mind we have turn our

attention on Green Chemical Technology(GCT) for valuable synthetic transformations. It is well known that thiamine hydrochloride(vitamin-B₁) is a cheap, non-toxic and biodegradable natural product. The structure of VB₁ consists of pyrimidine and a thiazole ring linked by methylene bridge (Figure 1). Due to structural similarities of VB₁with PTC It has been extensively used as a potent catalyst for various organic transformations.^{26,27}

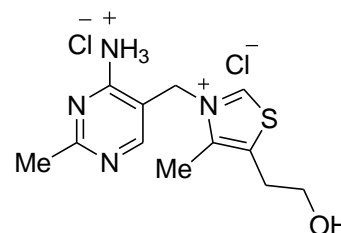


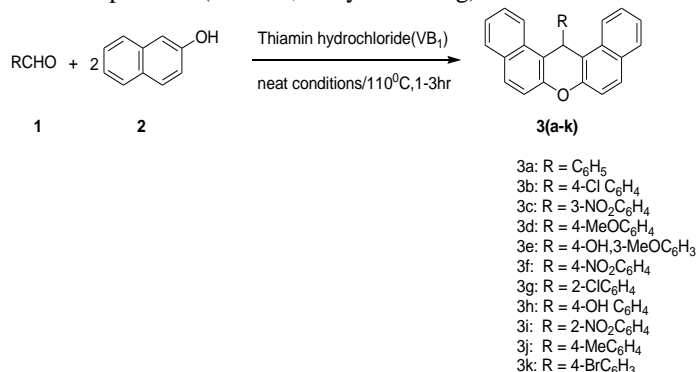
Figure 1. Thiamine hydrochloride(Vitamin-B₁).

Result and Discussion

In continuation to our ongoing research development of new catalytic methods for multicomponent reactions,²⁸ we explored the utility and catalyst efficiency of vit-B₁ for the synthesis of benzoxanthene derivatives by the reaction of two equivalents of β-naphthol and aldehydes under solventfree conditions (Scheme 1).

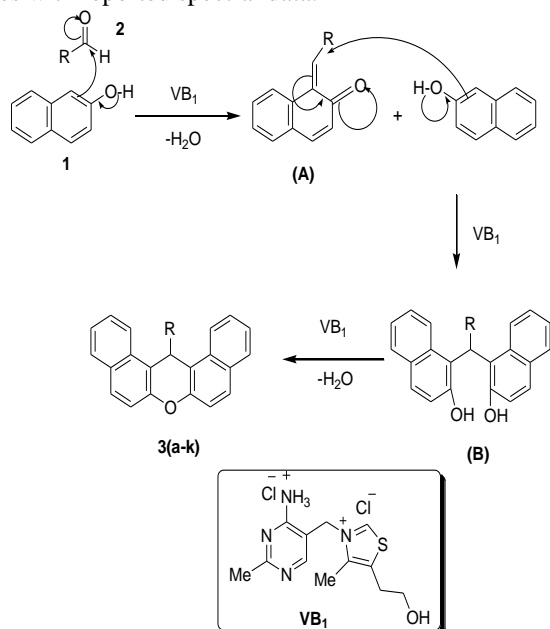
In order to optimize catalyst concentration and reaction temperature, we have conducted the reaction of two equivalents of β-naphthol (1) and benzaldehyde (2) at various temperatures in the presence of varied amount of thiamine hydrochloride (VB₁) and in absence of catalyst (Table 1). It has been found that reaction when conducted in absence of vit-B₁, no product formation was observed (as indicated by TLC) even after prolonged heating(10 hr). Next, we have conducted same reaction by varying amount of catalyst(5-15 mol%) at various temperatures (80-120 °C). Excellent yield of the product 3a(98%) was obtained when 15 mol% of catalyst at 110 °C temperature. Further increase in temperature to 120 °C and

catalyst amount 20 mol%, no reasonable enhancement in yield was observed. Hence, 15 mole% catalyst and 110°C temperature was chosen as an optimized reaction condition for further study. After assortment of appropriate reaction conditions, we have applied the same stratagem for various aromatic aldehydes with diverse functionality (Table 2). After vigilant optimization reaction has been extended for various types of aldehydes with electron donating as well as electron withdrawing functional groups (Table 2). Results obtained clearly indicated that aldehyde possessing electron withdrawing group underwent fast reaction and product is formed in excellent yields (Table 2, entry 3c, 3f and 3i). Whereas, sterically hindered aldehydes underwent slow reaction with comparatively slow yield of the final xanthene products (Table 2, entry 3e and 3g).



Scheme 1 Synthesis of 14-aryl-4H-dibenzo[a,j]xanthenes catalyzed by Vitamin-B₁.

The proposed mechanism of the VB₁ catalyzed xanthene formation is represented in Scheme 2. The condensation of β-naphthol (1) and aromatic aldehyde (2) takes place by addition dihydration and Michael addition. In the beginning, reaction may proceed via formation of intermediate (A) by the reaction of β-naphthol and aldehyde 2. Construction of intermediate 'B' by Michael addition of second β-naphthol molecule to 'A' which on further intramolecular cyclization and dehydration afforded xanthene derivatives. The compounds were characterized by IR, ¹H NMR, and mass spectral data; the spectral data obtained were matches with reported spectral data.^{10,17,24}



Scheme 2. Plausible mechanism of vitamin-B₁ catalyzed synthesis of 14-aryl-4H-dibenzo[a,j]xanthenes catalyzed by Vitamin-B₁

All reactions are carried out under solvent-free conditions.

*Isolated yield of the product

Experimental

All of the products are known compounds and were identified by comparison of their physical and spectral data with those of reported. Melting points were recorded in open capillary using paraffin bath and are uncorrected. Progress of reaction was studied using thin layer chromatography (TLC) in petroleum ether : ethyl acetate (4.5: 0.5) solvent system. IR spectra were recorded using KBr disc. ¹H NMR spectra were recorded 300 MHz instrument using CDCl₃ solvent and TMS as an internal standard.

General procedure for preparation of 14-aryl-4H-dibenzo (a, j) xanthenes catalyzed by VB₁

To a mixture of aldehyde (2 mmol) and β-naphthol (4 mmol), VB₁ (20 mole %) was added. Reaction mixture was heated in oil bath at 110°C for 1.5 h. Completion of reaction was indicated by TLC. After reaction was completed, reaction mixture was transferred in water to afford solid crude products. The product was further purified by recrystallization in ethanol (Ethanol: 4:1). The synthesized pure products were characterized by comparison of their physical data with those of known benzoxanthenes. The spectral data of some representative benzoxanthenes were given below.

Selected characterization data

14(4-Methoxyphenyl)-14H-dibenzo[a,j]xanthene (3d): IR (KBr, cm⁻¹): 3135, 1616, 1590, 1450, 1230, 1120, 820, 778; ¹H NMR (CDCl₃): δ = 6.52(s, 1H), 3.54(s, 3H), 7.07-8.34(m, 16H); Mass (m/z): 372(M⁺) (M.F. = C₂₈H₂₀O).

14(4-Hydroxyphenyl)-14H-dibenzo[a,j]xanthene (3h): IR (KBr, cm⁻¹): 3410, 1590, 1508, 1410, 1255, 814; ¹H NMR (CDCl₃): δ = 4.95(br, s, 1H), 6.40(s, 1H), 6.52-8.40(m, 16H); Mass (m/z): 374.12(M⁺) (M.F. = C₂₇H₁₈O₂).

14(4-Chlorophenyl)-14H-dibenzo[a,j]xanthene (3b): IR (KBr, cm⁻¹): 3140, 1620, 1588, 1450, 1230, 821, 780; ¹H NMR (CDCl₃): δ = 6.5 (s, 1H), 7.12-8.20(m, 16H); Mass (m/z): 392.02(M⁺) (M.F. = C₁₂₇H₁₇ClO).

14(2-Nitrophenyl)-14H-dibenzo[a,j]xanthene (3i): IR (KBr, cm⁻¹): 3350, 3120, 1602, 1590, 1520, 1357, 1242, 1150, 810, 749; ¹H NMR (CDCl₃): δ = 7.45(s, 1H), 7.11-8.40(m, 16H); Mass (m/z): 403.20(M⁺) (M.F. = C₂₈₂₇H₁₇NO₃).

Table 1. Effect of amount of catalyst on the formation of '3a'

Entry	Catalyst (mole %)	Yield '3a' (%)			
		Temp (°C): a=80; b=100; c=110; d=120			
1	00	00 ^{a,b,c,d}			
2	05	00 ^a	58 ^b	70 ^c	72 ^d
3	10	35 ^a	71 ^b	88 ^c	88 ^d
4	15	62 ^a	80 ^b	95 ^c	95 ^d
5	20	69 ^a	77 ^b	92 ^c	95 ^d

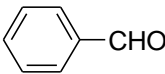
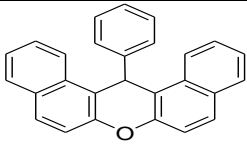
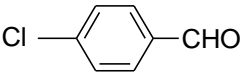
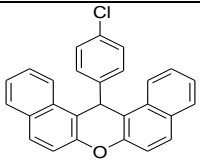
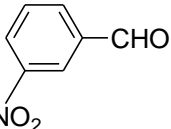
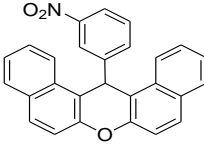
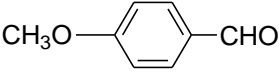
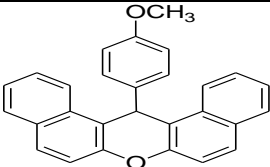
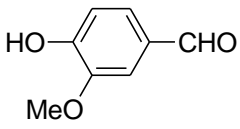
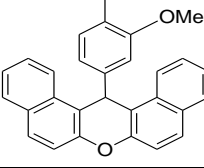
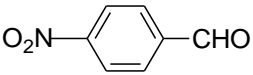
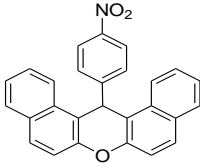
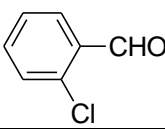
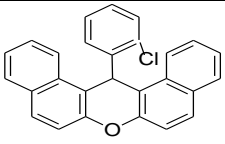
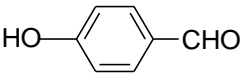
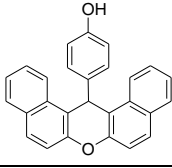
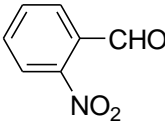
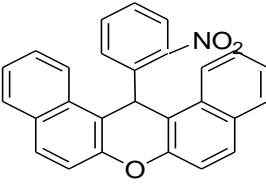
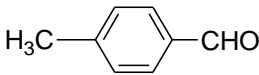
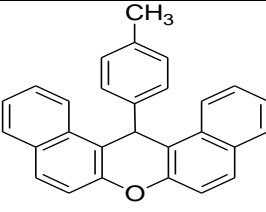
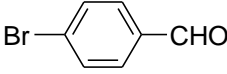
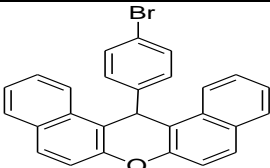
Conclusion

In conclusion, present method was found to be useful addition for development of 'Green Chemistry'. The benzoxanthene products were obtained in good to excellent yield by the reaction of two equivalents of β-naphthol and one equivalent of aromatic aldehyde catalyzed by (VB₁) under solvent free conditions. The method presented here was found to be important from an environmental point of view and less expensive than reported procedures.

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Table 2. Synthesis of 14-aryl-4H-dibenzo[a,j]xanthenes catalyzed by Vitamin-B₁.

Entry	Aldehyde(2)	Product (3)	Time (hr)	Yield (%)*	M.P.(°C) [Ref.]
1			1.2	98	220-221[10b]
2			1.4	90	234-236[10a]
3			1.2	88	210-212[10a]
4			1.4	92	196-198[10a]
5			1.5	87	240-242[10b]
6			1.3	94	192-194[10b]
7			1.0	85	220-221[10a]
8			1.2	92	210-212[17]
9			2.5	90	293-295[24]
10			3.0	92	218-220[10b]
11			2.0	94	295-297[10a]

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