Nanoparticle silica supported sulfuric acid (NPs SiO_2-H_2SO_4): a solid phase acidic catalyst for the one-pot synthesis of benzo[*a*]xanthene-11-one derivatives

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The reaction between aromatic aldehydes, dimedone (5,5-dimethyl-1,3-cyclohexane dione) and 2-naphthol catalysed by nanoparticle silica supported sulfuric acid (NPs SiO_2-H_2SO_4) in CH_2Cl_2 as a solvent at room temperature provided a simple and efficient one-pot route for the synthesis of benzo[*a*]xanthene-11-one derivatives in high yield. Benzoxanthenes are important heterocycles because of their antiviral, anti-inflammatory and antibacterial activities.

Keywords: nanoparticle silica supported sulfuric acid, dimedone, 2-naphthol, aromatic aldehydes, benzo[*a*]xanthene-11-one derivatives, green chemistry

Xanthenes and benzoxanthenes are important heterocycles that possess antiviral,[1] anti-inflammatory[2] and antibacterial[3] activities. These are used as antagonists for paralysing action of zoxazolamine[4,5] and in photodynamic therapy.[6,7] Furthermore, these compounds can be used as dyes,[8,9] in laser technologies[10,11] and as pH sensitive fluorescent materials for the visualisation of biomolecules.[12] The synthesis of benzo[*a*]xanthen-11-ones has been reported in the presence of Sr $(OTf)_2$,[13] $NaHSO_4$-SiO_2 under reflux in halogenated solvents for a long time,[14] ρTSA in the presence of ionic liquids,[15] indium trichloride,[16,17] P_2O_5 under solvent-free,[18] BF_3-Et_2O,[19] and TBAF.[20] We have now used nanoparticle silica supported sulfuric acid (NPs SiO_2-H_2SO_4) as a new and rapid method affording excellent yields. This provides a solid phase acidic green catalyst for the synthesis of benzo[*a*]xanthene-11-one derivatives at room temperature.

Results and discussion

In continution of our investigations of the application of solid acids in organic synthesis[21–23] we have investigated the synthesis of benzo[*a*]xanthene-11-one derivatives by the three-component condensation of an aromatic aldehyde **1**, dimedone **2**, and 2-naphthol **3** in the presence of 0.003 g NPs SiO_2-H_2SO_4 catalyst (Scheme 1).

The stable catalyst is easily prepared[23] for use inh preparation of benzo[*a*]xanthene-11-one derivatives. We have carried out a model study with 3-nitrobenzaldehyde dimedone and 2-naphthol using NPs SiO_2-H_2SO_4 (0.003 g) as catalyst at room temperature. In order to establish the better catalytic activity of NPs SiO_2-H_2SO_4, we have compared the reaction using other catalysts at room temperature and for 20 min. The results are listed in Table 1. Those synthetic methods which afforded good yields however, had the limitation of requiring a long reaction time, harsh reaction conditions and often expensive catalysts. The problems in the reported protocols prompted us to develop a new rapid method for the synthesis of benzo[*a*]xanthene-11-one derivatives.affording excellent yield and using a solid phase acidic green catalyst.

In order to determine the optimum quantity of NPs SiO_2–H_2SO_4, the reaction of 3-nitrobenzaldehyde, dimedone and 2-naphthol was carried out at room temperature using different quantities of NPs SiO_2-H_2SO_4 (Table 2). NPs SiO_2-H_2SO_4 of 0.003 g gave an excellent yield in 20 min (Table 2, entry 3).

The above reaction was also examined in various solvents (Table 3).

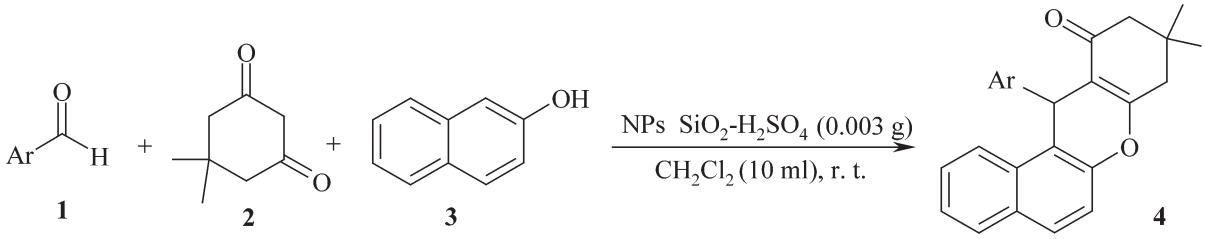
The results indicated that various solvents affected the efficiency of the reaction. Most of these solvents required a longer time and gave moderate yields. The best results were obtained when CH_2Cl_2 was used as solvent (Table 3, entry 1).

To study the scope of the reaction, a series of aromatic aldehydes, dimedone and 2-naphthol catalysed by NPs SiO_2-H_2SO_4 were examined. The results are shown in Table 4. In all cases, aromatic aldehyde substituted with either electron-donating or electron-withdrawing groups underwent the reaction smoothly and gave products in excellent yields.

Table 1 Evaluation of the activity of different catalysts for the condensation of 3-nitrobenzaldehyde, dimedone and 2-naphthol in NPs SiO_2-H_2SO_4

Entry	Catalyst	Time /min	Yield[a] /%
1	–	20	15
2	TBAF	20	40
3	Sr $(OTf)_2$	20	47
4	$NaHSO_4$-SiO_2	20	45
5	$InCl_3$	20	65
6	P_2O_5	20	50
7	ρTSA	20	55
8	BF_3-Et_2O	20	40
9	NPs SiO_2-H_2SO_4	20	95

[a]Isolated yield.



Scheme 1 Synthesis of benzo[*a*]xanthene-11-one derivatives by condensation of an aromatic aldehyde, dimedone and 2-naphthol using NPs SiO_2-H_2SO_4 (0.003 g) as catalyst.

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Table 2 Optimisation amount of NPs SiO_2-H_2SO_4 on the reaction of condensation of 3-nitrobenzaldehyde, dimedone and 2-naphthol in CH_2Cl_2 at room temperature

Entry	Catalyst	Time /min	Yield[a] /%
1	0.001	20	78
2	0.007	20	97
3	0.003	20	96
4	0.01	20	97

[a] Isolated yield.

Table 3 Effect of the solvent on the reaction between 3-nitrobenzaldehyde, dimedone and 2-naphthol by NPs SiO_2-H_2SO_4 (0.003 g)

Entry	Solvent	Time /min	Yield[a] /%
1	CH_2Cl_2	20	95
2	H_2O	20	80
3	EtOH	20	77
4	n-Hexane	20	64
5	Solvent-free	40	80

[a] Isolated yield.

Table 4 Reaction between an aromatic aldehyde, dimedone and 2-naphthol by NPs SiO_2-H_2SO_4 (0.003 g) in CH_2Cl_2 at room temperature

Entry	Ar	Product	Time/min	Yield%[a]	M.p./°C	
					Found	Reported [18]
1	C_6H_5	**4a**	20	82	149–151	151–153
2	3-$NO_2C_6H_4$	**4b**	20	96	170–172	168–170
3	4-ClC_6H_4	**4c**	20	86	180–182	180–182
4	2-ClC_6H_4	**4d**	20	87	178–180	179–180
5	4-$NO_2C_6H_4$	**4e**	20	83	180–182	178–180
6	4-$MeOC_6H_4$	**4f**	20	92	202–204	204–205
7	4-OHC_6H_4	**4g**	20	83	222–224	223–225
8	3-OHC_6H_4	**4h**	20	89	242–244	240–241
9	5-Br-2-OHC_6H_3	**4i**	20	85	270–272	266–268
10	2,4-$Cl_2C_6H_3$	**4j**	20	95	179–181	178–180
11	2-$MeOC_6H_4$	**4k**	20	90	161–163	163–165
12	4-MeC_6H_4	**4l**	20	82	177–179	176–178
13	5-NO_2-2-OHC_6H_3	**4m**	20	91	264–266	263–265
14	2-OH-3-$MeOC_6H_3$	**4n**	20	87	211–213	213–215

[a] Yields refer to the pure isolated products.

The compounds **4a–n** were characterised by their ^1H, ^{13}C NMR and IR spectroscopy and elemental analyses.[18]

In summary, we prepared NPs SiO_2-H_2SO_4 and have shown that it has advantages in the preparation of benzo[*a*]xanthene-11-ones such as shorter reaction times, simple work-up, and affords excellent yield. The solid phase acidic catalyst was re-usable for a number of times without appreciable loss of activity. The present method does not involve any hazardous organic solvent. Therefore, this procedure could be classified as green chemistry.

Experimental

Melting points were determined with an Electrothermal 9100 apparatus. Elemental analyses were performed using a Costech ECS 4010 CHNS-O analyser. IR spectra were recorded on a Shimadzu IR-470 spectrometer. ^1H and ^{13}C NMR spectra were recorded on Bruker DRX-500 Avance spectrometer for solutions in d_6-DMSO using TMS as an internal standard. The chemicals for this work were purchased from Fluka (Buchs, Switzerland) and were used without further purification. NPs SiO_2-H_2SO_4 was prepared as previously described in the literature.[23]

General procedure:

NPs SiO_2-H_2SO_4 (0.003 g) was added to a stirred mixture of the aromatic aldehyde (1 mmol), dimedone (1 mmol) and 2-naphthol in CH_2Cl_2 (10 mL). The reaction mixture was then stirred for 20 min at room temperature. The progress of the reaction was followed by TLC (*n*-hexane:ethylacetate). After completion of the reaction, the mixture was filtered to remove the catalyst. After evaporation of the solvent, the crude product was recrystallised from hot ethanol to obtain the pure compound.

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