

Silica supported perchloric acid ($\text{HClO}_4\text{-SiO}_2$): A mild, reusable and highly efficient heterogeneous catalyst for the synthesis of 14-aryl or alkyl-14-*H*-dibenzo[*a,j*]xanthenes

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Received 24 February 2007; received in revised form 8 May 2007; accepted 9 May 2007

Available online 13 May 2007

Abstract

Silica supported perchloric acid ($\text{HClO}_4\text{-SiO}_2$) is found to be a recyclable heterogeneous catalyst for a rapid and efficient synthesis of various 14-aryl or alkyl-14-*H*-dibenzo[*a,j*]xanthenes with good to excellent yields under reflux and solvent free conditions. The catalyst is easily prepared, stable, reusable and efficient under the reaction conditions.

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Keywords: Xanthenes; Solvent-free; Heterogeneous catalyst; Silica supported perchloric acid

1. Introduction

Xanthenes and benzoxanthenes are biologically important drug intermediates. They are cited as active oxygen heterocycles possessing antibacterial [1], anti-inflammatory [2], and antiviral properties [3]. These compounds are also utilized as antagonists for paralyzing action of zoxazolamine [4] and in photodynamic therapy [5]. The other useful applications of these heterocycles are as dyes [6], fluorescent materials for visualization of biomolecules [7] and in laser technologies [8]. Several polycyclic compounds containing xanthene skeleton are isolated from natural sources [9]. Xanthenes and benzoxanthenes are prepared by different methods including the reaction of aryloxymagnesium halides with triethylorthoformate [10], cyclodehydration [11], trapping of benzynes by phenols [12], intramolecular phenyl carbonyl coupling reactions of benzaldehydes and acetophenones [13], cyclization of polycyclic aryltriflate esters [14] and cyclocondensation between 2-hydroxy aromatic aldehydes and 2-tetralone [15],

Furthermore, 14-*H*-dibenzo [*a,j*]xanthenes and its analogues are prepared by reaction of 2-naphthol with 2-naphthol-1-methanol [16], formamide [17], CO [18], and aldehydes [19–26]. Many of these methods, however, suffer from longer reaction times, unsatisfactory yields, harsh reaction conditions and excessive use of reagents and catalysts. It is therefore important to find more convenient methods for the preparation of these compounds.

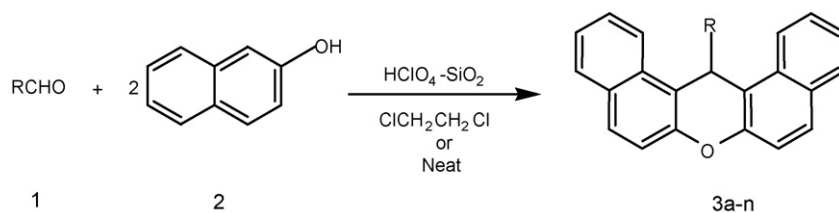
Heterogeneous catalysts have gained interesting attraction in recent years due to economic and environmental considerations. These catalysts are generally inexpensive and easily available. They can conveniently be handled and removed from the reaction mixture, thus making the experimental procedure simple and eco-friendly.

The leading contenders for environmentally acceptable processes are supported reagents. Use of silica-supported reagents in one-pot multi-component construction of heterocycles has received considerable importance in organic synthesis [27]. In particular, perchloric acid adsorbed on silica gel ($\text{HClO}_4/\text{SiO}_2$) [28] has emerged as an extremely useful catalyst in various organic transformations, including acylation of alcohols [28], acylation of aldehydes [29], 1,3-dithiolane/dithiane formation [30], tetrahydropyranlation [31], thio-acetalization [31], Ferrier rearrangement [32], Michael addition [33], cleavage of ketals and benzylidene acetals [34], the Hantzsch condensation

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Scheme 1. $\text{HClO}_4\text{-SiO}_2$ catalyzed synthesis of 14-aryl or alkyl-14-*H*-dibenzo[*a,j*] xanthenes.

[35], Synthesis of bis-indolylmethanes [36], glycosylation of sugars [37] and *N*-*tert*-butoxycarbonylation of amines [38], synthesis of tetrasubstituted imidazoles [39] and synthesis of poly-substituted quinolines [40].

In view of its inherent properties like environmental compatibility, greater selectivity, operational simplicity, moisture-insensitive, less noncorrosive nature and ease of isolation, it is therefore, interest to us to find out the behavior of the reagent system, HClO_4 supported on silica gel (230–400 mesh) in the synthesis of xanthene derivatives. To the best of our knowledge, there are no reports on the use of perchloric acid adsorbed on silica gel ($\text{HClO}_4/\text{SiO}_2$), for the synthesis of 14-aryl or alkyl-14-*H*-dibenzo[*a,j*]xanthenes. In continuation of our work on the development of efficient protocols for the synthesis of xanthene [41], an intermediate for the preparation of an antibacterial drug and in view of importance of heterogeneous acid catalysts in organic synthesis, we now wish to report perchloric acid adsorbed on silica gel ($\text{HClO}_4/\text{SiO}_2$) catalyzed highly efficient synthesis of 14-aryl or alkyl-14-*H*-dibenzo[*a,j*]xanthenes using one-pot condensation of 2-naphthol with wide variety of aldehydes under solvent free and reflux conditions (Scheme 1).

2. Results and discussion

$\text{HClO}_4\text{-SiO}_2$ was prepared according to the literature procedure [28]. In order to determine the most appropriate reaction conditions and evaluate the catalytic efficiency of $\text{HClO}_4\text{-SiO}_2$ catalyst, initially a model study was carried out on the synthesis of **3a** (Scheme 1). Among the tested solvents such as methanol, ethanol, DMF, CH_3CN , chloroform, 1,2-dichloroethane and solvent-free system, condensation of benzaldehyde and 2-naphthol was more facile and proceeded to give highest yield, under solvent free conditions (Table 1). Interestingly, it was found to be HClO_4 supported on silica gel with low loading

Table 1
Synthesis of **3a** using $\text{HClO}_4\text{-SiO}_2$ catalyst (1 mol%) in the different solvents

Entry	Solvent	Time (h)	Yield (%) ^a
1	Methanol	10	70
2	Ethanol	10	62
3	DMF	14	0
4	CH_3CN	12	40
5	CHCl_3	12	50
6	$\text{ClCH}_2\text{CH}_2\text{Cl}$	10	92
7	Solvent-free	10 (min)	95

^a Isolated yield.

(0.025 mmol/50 mg, 1 mol%) is an efficient catalyst and gave exclusively **3a** in 95% yield in 10 min under solvent free conditions.

In order to evaluate the generality of the process, several diversified examples illustrating the present method for the synthesis of 14-aryl or alkyl-14-*H*-dibenzo[*a,j*]xanthenes **3** was studied (Table 2). The reaction of 2-naphthol with various aromatic aldehydes bearing electron withdrawing groups (such as nitro, halide) or electron releasing groups (such as methyl, methoxy) and aliphatic aldehydes was carried out in the presence of $\text{HClO}_4\text{-SiO}_2$ as catalyst. The yields obtained were good to excellent without formation of any side products. The reaction worked well with aromatic (entries 1–10, Table 2) as well as aliphatic aldehydes (entries 12–14, Table 2), giving various xanthene derivatives in 86–98% yields. All the products obtained were characterized by spectroscopic methods such as IR, ^1H NMR, for unknown compound (^{13}C NMR and analytical data) and also by comparison with the reported spectral data and melting point.

Concerning the reaction mechanism, we proposed that a carbocation is initially formed; aryl- or alkyl-methanebisnaphthols are then formed in the second step, which then undergo dehydration to give the final product which is similar to the literature reports [25] (Fig. 1).

Table 3, compares our results (time, yield, reaction conditions) with results obtained by other groups. As can be seen, our method is simpler, more efficient, and uses no toxic solvents.

2.1. Reusability of catalyst

Next, we investigated the reusability and recycling of $\text{HClO}_4\text{-SiO}_2$. At first, we put *p*-bromobenzaldehyde, 2-naphthol and 0.01 mmol $\text{HClO}_4\text{-SiO}_2$ in 1,2-dichloroethane together, and then the mixture was refluxed. When the reaction was completed, the catalyst was separated by simple filtration and recovered $\text{HClO}_4\text{-SiO}_2$ was reused in subsequent reactions without significant decrease in activity even after five runs (Table 4).

The simplicity, together with the use of inexpensive, non-toxic and environmentally benign nature of $\text{HClO}_4\text{-SiO}_2$ catalyst under solvent free condition is other remarkable feature of the procedure. Chloroform was added to the reaction mixture, the catalyst was filtered and the filtrate was concentrated to give crude residue, which was crystallized in ethanol to give pure 14-aryl or alkyl-14-*H*-dibenzo[*a,j*]xanthenes **3** in excellent yields.

Table 2
HClO₄-SiO₂ catalyzed synthesis of 14-aryl or alkyl-14-*H*-dibenzo [*a,j*]xanthenes

Entry	R	Product ^a	Method A time (h)	Yield (%) ^b	Method B time (min)	Yield (%) ^b	Mp (°C)	
							Found	Reported
1	C ₆ H ₅	3a	10	92	10	95	184–185	185 [20]
2	4-BrC ₆ H ₅	3b	7	96	8	98	297–298	297 [20]
3	4-MeOC ₆ H ₅	3c	12	92	10	92	203–205	204 [20]
4	2-MeOC ₆ H ₅	3d	12	85	10	88	258–259	260 [20]
5	4-MeC ₆ H ₅	3e	9	92	8	92	227–229	229 [20]
6	4-ClC ₆ H ₅	3f	8	94	8	96	289–290	289 [20]
7	2-ClC ₆ H ₅	3g	10	86	10	88	214–216	215 [20]
8	4-NO ₂ C ₆ H ₅	3h	10	94	10	90	311–312	310 [20]
9	3-NO ₂ C ₆ H ₅	3i	12	88	10	90	210–211	211 [20]
10	4-FC ₆ H ₅	3j	9	94	10	96	239–240	239 [20]
11	C ₆ H ₅ CH ₂	3k	12	92	10	94	178–180	–
12	CH ₃ CH ₂	3l	15	82	20	86	150–151	152 [20]
13	(CH ₃) ₂ CH	3m	15	85	20	86	155–157	155–157 [41]
14	CH ₃ CH ₂ CH ₂	3n	15	86	20	88	152–154	–

^a Products are characterized by melting point, IR, ¹H NMR and comparison with literature.

^b Isolated yield.

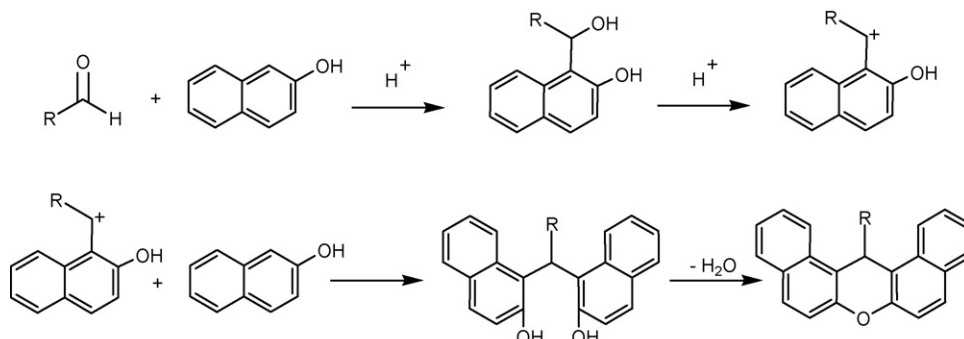


Fig. 1. Plausible mechanism for the catalytic activity of HClO₄-SiO₂.

Table 3
Comparison of our results with results obtained by other groups^a

Catalyst	Conditions	Yield (%)	Time (h)	References
K ₅ CoW ₁₂ O ₄₀ ·3H ₂ O	Neat/125 °C	91	2	[24]
I ₂	Neat/90 °C	90	2.5	[22]
<i>p</i> -TsOH	Neat/125 °C	89	4	[20]
LiBr	Neat/130 °C	82	1	[21]
Amberlyst-15	Neat/125 °C	94	2	[25]
Sulfamic acid	Neat/125 °C	93	8	[26]
HClO ₄ -SiO ₂	Neat/125 °C	95	10 (min)	Table 2

^a Based on benzaldehyde.

Table 4
The recycling of 0.01 mmol of HClO₄-SiO₂ in 1,2-dichloroethane

Entry	Time (h)	Yield (%) ^a
1	7	95
2	8	93
3	10	92
4	12	90
5	12	90

^a Isolated yield.

3. Conclusion

We described herein perchloric acid adsorbed on silica gel (HClO₄-SiO₂) catalyzed highly efficient, one-pot, protocol for the synthesis of 14-aryl or alkyl-14-*H*-dibenzo[*a,j*]xanthenes by the condensation of an aldehyde and 2-naphthol under solvent free and reflux conditions in excellent yields. The remarkable catalytic activity of HClO₄-SiO₂ exhibited is convincingly superior to the recently reported other catalytic methods with respect to reaction time (8–20 min in solvent free condition), amount of catalyst and the pure products were obtained by simple crystallization. Easy work up, inexpensive, ready availability of the catalyst makes the procedure an attractive alternative to the existing methods for the synthesis of xanthenes **3a–n**.

4. Experimental

The products (**3a–n**) were isolated and characterized by physical and spectral data. ¹H NMR and ¹³C NMR spectra were recorded on Bruker Avance-300 MHz spectrometers with 7–10 mM solutions in CDCl₃ in the presence of

tetramethylsilane as internal standard. IR spectra were recorded using a Perkin-Elmer 843 spectrometer with KBr plates. Melting points were determined on Electro thermal 9100, and are not corrected.

4.1. Preparation of $\text{HClO}_4/\text{SiO}_2$ catalyst

70% aqueous perchloric acid (1.8 g, 12.5 mmol) was added to a suspension of SiO_2 (230–400 mesh, 23.7 g) in ether (70 ml). The mixture was concentrated and the residue was heated at 100 °C for 72 h under vacuum to give $\text{HClO}_4\text{-SiO}_2$ (0.5 mmol/g) as free flowing powder (50 mg = 0.025 mmol of HClO_4).

4.2. General experimental procedure (Method A)

A mixture of an aldehyde (1 mmol), 2-naphtol (2 mmol) and $\text{HClO}_4\text{-SiO}_2$ (20 mg, 0.01 mmol, 1 mol%) in 1,2-dichloroethane (10 ml) was stirred at reflux for appropriate time according to Table 2. The progress of the reaction was monitored by TLC. After completion of the reaction, the reaction mixture was filtered and the organic solvent was concentrated in vacuum to afford crude product. The crystalline pure product was obtained by further recrystallization from ethanol.

4.3. General experimental procedure (Method B)

To a mixture of aldehyde (1 mmol), 2-naphtol (2 mmol) and $\text{HClO}_4\text{-SiO}_2$ (20 mg, 0.01 mmol, 1 mol%) were heated at 125 °C with stirring for appropriate time according to Table 2. After completion of reaction (monitored by TLC) the mixture was cooled to room temperature, CHCl_3 (15 ml) was added. The catalyst was filtered, solid was washed with CHCl_3 (5 ml), combined CHCl_3 solution was concentrated in vacuum to afford crude product. The crystalline pure product was obtained by further recrystallization from ethanol.

The spectral (IR, ^1H NMR, ^{13}C NMR) and analytical data for the unknown compounds are presented below:

Compound **3k**.

IR (KBr): 3061, 3019, 1617, 1587, 1511, 1488, 1451, 1397, 1241 cm^{-1} ;

^1H NMR (300 MHz, CDCl_3): δ = 3.27 (2H, d, J = 4.7 Hz), 5.80 (1H, t, J = 4.7 Hz), 6.12 (2H, d, J = 9.0 Hz), 6.84–7.20 (5H, m), 7.45–7.91 (8H, m), 8.25 (2H, d, J = 9.0 Hz);

^{13}C NMR (75 MHz, CDCl_3): δ = 33.0, 41.33, 115.27, 117.39, 122.18, 124.10, 126.10, 126.68, 127.18, 128.35, 128.88, 129.76, 130.84, 131.30, 137.55, 150.11;

Anal. Calcd. for $\text{C}_{28}\text{H}_{20}\text{O}$: C, 90.33; H, 5.37; found: C, 90.27; H, 5.37.

Compound **3n**.

IR (KBr): 3066, 2961, 2874, 1623, 1591, 1518, 1488, 1461, 1434, 1400, 1245 cm^{-1} ;

^1H NMR (300 MHz, CDCl_3): δ = 0.62 (3H, t, J = 7.2 Hz), 1.04 (2H, m), 2.03 (2H, m), 5.58 (1H, t, J = 4.6 Hz), 7.40 (2H, d, J = 8.8 Hz), 7.45–7.66 (4H, m), 7.79 (2H, d, J = 8.8 Hz), 7.89 (2H, d, J = 7.7 Hz), 8.27 (2H, d, J = 8.5 Hz);

^{13}C NMR (75 MHz, CDCl_3): δ = 14.8, 20.20, 42.0, 43.10, 115.40, 118.60, 122.48, 123.40, 126.24, 128.3, 128.48, 128.80, 133.60, 150.3;

Anal. Calcd. for $\text{C}_{24}\text{H}_{20}\text{O}$: C, 88.85; H, 6.21; found: C, 88.98; H, 6.39.

Acknowledgment

We thank the faculty of chemistry of Teacher Training University for supporting of this work.

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