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Iron(III) triflate under ultrasound facilitates the synthesis of benzo[*f*]chromenes

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ABSTRACT

Iron(III) triflate with the aid of ultrasonic irradiation efficiently catalyzes the three-component condensation reaction of naphthols, aromatic aldehydes and acetophenone in acetonitrile at 40 °C to afford the corresponding 1,3-diaryl-3*H*-benzo[*f*]chromene derivatives in high yields.

KEYWORDS

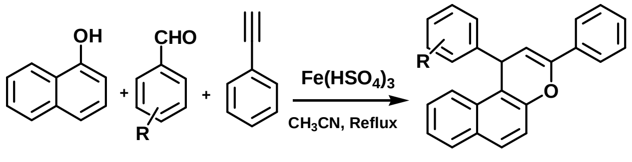
1,3-diaryl-3*H*-benzo[*f*]chromenes;
Naphthopyran;
One-pot;
Iron(III) triflate.

INTRODUCTION

Chromenes and fused chromenes are biologically active compounds with antibacterial activities,[1,2] antifungal activities,[3] antitumor activity[4] and hypotensive effects.[5] Some chromene derivatives also have various biological properties like molluscicidal activity[6], local anesthetic and antiarrhythmic activities,[7] antiallergenic effects,[8,9] and antiviral activity[10].

Ultrasound has increasingly been used in organic synthesis. A large number of ultrasonic reactions can be carried out in higher yield, shorter reaction time, or milder conditions[11–14]. As we know that the temperature of hot spots caused by the collapse of acoustic caves is generally as high as more than several hundred degrees, this energy can be transferred to the organic molecules and absorbed by them to dramatically raise their intrinsic energy leading to the apparent improvement of the reaction efficiency with increased rates and reduced reaction time.

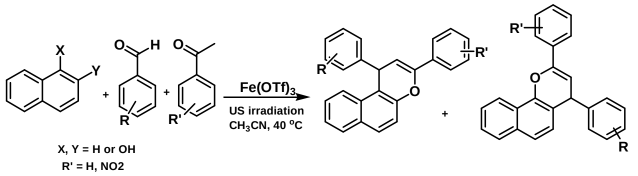
A few procedures have been reported for the synthesis of 1,3-diaryl-3*H*-benzo[*f*]chromene compounds such as Claisen rearrangement of alkynyl aryl ethers from propargylic alcohols and naphthols under acid catalysis.[15,16] Recently, we have disclosed an efficient acid catalyzed addition–cyclization reaction of naphthols, aldehydes and phenylacetylene affording the corresponding naphthopyran derivatives in high yields (Scheme 1). As an extension of this work, we then wondered if other nucleophile could be used instead of phenylacetylene. Acetophenone was also found to be a suitable reaction component in this reaction system to provide a series of disubstituted benzo[*f*]chromene derivatives with good to excellent yields.



Scheme 1

In general, Lewis acids such as $SnCl_2$, $SnCl_4$, $BF_3{\cdot}OEt_2$, $ZnCl_2$, $MgBr_2$, and $InCl_3$ have been used as catalysts in organic synthesis. However, sometimes these reactions could not be carried out efficiently when water is formed as a byproduct during the target product formation since it can decompose or deactivate these Lewis acids. During the past few years, the outstanding potential of a variety of metal triflates (trifluoromethylsulfonates) has been discovered, thus triggering much research endeavour.[17] Among the various metal triflates, iron(III) triflate [Fe $(OTf)_3$], is a novel Lewis acid, which has recently attracted attention as a catalyst[18-20].

In continuation of our interest in developing a versatile and efficient approach for synthesis of heterocyclic compounds[21,22], in the present study, a novel approach to the synthesis 1,3-diaryl-3*H*-benzo[*f*]chromenes is described. To our best knowledge, there is no report in literature on preparation of 1,3-diaryl-3H-benzo[*f*]chromene through one-pot condensation of naphthols, aldehydes, and acetophenone using $Fe(OTf)_3$ under ultrasonic irradiation. Herein, the details of this study are reported (Scheme 2). The choice of the iron(III) triflate [Fe(OTf)3] as a Lewis acid was based on the possible formation of water.



Scheme 2

EXPERIMENTAL

Chemicals were either prepared in our laboratories or purchased from Merck, Fluka and Aldrich Chemical Companies. All yields refer to isolated products. IR spectra were recorded on a Shimadzu-IR 470 spectrophotometer. ^{1}H NMR spectra was recorded on a Bruker 100-MHz spectrometer in chloroform as the solvent and TMS as internal standard. Flash column chromatography was performed with 300 and 400 meshes silica gel and analytical thin layer chromatography was performed on pre-coated silica gel plates (60F-254). Elemental analyses were performed on Thermo Finnigan EA1112 elemental analyzer. Sonication was performed in Kunshan KQ-250B ultrasonic cleaner with a frequency of 40 kHz and a power 250 W. The reaction flasks were located in the maximum energy area in the cleaner, and the addition or removal of water controlled the temperature of the water bath.

General procedure for the synthesis of 1,3-diaryl-3H-benzo[f]chromene derivatives

A mixture of naphthols (1 mmol), acetophenone (1 mmol), aldehydes (1 mmol) and $Fe(OTf)_3$ (0.05 mmol) in acetonitrile (10 mL) was taken in a 100 mL conical flask and the reaction mixture was irradiated in the water bath of the ultrasonic cleaner at 40 °C for a period as indicated in TABLE 2. The course of the reaction was followed by TLC. After completion of the reaction, the reaction was quenched by addition of water. The reaction mixture was extracted with ethyl acetate (20 mL) and washed with water. The aqueous layer containing $Fe(OTf)_3$ was separated and evaporated under reduced pressure to afford the catalyst which was dried at 75 °C for 4 h to give the recovered catalyst. The organic layer was dried over anhydrous sodium sulfate and concentrated under reduced pressure to give the crude products, which were purified by column chromatography on silica gel using ethyl acetate–hexane (1:9) as eluent to afford the pure product.

Representative spectral data for the selected products are as follows:

3-(4-Methoxyphenyl)-1-phenyl-3*H*-benzo[*f*]chromene (entry 3): ^{1}H 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-3*H*-benzo[*f*]chromene (entry 4): ^{1}H 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-4*H*-benzo[*h*]chromene (entry 8): ^{1}H 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-1*H*-benzo[*f*]chromene (entry 10): ^{1}H 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+).

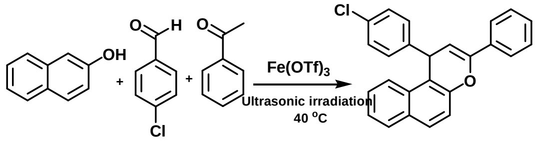
3-(4-Nitrophenyl)-1-p-tolyl-1*H*-benzo[*f*]chromene (entry 12): ^{1}H NMR (100 MHz, $CDCl_3$): δ 8.10 (d, 2H, J = 3.5 Hz), 7.55–7.70 (m, 5H), 6.95–7.55 (m, 7H), 6.20 (d, 1H, $J = 7.5$ Hz), 4.95 (d, 1H, $J = 7.5$ Hz), 2.2 (s, 3H). Anal. Calcd. for $C_{26}H_{19}NO_3$: C 79.37, H 4.87, N 3.56, Found: C 79.22, H 4.81, N 3.49. EIMS (m/z): 393 (M+).

4-(4-Chlorophenyl)-2-(4-nitrophenyl)-4*H*-benzo[*h*]chromene (entry 14): ^{1}H NMR (100 MHz, $CDCl_3$): δ 7.95 (d, 2H, J = 8.5 Hz), 7.82 (d, 1 H, J = 4.2 Hz), 7.65-7.50 (m, 4H), 7.05–7.43 (m, 7H), 6.20 (d, 1H, $J = 10.5$ Hz), 4.95 (d, 1H, $J = 10.5$ Hz). Anal. Calcd. for $C_{25}H_{16}NO_3Cl$: C 72.55, H 3.90, N 3.38, Found: C 72.47, H 3.86, N 3.33. EIMS (m/z): 413 (M+).

RESULTS AND DISCUSSION

As a starting point, 4-chlorobenzaldehyde was selected as a representative reactant in order to optimize the reaction conditions. The one-pot three-component condensation reaction of 2-naphthol, 4-chlorobenzaldehyde, and acetophenone in the presence of various solvents using catalytic amount of the $Fe(OTf)_3$ (5 mol%) under ultrasonic irradiation was conducted. The effect of different solvents such as $CHCl_3$, $ClCH_2CH_2Cl$, DMF, THF, CH_3CN, 1,4-dioxane, and EtOH on a model reaction under ultrasound irradiation at 40 °C was examined. The results were listed in TABLE 1. Acetonitrile was found to be the solvent of choice, giving the desired product in 91% yield (TABLE 2, entry 2).

TABLE 1 : Influence of solvent on Fe (III)-catalyzed synthesis of 1-(4-chlorophenyl)-3-phenyl-1*H*-benzo[*f*]chromene



Solvent	DMF	Dichloroethane	Dichloromethane	Chloroform	Acetonitrile	Dioxane	Ethanol
Yield[a,b]	72	50	35	55	91	70	84

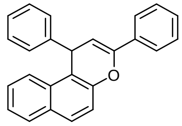
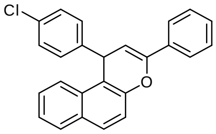
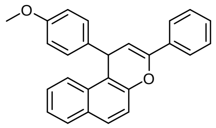
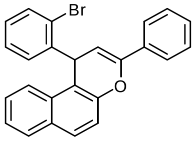
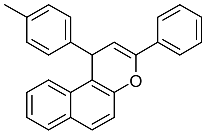
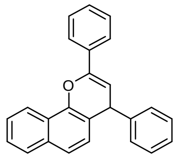
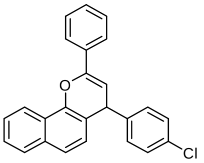
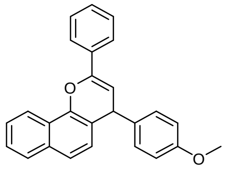
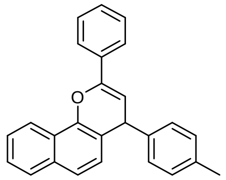
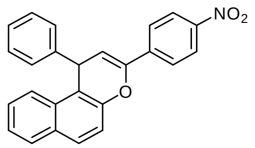
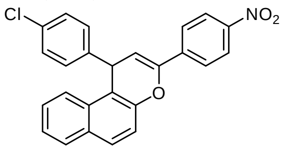
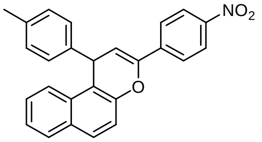
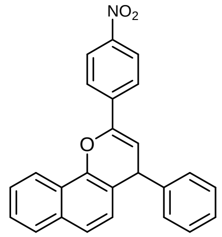
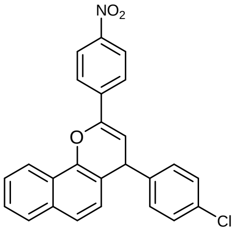
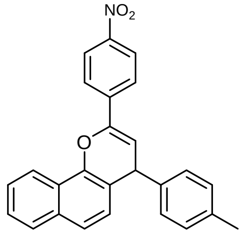
a) All the reactions were carried out at 40 °C under ultrasonication for 1 h.; b) Isolated yields.

To demonstrate the effect of ultrasound, the synthesis of 1-(4-chlorophenyl)-3-phenyl-1*H*-benzo[*f*]chromene (TABLE 2, entry 2) was investigated under stirring and reflux conditions using 5 mol% of the $Fe(OTf)_3$ in acetonitrile. Under stirring condition no corresponding desired benzo[*f*]chromene was detected even after long reaction time (8 h) whereas at reflux condition, the reaction could be completed within 5 h, to give the product in 77% yield. It was apparent that the ultrasound irradiation accelerates this transformation under milder conditions. As shown in TABLES 2, CH_3CN as solvent under ultrasound irradiation condition was chosen for the one-pot reaction of aldehydes, naphthols and acetophenone to give corresponding 1,3-diaryl-3*H*-benzo[*f*]chromene derivatives at 40 °C.

In order to extend the scope, acetophenone was treated with 1- or 2-naphthol and various aldehydes in the presence of $Fe(OTf)_3$ under ultrasound irradiation at 40 °C which successfully yielded the corresponding 1,3-diaryl-3H-benzo[*f*]chromene derivatives. In all cases, benzo[*f*]chromene derivatives were obtained in good yields. In the present procedure, aromatic aldehydes carrying either electron-donating or electron-withdrawing substituents on benzene ring reacted very well. Although the differences in the transformation times are slight, generally the electron-deficient substituents were superior to the electron-rich ones in this regard. Naphthopyran derivatives (entries 10 – 15) were also prepared efficiently by coupling of 1- or 2-naphthol with aromatic aldehydes and *p*-nitroacetophenone in the presence of $Fe(OTf)_3$ using the same conditions established before.

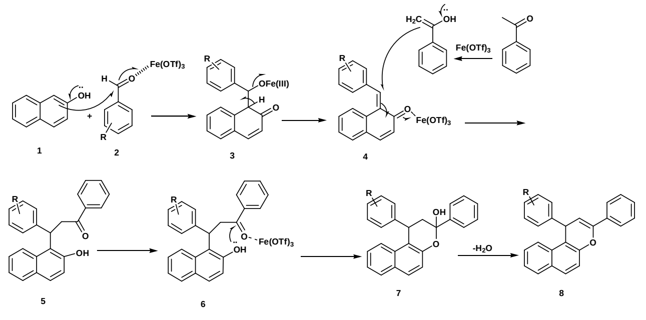
The suggested mechanism for the synthesis of 1,3-diaryl-3*H*-benzo[*f*]chromene was illustrated in Scheme 3. The reaction probably proceeds via *in situ* generation of *ortho*-quinone methide of 4 followed by Michael-type addition of enole of acetophenone to give intermediate 5, which is catalyzed by iron (III) triflate to

TABLE 2 : Additional reactions for the synthesis of benzo[*f*]chromenes using iron(III) triflate under ultrasonic irradiation[a]

Entry	Product	Time (min)	Yield (%)[b]
1		50	90
2		50	91
3		55	88
4		60	88
5		52	86
6		48	92
7		46	90
8		50	87
9		50	90
10		65	88
11		72	90
12		70	87
13		70	82
14		68	92
15		72	90

a) Reaction conditions: 1.0 mmol. of naphthol, 1.0 mmol. of aldehyde, 1.1 mmol. of acetophenone, 0.05 mmol catalyst, acetonitrile as the solvent, under ultrasonication.; b) Isolated yields

afford 6. Intramolecular cyclization of 6 gives 7 which undergoes dehydration to furnish product 8.



Scheme 3

CONCLUSION

In conclusion, a new, fast, general, and facile method for preparation of 1,3-diaryl-3*H*-benzo[*f*]chromene derivatives in the presence of iron(III) triflate under ultrasound irradiation is described. The catalyst system induced a remarkable acceleration for reactions. The salient features of this protocol were simple approach, mild reaction conditions, higher yields of products and shorter reaction time.

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