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$BF_3·SiO_2$: an efficient alternative for the synthesis of 14-aryl or alkyl-14*H*-dibenzo[*a*,*j*]xanthenes

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ABSTRACT

Silica-supported boron trifluoride ($BF_3·SiO_2$) is an efficient, readily available, and reusable catalyst for the synthesis of 14-aryl or alkyl-14*H*-dibenzo[*a*,*j*]xanthenes by condensation of 2-naphthol and aldehydes. This reaction under heating or sonication conditions is very simple, affording good to excellent yields of products.

The synthesis of benzoxanthenes with therapeutic and pharmacological properties such as antibacterial,[1] anti-inflammatory,[2] and antiviral[3] is currently of great interest. Furthermore, these heterocyclic compounds are used as sensitizers in photodynamic therapy,[4] as leuco-dyes in laser technology,[5] as antagonists of the paralyzing action of zoxazolamine,[6] and in fluorescent materials for visualization of biomolecules.[7] The reported protocol for the synthesis of 14-aryl or alkyl-14*H*-dibenzo[*a*,*j*]xanthene involves the mixing of 2-naphthol with aldehydes in the presence of a catalyst. This procedure is catalyzed with silica sulfuric acid,[8,9] Dowex-50W,[10] $NH_4H_2PO_4$,[11] I_2,[12,13] sulfamic acid,[14] $HClO_4$–SiO_2,[15] PW acid,[16] cyanuric chloride,[17] $Yb(OTf)_3$,[18] and alum.[19]

Homogeneous acidic catalysts such as H_2SO_4, HCl, and BF_3 are commonly used for organic synthesis. However, the above-mentioned catalysts have several disadvantages because they are corrosive, toxic or volatile, and generate large amounts of waste. Silica-supported boron trifluoride, $BF_3·SiO_2$,[20] is a bench-top catalyst which is easy to handle and enables better accessibility of the reactants to the active sites. $BF_3·SiO_2$ is a solid superacid and has surface species such as Al–OBF_2 and Si–OBF_2, and the ion pairs, Al–$OBF_3^-H^+$ or Si–$OBF_3^-H^+$.[21]

In continuation of our investigations on the applications of solid acids in organic synthesis,[22] we investigated the synthesis of 14-aryl and alkyl-14*H*-dibenzo[*a*,*j*] xanthenes in the presence of $BF_3·SiO_2$ under normal heating or sonication conditions. Herein, we report that $BF_3·SiO_2$ is an efficient and reusable catalyst for the synthesis of 14-aryl or alkyl-14*H*-dibenzo[*a*,*j*]xanthene derivatives, and is comparable with some other applied catalysts (Table 1). The reaction of 4-methylbenzaldehyde (1 mmol) with 2-naphthol (2 mmol) was investigated for optimization of the reaction conditions (Table 1). Reaction at different temperatures and various molar ratios of substrates in the presence of $BF_3·SiO_2$ revealed that the best conditions were solvent-free at 60 °C and a ratio of aldehyde (mmol): 2-naphthol (mmol): 37% $BF_3·SiO_2$ (g) of 1:2:0.08. However, the reaction conducted with 1-naphthol instead of 2-naphthol did not afford any product.

The feasibility of the ultrasonic-assisted synthesis of 14-(4-methylphenyl)-dibenzo[*a*,*j*]xanthene in the presence of 37% $BF_3·SiO_2$ was also demonstrated (Table 1). The results obtained show that reflux in chloroform under sonication conditions reduced the reaction time to 6 min.

The reusability of the $BF_3·SiO_2$ catalyst was also examined. After each run, the product was filtered, the solvent was evaporated, and the catalyst residue was washed with $CHCl_3$ and reused. Treatment with $CHCl_3$ removes tars more efficiently from the catalyst surface (Table 1, entries 15 and 16). The catalyst was reusable, although a gradual decline in activity was observed.

The applicability of the present method to a large scale process was examined with 50 mmol of 2-naphthol and 25 mmol of 4-methylbenzaldehyde under thermal conditions, which gave 14-(4-methylphenyl)-dibenzo[*a*,*j*]xanthene in 90% yield.

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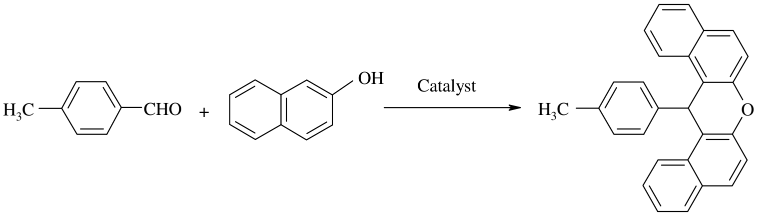
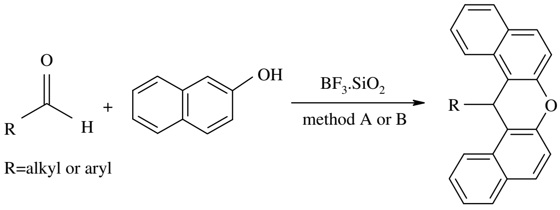
Table 1

Acid-catalyzed synthesis of 14-(4-methylphenyl)-dibenzo[*a*,*j*]xanthene via reaction of 2-naphthol (2 mmol) and 4-methylbenzaldehyde (1 mmol)



Entry	Catalyst (g)	Solvent	Conditions	Power (kHz)	Time (h)	Yield[a] (%)	Reference
1	37% $BF_3{\cdot}SiO_2$ (0.10)	Chloroform	rt	–	24	0	–
2	37% $BF_3{\cdot}SiO_2$ (0.10)	Ethanol	rt	–	24	0	–
3	37% $BF_3{\cdot}SiO_2$ (0.10)	Solvent-free	rt	–	24	0	–
4	37% $BF_3{\cdot}SiO_2$ (0.10)	Chloroform	Reflux	–	24	38	–
5	37% $BF_3{\cdot}SiO_2$ (0.10)	Ethanol	Reflux	–	24	42	–
6	37% $BF_3{\cdot}SiO_2$ (0.10)	Solvent-free	30 °C	–	3	42	–
7	37% $BF_3{\cdot}SiO_2$ (0.10)	Solvent-free	60 °C	–	3	96	–
8	37% $BF_3{\cdot}SiO_2$ (0.10)	Solvent-free	60 °C	–	1	95	–
9	37% $BF_3{\cdot}SiO_2$ (0.10)	Solvent-free	60 °C	–	0.25	94	–
10	25% $BF_3{\cdot}SiO_2$ (0.10)	Solvent-free	60 °C	–	0.25	74	
11	50% $BF_3{\cdot}SiO_2$ (0.10)	Solvent-free	60 °C	–	0.25	95	
12	37% $BF_3{\cdot}SiO_2$ (0.04)	Solvent-free	60 °C	–	0.25	42	–
13	37% $BF_3{\cdot}SiO_2$ (0.06)	Solvent-free	60 °C	–	0.25	73	–
14	37% $BF_3{\cdot}SiO_2$ (0.08)	Solvent-free	60 °C	–	0.25	94	–
15	37% $BF_3{\cdot}SiO_2$ (0.08) 2nd run	Solvent-free	60 °C	–	0.25	90	–
16	37% $BF_3{\cdot}SiO_2$ (0.08) 3rd run	Solvent-free	60 °C	–	0.25	87	–
17	37% $BF_3{\cdot}SiO_2$ (0.08)	Chloroform	Sonication/reflux	20	6 min	90	–
18	37% $BF_3{\cdot}SiO_2$ (0.08)	Chloroform	Sonication/reflux	20	4 min	67	–
19	37% $BF_3{\cdot}SiO_2$ (0.08)	Chloroform	Sonication/reflux	15	7 min	62	–
20	37% $BF_3{\cdot}SiO_2$ (0.08)	Chloroform	Sonication/25-35 °C	20	15 min	40	–
21	37% $BF_3{\cdot}SiO_2$ (0.08)	Ethanol	Sonication/reflux	20	15 min	0	–
22	37% $BF_3{\cdot}SiO_2$ (0.09)	Chloroform	Sonication/reflux	20	6 min	91	–
23	37% $BF_3{\cdot}SiO_2$ (0.09)	Solvent-free	60 °C	–	0.25	94	–
24	Silica sulfuric acid	Solvent-free	80 °C	–	45 min	86	8,9
25	Dowex-50 W	Solvent-free	100 °C		2	86	10
26	$NH_4H_2PO_4/SiO_2$	Water	Ultrasound/40 °C	–	40 min	88	11
27	I_2	Solvent-free	90 °C	–	0.4	93	12
28	I_2	Solvent-free	90 °C	–	3	88	13
29	Sulfamic acid	Solvent-free	125 °C	–	11	92	14
30	$HClO_4–SiO_2$	1,2-Dichloroethane	Reflux	–	9	92	15
31	$HClO_4–SiO_2$	Solvent-free	125 °C	–	8 min	92	15
32	PW acid	Solvent-free	100 °C	–	1.5	91	16
33	Cyanuric chloride	Solvent-free	110 °C	–	35 min	91	17
34	Alum	Water	100 °C	–	3	88	19

[a] Isolated yield.



Scheme 1.

The current method is simple, efficient, and less time-consuming for the synthesis of 14-aryl-14*H*-dibenzo [*a*,*j*] xanthene derivatives.

2-Naphthol and various aldehydes were used as substrates for the synthesis of 14-aryl-14*H*-dibenzo[*a*,*j*]xanthene derivatives under normal heating or sonication conditions (Scheme 1 and Table 2).[25]

In conclusion, we have demonstrated a simple method for the synthesis of 14-aryl or alkyl-14*H*-dibenzo[*a*,*j*]xanthenes using 37% $BF_3{\cdot}SiO_2$ as a reusable, eco-friendly, inexpensive, and efficient catalyst. Short reaction times, high yields, scale-up, and easy work-up are the advantages of this protocol.

Table 2

The reaction of 2-naphthol (1 mmol) and various aldehydes (0.5 mmol) in the presence of 37% $BF_3{\cdot}SiO_2$ (0.08 g)

Entry	R[a]	Yield[b] (%)		Mp (°C)	
		60 °C[c]	))))[d]	Found	Reported[Ref.]
1	CH_3CH_2	88	85	150–152	150–152[23]
2	$(CH_3)_2CH$	82	85	155–157	155–157[17]
3	$CH_3CH_2CH_2$	89	88	152–154	152–154[15]
4	C_6H_5	96	95	184–185	185[24]
5	4-Br–C_6H_4	97	98	297–298	297[17]
6	4-MeO–C_6H_4	93	91	203–205	203–205[17]
7	3-Cl–C_6H_4	96	95	209–211	210–213[11]
8	2-MeO–C_6H_4	88	88	258–259	258–259[17]
9	4-Me–C_6H_4	94	90	227–229	227–229[17]
10	4-Cl–C_6H_4	97	96	289–290	289[24]
11	2-Cl–C_6H_4	95	91	214–216	214–216[13]
12	4-O_2N–C_6H_4	93	94	311–312	311–312[13]
13	3-O_2N–C_6H_4	94	95	210–211	211[24]
14	3-H_3C–C_6H_4	91	93	198–197	198[12]
15	3-Br–C_6H_4	92	89	190–191	190–192[14]
16	2-O_2N–C_6H_4	94	91	214–215	214[12]

[a] All the products are known and were characterized by IR and ^1H NMR and by comparison of their physical properties with those reported in the literature.

[b] Isolated yield.

[c] The 2-naphthol (2 mmol) was stirred with aldehyde (1 mmol) in the presence of 0.08 g of freshly prepared 37% $BF_3{\cdot}SiO_2$ under neat conditions at 60 °C.

[d] The mixture of 2-naphthol (2 mmol) and aldehyde (1 mmol) was refluxed in chloroform in the presence of 0.08 g of 37% $BF_3{\cdot}SiO_2$ under sonication (20 kHz) for 6 min.

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25. *General procedure for the synthesis of aryl or alkyl-14H-dibenzo[a,j]xanthenes, method A*: A mixture of 2-naphthol (2 mmol), aldehyde (1 mmol), and 37% $BF_3 \cdot SiO_2$ (0.08 g) was heated at 60 °C. The progress of the reaction was monitored by TLC. After completion of the reaction, the mixture was washed with chloroform and filtered to recover the catalyst. The filtrate was evaporated, and the crude product was recrystallized from *iso*-propanol, and chloroform (80:20) to afford the pure 14-aryl or alkyl-14*H*-dibenzo[*a*,*j*]xanthene derivatives in 82–97% yields.

    Method B: In a two-necked flask, a mixture of 2-naphthol (2 mmol), aldehyde (1 mmol), 37% $BF_3 \cdot SiO_2$ (0.08 g), and chloroform (10 ml) was irradiated in a BANDELIN Sonopulse HD 3200 ultrasonic apparatus at reflux. After 6 min, the mixture was filtered to recover the catalyst, and the filtrate was evaporated. The residue was crystallized from *iso*-propanol and chloroform (80:20), and the pure products were obtained in 85–98% yields.