# An efficient method for synthesis of 3-arylbenzo[*f*] quinoline-1,2-dicarboxylates catalyzed by SnCl<sub>2</sub>

Qing Yan • Hongjun Zang • Jiaxuan Feng • Mingguang Li • Danni Yang • Hai Lu • Bowen Cheng

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**Abstract** A wide variety of 3-arylbenzo[f]quinoline-1,2-dicarboxylates and their dehydro derivatives have been synthesized by one-pot, three-component reaction of an aromatic aldehyde, naphthalene-2-amine, and dimethyl but-2-ynedioate in the presence of SnCl<sub>2</sub> under reflux in acetonitrile. This procedure has several advantages, for example high yield, short reaction time, easy work-up, little pollution, and low price of the catalyst.

**Keywords**  $SnCl_2 \cdot Imino Diels-Alder \cdot Aromatic aldehyde \cdot Dimethyl but-2-ynedioate \cdot Synthesis$ 

# Introduction

Multicomponent reactions (MCRs) are very important in organic synthesis because of the formation of carbon–carbon and carbon–hetero atom bonds [1–6]. Compared with classical stepwise synthesis, MCRs have the advantages of high atomeconomy, selectivity, and fewer byproducts, so these reactions are becoming increasingly attractive.

Benzoquinoline and its derivatives are famous for their diverse biological activity, for example antibacterial activity [7, 8], uridine diphosphate-glucuronosyl transferase activity [9, 10], antimicrobial activity [11], antimalarial activity [12], agonistic activity [13], and antipsychotic activity [14]. In recent years, much effort has been directed toward activating imine systems for cycloadditions by increasing their electron-deficient character, and many applications have been discovered [15, 16]. These applications have attracted the attention of organic chemists wishing to

Q. Yan  $\cdot$  H. Zang ( $\boxtimes$ )  $\cdot$  J. Feng  $\cdot$  M. Li  $\cdot$  D. Yang  $\cdot$  H. Lu  $\cdot$  B. Cheng

State Key Laboratory of Hollow Fiber Membrane Materials and Processes, Department of Environmental and Chemistry Engineering, Tianjin Polytechnic University, Tianjin, China e-mail: chemhong@126.com



Scheme 1 Synthesis of 3-arylbenzo[f]quinolone-1,2-dicarboxylates

develop efficient synthetic routes for highly functionalized benzoquinoline derivatives [17].

The imino Diels-Alder reaction enables easy preparation of six-membered nitrogen heterocycles and related fused ring heterocycles [18-22]. Lewis acid and Brønsted acid-catalyzed imino Diels–Alder reactions have been reported [23–31], and have been developed into convenient methods for synthesis of a wide variety of benzoquinoline derivatives. This method still has huge potential. Very recently, Wang [5] and Maiti et al. [6], reported one-pot synthesis of 3-arylbenzo[f]quinoline-1,2-dicarboxylate derivatives via an imino Diels-Alder reaction catalyzed by  $Yb(OTf)_3$  or SbCl<sub>3</sub>. As far as we are aware, there is no report of the use of SnCl<sub>2</sub>, a nontoxic and inexpensive catalyst, for synthesis of 3-arylbenzo[f]quinoline-1,2dicarboxylate derivatives. Our recent success in effective use of this catalyst for three-component coupling of aromatic aldehydes, 1-naphthylamine, and 5,5dimethylcyclohexane-1,3-dione and our continuing efforts in the synthesis of bioactive heterocyclic compounds [32] encouraged us to study three-component reaction of naphthylamines, aromatic aldehydes, and dialkyl acetylene dicarboxylates. A crucial aspect of this study was discovery of an efficient synthetic route to 3-arylbenzo[f]quinoline-1,2-dicarboxylate derivatives via an imino Diels-Alder reaction; we also found that SnCl<sub>2</sub> has highly catalytic activity in imino Diels–Alder reactions, with the advantages of low price and ready availability. In the work discussed in this report, we investigated reaction temperature, reaction time, different solvents, and the scope of this reaction with different aromatic aldehydes, aromatic amines, and dimethyl but-2-ynedioate.

We report a facile method of preparation of 3-arylbenzo[f]quinolone-1,2-dicarboxylate derivatives in the presence of SnCl<sub>2</sub> as an efficient catalyst in acetonitrile under reflux (Scheme 1).

#### **Results and discussion**

In the first set of experiments we investigated heating of 2-naphthylamine (1a, 1 mmol), 4-chlorobenzaldehyde (2, 1 mmol), and dimethyl but-2-ynedioate (3, 1.2 mmol) under reflux in a variety of solvents and with different catalysts as model reaction (Table 1). In the absence of catalyst only a trace of the expected product, 3-arylbenzo[f]quinolone-1,2-dicarboxylate (4), was obtained after 24 h (Table 1, entry 1). Obviously, the catalyst was an essential component of the reaction. Use of

CHO

COOCH<sub>2</sub>

	+ $+$ $+$ $+$ $+$ $+$ $+$ $+$ $+$ $+$	Catalyst MeCN reflux N OOCH <sub>3</sub> 3		CI
Entry	Catalyst/%	Solvent	Time (h)	Yield (%) <sup>a</sup>
1	_	MeCN	24	Trace
2	NH <sub>2</sub> SO <sub>3</sub> H/10	MeCN	24	Trace
3	ZnCl <sub>2</sub> /10	MeCN	24	Trace
4	SnCl <sub>2</sub> /10	MeCN	24	87
5	SnCl <sub>2</sub> /10	MeCN	8	55
6	SnCl <sub>2</sub> /10	MeCN	16	65
7	SnCl <sub>2</sub> /10	MeCN	32	88
8	SnCl <sub>2</sub> /10	Toluene	24	Trace
9	SnCl <sub>2</sub> /10	DMF	24	62
10	SnCl <sub>2</sub> /10	THF	24	59
11	SnCl <sub>2</sub> /1	MeCN	24	Trace
12	SnCl <sub>2</sub> /5	MeCN	24	64
13	SnCl <sub>2</sub> /15	MeCN	24	72
14	SnCl <sub>2</sub> /20	MeCN	24	69

Table 1 Optimization of the reaction conditions

Reaction conditions: 10 mL MeCN, 1.0 mmol 4-chlorobenzaldehyde, 1.0 mmol 2-naphthylamine, 1.1 mmol dimethyl but-2-ynedioate, and 0.1 mmol SnCl<sub>2</sub>

<sup>a</sup> Isolated yields

ZnCl<sub>2</sub> or NH<sub>2</sub>SO<sub>3</sub>H as catalyst also led to negative results (Table 1, entries 2, 3). We found SnCl<sub>2</sub> was an effective catalyst for the imino Diels-Alder reaction (Table 1, entry 4). These findings demonstrated SnCl<sub>2</sub> was important in the Diels-Alder reaction. A catalytic amount (0.1 equiv) of SnCl<sub>2</sub> was therefore used for synthesis of the 3-arylbenzo[f]quinolone-1,2-dicarboxylate derivatives. Reaction under reflux for 8, 16, 24, and 32 h gave 4 in 55, 65, 87, and 88 % yield, respectively (Table 1, entries 4–7), clearly showing that 24 h was the optimum reaction time. When different solvents (MeCN, THF, DMF, and toluene) were investigated (Table 1, entries 4, 8–10) it was found that MeCN was the best reaction medium, providing 3-arylbenzo[f]quinolone-1,2-dicarboxylate in 87 % yield (Table 1, entry 4); the nonpolar solvent toluene failed to afford the desired product (Table 1, entry 8). To determine the optimum amount of catalyst, the one-pot reaction was conducted with different amounts of  $SnCl_2$  (Table 1, entries 4, 11–14). Reaction with 10 mol% SnCl<sub>2</sub> as catalyst resulted in a good yield.

Encouraged by these results, we investigated the scope of the method by reaction of different aromatic aldehydes, 2-naphthylamine, and dimethyl but-2-ynedioate under the aforementioned optimized reaction conditions; the results are listed in

ĺ	NH +	$\begin{array}{c} CHO & CC \\ 12 \\ \hline R \\ 2a-k \end{array} + \begin{array}{c} \\ \\ CC $	$\begin{array}{c} \text{OOCH}_{3} \\ \hline \\ \underline{\text{SnCl}_{2} \ 10r} \\ \hline \\ \overline{\text{MeCN ref}} \\ \\ \text{OOCH}_{3} \\ \end{array}$	nmol Tux N <sub>2</sub>	COOCH <sub>3</sub> COO N 4a-k	R
Entry	R	Product 4	Time (h)	Yield (%) <sup>a</sup>	m.p. (°C)	
					Found	Reported
1	4-Chloro	4a	24	87	173–174	175–176 [5]
2	3-Chloro	4b	24	83	142-143	143–144 [5]
3	2,4-Dichloro	4c	24	80	210-212	209-210 [5]
4	2-Chloro	4d	24	73	171-173	_
5	4-Fluoro	4e	24	70	163-165	165–167 [ <mark>5</mark> ]
6	2-Bromo	4f	24	79	159-160	_
7	3-Nitro	4g	24	70	143-145	142–143 [ <mark>6</mark> ]
8	4-Nitro	4h	24	61	160-161	162 [ <mark>6</mark> ]
9	2-Methoxy	4i	24	82	181-182	_
10	4-Methoxy	4j	24	60	128-130	128–129 [6]
11	4-Hydroxy	4k	24	64	183–185	-

Table 2  $SnCl_2$ -catalyzed reaction of aromatic aldehydes, 2-naphthylamine. and dimethyl but-2-yne-dioate

Reaction conditions: 10 mL MeCN, 1.0 mmol aromatic aldehyde, 1.0 mmol 2-naphthylamine, 1.1 mmol dimethyl but-2-ynedioate, and 0.1 mmol  $\rm SnCl_2$ 

<sup>a</sup> Isolated yields

Table 2 (entries 1–11). It was apparent our procedure provided an opportunity for further chemical elaboration for synthesis of a variety of 3-arylbenzo[*f*]quinolone-1,2-dicarboxylate derivatives. A variety of aromatic aldehydes containing electron-donating and-electron withdrawing substituents reacted with 2-naphthylamine in good yields (Table 2, entries 1–11). The scope was then extended to reaction of aromatic aldehydes with 1-naphthylamine but the yield of the corresponding 3-arylbenzo[*f*]quinolone-1,2-dicarboxylate derivatives was moderate (Table 3, entries 1–3). Although transformation times and yields were different, the catalyst SnCl<sub>2</sub> was convincingly an essential component of the reaction.

According to the literature [5, 33], a probable mechanism for the synthesis of 3-arylbenzo[f]quinolone-1,2-dicarboxylate may be postulated as shown in Scheme 2. First, reaction may occur between the aromatic aldehyde and naphthalene-2-amine to form the Schiff base **a**. Imino Diels–Alder reaction between the SnCl<sub>2</sub>-activated Schiff base **b** and dimethyl but-2-ynedioate then occurs to form intermediate **c**, followed by isomerization to form 3,4-dihydrobenzo[f]quinolines, **d**, which will be further oxidized by air to afford the final aromatized 3-arylbenzo[f]quinoline-1,2-dicarboxylate, **4**.

	NH <sub>2</sub> +	$\begin{array}{c} CHO \\ \hline \\ $	$OCH_3$ $\frac{SnCl_2 10}{MeCN re}$ $OCH_3$	mmol flux N <sub>2</sub>		-R <sub>1</sub> H <sub>3</sub>
	1b	21-n	3	4m-o	COOCH <sub>3</sub>	
Entry	<i>R</i> 1	Product 4	Time	Yield (%) <sup>a</sup>	m.p. (°C)	
					Found	Reported
1	3-Nitro	41	20	73	143–145	146 [ <b>6</b> ]
2	4-Methyl	4m	22	75	163–164	164 [ <mark>6</mark> ]
3	4-Fluoro	4n	22	60	119-120	-

Table 3  $SnCl_2$ -catalyzed reaction of aromatic aldehydes, 1-naphthylamine, and dimethyl but-2-yne-dioate

Reaction condition: 10 mL MeCN, 1.0 mmol aromatic aldehyde, 1.0 mmol 1-naphthylamine, 1.1 mmol dimethyl but-2-ynedioate and 0.1 mmol  $SnCl_2$ 

<sup>a</sup> Isolated yields



Scheme 2 Possible mechanism for the reaction

## Experimental

All chemicals were commercially available and used as received. Reactions were monitored by TLC. All yields refer to isolated products. Melting points were measured on an X-4 digital microscopic melting-point apparatus and are uncorrected. <sup>1</sup>H NMR spectra were measured on a Bruker Avance 300 spectrometer with TMS as internal standard. Infrared spectra were recorded on a Thermo Scientific Nicolet 6700 FT-IR spectrometer using KBr optics. Elemental analysis was performed with a Perkin–Elmer auto-analyzer.

The structures of the new 3-arylbenzo[f]quinolone-1,2-dicarboxylate derivatives (4d, 4f, 4i, 4k, and 4n) were completely characterized on the basis of their IR and <sup>1</sup>H NMR spectra and by elemental analysis. Known compounds were identified by comparison of their melting points with values reported in the literature.

# General procedure for synthesis of 3-arylbenzo[*f*]quinolone-1,2-dicarboxylate derivatives

A mixture of 2-naphthylamine (1 mmol), aromatic aldehyde (1 mmol), and dimethyl but-2-ynedioate (1.2 mmol) was dissolved in MeCN (10 ml). The mixture was stirred at reflux in a 100-ml round-bottomed flask in the presence of SnCl<sub>2</sub> (1 mmol, 20 %) under an N<sub>2</sub> atmosphere at 80 °C. These results obtained are listed in Table 1. After completion of the reaction, as indicated by TLC, the MeCN was evaporated under reduced pressure, and water (20 ml) was added. The resulting solution was extracted with EtOAc (3 × 10 mL). The combined organic layers were dried over Na<sub>2</sub>SO<sub>4</sub> and concentrated. Products were purified by column chromatography on silica gel with ethyl acetate–petroleum (1:5 to 1:10) as eluent to afford the pure product.

Compound **4d**: Yellow solid; mp: 171–173 °C; IR (KBr): 2,935, 1,750, 1,721, 1,552, 1,436, 1,238, 1,136, 1,011, 952, 887, 835, 769, 738, 534 cm<sup>-1</sup>. <sup>1</sup>H NMR (400 MHz, CDCl3)  $\delta$  7.95 (d, J = 8.6 Hz, 1H), 7.58 (dd, J = 12.5, 8.4 Hz, 2H), 7.46 (dd, J = 7.2, 2.2 Hz, 1H), 7.41 (dd, J = 9.3, 6.3 Hz, 1H), 7.38–7.34 (m, 1H), 7.24–7.21 (m, 1H), 7.14 (pd, J = 7.4, 1.8 Hz, 2H), 6.74 (d, J = 8.8 Hz, 1H), 4.00 (s, 3H), 3.74 (s, 3H). Anal. Calcd for C<sub>23</sub>H<sub>16</sub>ClNO<sub>4</sub>: C 68.07, H 3.97, N 3.45; found: C 68.05, H 3.94, N 3.47.

Compound **4f**: Yellow solid; mp: 159–160 °C; IR (KBr): 2,955, 1,728, 1,555, 1,483, 1,439, 1,372, 1,242, 1,119, 1,076, 997, 832, 800, 747 cm<sup>-1</sup>. <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)  $\delta$  7.95 (d, J = 8.8 Hz, 1H), 7.65–7.51 (m, 3H), 7.49–7.45 (m, 1H), 7.41 (dd, J = 12.1, 3.4 Hz, 1H), 7.23 (d, J = 7.8 Hz, 1H), 7.18 (t, J = 8.1 Hz, 1H), 7.12–7.05 (m, 1H), 6.74 (d, J = 8.8 Hz, 1H), 4.00 (s, 3H), 3.74 (s, 3H). Anal. Calcd for C<sub>23</sub>H<sub>16</sub>BrNO<sub>4</sub>: C 61.35, H 3.58, N 3.11; found: C 61.36, H 3.59, N 3.14.

Compound **4i**: White solid; mp: 181–182 °C; IR (KBr): 2,955, 1,738, 1,718, 1,702, 1,599, 1,546, 1,430, 1,237, 1,119, 1,064, 1,026, 1,011, 833, 812, 737 cm<sup>-1</sup>. <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)  $\delta$  8.37–8.27 (m, 1H), 8.06 (s, 2H), 8.01–7.91 (m, 1H), 7.67 (pd, J = 7.1, 1.4 Hz, 2H), 7.58 (dd, J = 7.5, 1.7 Hz, 1H), 7.46–7.39 (m, 1H), 7.13 (t, J = 7.5 Hz, 1H), 6.95 (d, J = 8.3 Hz, 1H), 4.10 (s, 3H), 3.75 (s, 3H), 3.68 (s, 3H). Anal. Calcd for C<sub>24</sub>H<sub>19</sub>NO<sub>5</sub>: C 71.81, H 4.77, N 3.49; found: C 71.80, H 4.74, N 3.53.

Compound **4k**: White solid; mp: 183–185 °C; IR (KBr): 3,610, 2,945, 1,750, 1,721, 1,552, 1,436, 1,238, 1,136, 1,011, 952, 887, 835, 769, 738, 534 cm<sup>-1</sup>. <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)  $\delta$  8.36–8.29 (m, 1H), 8.09 (dd, J = 19.8, 9.0 Hz, 2H), 8.00–7.94 (m, 1H), 7.67 (tt, J = 8.7, 3.7 Hz, 2H), 7.59 (dd, J = 7.5, 1.6 Hz, 1H), 7.48–7.39 (m, 1H), 7.14 (t, J = 7.5 Hz, 1H), 6.95 (d, J = 8.1 Hz, 1H), 4.11 (s, 3H), 3.68 (s, 3H). Anal. Calcd for C<sub>23</sub>H<sub>17</sub>NO<sub>5</sub>: C 71.31, H 4.42, N 3.62; found: C 71.33, H 4.41, N 3.64.

Compound **4n**: Yellow solid; mp: 119–120 °C; IR (KBr): 2,953, 1,752, 1,557, 1,526, 1,430, 1,332, 1,232, 1,128, 996, 831, 747, 732, 694, 687 cm<sup>-1</sup>. <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)  $\delta$  7.94 (d, J = 8.9 Hz, 1H), 7.72 (d, J = 8.2 Hz, 1H), 7.67 (d, J = 8.0 Hz, 1H), 7.50 (dd, J = 9.0, 4.6 Hz, 1H), 7.39 (ddd, J = 11.8, 10.1, 7.0 Hz, 2H), 7.23–7.19 (m, 1H), 7.14 (d, J = 8.6 Hz, 1H), 7.07 (d, J = 8.6 Hz, 1H), 6.92 (t, J = 7.8 Hz, 1H), 4.08 (s, 2H), 3.77 (s, 3H). Anal. Calcd for C<sub>23</sub>H<sub>16</sub>FNO<sub>4</sub>: C 70.95, H 4.14, N 3.60; found: C 70.94, H 4.16, N 3.61.

### Conclusions

In conclusion, we report a one-pot, three-component reaction for synthesis of 3-arylbenzo[f]quinolone-1,2-dicarboxylate derivatives by imino Diels–Alder reaction of aromatic aldehydes, 2-naphthylamine, and dimethyl but-2-ynedioate in MeCN using 10 mol% SnCl<sub>2</sub> as catalyst. Compared with reactions reported in the literature, the main advantages of this procedure are milder conditions, economical steps, and inexpensive catalyst.

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