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Efficient example of cross-linked polymeric catalysed synthesis of 7*H*-benzo[*h*]indeno[1,2-*b*]quinolin-8-one and 8*H*-naphtho[2,3-*h*]indeno[1,2-*b*]quinolin-9-one

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Abstract. Cross-linked poly(2-acrylamido-2-methyl propane sulphonic acid) (AMPS) was found to be an efficient heterogeneous catalyst for direct synthesis of 7*H*-benzo[*h*]indeno[1, 2-*b*]quinolin-8-one and 8*H*-naphtho[2, 3-*h*]indeno[1, 2-*b*]quinolin-9-one derivatives through one-pot condensation of aromatic aldehydes, 1, 3-indandione and 1-naphthylamine or 1-antharacylamine. The catalyst could be recovered conveniently and reused without any loss of activity. Mild conditions, short reaction times, simplicity, easy workup, and good to excellent yields can be mentioned as the advantages of this research.

Keywords. Polymeric catalyst; direct synthesis; indeno[1, 2-*b*]quinolinone.

1. Introduction

Quinoline derivatives are reported to possess interesting pharmacological activities such as antiplasmodial, intrinsic, cytotoxic, functional, antibacterial, antiproliferative, antimalarial and anticancer activities.[1,2] Therefore, various methods such as the Skraup, Doebner–von Miller, Friedl¨ander, and Combes procedures have been developed for the synthesis of quinoline derivatives.[3,4] Partially hydrogenated quinoline cores are also present in some important bioactive compounds; for example, the 4-aza-analogues of podophyllotoxin, a plant lignan that inhibits microtubule assembly, revealed to be more potent and less toxic anticancer agents.[5] In view of the importance of benzoquinoline and its derivatives in various fields of chemistry, biology, and pharmacology, many efforts have been devoted to their synthesis.

Synthetic approach for the synthesis of such compounds has gained attraction among chemists. In the recent years, a three-component synthesis of indeno[1, 2-*b*]quinoline-7-one derivatives under microwave irradiation was reported.[6,7] Ji's group reported a green multicomponent approach to a new series of these derivatives, consisting of the reaction of either tetronic acid or 1,3-indanedione with various aldehydes and substituted anilines in water under microwave irradiation conditions.[8]

Polymer-supported reagents have been in use for many years and have been the subject of many review articles.[9,10] Synthesis using these reagents is attractive and suitable for parallel synthesis. Utility of polymer-supported catalysts is now well-recognized because of their ease of workup and separation of products and catalysts, and from the economical point of view, and for applications for industrial processes, recyclability, greater selectivity, enhanced stability, nontoxicity and noncorrosiveness.[11,12] Therefore, it is reasonable to assume that polymeric reagents will be employed with increasing regularity to conduct one- to multistage synthetic sequences.

As a part of our ongoing research aiming to develop novel heterocyclic compounds via multicomponent reactions[13–15] and following to our first report on the synthesis of indenoquinolinone derivatives,[16] herein, the direct synthesis of new 7*H*-benzo[*h*]indeno[1,2-*b*]quinolin-8-one and 8*H*-naphtho[2,3-*h*]indeno[1,2-*b*]quinolin-9-one catalysed by poly(2-acrylamido-2-methyl propane sulphonic acid) (AMPS) cross-linked with N,N′-methylene bisacrylamide (MBA) (scheme 1) is reported.

2. Experimental

2.1 *Materials and methods*

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

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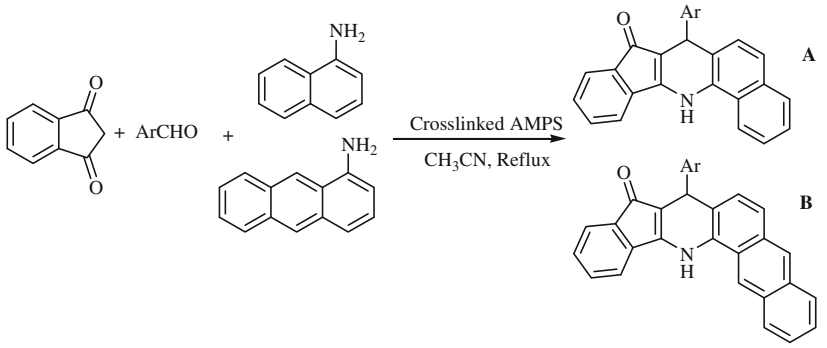


(A) Ar = C_6H_5 - (**1**); 4-$CH_3OC_6H_4$- (**2**); 4-$NO_2C_6H_4$- (**3**); 4-FC_6H_4-(**4**); 4-BrC_6H_4 (**5**); 1-naphthy-(**6**); 4-$Me_2NC_6H_4$-(**7**); 4-MeC_6H_4-(**8**).

(B) Ar = C_6H_5 - (**9**); 4-$NO_2C_6H_4$- (**10**); 2-furyl-(**11**); 4-$OMeC_6H_4$ (**12**);

Scheme 1. Synthesis of 7*H*-benzo[*h*]indeno[1,2-*b*]quinolin-8-one (**A**) and 8*H*-naphtho[2,3-*h*]indeno[1,2-*b*]quinolin-9-ones (**B**) **1–12**.

spectra were recorded on a Shimadzu-IR 470 spectrophotometer. ^{1}H NMR spectra was recorded on a Bruker 100-MHz spectrometer in DMSO as solvent and TMS as internal standard. Flash column chromatography was performed with 300 and 400 meshes silica gel and analytical thin-layer chromatography (TLC) 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 analyser. AMPS cross-linked with MBA was prepared according to our previous literature.[17]

2.2 *General procedure for synthesis of indeno[1,2-b]quinoline-7-ones*

A mixture of aryl aldehyde (1.0 equiv), 1,3-indandione (1.0 equiv), amine (1.0 equiv), polymeric catalyst (0.15 equiv), and CH_3CN (10 mL) was added to a round-bottomed flask. The mixture was heated at reflux condition for the appropriate time indicated by TLC. Upon completion the reaction, the heterogeneous catalyst was recovered by simple filtration. The catalyst was rinsed with a little amount of methanol and dried to be reused without loss of activity for further reactions. The solvent was removed from filtrate by distillation and crude product was purified by column chromatography on silica gel eluting by petroleum ether—AcOEt (5:1).

2.2a *7-Phenyl-8,13-dihydro-7H-benzo[h]indeno[1,2-b]quinolin-8-one (**1**)*: Isolated yield 90%; ^{1} HNMR: 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.

2.2b *7-(4-Methoxyphenyl)-8,13-dihydro-7H-benzo[h]indeno[1,2-b]quinolin-8-one (**2**)*: Isolated yield 90%; ^{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.

2.2c *7-(4-Nitrophenyl)-8,13-dihydro-7H-benzo[h]indeno[1,2-b]quinolin-8-one (**3**)*: Isolated yield 92%; ^{1}HNMR: 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.

2.2d *7-(4-Fluorophenyl)-8,13-dihydro-7H-benzo[h]indeno[1,2-b]quinolin-8-one (**4**)*: Isolated yield 92%; ^{1} HNMR: 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.

2.2e *7-(4-Bromophenyl)-8,13-dihydro-7H-benzo[h] indeno[1,2-b]quinolin-8-one (**5**)*: Isolated yield 90%; [1] HNMR: 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.

2.2f *7-(1-Naphthyl)-8,13-dihydro-7H-benzo[h]indeno [1,2-b]quinolin-8-one (**6**)*: Isolated yield 86%;[1] HNMR: 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.

2.2g *7-[4-(Dimethylamino)phenyl]-8,13-dihydro-7H-benzo[h]indeno[1,2-b]quinolin-8-one (**7**)*: Isolated yield 84%; [1] HNMR: 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.

2.2h *7-(4-Methylphenyl)-8,13-dihydro-7H-benzo[h] indeno[1,2-b]quinolin-8-one (**8**)*: Isolated yield 90%; [1] HNMR: 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.

2.2i *8-Phenyl-9,14-dihydro-8H-indeno[1,2-b]naphtho[2, 3-h]quinolin-9-one (**9**)*: Isolated yield 80%; [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.

2.2j *8-(4-Nitrophenyl)-9,14-dihydro-8H-indeno[1,2-b]naphtho[2,3-h]quinolin-9-one (**10**)*: Isolated yield 92%; [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.

2.2k *8-[4-(2-Furyl)phenyl]-9,14-dihydro-8H-indeno [1,2-b]naphtho[2,3-h]quinolin-9-one (**11**)*: Isolated yield 84%; [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.

2.2l *8-(4-Methoxyphenyl)-9,14-dihydro-8 H-indeno[1, 2-b] naphtho[2,3-h]quinolin-9-one (**12**)*: Isolated yield 86%; [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.

2.2m *N-(1-Anthracyl)-4-nitrobenzaldimine (intermediate **A**)*: To a solution of 4-nitrobenzaldehyde (1 mmol) in ethanol (10 ml), 1-aminonaphthalene (1 mmol) and a trace amount of *p*–toluenesulphonic acid were added. The mixture was heated under reflux for 2 h. The reaction mixture was cooled and the precipitate was filtered and crystallized from acetonitrile. The yield was 90%; IR: ν 3010, 2873, 1670, 1515, 1335, 1010, 832, 720 cm^{-1}; [1] HNMR: 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.

2.2n *2-(4-Nitrobenzylidenyl)-1,3-indanedione (intermediate **B**)*: A solution of 1,3-indanedione (1 mmol) and 4-nitrobenzaldehyde (1 mmol) in ethanol (10 ml) was heated under reflux for 2 h. Resultant precipitate was filtered, washed with ether and crystallized from acetonitrile. The yield was 80%; IR: ν 2915, 1665, 1570, 1405, 1185, 940, 810 cm^{-1}; [1] HNMR: 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.

3. Results and discussion

One-pot reaction of 1-aminonaphthalene or 1-aminoanthracene with aromatic aldehydes and 1,3-indanedione providing a series of indeno[1,2-*b*]quinolineone derivatives is described. First, the mixture of 4-nitrobenzaldehyde, 1-aminonaphthalene

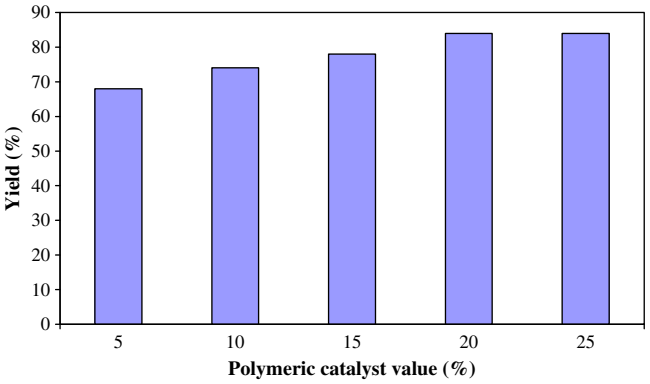


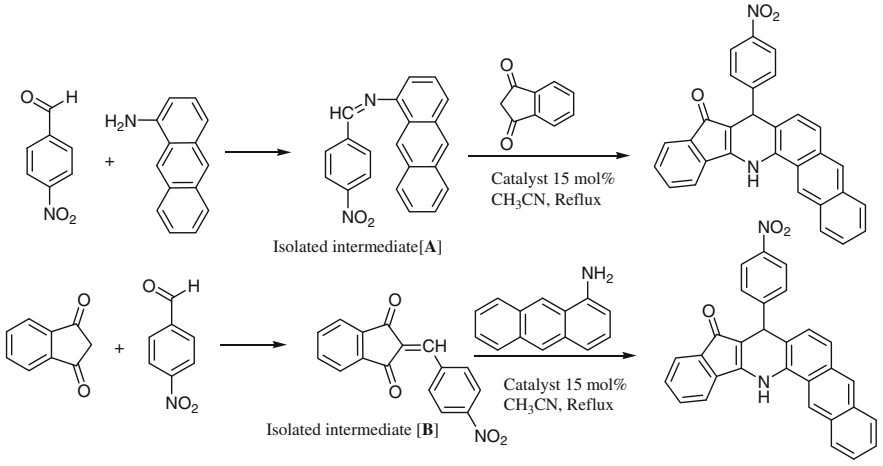
Figure 1. Optimization of quantity of polymeric catalyst for synthesise of 7-(4-nitrophenyl)-8,13-dihydro-7*H*-benzo[*h*]indeno[1,2-*b*]quinolin-8-one (**3**).

and 1,3-indandione to synthesize 7-(4-nitrophenyl)-8,13-dihydro-7*H*-benzo[*h*]indeno[1,2-*b*]quinolin-8-one (**3** in scheme 1) was chosen as the model reaction to determine the optimum value of polymeric catalyst which leads the reaction push forward efficiently. The mentioned reaction was carried out using 5, 10, 15, 20 and 25 mol% of the catalyst. As seen in figure 1, the amount of 20 mol% of cross-linked poly(2-acrylamido-2-methyl propane sulphonic acid) could be sufficient to obtain reasonable chemical yield of 85%. Furthermore, no target product was observed when the mixture was stirred under similar conditions in the absence of catalyst, even after refluxing for 8 h, thus highlighting the role of polymeric reagent as a catalyst. Reusability of the recovered catalyst using the model reaction was investigated and the catalyst was recovered successfully without any significant loss of its activity for 4 runs.

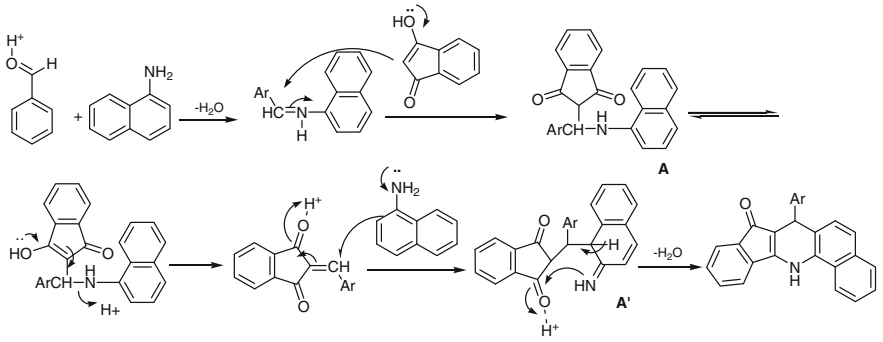
Generality of this process was demonstrated by employing the wide range of substituted aromatic aldehydes to synthesize indeno[1,2-*b*]quinolinone derivatives **1–12** (scheme 1). Various aromatic aldehydes possessing electron-withdrawing or electron-releasing substitutions were allowed to react with 1-amino naphthalene and 1,3-indanedione and all these reactions proceeded smoothly to give the corresponding 7*H*-benzo[*h*]indeno[1,2-*b*]quinolin-8-one products **1–8** in good to excellent yields (scheme 1). Encouraged by these results, attention was turned to 1-aminoanthracene, the reaction of which gave the corresponding 8*H*-naphtho[2,3-*h*]indeno[1,2-*b*]quinolin-9-ones **9–12** in good yields (scheme 1).

In order to gain an insight into the reaction mechanism, 4-nitrobenzaldehyde was allowed to react with 1-aminoanthracene and the expected Schiff base intermediate **A** was isolated and characterized. Subsequent treatment of intermediate **A** with 1,3-indanedione furnished product **11** identical with that obtained in the one-pot three-component reaction. In a similar fashion, intermediate **B** (scheme 2) from the reaction between 1,3-indanedione and 4-nitrobenzaldehyde was isolated and characterized. Its subsequent reaction with 1-aminoanthtracene also furnished compound **11**. Accordingly, both intermediates were conceivable during the synthesis.

To postulate the mechanism and figure out the true intermediate, we focused on the observation during the reaction. It was observed that upon addition of reactants into the flask, a yellow solid formed immediately which could be identified by spectral study. After analysing, it was revealed that the kinetic intermediate is a Schiff base obtained from the condensation of aldehyde and amine (intermediate **A**, scheme 2). According to this distinctive analysis, the reasonable mechanism is depicted in scheme 3. As shown, the condensation of aldehyde and aromatic amine furnished Schiff base. Addition of Schiff base to 1,3-indanone



Scheme 2. Multi-step route for synthesis of indeno[1,2-*b*]quinolinones regarding two different probable intermediates.



Scheme 3. Tentative mechanism for the synthesis of indeno[1,2-*b*]quinolinone derivatives.

then afforded intermediate **A**′, which upon intermolecular cyclization and dehydration resulted in the formation of corresponding product.

4. Conclusion

A three-component reaction yielding 7*H*-benzo[*h*] indeno[1,2-*b*]quinolin-8-one and 8*H*-naphtho[2,3-*h*] indeno[1,2-*b*]quinolin-9-one derivatives in a one-pot procedure using poly(2-acrylamido-2-methyl propane sulphonic acid) cross-linked with *N*, *N*′-methylene bisacrylamide as an efficient, acidic, heterogeneous and recyclable catalyst has been developed.

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