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One step synthesis of 14-alkyl- or aryl-14*H*-dibenzo[*a*,*j*]xanthenes using sodium hydrogen sulfate as catalyst

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Abstract A simple and environmentally benign procedure for the synthesis of 14-alkyl- or aryl-14*H*-dibenzo[*a*,*j*]xanthenes is described through a one-pot condensation of 2-naphthol with aryl or alkyl aldehydes in the presence of sodium hydrogen sulfate as a catalyst under solvent-free conditions.

Keywords 2-Naphthol; Dibenzoxanthenes; Sodium hydrogen sulfate.

Introduction

The synthesis of xanthenes, especially benzoxanthenes has attracted great interest in previous years due to their biological and pharmaceutical properties such as antiviral [1], antibacterial [2], and antiflammatory [3] activities as well as efficacy in photodynamic therapy and antagonists for paralyzing action of zoxazolamine [4]. Furthermore, these compounds represent a very important class of leuco-dyes [5].

Various methods are available for the construction of xanthenes and benzoxanthenes involving the reaction of 2-hydroxynaphtyl carbinol and resorcinol [6], trapping of benzynes by phenols [7], cyclocondensation reaction between 2-hydroxyaromatic aldehydes and 2-tetralone [8], interamolecular phenyl-carbonyl coupling reaction of benzaldehyes and acetophenones [9], cyclocondensation between 2-naphthol and 2-hydroxyaromatic alcohols [10], and cyclization of polycyclic aryltriflate esters [11]. In addition, the synthesis of benzoxanthenes has been achieved by the reaction of aldehydes with 2-naphthol by dehydration. In this context some methods and catalysts for the synthesis of benzoxanthenes have been reported such as acetic acid and sulfuric acid [12], acetic acid and hydrochloric acid [13], H_3PO_4 or $HClO_4$ [14], *p*-toluene sulfonic acid [15], sulfamic acid [16], I_2 [17], Amberlyst-15 [18], $K_5CoW_{12}O_{40}\cdot 3H_2O$ [19], LiBr [20], $HClO_4$–SiO_2 [21], cyanuric chloride [22], silica-sulfuric acid [23], heteropolyacid [24], Dowex-50W [25], and Selectfluor^{TM} [26].

However, these methodologies show varying degrees of success as well as limitations due to low yields, prolonged reaction times, use of toxic organic solvents, the requirement of special apparatus, or harsh reaction conditions. Thus, there is a certain need for the development of an alternate route for the production of xanthenes derivatives, which surpasses those limitations.

Following our systematic studies directed towards the development of practical, safe, and environmentally friendly procedures for several important organic transformations [27], we describe an efficient method for the condensation of aldehydes with 2-naphthol to the corresponding 14-alkyl or aryl-14*H*-dibenzo[*a*,*j*]xanthanes using catalytic amounts of sodium hydrogen sulfate under solvent-free conditions (Scheme 1).

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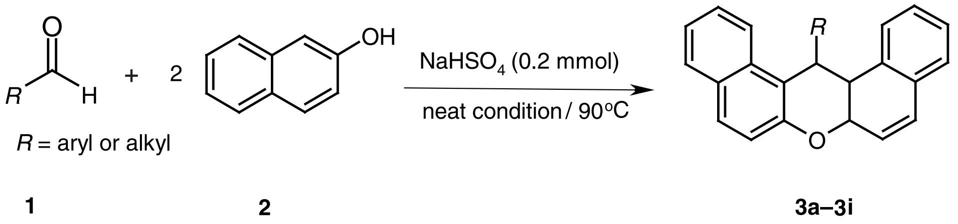


Scheme 1

Results and discussion

Recently, sodium hydrogen sulfate has emerged as a promising solid catalyst for acid catalyzed reactions, such as deprotection of 1,1-diacetates [28], cleavage of prenyl esters [29], bromination of carbonyl compounds [30], esterification of aliphatic carboxylic acids [31], and for silylation of phenols [27e].

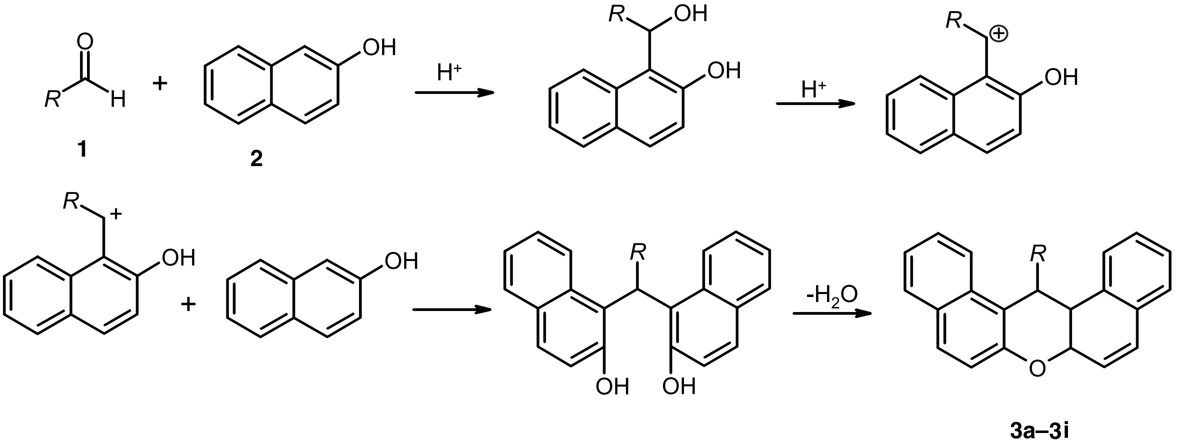
Sodium hydrogen sulfate ($NaHSO_4$) is a readily available and inexpensive reagent and can conveniently be handled and removed from the reaction mixture. Thus, the remarkable catalytic activity together with its operational simplicity make it the most suitable catalyst for the synthesis of dibenzoxanthenes.

14-Alkyl- or aryl-14*H*-dibenzo[*a*,*j*]xanthenes **3a**–**3i** were produced by heating the appropriate aldehyde and 2-naphthol in the presence of a catalytic amount of $NaHSO_4$ at 90°C in an oil bath without solvent (Scheme 1). After completion of the reaction, the catalyst ($NaHSO_4$) can be separated from the reaction mixture by washing the product with water. The reaction proceeds *via* condensation of 1 mol of aldehyde with 2 mol of 2-naphthol followed by intramolecular elimination of water from two hydroxyl groups to form the corresponding dibenzoxanthene as has been suggested earlier [18]. The reaction mechanism is shown in Scheme 2.

This method offers some advantages in term of simplicity of performance, solvent free condition, very low reaction time and a wide range of accessible aryl or alkyl dibenzoxanthenes can be synthesized. Several examples illustrating this novel and general method for the synthesis of dibenzoxanthenes are summarized in Table 1. All products are known compounds and structures of them were confirmed by comparison with their known physical and spectral (NMR and IR) data [12–26].

Various functionalities present in the aryl aldehydes, such as halogen, methoxy, and nitro groups were tolerated. In all these cases, the corresponding dibenzoxanthenes were obtained in good yields. Similar results were also obtained in the case of aliphatic aldehydes (Table 1, entries 8, 9). The synthesis of dibenzoxanthenes could not be achieved in the absence of catalyst ($NaHSO_4$). Table 2 compares our results with results obtained by other groups.

In conclusion, we have developed a simple method for the synthesis of 14-alkyl- or aryl-14*H*-dibenzo[*a*,*j*]xanthenes by condensation reaction of



Scheme 2

Table 1 Synthesis of 14-alkyl- or aryl-14*H*-dibenzo[*a*,*j*]xanthanes in the presence of sodium hydrogen sulfate

Entry	Aldehyde **1**	Product [Ref.][a]	Time/min	Yield/%
1	*Ph*	**3a** [12]	30	90
2	4-Cl*Ph*	**3b** [24]	40	91
3	4-F*ph*	**3c** [15]	40	91
4	4-(NO_2)*Ph*	**3d** [20]	40	88
5	3-(NO_2)*Ph*	**3e** [15]	40	86
6	4-(CH_3)*Ph*	**3f** [19]	40	90
7	2-(CH_3O)*Ph*	**3g** [15]	50	87
8	*n*-C_3H_7	**3h** [13b]	60	74
9	CH_3CHO	**3i** [13b]	60	75

[a] References referring the spectral data of known compounds

Table 2 Comparison of efficiency of various catalysts in synthesis of dibenzoxanthenes

Catalyst[a]	Conditions	Time/h	Yield/%	Ref.
H_2SO_4 (1.2 cm^3)	AcOH/80°C	73	60–90	[12]
p-Toluene sulfunic acid (0.02 mmol)	$ClCH_2CH_2Cl$/reflux	15–24	83–95	[15]
Sulfamic acid (0.1 mmol)	Solvent-free/125°C	6–12	90–95	[16]
I_2 (0.1 mmol)	Solvent-free/90°C	2.5–5	82–95	[17a]
Amberlyst-15 (0.01 g)	Solvent-free/125°C	0.5–2	80–94	[18]
$NaHSO_4$ (0.2 mmol)	Solvent-free/90°C	0.5–1	74–91	this work

[a] The amount of catalyst for 1 mmol aldehyde **1**

aldehydes and 2-naphthol in the presence of sodium hydrogen sulfate under solvent-free conditions. This method offers some advantages in terms of simplicity of performance, low reaction times, solvent-free condition, low cost, and it follows along the line of green chemistry. The catalyst is readily available and inexpensive and can conveniently be handled and removed from the reaction mixture.

Experimental

Products were characterized by comparison of their physical and spectral data with those of authentic samples. All yields refer to isolated products after column chromatography. IR and NMR spectra were recorded on Perkin Elmer 781 and Bruker DPX500 machines. The progress of the reactions was monitored by TLC.

Typical experimental procedure for the synthesis of ***3a–3i***

A mixture of aldehyde (1 mmol), 2-naphthol (2 mmol) and $NaHSO_4$ (0.2 mmol) was stirred at 90°C for the appropriate time indicated in Table 1. The progress of reactions was monitored by TLC (ethyl acetate/petroleum ether = 1/4). After completion of the reaction, the reaction mixture was cooled to 25°C, and water (5 cm^3) was added, and the mixture was stirred for 10 min. The obtained solid was collected by filtration and purified by short column chromatography on silica gel eluting with ethyl acetate/petroleum ether. Products were characterized by comparison of their physical and spectral data with those of authentic samples.

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