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Cellulose sulfuric acid: An efficient biodegradable and recyclable solid acid catalyst for the one-pot synthesis of aryl-14H-dibenzo[*a.j*]xanthenes under solvent-free conditions

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ABSTRACT

The condensation of β-naphthol with aromatic aldehydes in the presence of cellulose sulfuric acid under solvent-free media to afford the corresponding aryl-*14H*-dibenzo [*a.j*]xanthenes in excellent yields and short reaction times is described. The reaction work-up is very simple and the catalyst can be easily separated from the reaction mixture and reused several times in subsequent reactions.

1. Introduction

Xanthenes and benzoxanthene derivatives have received considerable interest from the pharmaceutical industry due to their wide range of interesting biological and therapeutic properties, such as antiviral [1], antibacterial [2], anti-inflammatory [3] activities, as well as their use in photodynamic therapy [4]. Such compounds are also utilized for antagonism of the paralyzing action of zoxazolamine [5]. Because of their interesting spectroscopic properties, these compounds have also found applications to dyes [6], pH-sensitive fluorescent materials for visualization of biomolecules [7], and utility in laser technologies [8]. Since they display a broad spectrum of biological and therapeutic properties, they are considered as high priority structures in combinatorial drug discovery and development. Consequently, many procedures have been developed for the synthesis of xanthenes and benzoxanthenes, which include trapping of benzynes by phenols [9], cyclocondensation between 2-hydroxy aromatic aldehydes and 2-tetralone [10] cyclodehydrations [11], and intramolecular phenyl carbonyl reaction of aldehydes with β-naphthol [12]. Furthermore, the synthesis of benzoxanthenes and their related products include the reaction of β-naphthol with formamide [13] carbon monoxide [14], 2-naphthol-1-methanol [15], aldehydes and cyclic 1,3-dicarbonyl compounds [16]. However, these methods have many disadvantages, such as the use of toxic solvents, prolonged reaction times, excess reagents, low yields and harsh reaction conditions. The synthesis of xanthenes has been improved by condensing β-naphthol with aldehydes in the presence of an acid catalyst such as sulfamic acid [17], Amberlyst-15 [18], AcOH-H_2SO_4 [19], *p*-TSA [20] and silica sulfuric acid [21]. Some of these methods suffer from severe drawbacks, including use of large amounts of expensive reagents and catalysts, low yield, use of toxic solvents and catalysts, long reaction times, special apparatus, and tedious workup procedures, which necessitate the development of an alternative route for the synthesis of these biologically active molecules. Cellulose is one of the most abundant natural biopolymers in the world and has been widely studied during the past several decades because it is a biodegradable material and a renewable resource. Its unique properties make it an attractive alternative to conventional organic or inorganic supports in catalytic applications.

Recently, the direction of science and technology has been shifting more towards eco-friendly, natural product resources and reusable catalysts. Thus, natural biopolymers are attractive candidates in the search for such solid support catalysts [22,23]. Recently, cellulose sulfuric acid has emerged as a promising biopolymeric solid support acid catalyst for acid-catalyzed reactions, such as the synthesis of α-aminonitriles [24], imidazoazines [25] and quino-

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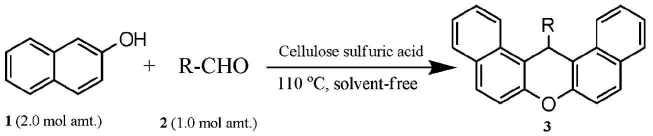
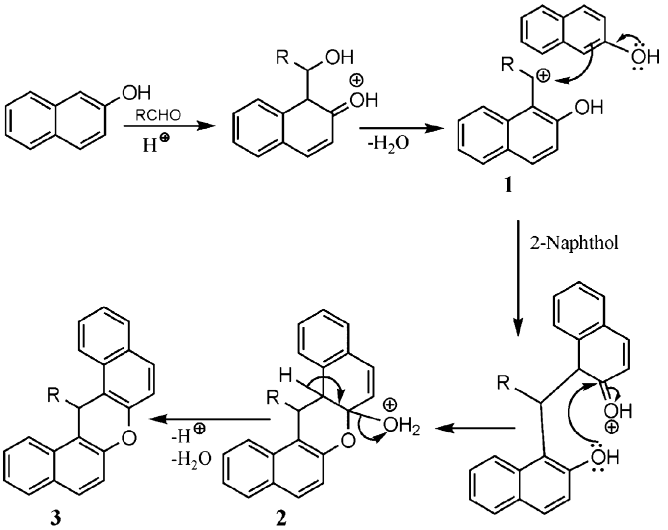


Scheme 1. Synthesis of aryl-14*H*-dibenzo[*a.j*]xanthenes with cellulose sulfuric acid.



Scheme 2. Plausible reaction mechanism for the formation of aryl-14*H*-dibenzo[*a.j*]xanthenes from β-naphthol.

Table 1
Effect of temperature on xanthene yield.

Entry	Temperature (°C)	Yield[a] (%)
1	110	95
2	120	94
3	100	86

[a] Isolated yield.

lines [26]. Cellulose sulfuric acid can be easily prepared by the reaction of inexpensive cellulose with chlorosulfonic acid; the number of acidic (H^+) sites in the cellulose sulfuric acid product is 0.50 meq/g [24].

We now report a new and efficient method for the synthesis of aryl-14*H*-dibenzo[*a.j*]xanthenes *via* the condensation of β-naphthol with different aromatic aldehydes using cellulose sulfuric acid as a catalyst under solvent-free conditions (Scheme 1). To the best of our knowledge, the use of cellulose sulfuric acid as a catalyst for the synthesis of aryl-14*H*-dibenzo[*a.j*]xanthenes has not been previously reported.

2. Results and discussion

The reaction likely proceeds *via* initial formation of carbocation (**1**). The oxonium species (**2**) is then formed on reaction with β-naphthol, which then undergoes dehydration to afford the desired product (**3**) (Scheme 2).

Initially, the condensation of β-naphthol with benzaldehyde in the presence of a catalytic amount (0.08 g) of cellulose sulfuric acid under solvent-free media at 110–115 °C temperature was examined as a model reaction (Table 1). When 1.0 mmol of benzaldehyde and 2.0 mmol of β-naphthol were used, the reaction was completed within 1.5 h to furnish the desired xanthene, phenyl-14*H*-dibenzo[*a.j*]xanthene, in 95% yield (Entry 1). Furthermore, the effect of reaction temperature was examined and the reaction proceeded smoothly at 120 °C, but there was no significant change in the yield of the product (Entry 2). It was also observed that the yield of xanthene product decreased to 86% when the reaction was carried out at 100 °C (Entry 3).

Table 2
Effect of catalysts on xanthene yield.

Entry	Catalyst	Yield[a] (%)	Quantity
1	Cellulose sulfuric acid	95	0.08 g
2	Silica sulfuric acid	89	0.08 g
3	*p*-Toluene sulfonic acid	91	0.1 mmol
4	Sulfuric acid in acetic acid	55	0.1 mmol
5	No catalyst	15	None

Reaction conditions: β-naphthol, 2.0 mmol; benzaldehyde, 1.0 mmol; 110–115 °C; and 1.5 h.

[a] Isolated yield.

The efficiency of the cellulose sulfuric acid reagent compared to various sulfur analog acidic catalysts was also examined (Table 2). In this study it was found that cellulose sulfuric acid is a more efficient and superior catalyst (Entry 1) over other acidic catalysts (Entries 2–4) with respect to reaction time and yield of the desired xanthene. It was also observed that the yield of the xanthene was only 15% in the absence of the cellulose sulfuric acid reagent (Entry 5).

The reusability of the catalyst was checked by separating the cellulose sulfuric acid from the reaction mixture by simple filtration, washing with CH_2Cl_2, and drying in a vaccum oven at 60 °C for 5 h prior to reuse in subsequent reactions The recovered catalyst can be reused at least three additional times in subsequent reactions without significant loss in product yield (Table 3).

Several syntheses of aryl-14*H*-dibenzo[*a.j*]xanthenes from the condensation of β-naphthol with a wide range of aromatic aldehydes utilizing cellulose sulfuric acid under solvent-free conditions at 110–115 °C were examined. All reactions were complete with in 1–3 h, as indicated in Table 4; in all cases the reactions afforded the desired products in excellent yields.

Table 3
The effect of reusability of cellulose sulfuric acid catalyst on the xanthene yield.

Run	Cycle	Yield[a] (%)
1	0	95
2	1	94
3	2	91
4	3	86

Reaction conditions: β-naphthol, 2.0 mmol; benzaldehyde, 1.0 mmol; cellulose sulfuric acid, 0.08 g; 110–115 °C; and 1.5 h.

[a] Isolated yield.

Table 4
Synthesis of aryl-14*H*-dibenzo[*a.j*]xanthenes with cellulose sulfuric acid.

Entry[a]	Aromatic aldehyde	Time (h)	Yield[b] (%)
1	Benzaldehyde	1.5	95
2	4-Methylbenzaldehyde	2.0	93
3	4-Chlorobenzaldehyde	1.0	97
4	4-Bromobenzaldehyde	2.0	92
5	4-Nitrobenzaldehyde	2.0	90
6	4-Methoxybenzaldehyde	1.5	95
7	2-Chlorobenzaldehyde	2.0	93
8	2-Nitrobenzaldehyde	2.5	90
9	2-Methoxybenzaldehyde	2.5	94
10	3-Bromobenzaldehyde	1.5	92
11	3-Nitrobenzaldehyde	2.0	90
12	2-Naphthaldehyde	3.0	84
13	4-Oxo-4*H*-chromene-3-carbaldehyde	3.0	83
14	6-Nitro-4-0xo-4*H*-chromene-3-carbaldehyde	3.0	81

Reaction conditions: β-naphthol, 2.0 mmol; aromatic aldehyde, 1.0 mmol; cellulose sulfuric acid, 0.08 g; 110–115 °C; and 1–3 h.

[a] All the compounds are known, characterized by IR, ^1H NMR, and mass spectral analysis, and compared with the authentic samples.

[b] Isolated yields.

From the results in Table 4, the slight variations in the yield of xanthene is likely due to the presence and nature of the different aromatic substituents on the aldehyde precursor, although it must be noted that in general, the yield of most xanthene products is greater than 90%. Thus, 4-chlorobenzaldehyde (Entry 3), and other benzaldehydes bearing electromeric 4-substituents (i.e. Entries 4 and 6) afford slightly better xanthene yields over benzaldehydes bearing electron withdrawing 4-substituents (Entry 5). This slight difference is also seen in 2-substituted benzaldehydes (Entries 7, 8 and 9). It was also observed that a more significant decrease in xanthene yield occurred when simple or substituted benzaldehydes precursors were replaced with polycyclic aromatic aldehyde precursors (compare Entries 1 and 12, and see Entries 13 and 14).

3. Experimental

3.1. Preparation of cellulose sulfuric acid

To a magnetically stirred mixture of 5.00 g of cellulose) in 20 ml of *n*-hexane, 1.00 g of chlorosulfonic acid (9 mmol) was added dropwise at 0 °C during 2 h. HCl gas was removed from the reaction vessel immediately. After the addition was complete, the mixture was stirred for 2 h. The mixture was then filtered and washed with 30 ml of acetonitrile and dried at room temperature to afford 5.25 g of cellulose sulfuric acid as a white powder. The number of H^+ sites on the cellulose–SO_3H was determined by acid-base titration to be 0.50 meq/g.

3.2. Procedure for the synthesis of aryl-14H-dibenzo[a.j]xanthenes

A mixture of β-naphthol (2 mmol), aromatic aldehyde (1 mmol) and cellulose sulfuric acid (0.08 g) was stirred at 110–115 °C for the appropriate time, as shown in Table 3. Completion of the reaction was indicated by TLC monitoring. The reaction mixture was cooled to ambient temperature, EtOAc was added, and the cellulose sulfuric acid was filtered off. The filtrate was concentrated to dryness, and the crude solid product was crystallized from EtOH to afford the pure aryl-14H-dibenzo[*a.j*]xanthene

4. Conclusions

In conclusion, cellulose sulfuric acid, an efficient, eco-friendly, reusable, and solid support biodegradable acid catalyst, has been prepared and utilized for the synthesis of biologically important aryl-14*H*-dibenzo[*a.j*]xanthenes *via* the condensation of β-naphthol with a wide range of aromatic aldehydes under solvent-free conditions. Prominent advantages of this new methodology are the reusability of the catalyst, the operational simplicity, and the high yields of product. We believe this methodology is superior to existing methodologies for the synthesis of aryl-14*H*-dibenzo[*a.j*] xanthenes.

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