Synthesis, Characterization, and Application of Cobalt Hydrogen Sulfate as a New Heterogeneous, Reusable and Efficient Catalyst in One-Pot Synthesis of 14-aryl-14H-dibenzo[a,j]xanthenes and 1,8-dioxooctahydroxanthenes¹

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Abstract—Cobalt hydrogen sulfate is synthesized and characterized by XRD, FTIR and TEM measurements. The efficiency of this readily available, cheap, non-toxic, heterogeneous and reusable catalyst is shown in the one-pot preparation of aryl- and alkyl-14H-dibenzoxanthenes and 1,8-dioxooctahydroxanthene derivatives by cyclocondensation of substituted benzaldehydes and β -naphthol or 5,5-dimethyl-1,3-cyclohexanedione respectively. Among advantages of these methods are high yields, a clean reaction strategy, simple methodology, green conditions and easy workup.

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Metal hydrogen sulfates are widely used as efficient reagents in synthetic organic chemistry. A broad range of reactions including protection, deprotection, oxidation, C–C, C–N, and C–O bond formation and cleavage took place in the presence of these reagents. In addition, stability, cheapness, and efficiency and in many cases heterogeneity and reusability are other important advantages of these reagents [1–5].

The synthesis of xanthene derivatives, especially benzoxanthenes, has attracted attention of organic chemists due to their wide range of biological and therapeutic properties such as antibacterial [6] and antiviral efficiency [7] and also because they can be used for photodynamic treatments (PDT) [8]. Benzoxanthenes are used in production of dyes [9], in laser technologies [10], and in manufacturing of fluorescent materials for visualization of biomolecules [11]. Many procedures are disclosed to synthesize xanthenes and benzoxanthenes like trapping of benzynes by phenols [12], cyclocondensation between 2-hydroxy aromatic aldehydes and 2-tetralone [13], interamolecular phenyl-carbonyl coupling reaction of benzaldehydes and acetophenones [14]. In addition, 14H-dibenzoxanthenes and related products are prepared by dehydration reaction of β -naphthol with aldehyde. In this context some methods and catalysts suitable for the synthesis of benzoxanthenes have been reported. Among these are acetic acid and sulfuric acid [15], silica and sulfuric acid [16], *p*-toluene sulfonic acid [17], amberlyst-15 [18], ferric hydrogen sulfate [19], and heteropolyacids (HPAs) [20]. On the other hand, the an increased application both in the field of medicinal chemistry and material science produced a renewed interest in the synthesis of 1,8-dioxooctahydroxanthene compounds. In recent years, synthesis of 1,8dioxooctahydroxanthenes was focused on the condensation of dimedone (5,5-dimethyl-1,3-cyclohexanedione) with various aromatic aldehydes, by using different catalysts such as silica sulfuric acid [21], Dowex-50W [22], HClO₄-SiO₂ and PPA-SiO₂ [23], NaHSO₄-SiO₂ and silica chloride [24], p-dodecylbenzenesulfonic acid [25], Fe³⁺-montmorillonite [26], amberlyst-15 [27], diammonium hydrogen phosphate [28], TMSC1 [29], tetrabutylammonium hydrogen sulphate [30], and hydrochloric acid [31].

In spite of potential utility of aforementioned routes for the synthesis of xanthenes derivatives, many of these methods have serious shortcomings. They use expensive reagents, strong acidic conditions, and long reaction times but afford low yields. Moreover, excess of reagents/catalysts and toxic organic solvents are involved in the synthesis. A possible approach to correct these problems is a search for new active, efficient and recyclable catalysts and simple work-up for the preparation of xanthenes under neutral, mild and practical conditions. In the present paper, we report a

¹ The article is published in the original.



Scheme 1. Synthesis of 14-aryl-14H-dibenzo[a,j]xanthenes.

one-pot synthesis of aryl-14H-dibenzoxanthene and 1,8-dioxooctahydroxanthene derivatives by the reaction of various aromatic aldehydes with β -naphthol or dimedone, respectively in the presence of Co(HSO₄)₂ as an heterogeneous catalyst (Scheme 1).

EXPERIMENTAL

All materials and solvents were procured from "Merck" and "Fluka" chemical companies. Melting points were determined in open capillary tubes using an IA 9000 melting point apparatus ("Electrothermal"). IR spectra were recorded using Avatar 370 FT-IR spectrometer ("Therma Nicolet"). ¹H NMR spectra were recorded with a Bruker-100 MHz instrument ("Bruker") using tetramethylsilane (TMS) as an internal standard. The mass spectra were scanned on a Varian Mat CH-7 instrument ("Varian") at 70 eV. Elemental analyses were obtained on a Flash EA microanalyzer ("Thermo Finnigan").

Preparation of $Co(HSO_4)_2$

A 50 ml suction flask was equipped with a dropping funnel. The gas outlet was connected to a vacuum system through an alkaline solution trap. Cobalt chloride (10 mmol) was charged into the flask and concentrated sulfuric acid 98% (30 mmol) was added drop wise over a period of 30 min at room temperature. Gaseous HCl was evolved immediately. After adding sulfuric acid, the mixture was shaken for 30 min at 100°C, while the residual HCl was removed by suction. Finally, Co(HSO₄)₂ was obtained in 95% yield.

General Procedure for the Preparation of 14-Arylor Alkyl-14H-Dibenzo[a,j]xanthenes 3a-1

A mixture of 2-naphthol (0.145 g, 1 mmol), aldehyde (0.5 mmol), and $Co(HSO_4)_2$ (0.025 g, 0.1 mmol)

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in 1,2-dichloroethane (**DCE**, 10 ml) was allowed to stir at reflux condition for appropriate time according to Table 1. TLC monitored the progress of the reaction. After reaction, the reaction mixture was filtered and the organic solvent was cooled and concentrated. The crystalline solid that was precipitated was recrystallized from ethanol to give a pure product. All products are known compounds, which were characterized by IR and ¹H NMR spectroscopic data and their melting points were compared with reported values.

14-(4-Hydroxyphenyl)-14H-dibenzo[a,j]xanthene **3d** (Table 1, entry 4): pink solid. Yield: 90%. M.p.: 140–141°C, ¹H NMR (CDCl₃ 100 MHz): 4.97 (br s, 1H, OH), 6.42 (s, 1H, CH), 6.56–8.36 (m, 16H, Ar–H). FTIR (KBr, cm⁻¹): 1592, 1511, 1401, 1250, 1242, 816.

General Procedure for the Preparation of 9-Aryl-1,8-Dioxooctahydroxanthene **5a–1**

A mixture of dimedone (2 mmol), aldehyde (1 mmol) and Co(HSO₄)₂ (0.1 mmol) was refluxed in dichloroethane. After the end of the reaction monitored by TLC, the reaction mixture was cooled to room temprature, extracted with EtOAc (3×15 mL), filtered to isolate the catalyst and the filtrate was concentrated to obtain crude product. The residue was crystallized in ethanol to obtain pure 9-aryl-1,8-dioxooctahydroxanthene **5a–I** as a crystalline solid. All the products obtained were fully characterized by spectroscopic methods such as IR, ¹H NMR, ¹³C NMR and mass spectroscopy and also by comparison of the spectral data with those reported in literature.

3,3,6,6-Tetramethyl-9-phenyl-3,4,6,7-tetrahydro-2H-xanthene-1,8(5H, 9H)dione **5a** (Table 2, entry 1): white solid. Yield: 90%. M.p.: 203– 205°C,¹H NMR (CDCl₃, 100 MHz): 7.24–7.19 (m,

Entry	Aldehyde	Product	Time, h	Yield ^b , %	$\frac{\text{Melting point, }^{\circ}C}{\text{observed reported}}$		Reference
1	C ₆ H ₄	3a	4	80	182-183	183-184	[19]
2	$4-O_2NC_6H_4$	3b	1	95	308-310	311-12	[19]
3	4-MeC ₆ H ₄	3c	4	90	239-240	238-240	[19]
4	4-HOC ₆ H ₄	3d	3	95	140-141	140-141	[16]
5	4-MeOC ₆ H ₄	3e	4	80	204-205	203-205	[19]
6	$4-BrC_6H_4$	3f	3	85	298-300	297-298	[19]
7	$4-ClC_6H_4$	3g	2	95	288-290	287-288	[16]
8	$3-O_2NC_6H_4$	3h	2.5	80	210-212	211-212	[17]
9	$2-ClC_6H_4$	3i	3	75	214-216	215	[17]
10	2-MeOC ₆ H ₄	3ј	5	70	260-261	258-260	[17]
11	C ₂ H ₅	3k	7	80	151-152	150-151	[19]
12	C ₅ H ₁₁	31	6	70	99–101	98-100	[19]

Table 1. Synthesis of 14-aryl-14H-dibenzo[a,j] xanthenes in the presence of Co(HSO₄)²

^a Reaction conditions: β -naphthol (2.0 mmol), aromatic aldehyde (1 mmol), Co(HSO₄)₂ (0.1 mmol), DCE (10 mL) reflux. ^b Yields of the isolated product.

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Entry	Aldehyde	Product	Time, h	Yield ^b , %	Melting point, °C observed reported		Reference
1	C ₆ H ₄	5a	4	85	203-205	204-205	[26]
2	$4-O_2NC_6H_4$	5b	3	90	226-228	225-227	[23]
3	$4-MeC_6H_4$	5c	4	95	218-220	217-218	[25]
4	4-HOC ₆ H ₄	5d	3.5	87	246-248	247-248	[26]
5	4-MeOC ₆ H ₄	5e	3	85	242-244	244-246	[26]
6	$4-BrC_6H_4$	5f	4	85	233-235	234-236	[26]
7	4-ClC ₆ H ₄	5g	3	95	228-230	229-230	[26]
8	$3-O_2NC_6H_4$	5h	4	80	168-170	170-172	[26]
9	$2-ClC_6H_4$	5i	5	75	229-231	228-230	[26]
10	$2-NO_2C_6H_4$	5j	6	75	258-260	258-260	[25]
11	3-OMeC ₆ H ₄	5k	4	80	178-180	177-180	[25]
12	2-OMeC ₆ H ₄	51	6	70	187-189	190-191	[25]

Table 2. Synthesis of 9-aryl-1,8-dioxooctahydroxanthenes in the presence of $Co(HSO_4)_2^a$

^a Reaction conditions: dimedone (2.0 mmol), aromatic aldehyde (1 mmol), Co(HSO₄)₂ (0.1 mmol), DCE (10 mL) reflux.

^b Yields of the isolated product.



Fig. 1. XRD pattern of Co(HSO₄)₂ nanoparticles.

2H, ArH), 7.14–7.09 (m, 1H, ArH), 7.04–7.01 (d, J = 7.93 Hz, 2H, ArH), 5.47 (s, 1H, CH), 2.47–2.25 (m, 8H, 4CH₂), 1.25 (s, 6H, 2CH₃), 1.11 (s, 6H, 2 2CH₃). FT–IR (KBr, cm⁻¹): 2962, 2928, 1592, 1372, 1159, 1041, 842, 774, 692.

9-(4-Chlorophenyl)-3,3,6,6-tetramethyl-3,4,6,7-tetrahydro-2H-xanthene-1,8(5H, 9H)-dione **5g** (Table 2, entry 7): white solid. Yield: 95%. M.p.: 228–230°C, ¹H NMR (100 MHz, CDCl₃): 7.25–7.18 (m, 2H, ArH), 6.97–6.95 (d, *J* = 8.12 Hz, 2H, ArH), 5.40 (s, 1H, CH), 2.46–2.25 (m, 8H, 4CH₂), 1.22 (s, 6H, 2CH₃), 1.11 (s, 6H, 2CH₃). FT-IR (KBr, cm⁻¹): 2960, 2929, 1589, 1305, 1093, 887, 833, 720, 658.

Catalyst Characterization

Powder X-ray diffraction (XRD). Figure 1 shows the X-ray diffraction patterns of the Co(HSO₄)₂ sample obtained by using Cu K_{α} radiation. The XRD patterns show characteristic peaks corresponding to Co(HSO₄)₂ crystallites as evidenced by the references of the ICDD database. The data of XRD shows that Co(HSO₄)₂ crystallizes in a monoclinic phase with a = 6.9630 Å, b = 7.5800 Å, c = 7.4700 Å and space group C2/c (Z = 4).

Based on the signal of the (311) peak, Co(HSO₄)₂ crystallites have an average size of 40 nm calculated using X-ray line broadening via the Scherrer equation.

Transmission electron microscopy (TEM) analysis. Figure 2 shows the TEM images of the $Co(HSO_4)_2$ nanoparticles taken with different magnifications. TEM images imply a homogeneous morphology of nanoparticles. The nanoparticles consist of uniform quasi-spherical crystallites with an average size of 40 nm. It can be seen that the obtained value is in agreement with the result indicated by XRD measurements.

Fourier transform infrared (FT-IR) and UV-Visible spectra of $Co(HSO_4)_2$. The FT-IR spectrum of the catalyst is shown in Fig. 3. The solid state IR spectrum

was recorded using the KBr disk technique. The spectrum shows a broad OH stretching absorption around 3374 cm⁻¹ for hydrogen sulfate anions in Co(HSO₄)₂, the FT-IR absorption of the O=S=O stretching modes lies at 1120 cm⁻¹, and that of the S–O stretching mode lies in the range 600–700 cm⁻¹. These characteristic bands are comparable with bands reported for sodium hydrogen sulfate and ferric hydrogen sulfate [32–35]. Also Fig. 4 compares the UV-Vis spectra of Co(HSO₄)₂ and Co(NO₃)₂. The characteristic peaks of Co²⁺ at $\lambda_{max} = 511$ nm can be readily recognized.



Fig. 2. TEM image of $Co(HSO_4)_2$ nanocatalyst.



Fig. 3. FT-IR spectrum of $Fe(HSO_4)_3(1)$ and $Co(HSO_4)_2(2)$.

RESULTS AND DISCUSSION

In order to optimize the reaction conditions and evaluate the catalytic efficiency of $Co(HSO_4)_2$, initially two model reactions were carried out to synthesize **3b** (Scheme 1) and **5b** (Scheme 2). Solvents such as *n*-hexane, CHCl₃, DMF, CH₃CN and 1,2-dichloroethane (DCE) were tested in the condensation of 4-nitrobenzalehyde and β -naphthol, and the reaction of 4-methylbenzalehyde and dimedone in the presence of 10 mol % of catalyst. DCE was superior to other solvents since it gave better yields in shorter reaction times.



Scheme 2. Synthesis of 9-aryl-1,8-dioxooctahydroxanthenes.

Under the optimal reaction conditions in the presence of 10 mol % of $Co(HSO_4)_2$ initial reactants were completely converted to give the products in the highest yields. One of the special advantages of cobalt hydrogen sulfate is its insolubility in organic solvents that makes its recovery very convenient. After the reaction was complete, the catalyst was separated by simple filtration, dried at 100°C under vacuum for 2 h and the recovered catalyst was reused in subsequent reactions without significant decreases in activity even after five runs.

After optimizing the reaction conditions we prepared a range of 1,8-dioxooctahydroxanthenes and aryl-14H-dibenzoxanthene derivatives. The results are shown in Tables 1 and 2. One important feature is

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Fig. 4. UV-Vis absorbance of $Co(HSO_4)_2$ (*1*) and $Co(NO_3)_2$ (*2*).

that aryl aldehydes, both possessing electron-withdrawing and electron-donating groups, afforded the corresponding products in good yields. In particular, aryl aldehydes with substrates at the para- and metapositions of the benzene ring gave products in high vield, whereas those with substrates at the ortho-position gave products in somewhat lower yields, probably due to steric hindrance. Work up procedures is very simple and include filtration of reaction mixture to separate the heterogeneous catalyst. The filtrate was concentrated to give a crude product which was then recrystallized from ethanol to give pure 14-aryl-14Hdibenzoxanthene (3a-l) and 9-aryl-1,8-dioxooctahydroxanthene (5a-l) in excellent yields. Absence of OH absorptions in the ¹H NMR and IR spectra confirms the structure of 14-aryl-14H-dibenzoxanthene. In all the ¹H NMR spectra (CDCl₃), the characteristic peak of 14-H-dibenzoxanthene appeared as a singlet in the range 5.5-7.0 ppm. On the other hand, in all the ¹H NMR spectra of 9-aryl-1,8-dioxooctahydroxanthene $(CDCl_3)$, the characteristic peak of 9H-dioxooctahydroxanthene appeared as a singlet in the 4.6-5.5 ppm region.

In conclusion, cobalt hydrogen sulfate is prepared for the first time by treatment of cobalt chloride with concentrated sulfuric acid. This catalyst was characterized by FT-IR, TEM and XRD. The efficiently of this new catalyst was demonstrated in the synthesis of 14-aryl-14H-dibenzoxanthenes and synthesis of 1,8dioxooctahydroxanthenes by using $Co(HSO_4)_2$ as a heterogeneous acid catalyst. The simplicity, together with the use of inexpensive, non-toxic, recyclable and environmentally friendly catalyst belongs to other remarkable features of the procedure.

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