Iranian Journal of Catalysis 3(2), 2013, 123-128

IRANIAN JOURNAL OF CATALYSIS

Cellulose sulfuric acid: an efficient biopolymer-based catalyst for the synthesis of 5*H*-dibenzo[*b,i*]xanthene-tetraones and spiro[dibenzo[*b,i*]xanthene-13,3'-indoline]-pentaones under solvent free conditions

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Received 16 May 2013; received in revised form 1 August 2013; accepted 29 August 2013

ABSTRACT

A practical and green method for the synthesis of 5*H*-dibenzo[*b,i*]xanthene-tetraones and spiro[dibenzo[*b,i*]xanthene-13,3'-indoline]-pentaones by the condensation of 2-hydroxynaphthalene-1,4-dione with aldehydes or isatins, respectively, in the presence of a catalytic amount of cellulose sulfuric acid (CSA) under solvent-free conditions at 100 °C is described. The significant features of this procedure are high yields of the products, simple work-up, solvent-free conditions, operational simplicity and non-toxicity of the catalyst. Moreover, cellulose sulfuric acid is successfully reused for four cycles without significant loss of activity.

***Keywords**: 2-Hydroxynaphthalene-1,4-dione; Cellulose sulfuric acid; Xanthenes; Solvent-free.*

1. Introduction

Solid acid catalysts for the synthesis of fine chemicals have attracted considerable attention from both environmental and economical points. The solid acids generally have high turnover numbers that can be easily separated from reaction mixtures [1]. Replacement of liquid acids with solid acids is desirable in the chemical industry [2,3]. Majority of the reported supports for catalytic applications are based on inorganic materials or functional synthetic polymers in which the synthesis of the supports involve high temperature calcinations or polymerization of petrochemical feed stocks [4,5]. Recently the emphasis of science and technology is shifting more towards sustainable resources and processes; in this regard biopolymers are attractive candidates to explore for supported catalysis [6-10]. 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 [11]. As a chemical raw material, it is generally well-known that it has been used in the form of fibers or derivatives for nearly 150 years for a wide spectrum of products and materials in daily life [12]. Cellulose as a biodegradable material can be used for several applications and also as support for bonding several functional groups which act as catalysts to yield clean efficient and fast chemical reactions [13]. Shabani et al have synthesized Cellulose sulfuric acid (CSA) by the reaction of inexpensive cellulose with chlorosulfonic acid (Scheme 1) [11]. The number of acidic (H^+) sites in the cellulose sulfuric acid is 0.50 meq/g in the basis of acid-base titration [11]. It has excellent catalytic properties, which are attributed to the high thermal stability and strong acid sites of sulfonic acid functional groups and make it an attractive alternative to conventional organic or inorganic supports in catalytic applications. Also, it has emerged as a promising biopolymeric solid-support acid catalyst for acid-catalyzed reactions, such as the synthesis of aryl-14*H*-dibenzo[*a.j*]xanthenes [14], 1,4-dihydropyridines [15], quinoxaline [16], α-amino nitriles [11], Pechmann condensation [17], thiadiazolo benzimidazoles [18], imidazoazines [19], quinolines [20], 3,3'-indolyloxindoles [21], 3,4-dihydropyrimidine-2(1*H*)-ones [22], 2,4,5-triarylimidazoles [23], *β*-acetamido carbonyl derivatives [24], Knoevenagel condensation [25], oxazolines, imidazolines and thiazolines [26].

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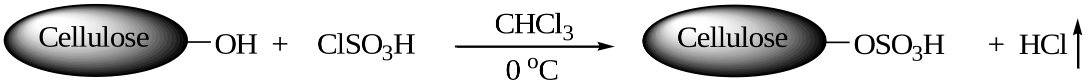


Scheme 1. Preparation of cellulose sulfuric acid (CSA).

Molecules with the quinone structure constitute one of the most interesting classes of compounds in organic chemistry, due to their biological properties, their industrial applications and their potential as intermediates in the synthesis of heterocycles [27]. Various biological properties including enzyme inhibition, antibacterial, antifungal, and anticancer activities have been reported for quinones and quinone derivatives [28-31]. The chemistry of quinone-annulated heterocycles is largely dependent on the substituent being either on the quinone or on adjacent rings [32,33]. These activities, combined with diverse chemical behavior make quinones attractive targets in organic synthesis [34-36].

Considering the above reports, the development of new and simple synthetic methods for naphthoquinone fragments is an interesting area. Herein we have reported a green and facile methodology for the synthesis of 5*H*-dibenzo[*b,i*]xanthene-tetraones and spiro[dibenzo[*b,i*] xanthene-13,3'-indoline]-pentaones in the presence of cellulose sulfuric acid (CSA) as an inexpensive and biodegradable solid acid catalysts at 100 °C (Scheme 2). To the best of our knowledge, there are only two reports in literature on the synthesis of 5*H*-dibenzo[*b,i*]xanthene-tetraones [34,36].

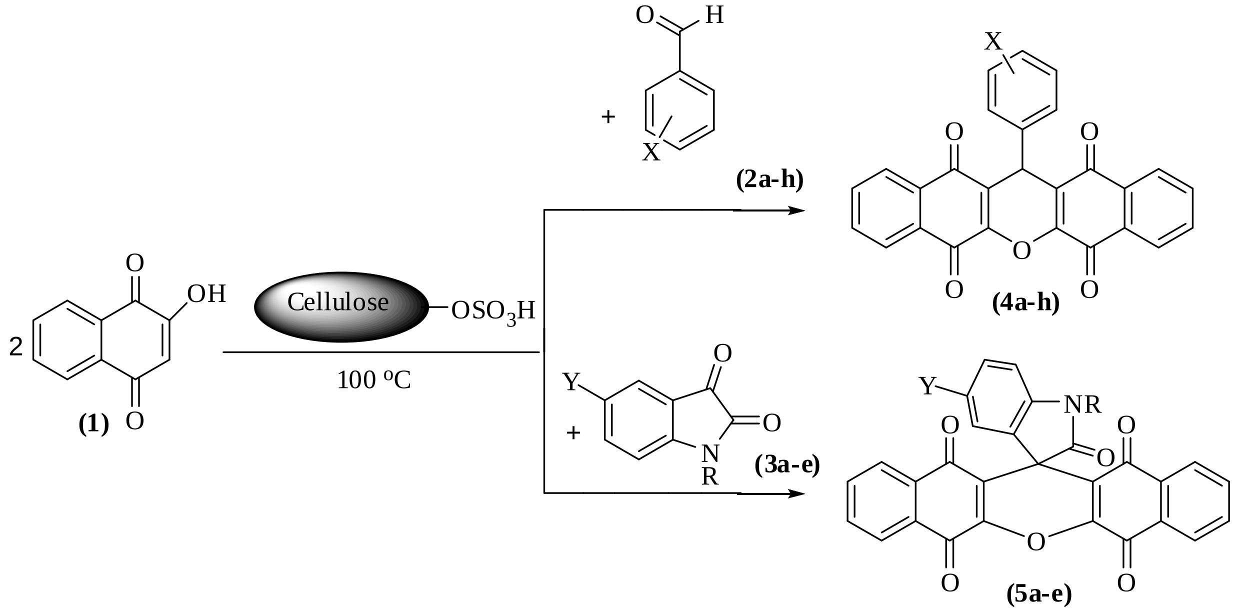
2. Experimental

2.1. General

All chemicals were purchased from Merck or Fluka Chemical Companies. The products were characterized by comparing the physical data with those of known samples or by their spectral data. Melting points were measured on an Electrothermal 9200 apparatus. IR spectra were obtained on a Shimadzu FTIR-8400S spectrometer. ^{1}H NMR spectra was determined on a BRUKER DRX-300 AVANCE spectrometer at 300.13 MHz.

2.2. Catalyst preparation

To a magnetically stirred mixture of cellulose (5.00 g, DEAE for column chromatography, Merck) in $CHCl_3$ (20 mL), chloro sulfonic acid (1.00 g, 9 mmol) was added drop wise at 0 °C during 2 h. After addition was complete, the mixture was stirred for 2 h until HCl was removed from reaction vessel. Then, the mixture was filtered and washed with methanol (30 mL) and dried at room temperature to obtain cellulose sulfuric acid as white powder (5.13 g).



Scheme 2. Synthesis of 5*H*-dibenzo[*b,i*]xanthene-tetraones and spiro[dibenzo[*b,i*]xanthene-13,3'-indoline]-pentaones in the presence of cellulose sulfuric acid (CSA).

*2.3. General procedure for the preparation of 5H-dibenzo[b,i]xanthene-tetraones **(4a)** and spiro[dibenzo[b,i]xanthene-13,3'-indoline]-pentaones **(5a)***

In a typical reaction, a mixture of 2-hydroxynaphthalene-1,4-dione (2 mmol, 0.348 g) and bezaldehyde (1 mmol, 0.106 g) or isatin (1 mmol, 0.147 g) in the presence of cellulose sulfuric acid (0.07 g) was heated at 100 °C. Reaction progress was monitored by TLC. After completion of the reaction, the reaction mixture was filtered and washed with CH_2Cl_2 (10 mL) to separate the catalyst. Then the filtrate's solvent was evaporated under reduced pressure and recrystallized from ethanol to afford the pure product **(4a)** or **(5a)**. The same procedure was also used for the other products listed in Table 1.

2.4. Selected spectral data

13-Phenyl-5*H*-dibenzo[*b*,*i*]xanthene-5,7,12,14(13*H*)-tetraone **(4a):** Red powder, m.p. 306-308 °C, IR (KBr, cm^{-1}): 3035, 1660, 1569; ^1H NMR (300.1 MHz, DMSO-d_6, ppm) δ: 5.09 (1H, s, CH), 7.16-8.08 (13H, m, H-Ar).

13-*p*-Tolyl-5*H*-dibenzo[*b*,*i*]xanthene-5,7,12,14(13*H*)-tetraone **(4b):** Brick-red powder m.p. 305-307 °C IR (KBr, cm^{-1}): 3088, 1663, 1608; ^1H NMR (300.1 MHz, DMSO-d_6, ppm) δ: 2.21 (3H, s, CH_3), 5.09 (1H, s, CH), 7.07-8.12 (12H, m, H-Ar).

13-(4-Chlorophenyl)-5*H*-dibenzo[*b*,*i*]xanthenes 5,7,12,14(13*H*)-tetraone **(4c):** Orange powder, m.p. 329-331 °C; IR (KBr, cm^{-1}): 3028, 1663, 1610; ^1H NMR (300.1 MHz, DMSO-d_6, ppm) δ: 5.10 (1H, s, CH), 7.26-8.07 (12H, m, H-Ar).

13-(4-Nitrophenyl)-5*H*-dibenzo[*b*,*i*]xanthenes 5,7,12,14(13*H*)-tetraone **(4h):** Orange powder, m.p. 354-356 °C; IR (KBr, cm^{-1}): 3038, 1665, 1608; ^1H NMR (300.1 MHz, DMSO-d_6, ppm) δ: 5.45 (1H, s, CH), 7.12-8.16 (12H, m, H-Ar).

Spiro[dibenzo[*b*,*i*]xanthene-13,3'-indoline]-pentaone **(5a):** Orange powder, m.p. 350 °C dec, IR (KBr, cm^{-1}): 3412, 3088, 1723, 1667, 1605. ^1H NMR (300.1 MHz, DMSO-d_6, ppm) δ: 6.79-8.13 (12H, m, H-Ar), 10.83 (1H, s, NH).

1'-Methylspiro[dibenzo[*b*,*i*]xanthene-13,3'-indoline]-pentaone **(5d):** Red powder, m.p. 365 °C dec, IR (KBr, cm^{-1}): 3398, 3123, 1730, 1665, 1603. ^1H NMR (300.1 MHz, DMSO-d_6, ppm) δ: 2.18 (3H, s, CH_3), 6.82-8.19 (11H, m, H-Ar), 10.84 (1H, s, NH).

3. Results and Discussion

We first studied a reaction between 2-hydroxynaphthalene-1,4-dione and benzaldehyde by screening the reaction conditions. To determine the optimum conditions, we examined the influence of the reaction temperature, the choice of solvent and the type of catalyst (Table 1).

Table 1. Optimization of the reaction conditions.[a]

Entry	Catalyst	Condition	Time (h)	Yield (%) [b]	Reference
1	-	Solvent-free/ 25 °C	24	Nil	-
2	-	Solvent-free/ 100 °C	24	Nil	-
3	*p*-TSA	Solvent-free/ 25 °C	24	Nil	-
4	*p*-TSA	Solvent-free/ 80 °C	7	74	36
5	*p*-TSA	Solvent-free/ 100 °C	3	81	34
6	$NaHSO_3/SiO_2$	Solvent-free/ 100 °C	3	75	-
7	*L*-proline	Solvent-free/ 100 °C	2.5	82	-
8	HOAc	Solvent-free/ 100 °C	3.5	64	-
9	CSA (0.03)	Solvent-free/ 100 °C	3.5	79	-
10	CSA (0.05)	Solvent-free/ 100 °C	2	86	-
11	CSA (0.07)	Solvent-free/ 25 °C	24	Nil	-
12	CSA (0.07)	EtOH/ reflux	3	80	-
13	CSA (0.07)	H_2O/ reflux	2.5	82	-
14	CSA (0.07)	Solvent-free/ 100 °C	1.5	93	-

[a] A mixture of 2-hydroxynaphthalene-1,4-dione **(1)** and benzaldehyde **(2a)**.

[b] Isolated yield.

Throughout the reaction, the conditions were optimized for a 100% conversion. It could be seen that the best result was obtain with (0.07 g) of catalyst under solvent-free condition at 100 °C (Table 1, Entry 14).

After optimizing the conditions, we next examined the generality of these conditions to other substrates using several aromatic aldehydes bearing electron-withdrawing and electron-donating groups (Scheme 2). The results are summarized in Table 2. As indicated in Table 2, in all cases the reaction gives the products in good yields and prevents problems associated with solvent use such as cost, handling, safety and pollution. Encouraged by these results, we attempted to expand the scope of this synthetic method by using isatins in place of aromatic aldehydes partner. The results showed that the reactions were completed within 4-6 h of heating, and the desired products were obtained in excellent yields (Table 2). We examined the effect of the amount of catalyst in this reaction. The best results were obtained using 0.07 g of catalyst. Using lower amounts of catalyst resulted in lower yields, and in the absence of catalyst the yield of the product was found to be nil (Table 2, Entry 1,2).

The structures of compounds **4a-h** and **5a-e** were confirmed by IR and ^{1}H NMR spectroscopy. The IR spectrum of compound **5d**, for example, show absorption bands at 3398, 3123, 1730, 1665, and 1603 cm^{-1} indicating the presence of N-H and C=O groups in this molecule. Aromatic protons of this compound were seen at δ 6.82-8.19 in its ^{1}H NMR spectrum resonating with proper integrals and splittings. Aliphatic region of this spectrum exhibits one singlet peak at δ 2.18 arising from protons of the methyl groups. In addition, there is one singlet signal appeared at δ 10.84 in the spectrum accounting for the presence of the N-H group in the molecule. Due to the very low solubility of products **4** and **5** we were unable to obtain ^{13}C NMR spectra for these products.

Table 2. Synthesis of 5*H*-dibenzo[*b,i*]xanthene-tetraones and spiro[dibenzo[*b,i*]xanthene-13,3'-indoline]-pentaones 4a-h and 5a-e.

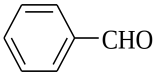
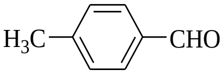
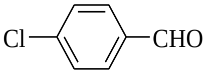
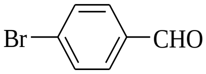
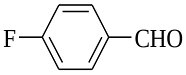
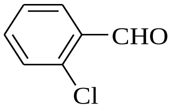
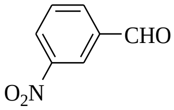
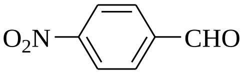
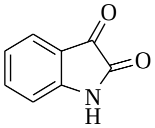
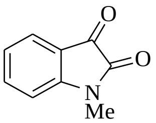
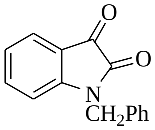
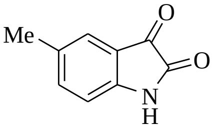
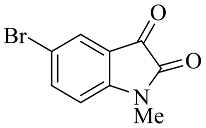
Entry	Aldehyde or Isatin	Product ^{a}	Time (h)	Yield (%) ^{b}	m.p. (°C)	
					Found	Reported
1	 **2a**	4a	1.5	93	306-308	305-307
2	 **2b**	4b	2.5	90	305-307	304-307
3	 **2c**	4c	1	89	329-331	330-332
4	 **2d**	4d	2	86	334-336	333-335
5	 **2e**	4e	1.5	92	268-270	270-272
6	 **2f**	4f	2	88	306-308	307-309
7	 **2g**	4g	1	94	339-341	340-342
8	 **2h**	4h	1.5	92	354-356	-

Table 2. *(Continued).*

9	 **3a**	5a	4	87	349 dec.	350 dec.
10	 **3b**	5b	4.5	92	358 dec.	360 dec.
11	 **3c**	5c	6	89	356 dec.	358 dec.
12	 **3d**	5d	5	90	365 dec.	-
13	 **3e**	5e	6	85	363 dec.	365 dec.

[a] All products were characterized by ^1H NMR and IR spectral data and comparision of their melting points with those of authentic samples.
[b] Isolated yield.
[c] References 34, 36.

We also investigated the reusability of the catalyst. For this purpose after completion of the model reaction, the cellulose sulfuric acid was separated from the reaction mixture by simple filtration, washing with CH_2Cl_2, and drying in a vacuum oven at 60 °C for 5 h prior to reuse in subsequent reactions. The recovered catalyst can be reused at least four additional times in subsequent reactions without significant loss in product yield (Table 3).

A plausible mechanism for the formation of 5*H*-dibenzo[*b*,*i*]xanthene-tetraones is shown in Scheme 3.

The dibenzo[*b*,*i*]xanthene synthesis presumably initiates by nuleophilic addition of the substrate 2-hydroxynaphthalene-1,4-dione **1** on the reactant aldehyde **2** activated by CSA. The resulting adduct **6** undergoes dehydration to give the key enone intermediate **7** which is likely activated by CSA to follow a Michael type addition by the second molecule of **1**. Cyclization of the intermediate **8** and subsequent loss of H_2O leads to the xanthene **4**.

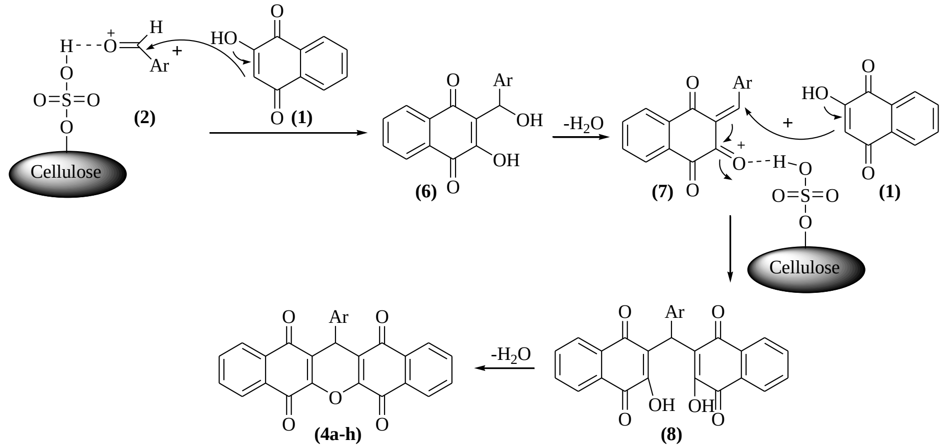
4. Conclusion

In summary, we have described green and simple method for the preparation of 5*H*-dibenzo[*b*,*i*]xanthene-tetraones and spiro[dibenzo[*b*,*i*] xanthene-13,3'-indoline]-pentaones, in the presence of cellulose sulfuric acid as an efficient and environment friendly bio-supported proton source catalyst under solvent-free conditions. Excellent yields, recyclability of the catalyst, simple experimental procedure and product isolation, the usage of nontoxic, noncorrosive and inexpensive solid acid catalyst are important features of the presented approach.

Table 3. The effect of CSA recycling on the **4a** yield. [a]

Entry	Cycle	Yield (%) [b]
1	fresh	93
2	first recycle	92
3	second recycle	92
4	third recycle	90
5	fourth recycle	89

[a] Reaction conditions: a mixture of 2-hydroxynaphthalene-1,4-dione **1** (2.0 mmol) and benzaldehyde **2a** (1.0 mmol) at 100 °C.
[b] Isolated yields.



Scheme 3. Plausible mechanism for the synthesis of 5*H*-dibenzo[*b*,*i*]xanthene-tetraones 4a-h in the presence of cellulose sulfuric acid CSA.

Acknowledgements

We gratefully acknowledge financial support from the Research Council of Islamic Azad University Rasht Branch.

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