Yb(OTf)₃: an efficient catalyst for the synthesis of 3-arylbenzo [*f*]quinoline-1,2-dicarboxylate derivatives via imino-Diels–Alder reaction

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ABSTRACT

A mild and facile method for the synthesis of 3-arylbenzo[*f*]quinoline-1,2-dicarboxylate derivatives is reported by an imino-Diels–Alder reaction in high yields (76–92%). This procedure includes a novel three-component reaction of aromatic aldehyde, naphthalen-2-amine, and but-2-ynedioate catalyzed by Yb(OTf)₃ in toluene. The results are obviously different from those of the simple substituted aniline-involved reactions catalyzed by ZnCl₂ or KOH in the literature.

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Multi-component reactions (MCRs) play an important role in modern synthetic organic chemistry since they generally occur in a single pot and exhibit a high atom–economy and selectivity. They also deliver fewer byproducts compared to the classical stepwise synthetic routes. In addition, for multi-component reactions involving the simultaneous molecular interaction of three or more components, they always gave diverse compounds as well as small and drug-like heterocycles through controlling of different reaction parameters such as temperature, pressure, solvent, and catalyst type.[1]

The synthesis of benzoquinoline derivatives has been the focus of great interest, because it was reported that its derivatives possess a broad spectrum of biological properties, such as antibacterial activity,[2] UDP (Uridine diphosphate)-glucuronosyl transferase activity,[3] antimicrobial activity,[4] antimalarial activity,[5] agonistic activity,[6] and antipsychotic activity.[7] Accordingly, novel strategies for the synthesis of benzoquinolines continue to receive considerable attention in the field of synthetic organic chemistry in recent years,[8] and among which imino-Diels–Alder reaction provides an easy access to the preparation of quinoline or benzoquinoline derivatives. The imines derived from aromatic amines act as heterodienes and undergo imino-Diels–Alder reaction with various dienophiles in the presence of acid catalysts.[9] The known reported dienophiles included enol from aldehyde or ketone,[9a–d] 2,3-dihydrofuran or 3,4-dihydro-2*H*-pyran,[9e–j] vinyl ether,[9l–n] and 1-vinylpyrrolidin-2-one.[9n–r] In view of the importance of the benzoquinoline and its

derivatives, searching for other dienophiles to construct novel benzoquinoline moieties is of increasing interest.

As a part of our ongoing program to synthesize benzoquinoline derivatives via imino-Diels–Alder reaction using various dienophiles,[10] in this Letter, we would like to report the synthesis of 3-arylbenzo[*f*]quinoline-1,2-dicarboxylate derivatives using but-2-ynedioate as dienophile via a one-pot imino-Diels–Alder reaction catalyzed by Yb(OTf)₃. Because over the past few years, Yb(OTf)₃ has emerged as a powerful catalyst for various organic transformations to afford the products in good to excellent yields. Owing to several advantages such as inexpensive, nontoxic, and eco-friendly nature, Yb(OTf)₃ has been used as a catalyst in the investigation of different organic reactions.[11]

Treatment of aromatic aldehyde 1, naphthalen-2-amine 2, and but-2-ynedioate 3 in toluene in the presence of 1 mol % Yb(OTf)₃ at 80 °C resulted in the corresponding 3-arylbenzo[*f*] quinoline-1,2-dicarboxylate derivatives 4a–o in high yields (Scheme 1). Obviously, this structure 4 was different from that of the simple substituted aniline-involved reactions reported by Zhang and Jiang[12] in 2008, which was carried out in refluxing toluene catalyzed by ZnCl₂, and in CH₃CN in the presence of KOH reported by the same team[13] in 2007, respectively.
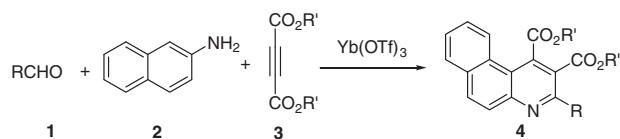
Scheme 1.

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Table 1
Synthesis of **4a** at different reaction conditions[a]

Entry	T (°C)	Solvent	Cat. (mol %)	Yield[b] (%)
1	80	Toluene	I_2/1	56
2	80	Toluene	Yb(OTf)$_3$/1	86
3	80	Toluene	Yb(OTf)$_3$/5	84
4	80	Toluene	Yb(OTf)$_3$/10	86
5	rt	Toluene	Yb(OTf)$_3$/1	Trace
6	50	Toluene	Yb(OTf)$_3$/1	65
7	110	Toluene	Yb(OTf)$_3$/1	85
8	80	Toluene	AgOTf/1	52
9	80	Toluene	Cu(OTf)$_2$/1	48
10	80	Toluene	Zn(OTf)$_2$/1	50
11	80	Toluene	Ca(OTf)$_2$/1	46
12	80	Toluene	Fe(OTf)$_2$/1	38
13	65	THF	Yb(OTf)$_3$/1	69
14	80	Benzene	Yb(OTf)$_3$/1	72
15	80	DMF	Yb(OTf)$_3$/1	70

[a] Reaction condition: 10 mL solvent, 2 mmol 4-fluorobenzaldehyde, 2 mmol naphthalen-2-amine, 2.1 mmol diethyl but-2-ynedioate.
[b] Isolated yields.

In our initial study, dimethyl but-2-ynedioate was applied to this imino-Diels–Alder reaction as dienophile to react with 4-fluorobenzaldehyde and naphthalen-2-amine catalyzed by iodine, with expected 3-arylbenzo[*f*]quinoline-1,2-dicarboxylate derivatives being obtained in lower yield (**4a** in 56% yield, Table 1, entry 1). In order to further enhance the rate of conversion, screening higher efficient Lewis acid catalyst is carried out in our lab; finally Yb(OTf)$_3$ (**4a** in 86% yield, Table 1, entry 2) was selected as an efficient catalyst. Subsequently, the above reaction was used as a model reaction to optimize the conditions. A summary of the optimization experiment was provided in Table 1. The results showed that at room temperature, trace amount of products was observed by TLC (Table 1, entry 1). To our delight, at 80 °C the reaction proceeded smoothly in high yield. Similar reactions were then carried out in the presence of 1%, 5%, and 10 mol % of Yb(OTf)$_3$. The results from Table 1 (entries 3–5) showed that 1 mol % of Yb(OTf)$_3$ at 80 °C is enough to give a high yield (86%). Higher loading of the catalyst did not improve the reaction condition to a great extent. Thus, the optimal reaction temperature and catalyst amount are 80 °C and 1 mol % Yb(OTf)$_3$, respectively. Moreover, different solvents and various trifuloromethanesulfonates were further investigated as shown in Table 1,
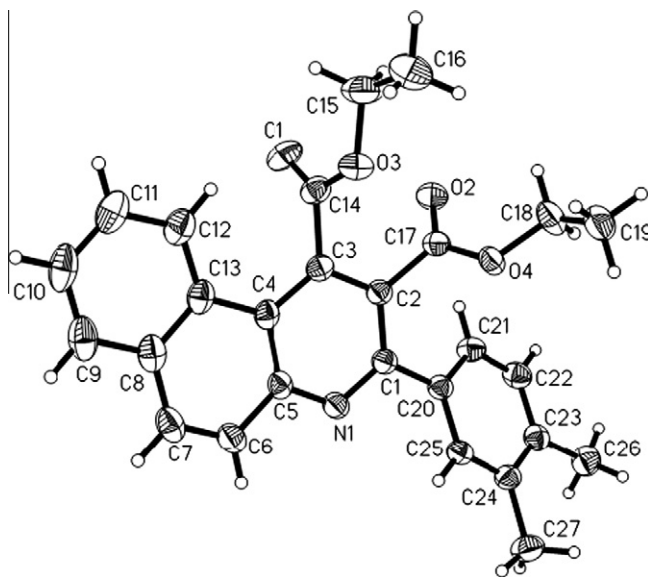
Table 2
Yb(OTf)$_3$ catalyzed reactions of aromatic aldehyde, naphthalen-2-amine and but-2-ynedioate[a],[15]

Products	R	R′	Time (h)	Yields[b] (%)
4a	4-FC$_6$H$_4$	Me	8	86
4b	4-ClC$_6$H$_4$	Me	9	84
4c	3-ClC$_6$H$_4$	Me	9	78
4d	4-CH$_3$C$_6$H$_4$	Me	12	89
4e	2,4-Cl$_2$C$_6$H$_3$	Me	8	92
4f	3,4-Cl$_2$C$_6$H$_3$	Me	8	86
4g	2-Thienyl	Me	10	79
4h	3-FC$_6$H$_4$	Et	12	78
4i	4-BrC$_6$H$_4$	Et	13	82
4j	4-CH$_3$OC$_6$H$_4$	Et	14	84
4k	4-NO$_2$C$_6$H$_4$	Et	8	87
4l	2,4-Cl$_2$C$_6$H$_3$	Et	9	76
4m	3,4-OCH$_2$OC$_6$H$_3$	Et	12	85
4n	3,4-Me$_2$C$_6$H$_3$	Et	12	85
4o	2-Thienyl	Et	13	77
4p	PhCH$_2$	Me	15	0[c]

[a] Reaction condition: 10 mL toluene, 2.0 mmol aromatic aldehyde, 2.0 mmol naphthalen-2-amine, 2.1 mmol but-2-ynedioate and 0.02 mmol Yb(OTf)$_3$.
[b] Isolated yields.
[c] The expected products were not found using other aliphatic aldehydes, such as propionaldehyde, *n*-butyl aldehyde, and *n*-heptaldehyde.

Figure 1. The crystal structure of the product **4n**.

we can conclude that the Yb(OTf)$_3$/toluene was the best system for this reaction.

In order to extend the above reaction (Scheme 1) to a library system, various kinds of arylaldehydes **1** (Table 2) were subjected to react with **2** and **3** to give the corresponding 3-arylbenzo[*f*]quinoline-1,2-dicarboxylate **4**, and representative examples are shown in Table 2. All of **1** gave the expected products at high yields, either bearing electron-withdrawing groups (such as halide, nitro) or electron-donating groups (such as alkyl group, or alkoxyl group) under the same reaction condition. To further demonstrate the scope and limitation of the substrates, aliphatic aldehydes, such as phenylacetaldehyde, propionaldehyde, *n*-butyl aldehyde, and *n*-heptaldehyde, were used as reactants to react with naphthalen-2-amine and dimethyl but-2-ynedioate. However, the desired products were neither found nor obtained successfully. All of the structures were characterized by ^{1}H NMR, IR, and HRMS. The structure of the product **4n** was additionally confirmed by an X-ray diffraction analysis,[14] and its crystal structure was shown in Figure 1.

According to the literatures,[16] we think that Yb(OTf)$_3$ catalyzes the reaction as a mild Lewis acid. The mechanism was tentatively proposed in Scheme 2. The Schiff base **I** may be formed by the reaction of aromatic aldehyde and naphthalene-2-amine firstly. And then imino-Diels–Alder reaction between the Yb(OTf)$_3$-activated Schiff base **II** and but-2-ynedioate takes place to form intermediate **III**, followed by isomerization to give 3,4-dihydrobenzo[*f*]quinolines **IV**, which is further oxidized by air to afford the final aromatized 3-arylbenzo[*f*]quinoline-1,2-dicarboxylate **4**.
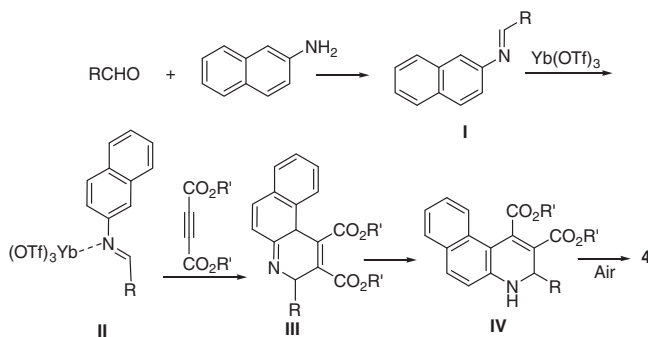
Scheme 2.

In conclusion, we have discovered an effective method for the syntheses of 3-arylbenzo[*f*]quinoline-1,2-dicarboxylate derivatives by an imino-Diels–Alder reaction of aromatic aldehyde, naphthalen-2-amine, and but-2-ynedioate in toluene using 1 mol % Yb(OTf)$_3$ as catalyst. The note-worthy features of this procedure are mild reaction conditions, economical steps, high yields, and operational simplicity.

Acknowledgments

Supplementary data

Supplementary data associated with this article can be found, in the online version, at doi:10.1016/j.tetlet.2010.08.074.

References and notes

1. (a) Vijjay, N. C.; Rajesh, A. U.; Vinod, S.; Bindu, A. R.; Sreekanth, J. S.; Lakshmi, B. *Acc. Chem. Res.* **2003**, *36*, 899–907; (b) Tietze, L. F. *Chem. Rev.* **1996**, *96*, 115–136; (c) Nicolaou, K. C.; Edmonds, D. J.; Bulger, P. G. *Angew. Chem., Int. Ed.* **2006**, *45*, 7134–7186; (d) Weber, L.; Illgen, K.; Almstetter, M. *Synlett* **1999**, 366–374; (e) Wang, Z.; Zhou, L.; El-Boubbou, K.; Ye, X.-S.; Huang, X. *J. Org. Chem.* **2007**, *72*, 6409–6420; (f) Liéby-Muller, F.; Constantieux, T.; Jean Rodriguez, J. *J. Am. Chem. Soc.* **2005**, *127*, 17176–17177; (g) Sunderhaus, J. D.; Dockendorff, C.; Martin, S. F. *Org. Lett.* **2007**, *9*, 4223–4226.

2. (a) Selvi, G.; Rajendran, S. P. *J. Asian Chem. Res.* **2004**, *16*, 1017–1022; (b) Bahuguna, R. P.; Joshi, B. C. *Indian J. Heterocycl. Chem.* **1994**, *3*, 265–268.

3. (a) Carr, B. A.; Franklin, M. R. *Xenobiotica* **1998**, *28*, 949–956; (b) Le, H. T.; Lamb, J. G.; Franklin, M. R. *J. Biochem. Toxicol.* **1996**, *11*, 297–303.

4. Bahuguna, R. P.; Joshi, B. C.; Mangal, H. N. *J. Indian Chem. Soc.* **1992**, *69*, 401–402.

5. Mikhailitsyn, F. S.; Kozyreva, N. P.; Rabinovich, S. A.; Maksakovskaya, Y. V.; Kulikovskaya, I. M.; Dadasheva, N. R.; Lebedeva, M. N.; Bekhli, A. F.; Lychko, N. D.; Uvarova, N. A. *Med. Parazitol. Parazit. Bolezni.* **1992**, 50–53. ; *Chem. Abstr.* **1992**, *117*, 251317.

6. Nozulak, J.; Vigouret, J. M.; Jaton, A. L.; Hofmann, A.; Dravid, A. R.; Weber, H. P.; Kalkman, H. O.; Walkinshaw, M. D. *J. Med. Chem.* **1992**, *35*, 480–489.

7. Szmuszkovicz, J.; Darlington, W. H.; Von Voigtlander, P. F. 1988, WO 8804292 A1. *Chem. Abstr.* **1988**, *110*, 75335.

8. (a) Lo, K. K.-W.; Zhang, K. Y.; Chung, C.-K.; Kwok, K. Y. *Chem. Eur. J.* **2007**, *13*, 7110–7120; (b) Pratap, R.; Ram, V. J. *Tetrahedron Lett.* **2007**, *48*, 2755–2759; (c) Kadutskii, A. P.; Kozlov, N. G. *Russ. J. Org. Chem.* **2006**, *42*, 855–859; (d) Gusak, K. N.; Kozlov, N. G. *Russ. J. Org. Chem.* **2007**, *43*, 706–718; (e) Kozlov, N. G.; Gusak, K. N. *Russ. J. Org. Chem.* **2007**, *43*, 241–248; (f) Bhargava, G.; Mohan, C.; Mahajan, M. P. *Tetrahedron* **2008**, *64*, 3017–3024; (g) Jachak, M. N.; Kendre, D. B.; Avhale, A. B.; Toche, R. B.; Sabnis, R. W. *J. Heterocycl. Chem.* **2007**, *44*, 1525–1528; (h) Okada, E.; Shibata, D.; Tsukushi, N.; Dohura, M.; Medebielle, M. *Heterocycles* **2009**, *79*, 395–401; (r) Kise, N.; Isemoto, S.; Sakurai, T. *Org. Lett.* **2009**, *11*, 4902–4905; (i) Wang, X.-S.; Zhang, M.-M.; Li, Q.; Yao, C.-S.; Tu, S.-J. *Synlett* **2007**, 3141–3144; (j) Rong, L.; Han, H.; Jiang, H.; Tu, S. *J. Heterocycl. Chem.* **2009**, *46*, 465–468; (k) Kadutskii, A. P.; Kozlov, N. G.; Pashkovskii, F. S. *Russ. J. Org. Chem.* **2009**, *45*, 399–403; (l) Kozlov, N. G.; Lysenko, G. N.; Ogorodnikova, M. M.; Gusak, K. N. *Russ. J. Org. Chem.* **2009**, *45*, 434–437; (m) Kozlov, N. G.; Gusak, K. N. *Russ. J. Org. Chem.* **2008**, *44*, 1049–1053; (n) Mamane, V.; Louerat, F.; Iehl, J.; Abboud, M.; Fort, Y. *Tetrahedron* **2008**, *64*, 10699–10705; (o) Atta, A. H.; Abd El-Gawad, I. I.; El-Tamany, E. H.; Mohammed, N. M. *Orient. J. Chem.* **2008**, *24*, 801–806.

9. (a) Wang, X.-S.; Li, Q.; Zhang, M.-M.; Yao, C.-S.; Tu, S.-J. *J. Heterocycl. Chem.* **2008**, *45*, 1027–1031; (b) Kozlov, N. G.; Gusak, K. N.; Skatetskii, V. V. *Russ. J. Org. Chem.* **2006**, *42*, 112–117; (c) Lin, X. F.; Cui, S. L.; Wang, Y. G. *Tetrahedron Lett.* **2006**, *47*, 3127–3130; (d) Wang, X.-S.; Li, Q.; Wu, J.-R.; Li, Y.-L. *Synth. Commun.* **2009**, *39*, 702–715; (e) Lin, X. F.; Cui, S. L.; Wang, Y. G. *Tetrahedron Lett.* **2006**, *47*, 4509–4512; (f) Xia, M.; Lu, Y.-D. *Synlett* **2005**, 2357–2361; (g) Li, Y.-C.; Zhang, J.-M.; Dong, L.-T.; Yan, M. *Chin. J. Chem.* **2006**, *24*, 929–932; (h) Ma, Y.; Qian, C.; Xie, M.; Sun, J. *J. Org. Chem.* **1999**, *64*, 6462–6467; (i) Nagaiah, K.; Sreenu, D.; Srinivasa Rao, R.; Vashishta, G.; Yadav, J. S. *Tetrahedron Lett.* **2006**,

47, 4409–4413; (j) Kobayashi, S.; Araki, M.; Ishitani, H.; Nagayama, S.; Hachiya, I. *Synlett* **1995**, 233–234; (k) Kobayashi, S.; Ishitani, H.; Nagayama, S. *Synthesis* **1995**, 1195–1201; (l) Sridharan, V.; Avendaño, C.; Menéndez, J. C. *Tetrahedron* **2009**, *65*, 2087–2096; (m) Sridharan, V.; Avendaño, C.; Menéndez, J. C. *Synthesis* **2008**, 1039–1044; (n) Legros, J.; Crousse, B.; Ourévitch, M.; Bonnet-Delpon, D. *Synlett* **2006**, 1899–1902; (o) Astudillo, L. S.; Gutiérrez, C. M.; Gaete, H.; Kouznetsov, V. V.; Meléndez, C. M.; Palenzuela, J. A.; Vallejos, G. G. *Lett. Org. Chem.* **2009**, *6*, 208–212; (p) Srinivasa, A.; Mahadevan, K. M.; Hulikal, V. *Synth. Commun.* **2009**, *39*, 93–101; (q) Meléndez Gómez, C. M.; Kouznetsov, V. V.; Sortino, M. A.; Álvarez, S. L.; Zacchino, S. A. *Bioorg. Med. Chem.* **2008**, *16*, 7908–7920; (r) Kouznetsov, V. V.; Cruz, U. M.; Zubkov, F. I.; Nikitina, E. V. *Synthesis* **2007**, 375–384; (s) Savitha, G.; Perumal, P. T. *Tetrahedron Lett.* **2006**, *47*, 3589–3593.

10. (a) Wang, X. S.; Li, Q.; Wu, J. R.; Li, Y. L.; Yao, C. S.; Tu, S. J. *Synthesis* **2008**, 1902–1910; (b) Wang, X. S.; Li, Q.; Yao, C. S.; Tu, S. J. *Eur. J. Org. Chem.* **2008**, 3513–3518; (c) Wang, X. S.; Li, Q.; Yao, C. S.; Tu, S. J. *J. Comb. Chem.* **2009**, *11*, 433–437; (d) Wang, X. S.; Zhou, J.; Yin, M. Y.; Yang, K.; Tu, S. J. *J. Comb. Chem.* **2010**, *12*, 266–269.

11. (a) Vidadala, S. R.; Thadke, S. A.; Hotha, S. *J. Org. Chem.* **2009**, *74*, 9233–9236; (b) Hong, D.; Yang, Y.-Y.; Wang, Y.-G.; Lin, X.-F. *Synlett* **2009**, 1107–1110; (c) Rao, W.; Zhang, X.; Sze, E. M. L.; Chan, P. W. H. *J. Org. Chem.* **2009**, *74*, 1740–1743; (d) Genovese, S.; Epifano, F.; Pelucchini, C.; Curini, M. *Eur. J. Org. Chem.* **2009**, 1132–1135; (e) Ding, Q.; Wang, Z.; Wu, J. *Tetrahedron Lett.* **2009**, *50*, 198–200; (f) Huang, W.; Shen, Q.-S.; Wang, J.-L.; Zhou, X.-G. *Chin. J. Chem.* **2008**, *26*, 729–735; (g) Mihara, H.; Xu, Y.; Shepherd, N. E.; Matsunaga, S.; Shibasaki, M. *J. Am. Chem. Soc.* **2009**, *131*, 8384–8385; (h) Su, W.; Yang, D.; Jin, C.; Zhang, B. *Tetrahedron Lett.* **2008**, *49*, 3391–3394; (i) Liu, L.-P.; Shi, M. *Tetrahedron* **2007**, *63*, 4535–4542; (j) Su, W.-K.; Hong, Z.; Shan, W.-G.; Zhang, X.-X. *Eur. J. Org. Chem.* **2006**, 2723–2726; (k) Cheng, K.; Lin, L.; Chen, S.; Feng, X. *Tetrahedron* **2005**, *61*, 9594–9599; (l) Wang, L.; Sheng, J.; Tian, H.; Han, J.; Fan, Z.; Qian, C. *Synthesis* **2004**, 3060–3064; (m) Lebold, T. P.; Kerr, M. A. *Org. Lett.* **2009**, *11*, 4354–4357.

12. Zhang, M.; Jiang, H. F. *Eur. J. Org. Chem.* **2008**, 3519–3523.

13. Zhang, M.; Jiang, H. F.; Wang, A. Z. *Synlett* **2007**, 3214–3218.

14. *Crystal data for* **4n**: $C_{27}H_{25}NO_4$; $M = 427.48$, colorless block crystals, $0.46 \times 0.16 \times 0.12$ mm, Triclinic, space group $P\bar{1}$, $a = 7.6114(2)$, $b = 10.7371(3)$, $c = 14.9116(5)$ Å, $\alpha = 101.774(2)$, $\beta = 96.265(2)$, $\gamma = 109.891(2)°$, $V = 1100.52(6)^3$, $Z = 2$, $D_c = 1.290$ g cm^{-3}. $F(0\,0\,0) = 452$, $\mu(MoK\alpha) = 0.086$ mm^{-1}. Intensity data were collected on Rigaku Mercury diffractometer with graphite monochromated MoKα radiation ($\lambda = 0.71073$ Å) using *phi* and *omega* scan mode with $2.84° < \theta < 25.20°$. Unique reflections (3937) were measured and 3154 reflections with $I > 2\sigma(I)$ were used in the refinement. The structure was solved by direct methods and expanded using Fourier techniques. The final cycle of full-matrix least squares technique to $R = 0.0400$ and $wR = 0.0501$.

15. *General procedure for the syntheses of* 3-arylbenzo[*f*]quinoline-1,2-dicarboxylate *derivatives* **4a–o**: A dry 50 mL flask was charged with aromatic aldehyde (2.0 mmol), naphthalen-2-amine (0.286 g, 2.0 mmol), but-2-ynedioate (2.1 mmol), Yb(OTf)$_3$ (0.012 g, 0.02 mmol), and toluene (10 mL). The reaction mixture was stirred at 80 °C for 8–14 h. After completion of the reaction as indicated by TLC, another portion of toluene was added to the mixture until all the yellow solid was dissolved when the mixture was cooled to room temperature. The organic layer was washed with water, and then dried over anhydrous MgSO$_4$. The toluene was recovered by reduced pressure, and the crude products were purified by recrystallization from 95% EtOH to give **4**. Selected data: dimethyl 3-(4-fluorophenyl)benzo[*f*]quinoline-1,2-dicarboxylate **4a**: mp: 165–167 °C. ^{1}H NMR (DMSO-d_6, 400 MHz): δ_H 3.74 (s, 3H, CH$_3$), 4.08 (s, 3H, CH$_3$), 7.40 (t, $J = 8.4$ Hz, 2H, ArH), 7.69–7.73 (m, 2H, ArH), 7.81–7.84 (m, 2H, ArH), 8.04 (d, $J = 9.2$ Hz, 1H, ArH), 8.18–8.21 (m, 2H, ArH), 8.33 (d, $J = 9.2$ Hz, 1H, ArH). ^{13}C NMR (CDCl$_3$, 100 MHz): δ_C 169.5, 168.1, 164.7, 162.2, 154.8, 149.7, 138.5, 135.7, 135.6, 133.7, 132.9, 130.6, 130.5, 129.4, 128.2, 128.0, 127.5, 125.3, 124.1, 119.5, 115.7, 115.5, 53.4, 52.9. IR (KBr, ν, cm^{-1}): 2957, 1750, 1722, 1601, 1549, 1509, 1439, 1450, 1386, 1328, 1311, 1272, 1240, 1222, 1209, 1198, 1182, 1169, 1158, 1126, 1116, 1064, 1003, 840, 821, 809, 763. Diethyl 3-(3,4-dimethylphenyl)benzo[*f*]quinoline-1,2-dicarboxylate **4n**: mp: 153–155 °C. ^{1}H NMR (DMSO-d_6, 400 MHz): δ_H 1.09 (t, $J = 7.2$ Hz, 3H, CH$_3$), 1.35 (t, $J = 7.2$ Hz, 3H, CH$_3$), 2.32 (s, 6H, 2CH$_3$), 4.19 (q, $J = 7.2$ Hz, 2H, CH$_2$), 4.55 (q, $J = 7.2$ Hz, 2H, CH$_2$), 7.30 (d, $J = 7.6$ Hz, 1H, ArH), 7.37 (d, $J = 1.6$ Hz, 1H, ArH), 7.45 (s, 1H, ArH), 7.79–7.83 (m, 2H, ArH), 8.04 (d, $J = 8.8$ Hz, 1H, ArH),*v* 8.18 (dd, $J = 6.0$ Hz, $J' = 3.2$ Hz, 1H, ArH), 8.27 (dd, $J = 6.0$ Hz, $J' = 3.2$ Hz, 1H, ArH), 8.31 (d, $J = 9.2$ Hz, 1H, ArH). ^{13}C NMR (CDCl$_3$, 100 MHz): δ_C 169.2, 167.9, 156.3, 149.6, 138.4, 137.3, 136.7, 133.1, 132.8, 129.8, 129.6, 129.2, 128.3, 127.7, 127.1, 126.0, 125.5, 124.6, 119.2, 77.3, 77.0, 76.7, 62.7, 62.0, 19.8, 19.6, 13.8, 13.6. IR (KBr, ν, cm^{-1}): 2977, 2939, 2920, 2902, 1739, 1717, 1608, 1504, 1476, 1450, 1411, 1384, 1371, 1348, 1325, 1308, 1294, 1269, 1238, 1201, 1181, 1148, 1139, 1107, 1066, 1023, 999, 859, 749. HRMS (ESI, *m/z*): calcd for $C_{27}H_{25}NO_4$, (M+H$^+$) 428.1862, found: 428.1889.

16. Kudale, A. A.; Kendall, J. K.; Miller, D. O.; Collins, J. L.; Bodwell, G. J. *J. Org. Chem.* **2008**, *73*, 8437–8447.