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Research Article

Novel Approach for the Synthesis of 1,3-diaryl-3h-benzo[*f*]chromenes

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ABSTRACT

A novel, simple and facile procedure for the synthesis of 1,3-diaryl-3H-benzo[*f*]chromene derivatives is described. The procedure takes place by the one-pot condensation of naphthols, aromatic aldehydes and acetophenone in the presence of ferric hydrogensulfate as the catalyst.

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

1. INTRODUCTION

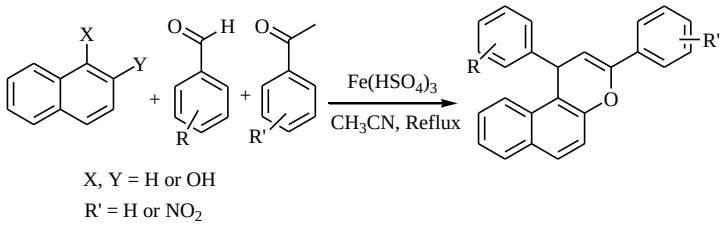
The development of "one-pot reactions" represents a great challenge in organic synthesis today. Indeed, this strategy allows the construction of highly complex molecules from relatively simple reagents under economically favorable conditions. Benzo- and naphthopyran derivatives are an important class of heterocyclic compounds possessing biological and pharmacological activities, such as anticoagulant, spasmolytic, diuretic, anticancer and antianaphylactin activities [1-2]. A variety of naphthopyran derivatives have been isolated and identified as natural phytochemicals [3-4].

Different synthetic approaches to benzo[*f*]chromenes are reported in the literature including Claisen rearrangement of alkynyl aryl ethers from propargylic alcohols and naphthols under acid catalysis [5], addition of Grignard reagents to coumarins and chromanones Dieckmann and aldol-type condensation of convenient aromatic carbonyl compounds [6], three component coupling reaction [7]. In addition, we have recently reported synthesis of 1,3-diaryl-3H-benzo[*f*]chromenes using ferric hydrogensulfate via one-pot three component reaction of β-naphthol, phenylacetylene and aromatic aldehydes [8]. In continuation, as part of our research program directed towards the development of highly expedient and efficient methods and the syntheses of diverse heterocyclic compounds [9], we herein disclose a new, convenient, and one-pot synthesis of 1,3-diaryl-3H-benzo[*f*]chromene from aldehydes, naphthols and acetophenone catalyzed by [$Fe(HSO_4)_3$] in good to excellent yields (Scheme 1).

2. EXPERIMENTAL

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

A dry 25 mL flask was charged with aromatic aldehyde (1 mmol), β-naphthol (1 mmol), phenylacetylene (1 mmol), $Fe(HSO_4)_3$ (0.1 mmol), and CH_3CN (10 mL). The reaction mixture was stirred at reflux conditions for the appropriate time. After completion of the reaction as indicated by TLC, another portion of CH_3CN was added to the mixture until all the pale yellow solid was dissolved when the mixture was cooled to room temperature. Then, the catalyst was recovered by filtration and the solvent was removed under reduced pressure, and the crude products were purified by short column chromatography on silica gel (Merck, 100–200 mesh, ethyl acetate–hexane. Representative ^1H NMR spectral data for the selected products are as follows:



Scheme 1

3-(4-Methoxyphenyl)-1-phenyl-3H-benzo[f]chromene (entry 3): ^1H NMR (100 MHz, $CDCl_3$): 7.46–7.55 (m, 10H), 6.96–7.25 (m, 5H), 5.80 (d, 1H, J = 3.5 Hz), 4.80 (d, 1H, J = 3.5 Hz), 3.75 (s, 3H). Anal. Calcd. for $C_{26}H_{20}O_2$: C 85.69, H 5.53, Found: C 85.51, H 5.48. Ms (m/z): 364 (M+).

3-(2-Bromophenyl)-1-phenyl-3H-benzo[f]chromene (entry 4): ^1H NMR (100 MHz, $CDCl_3$): δ 7.55–7.70 (m, 7H), 7.20–7.50 (m, 8H), 6.10 (d, 1H, *J* = 5 Hz), 4.85 (d, 1H, *J* = 5 Hz). Anal. Calcd. for $C_{25}H_{17}BrO$: C 72.65, H 4.15, Found: C 72.49, H 4.09. EIMS (m/z): 412 (M+).

4-(4-Methoxyphenyl)-2-phenyl-4H-benzo[h]chromene (entry 8): ^1H NMR (100 MHz, $CDCl_3$): δ 7.82 (d, J = 5.5 Hz, 1H), 7.25–7.62 (m, 9H), 7–7.25 (m, 6H), 6.90 (d, 2H, *J* = 5 Hz), 6.05 (d, 1H, J = 8.2 Hz), 4.90 (d, 1H, *J* = 5 Hz). Anal. Calcd. for $C_{26}H_{20}O_2$: C 85.69, H 5.53, Found: C 85.52, H 5.48. EIMS (m/z): 364 (M+).

3-(4-Nitrophenyl)-1-phenyl-1H-benzo[f]chromene (entry 10): ^1H NMR (100 MHz, $CDCl_3$): δ 8.15 (d, 2H, J = 3.5 Hz), 7.55–7.70 (m, 7H), 7.10–7.45 (m, 5H), 7.05 (d, 1H, *J* = 3.5 Hz), 6.05 (d, 1H,

J = 9 Hz), 4.85 (d, 1H, *J* = 9 Hz). Anal. Calcd. for $C_{25}H_{17}NO_3$: C 79.14, H 4.52, N 3.69, Found: C 79.08, H 4.45, N 3.61. EIMS (m/z): 379 (M+).

3-(4-Nitrophenyl)-1-p-tolyl-1H-benzo[f]chromene (entry 12): ^{1}H NMR (100 MHz, $CDCl_3$): δ 8.10 (d, 2H, J = 3.5 Hz), 6.95–7.55 (m, 7H), 7.55–7.70 (m, 5H), 6.20 (d, 1H, *J* = 7.5 Hz), 4.95 (d, 1H, *J* = 7.5 Hz), 2.2 (s, 3H). Anal. Calcd. for $C_{26}H_{19}N_3O$: C 79.37, H 4.87, N 3.56, Found: C 79.22, H 4.81, N 3.49.

3. RESULTS AND DISCUSSION

This research is an extension of our previous results describing the synthesis of 1,3-diaryl-3H-benzo[*f*]chromene [8] by one-pot reaction from naphthols, aromatic aldehydes and phenylacetylene in acetonitrile in the presence of ferric hydrogensulfate. In the present study, the target products have been synthesized through new approach in good to excellent yields.

Table 1: Influence of solvent on ferric hydrogensulfate-catalyzed reaction of 2-naphthol, p-chlirobenzaldehyde and acetophenone

Solvent	Ethanol	Methanol	Dichloromethane	Chloroform	Acetonitrile	Dioxane	THF
Yield[a,b]	82	75	50	55	93	80	60

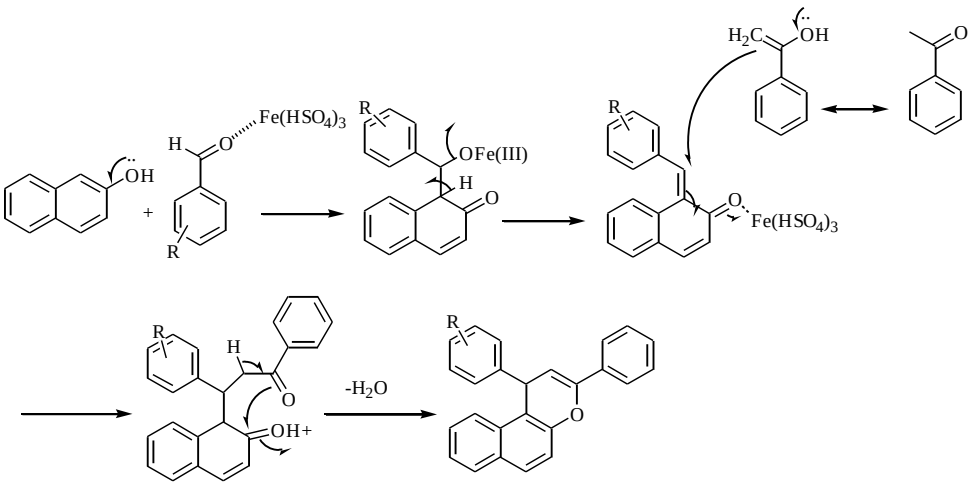
a) All the reactions were carried out at reflux condition for 4 h.

b) Isolated yields.

In an initial endeavor, we carried out the reaction of 2-naphthol, 4-chlorobenzaldehyde and acetophenone in the presence of catalytic amount of the catalyst (10 mol%) using the different solvents (Table 1). We screened different solvents such as ethanol, methanol, dichloromethane, tetrahydrofuran, acetonitrile, chloroform, dioxane at reflux condition. As shown in the Table 1, the best yield was obtained when acetonitrile was used as a solvent in the presence of 10 mol% catalyst. In case of the protic solvents the yields are better than aprotic solvent. To determine the role of the used catalyst, the model reaction was carried out in acetonitrile in the absence of ferric hydrogensulfate. No corresponding naphthochromene was observed in the absence of the catalyst highlighting the role of the catalyst to promote the reaction. A wide variety of aromatic aldehydes underwent smooth coupling with 2-naphthol and acetophenone under identical conditions (Table 2, entries 1-5). The reaction was amenable to a wide variety of substituents on araldehydes. The nature of functional groups on the aromatic ring of the aldehyde exerted a slight influence on the reaction time as well as reaction yield.

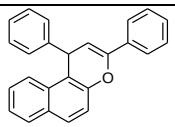
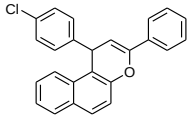
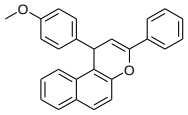
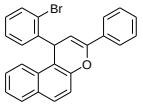
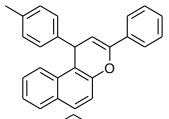
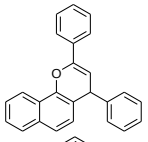
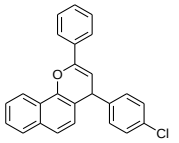
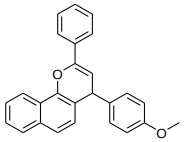
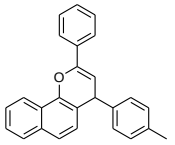
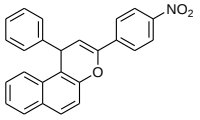
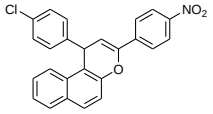
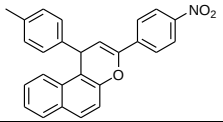
Besides 2-naphthol, 1-naphthol also participated in the three-component coupling reaction (Table 2, entries 6-9). Naphthopyran derivatives 10 - 12 were also prepared efficiently by means of coupling of 2-naphthol, aromatic aldehydes and *p*-nitroacetophenone in the presence of $Fe(HSO_4)_3$ using the similar reaction conditions.

The suggested mechanism for the synthesis of 1,3-diaryl-3H-benzo[*f*]chromene was depicted in Scheme 2. The reaction probably proceeds via *in situ* generation of *ortho*-quinone methides followed by Michael-type addition of enolized acetophenone to the *ortho*-quinone methides, dehydration, and heterocyclization leading to synthesis of the 1,3-diaryl-3H-benzo[*f*]chromene product.



Scheme 2

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

Entry	Naphthol	Aldehyde	Product	Time (min)	Yield (%)[b]
1	2-naphthol			3.5	90
2	2-naphthol			3	93
3	2-naphthol			4	90
4	2-naphthol			4	90
5	2-naphthol			4	90
6	1-naphthol			3	93
7	1-naphthol			3	94
8	1-naphthol			4	90
9	1-naphthol			4	92
10	2-naphthol			4.5	90
11	2-naphthol			5	88
12	2-naphthol			5	85

a) Reaction conditions: 1.0 equiv. of naphthol, 1.0 equiv. of aldehyde, 1.1 equiv. of acetophenone, 10 mol% ferric hydrogenesulfate, acetonitrile as the solvent, reflux conditions, b) The products were identified by ^{1}HNMR, IR and Mass spectroscopy, c) Isolated yields.

4. CONCLUSION

In summary, we have developed a convenient and efficient method for the synthesis of 1,3-diaryl-3H-benzo[*f*]chromene, via three-component reaction offering various advantages, such as mild condition, high yield, general applicability, and the use of inexpensive and highly reusable ferric hydrogensulfate. Eventually, this approach could make a valuable contribution to the existing procedures in the field of naphthopyran synthesis.

5. REFERENCES

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