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PII: S0040-4039(16)31593-3
DOI: http://dx.doi.org/10.1016/j.tetlet.2016.11.102
Reference: TETL 48388

To appear in: *Tetrahedron Letters*

Received Date: 1 October 2016
Revised Date: 21 November 2016
Accepted Date: 23 November 2016

Please cite this article as: Asadi, B., Landarani-Isfahani, A., Mohammadpoor-Baltork, I., Tangestaninejad, S., Moghadam, M., Mirkhani, V., Amiri Rudbari, H., Microwave-assisted, regioselective one-pot synthesis of quinolines and *bis*-quinolines catalyzed by Bi(III) immobilized on triazine dendrimer stabilized magnetic nanoparticles, *Tetrahedron Letters* (2016), doi: http://dx.doi.org/10.1016/j.tetlet.2016.11.102

Tetrahedron Letters
journal homepage: www.elsevier.com

Microwave-assisted, regioselective one-pot synthesis of quinolines and *bis*-quinolines catalyzed by Bi(III) immobilized on triazine dendrimer stabilized magnetic nanoparticles

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ARTICLE INFO

Article history:
Received
Received in revised form
Accepted
Available online

Keywords:
Quinoline
Bismuth
Microwave irradiation
Multicomponent reaction (MCR)
Dendrimers

ABSTRACT

Fe_3O_4-TDSN-Bi(III) was utilized as an efficient and reusable catalyst for the regioselective one-pot synthesis of quinoline derivatives from arylamines, arylaldehydes and methyl propiolate under microwave irradiation and solvent-free conditions. Also, *bis*-quinolines were obtained in high yields from dialdehydes or diamines. Atom-economy, high to excellent yields, easy work-up, as well as simple catalyst recovery and reusability are the key features of this procedure.

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1. Introduction

Multicomponent reactions (MCRs) have recently gained significant attention owing to the wide range of applications in synthesis. These reactions possess valuable advantages over conventional linear syntheses, allowing the formation of several bonds and the construction of novel and complex molecular structures from simple precursors with a minimum number of synthetic steps.[1]

Quinolines are an important class of heterocyclic compounds possessing potent biological activities including anticancer,[2] antimalarial,[3] antiasthmatic,[4] antidiabetic,[5] antibacterial,[6] antileishmaniasis,[7] and antitumor[8] properties. Additionally, this skeleton is found in natural products and is the main structural unit of several agrochemicals,[9] and dye-sensitized solar cells.[10] Representative functionalized quinoline based drugs include camptothecin (anticancer)[11] and cryptolepine (antimalarial).[12]

Many synthetic methods for the preparation of quinolines have been reported in the literature,[13] however, some of these approaches require either high temperatures, harmful organic solvents, strongly acidic media and/or non-reusable catalysts. Furthermore, in some cases high catalyst loadings (up to 30 mol%) are necessary to achieve reasonable yields.

Although there are a few reports dealing with the regioselective preparation of 2,3-disubstituted quinolines,[14] it is still necessary to develop additional methods.

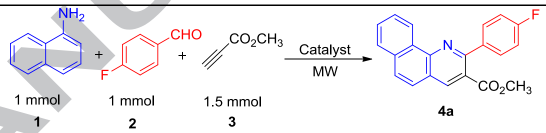
Recently, we reported Fe_3O_4-TDSN-Bi(III) as an efficient and recyclable catalyst for the synthesis of aminonaphthoquinones, as well as symmetric and unsymmetric *bis*-aminonaphthoquinones.[15] In a continuation of our research on the applications of this catalyst and the synthesis of quinoline derivatives,[16] herein, we report an efficient microwave-assisted, regioselective synthesis of quinolines, as well as symmetric and unsymmetric *bis*-quinolines, using a one-pot, three-component reaction between arylamines, arylaldehydes and methyl propiolate catalyzed by Fe_3O_4-TDSN-Bi(III) under solvent-free conditions.

2. Results and Discussion

The Fe_3O_4-TDSN-Bi(III) catalyst was prepared according to our previously reported procedure.[15] At the outset of this study, the reaction of 1-naphthylamine **1**, 4-fluorobenzaldehyde **2** and methyl propiolate **3** was investigated for optimization of the reaction conditions (Table 1). The reaction was first performed in the absence of catalyst under microwave (MW) irradiation[17] (360 W) at 85 °C in order to explore the role of catalyst. Under these conditions, no product was observed, even after 30 min (Entry 1). The reaction was then examined in the presence of 8 mol% of various Lewis acids including $ZnCl_2$, $MnCl_2$, $AlCl_3$, $FeCl_3$, $BiCl_3$, $Bi(NO_3)_3{\cdot}5H_2O$ and $Bi(OTf)_3$ for 2 min (Entries 2-8). These catalysts were only moderately effective, giving the desired product in 15-72% yield. An improved yield was observed when Fe_3O_4-TDSN-Bi(III) was used, and the desired product was obtained in 97% yield (Entry 9). Next, reaction parameters such as the catalyst loading, temperature, reaction time, and MW power were optimized. Accordingly, the reaction was repeated under solvent-free conditions and MW irradiation with different catalyst loadings (Entries 9-11), and the maximum yield (97%) was observed with 8 mol% of catalyst (Entry 9). The effect of temperature was studied by carrying out the model reaction at different temperatures and the best results were obtained at 85 °C (Entries 9 and 12). Increasing the temperature to 95 °C had no effect on the yield (Entry 13). Extending the reaction time (Entry 14) and the MW power (Entry 15) also did not improve the yield, while decreasing these parameters resulted in lower yields (Entries 16 and 17). To probe the effect of MW irradiation versus conventional heating, the model reaction was repeated using conventional heating (85 °C) to give the desired product in 40% yield after 4 hours (Entry 18). This confirmed that the increase in reaction rate was primarily due to the effect of MW irradiation. According to Table 1, the optimal reaction conditions were 1-naphthylamine (1 mmol), 4-fluorobenzaldehyde (1 mmol) and methyl propiolate (1.5 mmol) in the presence of Fe_3O_4-TDSN-Bi(III) (8 mol%, 133 mg) at 360 W, 85 °C.

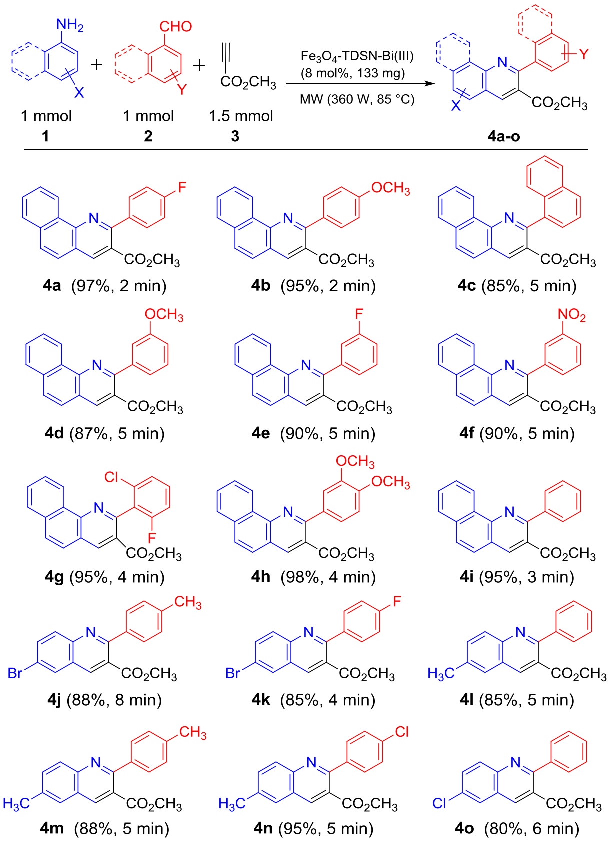
To examine the scope of this methodology, 1-naphthylamine and methyl propiolate were treated with a wide range of arylaldehydes containing electron-withdrawing and electron-donating substituents at the *ortho*-, *meta*-, and *para*-positions of the aromatic ring under MW irradiation to afford the corresponding benzo[*h*]quinoline-3-carboxylate derivatives. The electronic nature of the substituents on the aromatic ring had little influence on the reaction process (Scheme 1, **4a-i**). Likewise, substituted anilines reacted well with various arylaldehydes and methyl propiolate to furnish the corresponding quinoline-3-carboxylate derivatives in high yields (Scheme 1, **4j-o**).

Table 1. Influence of Reaction Parameters on the Yield of **4a**.



Entry	Catalyst (mol%)	T (°C)	Time (min)	Yield **4a** (%)[a]
1	-	85	30	0
2	$ZnCl_2$ (8)	85	2	20
3	$MnCl_2$ (8)	85	2	25
4	$AlCl_3$ (8)	85	2	15
5	$FeCl_3$ (8)	85	2	50
6	$BiCl_3$ (8)	85	2	35
7	$Bi(NO_3)_3{\cdot}5H_2O$ (8)	85	2	40
8	$Bi(OTf)_3$ (8)	85	2	72
9	Fe_3O_4-TDSN-Bi(III) (8)	85	2	97
10	Fe_3O_4-TDSN-Bi(III)(10)	85	2	97
11	Fe_3O_4-TDSN-Bi(III) (6)	85	2	70
12	Fe_3O_4-TDSN-Bi(III) (8)	75	2	80
13	Fe_3O_4-TDSN-Bi(III) (8)	95	2	97
14	Fe_3O_4-TDSN-Bi(III) (8)	85	5	97
15[b]	Fe_3O_4-TDSN-Bi(III) (8)	85	2	97
16	Fe_3O_4-TDSN-Bi(III) (8)	85	1	81
17[c]	Fe_3O_4-TDSN-Bi(III) (8)	85	2	70
18[d]	Fe_3O_4-TDSN-Bi(III) (8)	85	240	40

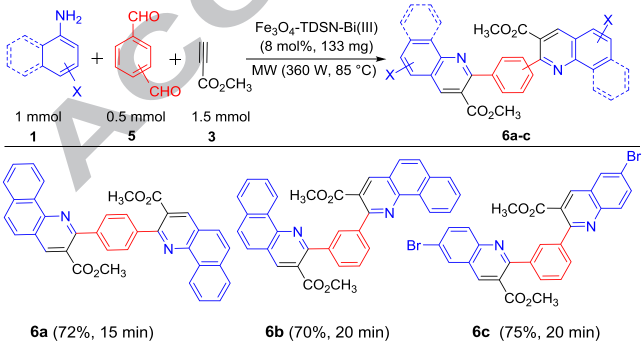
[a] Isolated yield. [b] Reaction performed with an applied power of 420 W. [c] Reaction performed with an applied power of 300 W. [d] Reaction carried out under conventional heating conditions.



Scheme 1. Scope of the quinoline synthesis catalyzed by Fe_3O_4-TDSN-Bi(III).

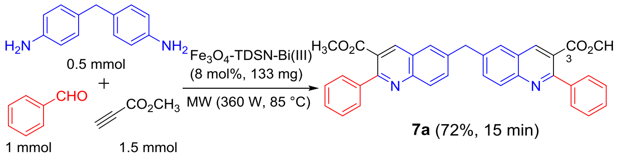
Benzo[*h*]quinoline-3-carboxylate derivatives were rapidly accessible on gram scales. On a 10 mmol scale, 1-naphthylamine, reacted with 4-fluorobenzaldehyde and methyl propiolate in the presence of Fe_3O_4-TDSN-Bi(III) (0.8 mol%) at 360 W, 85 °C, to give benzo[*h*]quinoline-3-carboxylate **4a** in 70% yield after 25 min.

Encouraged by this success, we next turned our attention to extending the substrate scope of this reaction to access *bis*-quinolines. The reaction of dialdehydes including terephthaldialdehyde and isophthaldialdehyde with arylamines and methyl propiolate proceeded rapidly to give the corresponding symmetric *bis*-quinolines **6a-c** in high yields (Scheme 2).



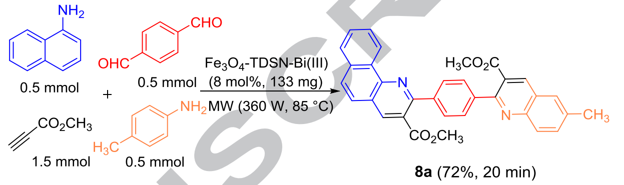
Scheme 2. Synthesis of symmetric *bis*-quinolines from dialdehydes catalyzed by Fe_3O_4-TDSN-Bi(III).

In another approach for the synthesis of *bis*-quinolines, treatment of 4,4'-diaminodiphenylmethane with benzaldehyde and methyl propiolate gave the desired symmetric *bis*-quinoline **7a** in 72% yield (Scheme 3).



Scheme 3. Synthesis of a symmetric *bis*-quinoline from diamine catalyzed by Fe_3O_4-TDSN-Bi(III).

Importantly, the reaction of terephthaldialdehyde with two different amines and methyl propiolate gave the related unsymmetric *bis*-quinoline **8a** in 72% yield (Scheme 4).



Scheme 4. Synthesis of a unsymmetric *bis*-quinoline catalyzed by Fe_3O_4-TDSN-Bi(III).

The products were identified by FT-IR, MS, ^{1}H NMR and ^{13}C NMR spectra as well as elemental analysis. Additionally, the structures of **4d** (CCDC 1478724) and **4h** (CCDC 1478723) were confirmed by single crystal X-ray analysis (Fig. 1, ESI Tables 1-4). The products were obtained by recrystallization from EtOH and dried under reduced pressure.

The product formation can take place *via* two pathways,[13j,14a] leading to either 2-substituted-quinoline-3-carboxylates or 2-substituted-quinoline-4-carboxylates. The reaction in the presence of Fe_3O_4-TDSN-Bi(III) afforded 2-substituted-quinoline-3-carboxylate products which were confirmed by NMR spectra and single crystal X-ray studies. A possible mechanism for formation of the quinolines, which involves air, is discussed in the ESI. Note that, 2-substituted-quinoline-3-carboxylate derivatives have an added advantage of being able to undergo nucleophilic substitution at the 4-position owing to blocking of the 2-position compared to the 2-substituted-quinoline-4-carboxylate derivates.[18]

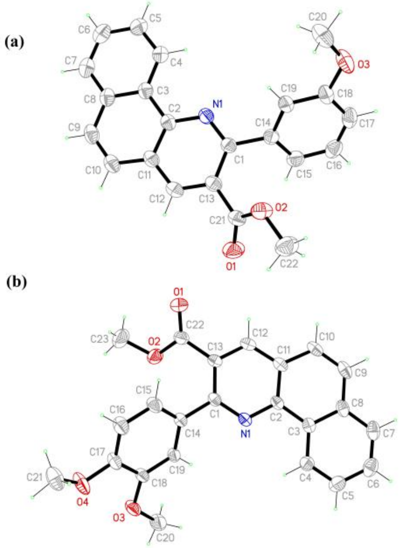


Figure 1. Molecular structures of (a) **4d** and (b) **4h**. Non-H atoms are represented as 30% probability displacement ellipsoids.

Catalyst recovery and reusability is an important property of this catalyst. The reusability of Fe_3O_4-TDSN-Bi(III) was probed in the synthesis of **4a**. Upon reaction completion, the mixture was cooled to room temperature and diluted with cold ethanol. The catalyst was separated using an external magnet, washed several times with ethanol, dried and then reused for subsequent reactions. The catalyst could be reused at least 6 times without considerable loss of activity (Table 2). No quantifiable amount of leached bismuth from the Fe_3O_4-TDSN-Bi(III) catalyst was detected (<1%) as determined by ICP-OES. This excellent reusability and high activity clearly show that the catalyst is stable under the reaction conditions.

Table 2. Reusability of the Fe_3O_4-TDSN-Bi(III) catalyst in the synthesis of **4a**.[a]

Run	1	2	3	4	5	6	7
Yield (%)[b]	97	97	96	94	94	92	92

[a] Reaction conditions: 1-naphthylamine (1 mmol), 4-fluorobenzaldehyde (1 mmol), methyl propiolate (1.5 mmol), Fe_3O_4-TDSN-Bi(III) (8 mol%, 133 mg), 360 W, 85 °C. [b] Isolated yield.

In summary, we have developed an efficient microwave-promoted synthesis of quinoline derivatives *via* a one-pot, three-component reaction of arylamines, arylaldehydes and methyl propiolate using Fe_3O_4-TDSN-Bi(III) as a recoverable heterogeneous catalyst. Additionally, this catalytic system was used for the multicomponent synthesis of symmetric and unsymmetric *bis*-quinolines. To date, this is the first report on the regioselective synthesis of symmetric and unsymmetric *bis*-quinolines *via* a one-pot, multicomponent reaction of dialdehydes/diamines under MW irradiation and solvent-free conditions, and therefore, can be considered as a useful method for the preparation of these compounds. This method presents several distinctive advantages, such as high reaction rates, high to excellent yields, a simple work-up procedure and easy recovery of the catalyst.

Acknowledgments

The authors are grateful to the Research Council of the University of Isfahan for financial support of this work.

Supplementary data

Supplementary data (general procedure and copies of ^1H and ^{13}C NMR spectra of the products) associated with this article can be found in the online version at ….

References and notes

1. (a) Cioc, R. C.; Ruijter, E.; Orru, R. V. A. *Green Chem*. **2014**, *16*, 2958-2975; (b) Amanpour, T.; Zangger, K.; Belaj, F.; Bazgir, A.; Dallinger, D. ; Kappe, C. O. *Tetrahedron* **2015**, *71*, 7159-7169; (c) Stalling, T.; Pauly, J.; Kröger, D.; Martens, J. *Tetrahedron* **2015**, *71*, 8290-8301.
2. (a) Afzal, O.; Kumar, S.; Haider, M. R.; Ali, M. R.; Kumar, R.; Jaggi, M.; Bawa, S. *Eur. J. Med. Chem*. **2015**, *97*, 871-910; (b) Shobeiri, N.; Rashedi, M.; Mosaffa, F.; Zarghi, A.; Ghandadi, M.; Ghasemi, A.; Ghodsi, R. *Eur. J. Med. Chem*. **2016**, *114*, 14-23.
3. Gorka, A. P.; de Dios, A.; Roepe, P. D. *J. Med. Chem*. **2013**, *56*, 5231-5246.
4. Gaurav, A.; Singh, R. *Med. Chem. Res*. **2014**, *23*, 5008-5030.
5. Lee, H. W.; Lee, H. S.; Park, J. H.; Cheong, J. J.; Kwon, H. B.; Kim, K. O.; Ku, C. S.; Kim, M. J.; Park, Y. J.; Ryu, H. W.; Song, H. H. *J. Appl. Biol. Chem.* **2015**, *58*, 1-3.
6. Hazra, A.; Mondal, S.; Maity, A.; Naskar, S.; Saha, P.; Paira, R.; Sahu, K.B.; Paira, P.; Ghosh, S.; Sinha, C.; Samanta, A.; Banerjee, S.; Mondal, N. B. *Eur. J. Med. Chem*. **2011**, *46*, 2132-2140.
7. Di Pietro, O.; Vicente-García, E.; Taylor, M. C.; Berenguer, D.; Viayna, E.; Lanzoni, A.; Sola, I.; Sayago, H.; Riera, C.; Fisa, R.; Clos, M. V.; Pérez, B.; Kelly, J. M.; Lavilla, R.; Muñoz-Torrero, D. *Eur. J. Med. Chem*. **2015**, *105*, 120-137.
8. Hu, H.; Jiang, M.; Xie, L.; Hu, G.; Zhang, C.; Zhang, L.; Zhou, S.; Zhang, M.; Gong, P. *Chem. Res. Chin. Univ*. **2015**, *31*, 746-755.
9. Neuhaus, J. D.; Morrow, S. M.; Brunavs, M.; Willis, M. C. *Org Lett.* **2016**, *18*, 1562-1565.
10. Vougioukalakis, G. C.; Stergiopoulos, T.; Kontos, A. G.; Pefkianakis, E. K.; Papadopoulos, K.; Falaras, P. *Dalton Trans*. **2013**, *42*, 6582-6591.
11. (a) Kim, S. H.; Kaplan, J. A.; Sun, Y.; Shieh, A.; Sun, H. L.; Croce, C. M.; Grinstuff, M. W.; Parquette, J. R. *Chem. Eur. J.* **2015**, *21*, 101-105; (b) Liu, Y. Q.; Li, W. Q.; Morris-Natschke, S. L.; Qian, K.; Yang, L.; Zhu, G. X.; Wu, X. B.; Chen, A. L.; Zhang, S. Y.; Nan, X.; Lee, K. H. *Med. Res. Rev*. **2015**, *35*, 753-789.
12. Forkuo, A. D.; Ansah, C.; Boadu, K. M.; Boampong, J. N.; Ameyaw, E. O.; Gyan, B. A.; Arku, A. T.; Ofori, M. F. *Malar. J.* **2016**, *15*, 1-12.
13. (a) Sarmah, M. M.; Bhuyan, D.; Prajapati, D. *Synlett* **2013**, *24*, 2245-2248; (b) Anvar, S.; Mohammadpoor-Baltork, I.; Tangestaninejad, S.; Moghadam, M.; Mirkhani, V.; Khosropour, A. R.; Kia, R. *RSC Adv*. **2012**, *2*, 8713-8720; (c) Kumar, A.; Rao, V. K. *Synlett* **2011**, *15*, 2157-2162; (d) Kulkarni, A.; Török, B. *Green Chem*. **2010**, *12*, 875-878; (e) Koley, S.; Chanda, T.; Ramulu, B. J.; Chowdhury, S.; Singh, M. S. *Adv. Synth. Catal.* **2016**, *358*, 1195-1201; (f) Reddy, M. S.; Thirupathi, N.; Kumar, Y. K. *RSC Adv*. **2012**, *2*, 3986-3992; (g) Reddy, B. S.; Venkateswarlu, A.; Reddy, G. N.; Reddy, Y. R. *Tetrahedron Lett*. **2013**, *54*, 5767-5770; (h) Zheng, Q.; Ding, Q.; Liu, X.; Zhang, Y.; Peng, Y. *J. Organomet. Chem*. **2015**, *783*, 77-82; (i) Xu, X.; Zhang, X.; Liu, W.; Zhao, Q.; Wang, Z.; Yu, L.; Shi, F. *Tetrahedron Lett*. **2015**, *56*, 3790-3792; (j) Cao, K.; Zhang, F. M.; Tu, Y. Q.; Zhuo, X. T.; Fan, C. A. *Chem. Eur. J.* **2009**, *15*, 6332-6334; (k) Huma, H. S.; Halder, R.; Kalra, S. S.; Das, J.; Iqbal, J. *Tetrahedron Lett*. **2002**, *43*, 6485-6488; (l) Prajapati, S. M.; Patel, K. D.; Vekariya, R. H.; Panchal, S. N.; Patel, H. D. *RSC Adv*. **2014**, *4*, 24463-24476; (m) Bharate, J. B.; Vishwakarma, R. A.; Bharate, S. B. *RSC Adv*. **2015**, *5*, 42020-2053.
14. (a) Li, Y. F.; Wu, Z. G.; Shi, J.; Pan, Y.; Bu, H. Z.; Ma, H. F.; Gu, J. C.; Huang, H.; Wang, Y. Z.; Wu, L. *Tetrahedron* **2014**, *70*, 8971-8975; (b) Bharate, J. B.; Bharate, S. B.; Vishwakarma, R. A. *ACS Comb. Sci*. **2014**, *16*, 624−630; (c) Selig, P.; Raven, W. *Org. Lett*. **2014**, *16*, 5192−5195; (d) Chen, D. S.; Li, Y. L.; Liu, Y.; Wang, X. S. *Tetrahedron*, **2013**, *69*, 7045-7050; (e) Yu, Z. H.; Zheng, H. F.; Yuan, W.; Tang, Z. L.; Zhang, A. D.; Shi, D. Q.; *Tetrahedron*, **2013**, *69*, 8137-8141; (f) Wang, K.; Herdtweck, E.; Dömling, A.; *ACS Comb. Sci*. **2012**, *14*, 316-322; (g) Vander Mierde, H. .; Van Der Voort, P.; Verpoort, F. *Tetrahedron Lett*. **2008**, *49*, 6893-6895; (h) Yan, M. C.; Tu, Z.; Lin, C.; Ko, S.; Hsu, J.; Yao, C. F. *J. Org. Chem*. **2004**, *69*, 1565-1570.
15. Asadi, B.; Mohammadpoor-Baltork, I.; Tangestaninejad, S.; Moghadam, M.; Mirkhani, V.; Landarani-Isfahani, A. *New J. Chem*. **2016**, *40*, 6171-6184.
16. (a) Mohammadpoor-Baltork, I.; Tangestaninejad, S.; Moghadam, M.; Mirkhani, V.; Anvar, S.; Mirjafari, A. *Synlett* **2010**, *20*, 3104-3112; (b) Anvar, S.; Mohammadpoor-Baltork, I.; Tangestaninejad, S.; Moghadam, M.; Mirkhani, V.; Khosropour, A. R.; Landarani-Isfahani, A.; Kia, R. *ACS Comb. Sci.* **2014**, *16*, 93-100.
17. The microwave system used in these experiments includes the following items: Micro-SYNTH labstation, equipped with a glass door, a dual magnetron system with pyramid-shaped diffuser, 1000 W delivered power, exhaust system, magnetic stirrer, ‘‘quality pressure’’ sensor for flammable organic solvents, and a ATCFO fibre optic system for automatic temperature control.
18. Yamaguchi, K.; Xu, N.; Jin, X.; Suzuki, K.; Mizuno, N. *Chem. Commun.* **2015**, *51*, 10034-10037.

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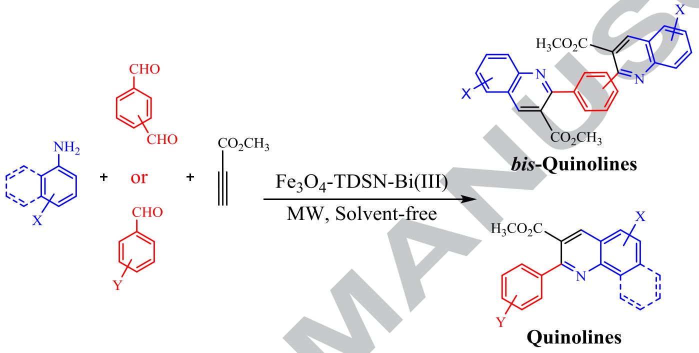

Highlights

- Fe_3O_4-TDSN-Bi(III) was applied to the regioselective one-pot synthesis of quinolines.
- *Bis*-quinolines were obtained from dialdehydes or diamines.
- The catalyst could be separated and reused six times without a decrease in activity.