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Efficient, Solvent-Free Method for the One-Pot Condensation of β-Naphthol, Aromatic Aldehydes, and Cyclic 1,3-Dicarbonyl Compounds Catalyzed by Silica Sulfuric Acid

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EFFICIENT, SOLVENT-FREE METHOD FOR THE ONE-POT CONDENSATION OF β-NAPHTHOL, AROMATIC ALDEHYDES, AND CYCLIC 1,3-DICARBONYL COMPOUNDS CATALYZED BY SILICA SULFURIC ACID

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GRAPHICAL ABSTRACT



Abstract Silica sulfuric acid as a reusable and efficient catalyst has been used for the preparation of 12-aryl-8,9,10,12-tetrhydro benzo[a]xanthene-11-one derivatives from the one-pot multicomponent reaction of aromatic aldehydes, β -naphthol, and a cyclic diketone under solvent-free conditions. Good yields, simple procedure, easy workup, short reaction times, and mild conditions are the advantages of this methodology.

Keywords Benzoxanthene; multicomponent reaction; one-pot synthesis; silica sulfuric acid

INTRODUCTION

Xanthenes and benzoxanthenes have attracted considerable interest because of their biological activities such as anti-inflammatory, antibacterial, and antiviral activities.^[1-3] These are being utilized as antagonists for the paralyzing action of zoxazolamine^[4] and in photodynamic therapy.^[5] Furthermore, these compounds can be used as dyes, as pH-sensitive fluorescent materials for the visualization of biomolecular assemblies, and in laser technologies.^[6,7] Thus, the synthesis of xanthene derivatives is of great importance.

A number of methods for the synthesis of tetrahydrobenzo[a]xanthen-11-ones have been reported. Generally they are synthesized by three-component condensation of cyclic 1,3-diketones with an aldehyde and β -naphthol, which entails the

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use of *para*-toluenesulfornic acid (p-TSA) in ionic liquid,^[8] perchloric acid adsorbed on silica gel,^[9] dodecatungstophosphoric acid,^[10] indium(III) chloride,^[11] strontium triflate,^[12] cyanuric chloride,^[13] iodine,^[14] and tetrabutyl ammonium fluoride.^[15]

Recently, silica sulfuric acid (SSA) has drawn much interest in numerous organic transformations^[16–20] because of its environmental compatibility, greater selectivity, experimental simplicity, ease of handling, noncorrosive nature and ease of isolation.

RESULTS AND DISCUSSION

In continuation of our studies to develop of green methods for the synthesis of organic compounds,^[21] we report herein the results of the preparation of 12-aryl-8,9, 10,12-tetrhydro benzo[*a*]xanthene-11-one derivatives catalyzed by SSA under solvent-free conditions at 100 °C (Scheme 1). To the best of our knowledge, there has been no report on the use of SSA as a catalyst in preparation of these compounds.

At first, the amount of catalyst required for the reaction of β -naphthol (1 mmol), dimedone (1 mmol), and benzaldehyde (1 mmol) was investigated under solvent-free condition at 100 °C. The results are summarized in Table 1. As shown from Table 1, this transformation does not take place in the absence of catalyst. The best result was obtained when using 0.10 g (0.26 mmol) of catalyst.

As the synthesis of 12-aryl-8,9,10,12-tetrhydrobenzo[a]xanthene-11-one derivatives was reported using 1.1–1.2 mmol of dimedone,^[8–13] the optimum amount of dimedone was also examined. As it can be seen from Table 2, it was possible to achieve the reaction with less dimedone than in other studies.

Further experimentation revealed that the reaction was completed in 30 min by heating the reaction mixture in an oil bath maintained at 100 °C in solvent-free condition. Lower yield was obtained when the reaction was carried out in different solvents (Table 3).

To broaden the scope of this new protocol, we used several aromatic aldehydes, including both electron-withdrawing and electron-donating groups, β -naphthol, and cyclic 1,3-diketones in the presence of 0.1 g SSA under solvent-free conditions at 100 °C. The results are summarized in Table 4.

The reaction proceeds efficiently with various kinds of aromatic aldehydes in good to excellent yields within short reaction time (30–45 min). As indicated in Table 4, the yield of the reaction with *ortho*-substituted aldehydes was less (Table 4, entries 4 and 7). In addition, aldehydes bearing electron-donating groups need longer reaction times as compared to aldehydes containing electron-withdrawing groups.



Scheme 1. Synthesis of 12-aryl-8,9,10,12-tetrahydrobenzo[a]xanthen-11-one derivatives.

CLEAN SYNTHESIS OF BENZOXANTHENES

Table 1. Optimization of silica sulfuric acid in condensation of β -naphthol, dimedone, and benzaldehyde in solvent-free conditions at 100 °C

Entry	SSA (g)	Time (min)	Yield (%)
1	0.0	30	0.0
2	0.05	30	40
3	0.08	30	65
4	0.10	30	95
5	0.15	30	95

Table 2. Optimization of dimedone in synthesis of 12-phenyl-8,9,10,12-tetrahydrobenzo[a]xanthene-11-one in solvent-free conditions at 100 °C

Entry	Dimedone (mmol)	Yield (%)
1	1.2	85
2	1.1	95
3	1	95

 Table 3. Optimization of temperature and medium of reaction in synthesis of 12-phenyl-8,9,10,12-tetrahydrobenzo[a]xanthene-11-one

Entry	Temp. (°C)	Condition	Time (min)	Yield (%)
1	80	Neat	30	60
2	100	Neat	30	95
3	120	Neat	30	95
4	Reflux	EtOH	30	Trace
5	Reflux	H_2O	30	Trace
6	Reflux	CH ₃ CN	30	Trace
7	Reflux	CICH ₂ CH ₂ Cl	30	20

Table 4. Synthesis of 12-aryl-8,9,10,12-tetrahydrobenzo[a]xanthen-11-one derivatives

Entry	ArCHO	R_1 and R_2	Time (min)	Yield (%) ^a	Mp (°C)
1	PhCHO	Me	30	95	149–151 ^[14]
2	4-MeC ₆ H₄CHO	Me	45	80	174-176 ^[14]
3	4-OMeC ₆ H ₄ CHO	Me	45	80	210-211[15]
4	2-ClC ₆ H ₄ CHO	Me	35	75	179–180 ^[11]
5	4-ClC ₆ H ₄ CHO	Me	30	90	167–169 ^[9]
6	4-NO ₂ C ₆ H ₄ CHO	Me	30	95	177-178 ^[14]
7	$2-NO_2C_6H_4CHO$	Me	40	75	223-225 ^[11]
8	3-NO ₂ C ₆ H ₄ CHO	Me	30	90	167-168 ^[11]
9	$4-BrC_6H_4CHO$	Me	30	95	185-187 ^[13]
10	2-Naphthaldehyde	Me	35	85	230-232[15]
11	4-FC ₆ H₄CHO	Me	30	95	184–186 ^[15]
12	PhCHO	H, Ph	35	80	118-124
13	4-ClC ₆ H ₄ CHO	H, Ph	30	85	181–183

^aIsolated yields.

Entry	Catalyst	Conditions	Time (min)	Yield (%)	Ref.
1	p-TSA ^a	[bmim]BF4/neat	180	90	8
2	HClO ₄ -SiO ₂	80°C/neat	72	89	9
3	Dodecatungsto phosphoric acid	60 °C/neat	70	86	10
4	InCl ₃	120 °C/neat	30	84	11
5	$Sr(OTf)_2$	1,2-Dichloroethane/80 °C	300	85	12
6	TCT	80°C/neat	50	90	13
7	$TBAF^b$	H ₂ O/reflux	540	99	15
8	NaHSO ₄ /SiO ₂	CH ₂ Cl ₂ /reflux	300	91	23
9	Silica sulfuric acid	100°C/neat	30	95	

Table 5. Comparison of results using silica sulfuric acid with results obtained by other workers for the synthesis of 9,10-dihydro-9,9-dimethyl-12-phenyl-8H-benzo[*a*]xanthen-11(12H)-one

^ap-Toluenesulfonic acid.

^bTetrabutyl ammonium fluoride.

As an aspect of green chemistry, the recyclability of the catalyst was tested. The catalyst was separated from the reaction mixture, washed with ethyl acetate, and dried at 100 °C for 24 h to give recycled SSA. The reaction of 4-bromobenzaldehyde, β -naphthol, and dimedone was repeated with recycled catalyst, and the yields were found to remain in the range of 85% for three runs.

In Table 5 the efficiency of our method for the synthesis of 12-aryl-8,9,10,12tetrhydro benzo[*a*]xanthene-11-one is compared with some other published studies. Each of these methods have their own advantages, but they often suffer from some disadvantages, including expensive reagent or catalyst, use of corrosive reagent, long reaction time, and nonrecyclable catalyst.

In conclusion, we have shown that the silica-based solid acid catalyst, which can be easily prepared from commercially available starting materials, efficiently catalyzes the synthesis of 12-aryl-8,9,10,12-tetrhydrobenzo[*a*]xanthene-11-one derivatives through the condensation of aromatic aldehydes and β -naphthol with 1,3-dicarbonyl compounds. The low cost, recyclability, and easy preparation of this catalyst may allow of these compounds on a large scale.

EXPERIMENTAL

Chemicals were purchased from the Fluka, Merck, and Aldrich chemical companies. Melting points were determined on an Electrothermal 9100 instrument and are not corrected. Thin-layer chromatography (TLC) on commercial aluminumbacked plates of silica gel 60 F254 was used to monitor the progress of reactions. ¹H NMR and ¹³C NMR spectra were recorded on Bruker Avance 300-MHz spectrometers with 7- to 10 mM solutions in CDCl₃ in the presence of tetramethylsilane as internal standard. Infrared (IR) spectra were recorded using a Perkin-Elmer 843 spectrometer with KBr plates. Elemental analyses were performed on a Perkin-Elmer CHN analyzer, 2400 series II.

Preparation and Recycling of Silica Sulfuric Acid

SSA was prepared according to the Zolfigol procedure.^[22] The catalyst was separated from the reaction mixture, washed with ethyl acetate, and dried at $100 \,^{\circ}$ C

for 24 h to give recycled SSA. The reaction of 4-bromobenzaldehyde, β -naphthol, and dimedone was repeated with recycled catalyst, and the yields were found to remain in the range of 85% for three runs.

General Procedure for the Synthesis of 12-Aryl-8,9,10,12tetrahydrobenzo[*a*]xanthen-11-one Derivatives

Aldehyde (1.0 mmol), β -naphthol (1.0 mmol), 5,5-dimethyl-1,3-cyclohexane dione or 5-phenyl-1,3-cyclohexane dione (1.0 mmol), and SSA (0.1 g, 0.26 mmol) were taken in a 10-ml round-bottomed flask. The mixture was stirred at 100 °C for an appropriate time as mentioned in Table 4. After completion of the reaction as monitored by TLC, the mixture was quenched with water (~10 mL) and filtered off. The solid was washed with ethyl acetate (10 mL) and filtered to recover the catalyst. The solvent was evaporated, and the crude product was recrystallized from EtOH.

The known compounds were identified by comparison of melting points with literature reports.

Spectral (IR, ¹H NMR, and ¹³C NMR) and Analytical Data of New Compounds

9,10-Dihydro-9,12-diphenyl-8H-benzo[*a*]**xanthen-11(12H)-one (Table 4, Entry 12).** Mp 118–124 °C; IR (KBr): $\nu \max/\text{cm}^{-1}$: 1700, 1400, 1200, 700. ¹H NMR (300 MHz, CDCl₃, Me₄Si) as a mixture of diastereomers: δ 7.40–7.17 (m, 32H), 4.91 (s, 1H), 4.92 (s, 1H), 3.49 (quintet, J = 5.57 Hz, 1H), 3.34 (quintet, J = 4.95, 1H), 3.00–2.81 (m, 4H), 2.74–2.53 (m, 4H); ¹³C NMR (75 MHz, CDCl₃) as a mixture of diastereomers: δ 31.77, 31.94, 34.62, 34.75, 38.22, 38.76, 43.70, 44.02, 195.65, 195.51, 163.36, 163.21, 162.54, 162.43, 143.81, 142.10, 142.01, 128.88, 128.80, 128.72, 128.59, 128.51, 128.39, 128.30, 128.14, 127.99, 127.25, 127.16, 127.02, 126.72, 126.63, 126.57. Anal. calc. for C₂₉H₂₂O₂: C, 86.56; H, 5.47. Found: C, 86.00; H, 6.01.

12-(4-Chlorophenyl)-9,10-dihydro-9-phenyl-8H-benzo[a]xanthen-11-(**12H)-one (Table 4, Entry 13).** Mp 181–183 °C, IR (KBr): $\nu \max/\text{cm}^{-1}$: 1700, 1550, 1450, 1300. ¹H NMR (300 MHz, CDCl₃, Me₄Si) as a mixture of diastereomers: δ 7.93–7.77 (m, 6H), 7.45–7.12 (m, 24 H), 5.78 (s, 1H), 5.76 (s, 1H), 3.52–3.49 (m, 1H), 3.35–3.33 (m, 1H), 3.00–2.81 (m, 4H), 2.79–2.54 (m, 4H); ¹³C NMR (75 MHz, CDCl₃) as a mixture of diastereomers: δ 34.24, 34.34, 35.12, 35.26, 38.29, 38.93, 43.98, 43.76, 114.91, 116.98, 123.51, 126.62, 126.70, 127.05, 127.17, 127.19, 128.35, 128.52, 128.54, 128.73, 128.87, 128.93, 129.20, 129.88, 129.95, 141.86, 142.32, 142.91, 147.70, 162.71, 163.52, 164.11, 165.09, 195.56, 196.06. Anal. calc. for C₂₉H₂₁ClO₂: C, 79.72; H, 4.81; Found: C, 78.43; H, 4.79.

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