Chemistry of Heterocyclic Compounds, Vol. 44, No. 2, 2008

SILICA SULFURIC ACID: A SIMPLE, EFFICIENT, AND REUSABLE HETEROGENEOUS CATALYST FOR THE ONE-POT SYNTHESIS OF ARYL-14H-DIBENZO-[*a,j*]XANTHENES UNDER CONVENTIONAL HEATING AND SOLVENT-FREE CONDITIONS

Raveendra K. Hunnur[1], B. Sunilkumar[1], P. S. Kumar[1], N. Srinivasulu[1], R. H. Udupi[1], and V. Hima bindu[2]

A novel approach towards the one-pot synthesis of aryl-14H-dibenzo[a,j]xanthenes is described from a known reaction between substituted aldehydes and β-naphthol in the presence of heterogeneous catalyst silica sulfuric acid under conventional heating as well as solvent-free conditions to afford good to excellent yields. The catalyst is reusable; it can be used several times without any decrease in the product yield.

Keywords: organic solvent, silica sulfuric acid, xanthenes, solvent-free conditions.

Considerable interest has been focused on the synthesis of xanthenes; in particular, benzoxanthenes have attracted much attention in recent years because of their wide range of biological and pharmacological applications, such as antiviral [1], attention [2], and anti-inflammatory [3] properties. They also exhibited efficacy in photodynamic therapy [4, 5] and are antagonists against the paralyzing action of *zoxazolamine* [6, 7]. In addition, these compounds have also been employed as dyes [8, 9], in laser technologies [10, 11], and in fluorescent materials for visualization of biomolecules [12].

The most commonly employed methods are available for the synthesis of xanthenes, and the synthesis of benzoxanthenes involves cycloacylation of carbamates [13], cyclodehydration [14-18], cyclocondensation between 2-hydroxy aldehydes and 2-tetralone [19], trapping of benzynes by phenols [20, 21], intramolecular coupling reaction of benzaldehyde and acetophenones [22], aldehydes and β-naphthols by dehydration [15, 23-25], and β-naphthol with: i) formamide [26], ii) carbon monoxide [27], aldehyde acetals, and 2-naphthol-1-methanol [28]. Although some of these methods are useful, the majority of the above methods suffer from at least one of the following disadvantages: low yield, prolonged reaction time, use of toxic organic solvents, excess of reagents and catalysts, high cost, and susceptibility to moisture. There is still a need for an efficient economical and excellent yielding catalyst that can work under mild conditions and shorter reaction time and avoid the use of toxic reagents and solvents.

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[1] Department of Pharmaceutical Chemistry, N.E.T. College of Pharmacy, Raichur-584103 (Karnataka), India. [2] Jawaharlal Nehru Technological University, Kukatapally, Hyderabad-500 072 (A.P), India; e-mail: ravi_hunnur@yahoo.com Translated from Khimiya Geterotsiklicheskikh Soedinenii, No. 2, pp. 196-201, February, 2008. Original article submitted August 26, 2007.

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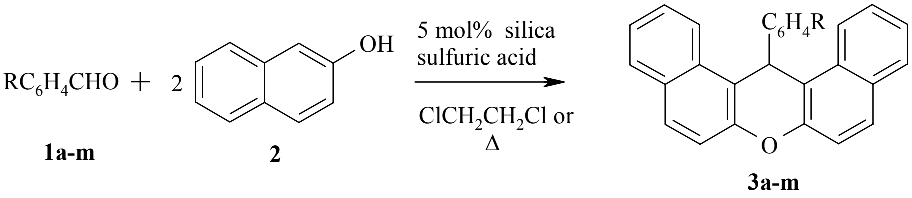
The use of solid acid catalysts plays a prominent role in organic synthesis; the importance of these catalysts is growing because of their ecofriendly nature as attention is directed towards the development of clean and green technologies for important organic molecules to promote environmental safety.

In general, solid acid catalysts are mainly based on clay [29–31] and silica. In terms of convenience, silica-based catalysts are inexpensive, easy to prepare, and insoluble in most of the organic solvents, which means that they have the advantage of recovery and recycle from various reactions. Therefore, we have found that silica sulfuric acid has many advantages over sulfuric acid alone. This reagent is safe, easy to handle, nontoxic, environmentally benign and presents fewer disposal problems. Recently, silica sulfuric acid has been used as a solid acid catalyst in many reactions such as nitration of aromatic compounds [32], oxidation of thiols to disulfides [33], three-component Biginelli reaction [34], preparation of 1,1-diacetates [35], and deprotection of tetrahydropyranyl ethers [36], acetals, and ketals [37].

In continuation of our work aiming at the synthesis of benzoxanthenes, we herein developed a green reaction of aromatic aldehyde 1 with β-naphthol 2 in solvent 1,2-dichloroethane and solvent-free conditions using heterogeneous catalyst silica sulfuric acid to afford a series of aryl-14H-dibenzo[*a,j*]xanthenes 3.



Choosing an appropriate solvent is of crucial importance for the above reaction. To search for the optimal solvent, the reaction of 4-methylsulfanylbenzaldehyde (**1a**) with β-naphthol **2** in the presence of catalyst silica sulfuric acid (5 mol%) was examined using various solvents like 1,2-dichloroethane, ethyl acetate, acetonitrile, methanol, and 1,4-dioxane at 80°C (Table 1). Among the different solvents investigated, 1,2-dichloroethane was found to be the best in terms of yield and quality. The above reaction has been carried out in 1,2-dichloroethane at 80°C for 2-3, h from which we obtained 14-(4-methylsulfanylphenyl)-14H-dibenzo[*a,j*]xanthene (**3a**) with 92%.

It is interesting to note that 4-fluorobenzaldehyde (**1b**) heated with β-naphthol **2** at 120°C in the presence of silica sulfuric acid (5 mol%) under solvent-free conditions afforded 14-(4-fluorophenyl)-14H-dibenzo[*a,j*]xanthene (**3b**) obtained within 1-2 h in 96% yield (Table 1).

The formation of product was characterized by IR, ^{1}H NMR, ^{13}C NMR, and mass-spectral studies; further structure of compound 3b was confirmed by X-ray diffraction studies [38].

Table 1. Effect of Solvents on the Reaction of 4-Methylsulfanylbenz-aldehyde **3a** and β-Naphthol in the Presence of Silica Sulfuric Acid*

Entry	Solvent	Time, h	Yield, %
1	$ClCH_2CH_2Cl$	16	92
2	EtOAc	18	65
3	MeCN	20	40
4	MeOH	17	50
5	1,4-Dioxane	19	70
6	Solvent-free conditions	3	96*^{2}

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* 5 mol% of silica sulfuric acid, 80°C.

*^{2} The reaction was carried out with 4-fluorobenzaldehyde.

TABLE 2. Synthesis of (2-Aryl)-14H-dibenzo[*a,j*]xanthenes **3a–m** in the Presence of Catalyst Silica Sulfuric Acid*

Compound	R	Method A		Method B		Mp, °C
		Time, h	Yield, %	Time, h	Yield, %	
3a	4-SMe	10	92	2.0	92	216
3b	4-F	8	88	2.5	95	239 [16]
3c	3-F	8.5	90	3.0	93	259 [18]
3d	2-F	10	84	2.5	94	209
3e	H	9	90	2.5	94	183 [15]
3f	3,4-OCH$_2$O	9	85	2.0	94	232
3g	4-OH	8	85	3.0	92	140 [39]
3h	4-Cl	9.5	93	2.0	95	287 [16]
3i	3-Cl	10	87	2.5	91	193
3j	2-Cl	9.0	88	3.0	91	215 [16]
3k	4-NO$_2$	9.0	92	3.0	95	310 [15]
3l	2-NO$_2$	10	86	3.0	93	293 [18]
3m	4-OMe	9	86	2.0	92	204 [16]

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* A – $ClCH_2CH_2Cl$, reflux; B – solvent-free, 120°C.

In comparison with the conventional method, the yield of the reaction under solvent-free conditions is higher and the reaction time is shorter. Therefore, we employed the above conditions for the conversion of various aldehydes 1a-m with β-naphthol 2 to the corresponding benzoxanthenes 3a-m in the presence of silica sulfuric acid (5 mol%) using both methods (Table 2).

Both of the above methods include a simple workup; the catalyst can be separated through filtration. We also checked the reusability of silica sulfuric acid by separation and reloading in a new run and found that the catalyst could be reused several times without decrease in the productivity. An example shown for the reaction of 4-fluorobenzaldehyde with β-naphthol (Table 2) in the presence of recovered silica sulfuric acid afforded the corresponding benzo- xanthene in good yield.

In conclusion, we have demonstrated a new efficient method for the synthesis of xanthenes using a catalytic amount of silica sulfuric acid as a heterogeneous catalyst. In contrast to the other catalyst, storage and handling of this catalyst does not require special precautions, and it can be stored on bench top for months without losing its catalytic activity. We believe that the above used catalyst in the present methodology addresses the current drive toward green chemistry due to the cheapness and easy availability of the substrate, simple workup, high yield, easy handling, nontoxicity of the catalyst, economy, and reusability of the catalyst.

EXPERIMENTAL

The infrared spectra were recorded on a Nicolet impact 410 FTIR spectrometer using KBr pellet technique. The ^1H and ^{13}C NMR spectra were recorded on a Varian 300 spectrometer (300 and 75 MHz respectively), with TMS as an internal standard; the electron impact mass spectra (EIMS) were recorded on a MI Ver.14 on a UIC 002002 EI-70 eV spectrometer, and elemental analyses were carried out in a Heraeus CHN rapid analyzer. Finally melting points were determined by the open capillary method and are uncorrected.

Preparation of silica sulfuric acid. A 500-ml suction flask equipped with a constant-pressure dropping funnel and a gas inlet tube for conducting HCl gas over an absorbing solution (i.e., water) was used. It was charged with silica gel (60.0 g), and chlorosulfonic acid (46.6 g, 0.4 mol) was added dropwise at room temperature over a period of 30 min. HCl gas evolved from the reaction vessel immediately after the addition of a few drops of chlorosulfonic acid. The mixture was shaken at room temperature for 30 min to obtain white solid silica sulfuric acid (92 g).

General Method. A. To a stirred solution of aldehyde (1 mol) in 1,2-dichloroethane (15 ml) was added β-naphthol (2 mol) and silica sulfuric acid (5 mol%). The reaction mixture was heated to reflux for the appropriate time according to Table 2. The progress of the reaction was monitored by TLC and, upon completion, the catalyst was filtered off, and the solvent was removed in vacuo to yield the crude product, which was crystallized from ethanol.

B. To a mixture of aldehyde (1 mol) and β-naphthol (2 mol), silica sulfuric acid (5 mol%) was added. The reaction mixture was stirred at 120°C for the appropriate time, as shown in Table 2. The reaction was followed by thin layer chromatography. After the completion of the reaction, the catalyst was filtered off by adding methylene dichloride, and the solvent was evaporated in vacuo to yield the crude product, which was crystallized from ethanol.

14-(4-Methylsulfanylphenyl)-14H-dibenzo[*a,j*]xanthene (3a). White solid; mp 216°C. IR spectrum, ν, cm^{-1}: 3057, 1634, 1621, 1592, 1514, 1470, 1457, 1248. ^{1}H NMR spectrum (CDCl$_3$), δ, ppm: 2.31 (3H, s); 6.46 (1H, s); 7.03-8.38 (16H, m). ^{13}C NMR spectrum (CDCl$_3$), δ, ppm: 16.1, 37.9, 117.5, 118.4, 123.0, 124.7, 127.2, 129.1, 129.2, 129.3, 131.5, 131.8, 136.6, 142.4, 149.1. Mass spectrum, *m/z*: 404 (M+). Found, %: C 83.20; H 4.96. $C_{28}H_{20}OS$. Calculated, %: C 83.17; H 4.98.

14-(4-Fluorophenyl)-14H-dibenzo[*a,j*]xanthene (**3b**). Brown solid; mp 237°C. IR spectrum, ν, cm^{-1}: 3068, 3034, 1622, 1592, 1502, 1458, 1432, 1412, 1399. ^{1}H NMR spectrum (CDCl$_3$), δ, ppm: 6.50 (1H, s); 6.82-8.37 (16H, m). ^{13}C NMR spectrum, δ, ppm: 37.6, 115.6, 115.9, 117.5, 118.4, 122.9, 124.7, 127.3, 129.3, 129.4, 130.0, 130.1, 131.5, 131.7, 141.2, 149.1, 159.9, 163.2. Mass spectrum, *m/z*: 376 (M+). Found, %: C 86.12; H 4.51. $C_{27}H_{17}FO$. Calculated, %: C 86.15; H 4.55.

14-(2-Fluorophenyl)-14H-dibenzo[*a,j*]xanthene (**3d**). Pale yellow solid; mp 209 °C. IR spectrum, ν, cm^{-1}: 3154, 2873, 1634, 1623, 1608, 1593, 1545, 1516, 1483, 1459. ^{1}H NMR spectrum (CDCl$_3$), δ, ppm: 6.79 (1H, s); 6.82–8.41(16H, m). ^{13}C NMR spectrum (CDCl$_3$), δ, ppm: 30.1, 115.3, 115.7, 117.1, 118.4, 122.7, 122.8, 124.8, 125.5, 127.6, 128.5, 128.6, 129.1, 129.4, 131.3, 131.5, 132.0, 132.8, 133.0, 149.3, 156.5, 159.8. Mass spectrum, *m/z*: 376 (M+). Found, %: C 86.10; H 4.51. $C_{27}H_{17}FO$. Calculated, %: C 86.15; H 4.55.

14-Benzo[1,3]dioxol-5-yl-14H-dibenzo[*a,j*]xanthene (**3f**). White solid; mp 232°C. IR spectrum, ν, cm^{-1}:2994, 1621, 1592, 1548, 1514, 1500, 1484, 1458, 1432, 1398, 1354, 1279, 1247. ^{1}H NMR spectrum (DMSO-d$_6$), δ, ppm: 5.75 (2H, s); 6.42 (1H, s); 6.60–8.40 (15H, m). ^{13}C NMR (DMSO-d$_6$), δ, ppm: 42.3, 106.1, 112.9, 113.8, 122.4, 122.9, 123.1, 126.4, 128.1, 129.6, 131.2, 132.0, 132.1, 133.7, 134.0, 134.1, 136.1, 136.3, 144.3, 151.1, 153.0, 153.6. Mass spectrum, *m/z*: 402 (M+). Found, %: C 83.53; H 4.59. $C_{28}H_{18}O_3$. Calculated, %: C 83.57; H 4.51.

4-(14H-Dibenzo[*a,j*]xanthen-14-yl)phenol (**3g**). Pink solid; mp 140°C. IR spectrum, ν, cm^{-1}: 3554, 3404, 3176, 1621, 1612, 1592, 1558, 1550, 1511, 1458, 1431, 1401. ^{1}H NMR spectrum (DMSO-d$_6$), δ, ppm: 4.97 (broad 1H, OH); 6.41 (1H, s); 6.56–8.36 (16H, m). Mass spectrum, *m/z*: 374 (M+). Found, %: C 86.11; H 4.88. $C_{27}H_{18}O_2$. Calculated, %: C 86.61; H 4.85.

14-(3-Chlorophenyl)-14H-dibenzo[*a,j*]xanthene (3i). Brown solid; mp 193°C. IR spectrum, ν, cm^{-1}: 3068, 1634, 1623, 1592, 1573, 1515, 1473, 1458, 1432, 1399, 1354. ^{1}H NMR spectrum (CDCl$_3$), δ, ppm: 6.4 (1H, s); 6.96–8.32 (16H, m). ^{13}C NMR spectrum (CDCl$_3$), δ, ppm: 38.2, 117.0, 118.5, 122.8, 124.8, 126.9, 127.2, 127.4, 128.8, 129.3, 129.61, 130.0, 131.5, 131.7, 134.8, 147.3, 149.2. Found, %: C 82.51; H 4.30. $C_{27}H_{17}ClO$. Calculated, %: C 82.54; H 4.36.

We are thankful to SIF, Indian Institute of Science, Bangalore, USIC Karnataka University, Dharwad, and IICT, Hyderabad for providing spectral data.

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