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Efficient one-pot synthesis of 1,3-diaryl-3*H*-benzo[*f*]chromenes using ferric hydrogensulfate

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Abstract

An efficient and easy method for one-pot three-component synthesis of 1,3-disubstituted-3*H*-benzo[*f*]chromenes by the condensation of naphtol, aromatic aldehyde derivatives and phenylacetylene in the presence of ferric hydrogensulfate [$Fe(HSO_4)_3$], has been described. The catalyst displayed high activity which afforded the corresponding 1,3-disubstituted-3*H*-benzo[*f*]chromenes in satisfying yields. Alkyl-substituted phenols were examined and the corresponding benzopyran derivatives were synthesized in moderate yields. Heterogeneous nature of the using catalyst made it reusable for further chemical reactions.

Keywords: 1,3-Disubstituted-3*H*-benzo[*f*]chromenes; Ferric hydrogensulfate; One-pot synthesis; Naphtopyran; Benzopyran

Naphtopyrans are an important class of photochromic compounds and the classical molecules which have the ability to generate a yellow colour on being irradiated with UV light [1]. Their photochromic behavior is based on a reversible pyran ring opening induced upon near UV irradiation that converts a colourless form to a set of quasi-planar forms constituting a system with a distinct absorption spectrum [1,2]. 2-Amino-4*H*-chromenes and their derivatives are of considerable interest as they possess a wide range of biological properties [3,4] such as spasmolytic, diuretic, anticoagulant, anticancer [5], antitumor, antiproliferative, antiviral and antianaphylactic activities [6,7]. Thus, the development of a new methodology for the direct synthesis of 1,3-disubstituted-3*H*-benzo[*f*]chromenes which does not need to use a stoichiometric amount of highly reactive catalyst and can be carried out under mild conditions would be highly desirable. However, recently some studies have been devoted to the preparation of benzo[*f*]chromenes [8–12].

In the present study, ferric hydrogenesulfate [$Fe(HSO_4)_3$], was introduced as an efficient catalyst for synthesis of the 1,3-disubstituted-3*H*-benzo[*f*]chromenes (naphthopyrans) by one-pot three-component coupling of naphthol, phenylacetylene and aromatic aldehyde derivatives (Scheme 1).

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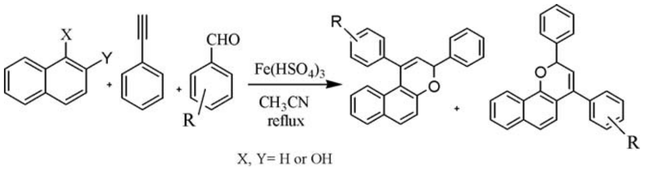


Scheme 1.

1. Experimental

Chemicals were either prepared in our laboratories or purchased from Merck, Fluka and Aldrich Chemical Companies. All yields refer to isolated products. The products were characterized by comparison of their physical data with those of known samples or by their spectral data. IR spectra were recorded on a Shimadzu-IR 470 spectrophotometer. ^{1}H NMR spectra were recorded on a Bruker 100-MHz spectrometer in chloroform as the solvent and TMS as internal standard. Ferric hydrogensulfate was prepared according to previously reported procedure [13,14].

1.1. General procedure to synthesis of 1,3-disubstituted-3H-benzo[f]chromenes

A mixture of naphthol (1 mmol), phenylacetylene (1.1 mmol), aldehyde (1 mmol) and ferric hydrogensulfate (0.1 mmol) was refluxed in acetonitril for the appropriate time (Table 1). The reaction was followed by TLC and after completion of the reaction the catalyst was recovered through filtration simply. The residue was concentrated in vacuo. The resulting crude product was purified by column chromatography on silica gel to afford the pure product.

Representative ^{1}H NMR spectral data for the selected products:

1,3-Diphenyl-3*H*-benzo[*f*]chromene (entry **1**): ^{1}H NMR (100 MHz, $CDCl_3$): δ 6.90–7.10 (m, 7H), 7.25–7.40 (m, 5H), 7.40–7.55 (m, 4H), 5.9 (d, 1H, $J = 1.5$ Hz), 4.90 (d, 1H, $J = 1.5$ Hz).

3-(2-Bromophenyl)-1-phenyl-3*H*-benzo[*f*]chromene (entry **2**): ^{1}H NMR (100 MHz, $CDCl_3$): δ 7.20–7.50 (m, 8H), 7.55–7.70 (m, 7H), 6.10 (d, 1H, $J = 5$ Hz), 4.85 (d, 1H, $J = 5$ Hz).

3-(4-Methoxyphenyl)-1-phenyl-3*H*-benzo[*f*]chromene (entry **3**): ^{1}H NMR (100 MHz, $CDCl_3$): δ 7.46–7.55 (m, 10H), 6.96–6.99 (m, 5H), 5.80 (d, 1H, $J = 3.5$ Hz), 4.80 (d, 1H, $J = 3.5$ Hz), 3.75 (s, 3H).

2. Result and discussion

Using β-naphtol, phenylacetylene as the alkyne and benzaldehyde as the aldehyde component in a stoichiometric ratio of 1:1.1:1 and 0.1 equiv. ferric hydrogensulfate (based on the aldehyde component), we designed a reaction as a model in order to find the optimum reaction solvent and the results are shown in Table 1.

As it can be seen in Table 1, among the various solvents investigated, CH_3CN was found to be the best choice. However, benzene and toluene afforded satisfying yields. Moderate and poor yields were obtained when the reactions were carried out in $C_2H_4Cl_2$ and THF respectively. As it can be seen in Table 1, the catalyst could be reused without significant loss of its catalytic activity until at least 5 times.

Table 1
Influence of solvent on $Fe(HSO_4)_3$-catalyzed reaction of β-naphtol, phenyl acetylene and benzaldehyde and reusability study.

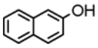
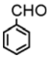
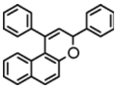
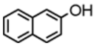
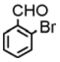
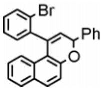
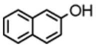
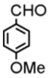
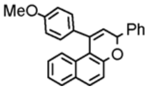
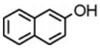
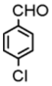
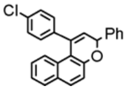
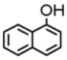
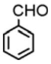
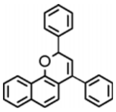
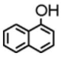
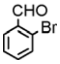
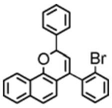
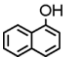
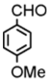
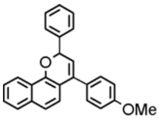
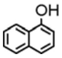
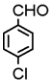
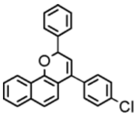
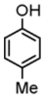
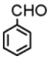
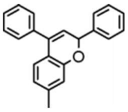
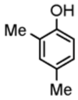
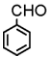
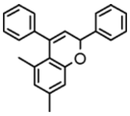
Solvent	Acetonitril	Toluene	Benzene	Dichloroethane	THF
Yield[a,b]	82	73	68	42	~20
Reusability[c]	78[d]	76[e]	~75[f]	70[g]	70[h]

[a] All the reactions were carried out under reflux conditions for 5 h.

[b] Isolated yields.

[c] Reusability of the recovered catalyst was investigated in CH_3CN as the optimum solvent.[d–h] Reusability of the recovered catalyst in new runs from run 2(d) to run 6(h).

Table 2
Results of one-pot three-component synthesis of naphtopyran and benzopyran derivatives[a].

Entry	Naphtol	Aldehyde	Product[b]	Time (h)	Yield (%)[c]
1				3.5	82
2				4	76
3				4.5	71
4				2	84
5				4	75
6				4	77
7				6	72
8				2.5	80
9				5.5	67
10				7	55

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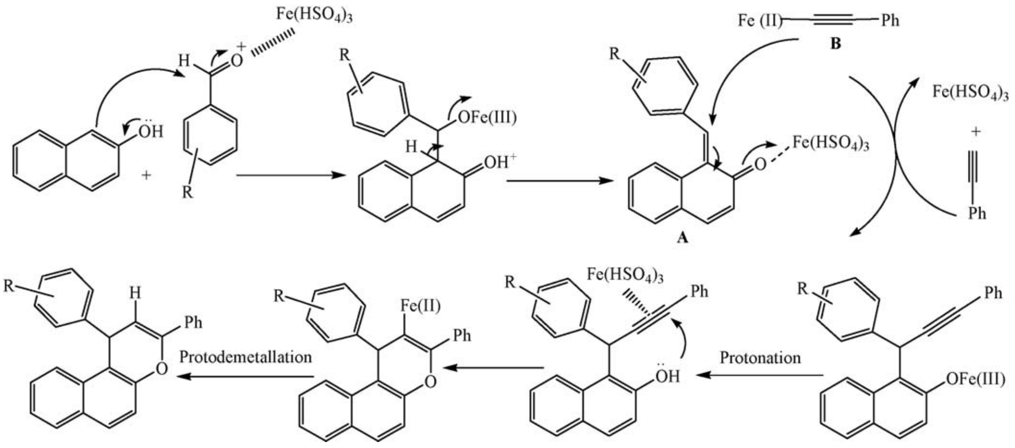
[a] Reaction conditions: 1.0 equiv. of naphthol, 1.0 equiv. of aldehyde, 1.1 equiv. of phenylacetylene, 10 mol% ferric hydrogenesulfate and reflux condition.

[b] The products were identified by ^{1}HNMR and IR spectra.

[c] Isolated yields.

To generalize the study, α- and β-naphtol, various aldehydes derivatives and phenylacetylene were employed in the multi-component one-pot reaction. The results are illustrated in Table 2. Electron withdrawing substitution on aldehyde compounds accelerated the multi-component reaction to some extent, however aromatic aldehydes bearing electron releasing group could react successfully and afford the corresponding products in good yields. In order to extend our study, alkyl-substituted phenols were examined under the optimized reaction conditions. Although the reactions were done properly, but the corresponding benzopyrans were obtained in longer times. The reaction was carried out using phenol and phenol with electron withdrawing substitutions (*e.g.* 4-chlorophenol and 4-nitrophenol) instead of alkyl-substituted phenols. The reactions were failed and no corresponding products were isolated.



Scheme 2.

The proposed mechanism for three-component synthesis of naphtopyran derivatives has been shown in Scheme 2. The reaction probably precedes *via in situ* generation of *ortho*-quinone methides (A) (OQMs) [15]. On the basis of several literatures [16,17], it is believed that the coupling reaction proceeds by terminal C–H bond activation by ferric hydrogensulfate catalyst. The Fe-alkyl acetylide (B) intermediate would attack on OQMs (A) by a Michael-type addition or by a Diels–Alder reaction (Scheme 2). Protometallation regenerates the catalyst for further reactions. Replacement of the phenylacetylene with 1-phenyl-1-propyne could not afford the corresponding product and the reaction of naphtols, 1-phenyl-1-propyne and benzaldehyde was failed. According to, although the Diels–Alder reaction might be conceivable, but due to failure of the reaction using 1-phenyl-1-propyne, the mentioned mechanism in Scheme 2 is more probable.

3. Conclusion

In conclusion, 1,3-disubstituted-3*H*-benzo[*f*]chromenes (naphthopyran and benzopyran derivatives) were synthesized successfully in the presence of catalytic amount of ferric hydrogensulfate as an efficient, inexpensive and heterogeneous catalyst. This new approach provided moderate to high yield of the corresponding products with the simple experimental and work up procedure.

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