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Solvent-free one pot synthesis of indenoquinolinones catalyzed by iron(III) triflate

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Abstract

A green three-component one pot condensation synthesis of 16 indenoquinolinone from aromatic aldehydes, 1-aminonaphthalene or 1-aminoanthracene and 1,3-indanedione catalyzed by $Fe(OTf)_3$ is described. The isolated yields ranged from 80% to 92%.

Keywords: indenoquinolinone; iron triflate; one pot synthesis.

Introduction

Heterocycles are used as scaffolds for creating pharmacophores to yield potent and selective drugs (Hermakens et al., 1997). This is especially true for six-membered ring heterocyclic compounds, which are core components of a large number of substances that possess a wide range of interesting biological activities (Avendano and Menendez, 2008). With an emphasis on the search for atom efficient transformations of readily available starting materials into complex organic molecules (Trost, 1995), reactions that provide maximum diversity are particularly desirable. Here, expeditious domino (Padwa and Bur, 2007) and multicomponent (Zhu and Bienaime, 2005) reactions (MCRs) have emerged as powerful strategies.

In view of the importance of benzoquinolines and their derivatives in various fields of chemistry, biology and pharmacology, significant efforts have been devoted to their synthesis. Quinoline derivatives are reported to possess interesting pharmacological activities such as anti-plasmodial, anti-bacterial and anti-proliferative activities (Tu et al., 2006a; Wang et al., 2007). Therefore, various methods such as the Skraup, Doebner–von Miller, Friedläänder and Combes procedures have been developed for the synthesis of quinoline derivatives (Jiang and Si, 2002; Theoclitou and Robinson, 2002).

In recent years, a multicomponent approach for the synthesis of indenoquinolinone derivatives has been reported (Tu et al., 2006b; Wang et al., 2008). The approach involves the reaction of either tetronic acid or 1,3-indanedione with various aldehydes and substituted anilines in water under microwave irradiation conditions. Furthermore, a one pot synthesis of indenoquinoline derivatives by condensing 1-aminonaphthalene, aldehydes and 1,3-indandione has been reported (Heravi et al., 2010).

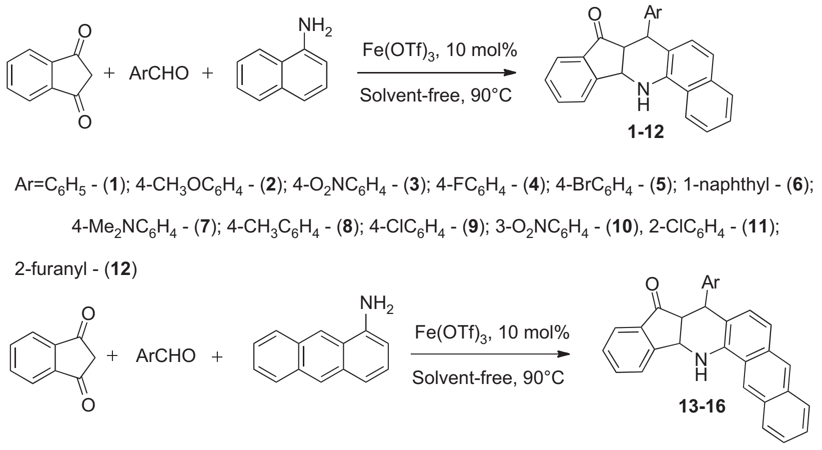
In contemporary organic synthesis, Lewis acid catalyzed reactions have gained increasing interest because of the unique reactivity and selectivity that can be achieved under mild conditions (Santelli and Pons, 1995). During the past few years, the outstanding potential of a variety of metal triflates (trifluoromethylsulfonates) has been discovered, thus triggering much research endeavor. The triflate anion is both weakly nucleophilic and coordinating, rendering the metal counter ion more cationic and thus a stronger Lewis acid.

In continuation of our interest in MCRs (Damavandi, 2011; Eshghi et al., 2011), herein, the metal triflates catalyzed one pot reaction of 1-aminonaphthalene or 1-aminoanthracene, aromatic aldehydes and 1,3-indanedione providing a series of indeno[1,2-*b*]quinolineone derivatives is described. To the best of our knowledge, this is the first report on the use of $Fe(OTf)_3$ as a catalyst for the synthesis of such compounds.

Results and discussion

First, the mixture of 4-nitrobenzaldehyde, 1-aminonaphthalene and 1,3-indandione was chosen as a model reaction to determine whether 5 mol% $Fe(OTf)_3$ was an efficient catalyst. The reaction mixture was stirred at 90°C for 4h and the corresponding indenoquinolinone (**3** in Scheme 1) was obtained in 80% yield. No target product was observed when the mixture was stirred under similar conditions in the absence of $Fe(OTf)_3$, even after heating for 6 h, thus highlighting the role of $Fe(OTf)_3$ as a catalyst. Next the amount of the $Fe(OTf)_3$was changed from 5 to 20 mol%. The results showed that the reaction yield was improved when the amount of $Fe(OTf)_3$ increased from 5 to 10 mol%. However, the yield was minimally affected when the amount of $Fe(OTf)_3$ was further increased from 10 to 20 mol% (92%). Therefore, 10 mol% of $Fe(OTf)_3$ was considered to be suitable.

Several metal triflates were investigated in an attempt to further optimize the reaction. The ferric catalyst $Fe(OTf)_3$ showed the most effective catalytic effect, whereas $Zn(OTf)_2$, $Cu(OTf)_2$ and triflic acid (HOTf) showed relatively lower catalytic efficiency. The recyclability of $Fe(OTf)_3$ was also investigated. The catalyst could be reused without any loss of activity.



Ar=C_6H_5 - (**1**); 4-$CH_3OC_6H_4$ - (**2**); 4-$O_2NC_6H_4$ - (**3**); 4-FC_6H_4 - (**4**); 4-BrC_6H_4 - (**5**); 1-naphthyl - (**6**); 4-$Me_2NC_6H_4$ - (**7**); 4-$CH_3C_6H_4$ - (**8**); 4-ClC_6H_4 - (**9**); 3-$O_2NC_6H_4$ - (**10**), 2-ClC_6H_4 - (**11**); 2-furanyl - (**12**)

Ar=C_6H_5 - (**13**); 4-$O_2NC_6H_4$ - (**14**); 2-furanyl - (**15**); 4-$CH_3OC_6H_4$ - (**16**)

Scheme 1 Synthesis of indeno[1,2-*b*]quinolinone derivatives **1**–**16**.

The generality of this process was demonstrated by the wide range of substituted aromatic aldehydes used to synthesize indenoquinolinone derivatives **1–16** (Scheme 1). Various aromatic aldehydes were allowed to react with 1-aminonaphthalene and 1,3-indanedione and all these reactions proceeded smoothly to give the corresponding products **1–12** in good to excellent yields (Scheme 1). Encouraged by these results the attention was turned to 1-aminoanthracene, the reaction of which gave the corresponding indeno[1,2-*b*]quinoline-7-ones **13–16** in good yields (Scheme 1).

In order to gain an insight into the reaction mechanism, 4-nitrobenzyldehyde was allowed to react with 1-aminoanthracene and the expected Schiff base **A** was isolated and characterized. A subsequent treatment of compound **A** with 1,3-indanedione furnished product **14** that was identical with that obtained in the one pot reaction. In a similar way, the intermediate product **B** (Scheme 2) from the reaction between 1,3-indanedione and 4-nitrobenzaldehyde was isolated and characterized. Its subsequent reaction with 1-aminoanthtracene yielded compound **14**.

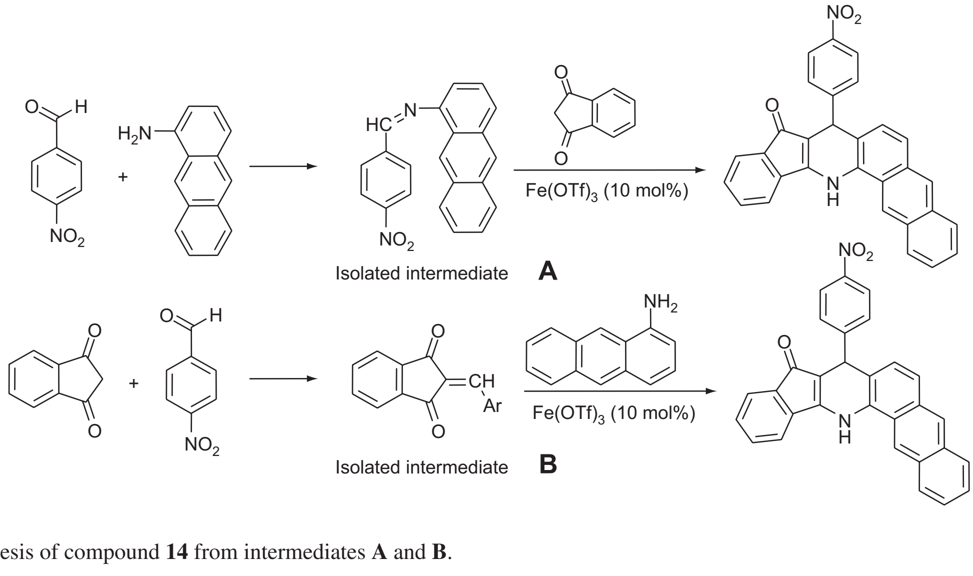
Conclusion

A simple three-component reaction yielding indenoquinolinone derivatives in a one pot procedure using iron(III) triflate as an efficient and recyclable catalyst has been developed.

Experimental

General

Chemicals were either prepared in our laboratories or purchased from Merck, Fluka and Aldrich Chemical Companies. All yields



Scheme 2 Synthesis of compound **14** from intermediates **A** and **B**.

refer to isolated products. IR spectra were recorded in KBr disks on a Shimadzu-IR 470 spectrophotometer. ^{1}H NMR spectra was recorded on a Bruker 100-MHz spectrometer in DMSO-d_6 with TMS as internal standard. Flash column chromatography was performed using 300- and 400-mesh silica gel and analytical thin layer chromatography was performed on pre-coated silica gel plates (60F-254). Mass spectra were recorded with a Shimadzu QP 1100 EX mass spectrometer operating at an ionization potential of 70 eV. Elemental analyses were performed on Thermo Finnigan EA1112 elemental analyzer.

General procedure for preparation of indeno[1,2-*b*]quinoline-7-ones (1–16)

A mixture of aryl aldehyde (1 mmol), 1,3-indanedione (1 mmol), amine (1 mmol), Fe(OTf)$_3$ (10 mol%) was added to a round bottomed flask. The mixture was heated at 90°C between 3–5 h as indicated by TLC analysis. Upon completion of the reaction, the mixture was extracted with AcOEt (3×10 ml) and washed with aq. NaHCO$_3$ solution (2×10 ml) and brine (2×5 ml). Then the organic phase was dried over MgSO$_4$ and concentrated under reduced pressure. The crude product was chromatographed on silica gel eluting with petroleum ether–AcOEt (5:1).

7-Phenyl-8,13-dihydro-7*H*-benzo[*h*]indeno[1,2-*b*]quinolin-8-one (1): Isolated yield 90%; m.p. 309–310°C; ^{1}H NMR: δ 9.85 (1H, s, NH), 7.85 (2H, d, *J*=3.5 Hz, ArH), 7.75 (2H, d, *J*=3.7 Hz, ArH), 7.65–7.45 (4H, m, ArH), 7.45–7.10 (7H, m, ArH), 5.10 (1H, s, CH); EIMS: m/z 359 (M$^+$). Analysis: calculated for $C_{26}H_{17}NO$: C, 86.88; H, 4.77; N, 3.90. Found: C, 86.72; H, 4.69; N, 3.87.

7-(4-Methoxyphenyl)-8,13-dihydro-7*H*-benzo[*h*]indeno[1,2-*b*]quinolin-8-one (2): Isolated yield 90%; m.p. 313–314°C; ^{1}H NMR: δ 10.10 (1H, s, NH), 7.80 (1H, d, *J*=7.3 Hz, ArH), 7.65–7.45 (4H, m, ArH), 7.55–7.10 (7H, m, ArH), 6.93 (2H, d, *J*=4.2 Hz, ArH), 5.25 (1H, s, CH), 3.65 (3H, S, OMe); EIMS: m/z 389 (M$^+$). Analysis: calculated for $C_{26}H_{19}NO_2$: C, 83.27; H, 4.92; N, 3.60. Found: C, 83.12; H, 4.89; N, 3.55.

7-(4-Nitrophenyl)-8,13-dihydro-7*H*-benzo[*h*]indeno[1,2-*b*]quinolin-8-one (3): Isolated yield 92%; m.p. 348–350°C; ^{1}H NMR: δ 11.22 (1H, s, NH), 7.92 (1H, d, *J*=9 Hz, ArH), 7.78–7.45 (6H, m, ArH), 7.36–7.10 (7H, m, ArH), 5.40 (1H, s, CH); EIMS: m/z 404 (M$^+$). Analysis: calculated for $C_{26}H_{16}N_2O_3$: C, 77.22; H, 3.99; N, 6.93. Found: C, 77.12; H, 3.92; N, 6.89.

7-(4-Fluorophenyl)-8,13-dihydro-7*H*-benzo[*h*]indeno[1,2-*b*]quinolin-8-one (4): Isolated yield 92%; m.p. 336–338°C; ^{1}H NMR: δ 9.80 (1H, s, NH), 7.90–7.67 (4H, m, ArH), 7.55–7.40 (4H, m, ArH), 7.35–7.10 (7H, m, ArH), 5.15 (1H, s, CH). EIMS: m/z 377 (M$^+$). Analysis: calculated for $C_{26}H_{16}FNO$: C, 82.74; H, 4.27; N, 3.71. Found: C, 82.48; H, 4.19; N, 3.74.

7-(4-Bromophenyl)-8,13-dihydro-7*H*-benzo[*h*]indeno[1,2-*b*]quinolin-8-one (5): Isolated yield 90%; m.p. 334–335°C; ^{1}H NMR: δ 10.10 (1H, s, NH), 7.83 (1H, m, ArH), 7.75–7.50 (8H, m, ArH), 7.35–7.05 (5H, m, ArH), 5.25 (1H, s, CH); EIMS: m/z 437 (M$^+$). Analysis: calculated for $C_{26}H_{16}BrNO$: C, 71.25; H, 3.68; N, 3.20. Found: C, 71.17; H, 3.65; N, 3.18.

7-(1-Naphthyl)-8,13-dihydro-7*H*-benzo[*h*]indeno[1,2-*b*]quinolin-8-one (6): Isolated yield 86%; m.p. 280–282°C; ^{1}H NMR: δ 9.95 (1H, s, NH), 7.85–7.70 (4H, m, ArH), 7.70–7.60 (4H, m, ArH), 7.55–7.05 (9H, m, ArH), 5.30 (1H, s, CH). EIMS: m/z 409 (M$^+$). Analysis: calculated for $C_{30}H_{19}NO$: C, 88.00; H, 4.68; N, 3.42. Found: C, 88.15; H, 4.71; N, 3.46.

7-[4-(Dimethylamino)phenyl]-8,13-dihydro-7*H*-benzo[*h*]indeno[1,2-*b*]quinolin-8-one (7): Isolated yield 84%; m.p. 323–325°C; ^{1}H NMR: δ 10.55 (1H, s, NH), 7.80–7.55 (3H, m, ArH), 7.50–7 (7H, m, ArH), 6.95 (2H, d, *J*=5.2 Hz, ArH), 6.65 (2H, d, *J*=5.5 Hz, ArH), 5.25 (1H, s, CH), 2.90 (6H, s, NMe$_2$); EIMS: m/z 402 (M$^+$). Analysis: calculated for $C_{28}H_{22}N_2O$: C, 83.56; H, 5.51; N, 6.96. Found: C, 83.48; H, 5.45; N, 6.91.

7-(4-Methylphenyl)-8,13-dihydro-7*H*-benzo[*h*]indeno[1,2-*b*]quinolin-8-one (8): Isolated yield 90%; m.p. 315–317°C; ^{1}H NMR: δ 10.70 (1H, s, NH), 7.75–7.65 (14H, m, ArH), 5.55 (1H, s, CH), 2.20 (3H, s, Me). EIMS: m/z 373 (M$^+$). Analysis: calculated for $C_{27}H_{19}NO$: C, 86.84; H, 5.13; N, 3.75. Found: C, 86.77; H, 5.19; N, 3.71.

7-(4-Chlorophenyl)-8,13-dihydro-7*H*-benzo[*h*]indeno[1,2-*b*]quinolin-8-one (9): Isolated yield 90%; m.p. 316–318°C; ^{1}H NMR: δ 9.85 (1H, s, NH), 7.75–7.45 (8H, m, ArH), 7.40 (2H, m, ArH), 7.25–7.0 (4H, m, ArH), 4.95 (1H, s, CH); EIMS: m/z 393 (M$^+$). Analysis: calculated for $C_{26}H_{16}ClNO$: C, 79.29; H, 4.09; N, 3.56. Found: C, 79.21; H, 4.03; N, 3.51.

7-(3-Nitrophenyl)-8,13-dihydro-7*H*-benzo[*h*]indeno[1,2-*b*]quinolin-8-one (10): Isolated yield 90%; m.p. 334–355°C; ^{1}H NMR: δ 10.50 (1H, s, NH), 8.05 (2H, m, ArH), 7.75–7.65 (2H, m, ArH), 7.55–7.07 (10H, m, ArH), 5.35 (1H, s, CH); EIMS: m/z 404 (M$^+$). Analysis: calculated for $C_{26}H_{16}N_2O_3$: C, 77.22; H, 3.99; N, 6.93. Found: C, 77.18; H, 4.05; N, 6.97.

7-(2-Chlorophenyl)-8,13-dihydro-7*H*-benzo[*h*]indeno[1,2-*b*]quinolin-8-one (11): Isolated yield 88%; m.p. 335–337°C; ^{1}H NMR: δ 9.85 (1H, s, NH), 7.75–7.45 (8H, m, ArH), 7.40 (2H, m, ArH), 7.25–7.0 (4H, m, ArH), 4.95 (1H, s, CH); EIMS: m/z 393 (M$^+$). Analysis: calculated for $C_{26}H_{16}ClNO$: C, 79.29; H, 4.09; N, 3.56. Found: C, 79.21; H, 4.03; N, 3.51.

7-(2-Furyl)-8,13-dihydro-7*H*-benzo[*h*]indeno[1,2-*b*]quinolin-8-one (12): Isolated yield 85%; m.p. 293–295°C; ^{1}H NMR: δ 9.90 (1H, s, NH), 7.85–7.75 (2H, m, ArH), 7.73–7.40 (5H, m, ArH), 7.40–7.0 (5H, m, ArH), 6.25 (1H, t, ArH), 4.95 (1H, s, CH); EIMS: m/z 349 (M$^+$). Analysis: calculated for $C_{24}H_{15}NO_2$: C, 82.50; H, 4.33; N, 4.01. Found: C, 82.33; H, 4.30; N, 3.98.

8-Phenyl-9,14-dihydro-8*H*-indeno[1,2-*b*]naphtho[2,3-*h*]quinolin-9-one (13): Isolated yield 80%; m.p. 336–338ºC; ^{1}H NMR: δ 9.55 (1H, s, NH), 7.80–7.70 (4H, m, ArH), 7.65–7.50 (6H, m, ArH), 7.35 (2H, d, *J*=4.7 Hz, ArH), 7.25–7.05 (5H, m, ArH), 5.30 (1H, s, CH); EIMS: m/z 409 (M$^+$). Analysis. calculated for $C_{30}H_{19}NO$: C, 88.00; H, 4.68; N, 3.42. Found: C, 88.11; H, 4.62; N, 3.39.

8-(4-Nitrophenyl)-9,14-dihydro-8*H*-indeno[1,2-*b*]naphtho[2,3-*h*]quinolin-9-one (14): Isolated yield 92%; m.p. 366–367°C; ^{1}H NMR: δ 10.55 (1H, s, NH), 7.75 (2H, d, *J*=8.5 Hz, ArH), 7.65–6.90 (14H, m, ArH), 5.40 (1H, s, CH); EIMS: m/z 454 (M$^+$). Analysis: calculated for $C_{30}H_{18}N_2O_3$: C, 79.28; H, 3.99; N, 6.16. Found: C, 79.21; H, 3.90; N, 6.12.

8-[4-(2-Furyl)phenyl]-9,14-dihydro-8*H*-indeno[1,2-*b*] naphtho[2,3-*h*]quinolin-9-one (15): Isolated yield 84%; m.p. 351–352°C; ^{1}H NMR: δ 9.75 (1H, s, NH), 7.75–7.50 (6H, m, ArH), 7.45–7.10 (8H, m, ArH), 6.35 (1H, t, ArH), 5.25 (1H, s, CH); EIMS: m/z 399 (M$^+$). Analysis: calculated for $C_{28}H_{17}NO_2$: C, 84.19; H, 4.29; N, 3.51. Found: C, 84.10; H, 4.22; N, 3.48.

8-(4-Methoxyphenyl)-9,14-dihydro-8*H*-indeno[1,2-*b*] naphtho[2,3-*h*]quinolin-9-one (16): Isolated yield 86%; m.p. 343–345°C; ^{1}H NMR: δ 9.95 (1H, s, NH), 7.75–7.25 (16H, m, ArH), 5.60 (1H, s, CH), 3.65 (3H, s, OMe); EIMS: m/z 439 (M$^+$). Analysis: calculated for $C_{31}H_{21}NO_2$: C, 84.72; H, 4.82; N, 3.19. Found: C, 84.66; H, 4.77; N, 3.14.

N-(1-Anthracyl)-4-nitrobenzaldimine (A)

To a solution of 4-nitrobenzaldehyde (1 mmol) in ethanol (10 ml), 1-aminonaphthalene (1 mmol) and a trace amount of *p*-toluenesulfonic acid were added. The mixture was heated under reflux for 2h. The reaction mixture was cooled and the precipitate was filtered and crystallized from acetonitrile. The yield was 90%; m.p. 155–157°C; IR: ν 3010, 2873, 1670, 1515, 1335, 1010, 832, 720 cm^{-1}; ^{1}H NMR: δ 8.35 (1H, s, CHN), 8.08 (2H, d, *J*=5.4 Hz, ArH), 7.90–7.80 (3H, m, ArH), 7.75–7.55 (4H, m, ArH), 7.50–7.38 (2H, m, ArH), 7.20 (1H, m, ArH), 7.05 (1H, t, *J*=7.3 Hz, ArH). Analysis: calculated for $C_{21}H_{14}N_2O_2$: C, 77.29; H, 4.32; N, 8.58. Found: C, 77.19; H, 4.29; N, 8.54.

2-(4-Nitrobenzylidenyl)-1,3-indanedione (B)

A solution of 1,3-indanedione (1 mmol) and 4-nitrobenzaldehyde (1 mmol) in ethanol (10 ml) was heated under reflux for 1 h. The resultant precipitate was filtered, washed with ether and crystallized from acetonitrile. The yield was 80%; m.p. 181–183°C; IR: ν 2915, 1665, 1570, 1405, 1185, 940, 810 cm^{-1}; ^{1}H NMR: δ 8.55 (1H, s, CH), 8.10 (2H, d, *J*=6.4 Hz, ArH), 7.85–7.50 (4H, m, ArH), 7.45–7.20 (2H, m, ArH). Analysis: calculated for $C_{16}H_9NO_4$: C, 68.82; H, 3.25; N, 5.02. Found: C, 68.64; H, 3.20; N, 4.58.

Acknowledgements

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