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Silica@PMA Core-Shell Structure as Recyclable Catalyst for the Synthesis of Quinolines

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ABSTRACT

2-Amino aryl ketones react with aliphatic ketones in 1,2-dichloroethane at room temperature in the presence of a catalytic amount of a PMA-Silica catalyst to afford the corresponding quinolines in high yields. The supported catalyst exhibited excellent activity and stability and it could be reused for at least six times without any loss of activity.

Keywords: PMA-SiO₂, Heterogeneous catalysis, Aryl ketones, Quinolines

INTRODUCTION

Most of the natural and synthetic compounds are containing one of the most important hetero cyclic compound quinoline.¹ Quinoline is a colourless, hygroscopic, strong odor compound, slightly soluble in water and sparingly soluble in all organic solvents. Diversity analogues containing quinolines are biologically active towards various diseases.² Most of the natural and synthetic compounds having quinoline derivatives are attractive N-containing heterocycles and these heterocyclic scaffolds have great significance in the fields of medicinal³ and industrial chemistry,⁴ and have attracted much interest in synthetic chemistry and medicinal chemistry. These compounds exhibit various biological activities, such as anti-inflammatory,⁵ antibacterial,⁶ antiviral,⁷ anti-HIV⁸ and antitumor properties.⁹ Some of the highly demanded drugs containing quinoline moiety are shown in Figure 1. In addition to that, quinolines have been widely used in the preparation of nano structures in the field of organic light-emitting diodes.

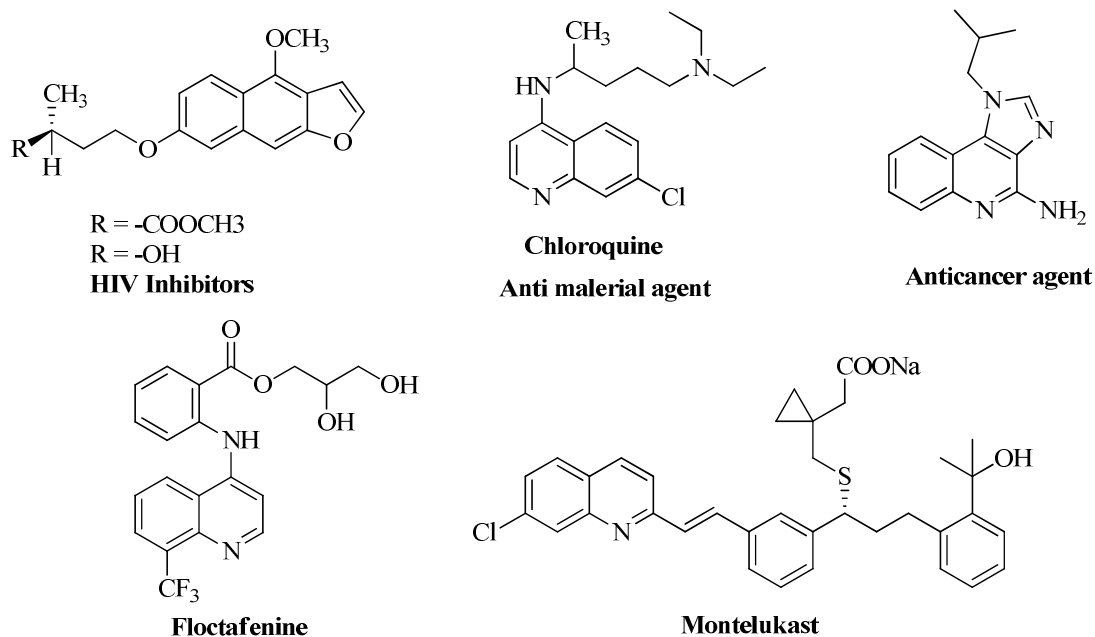


Figure 1: Biologically active quinoline derivatives

Because of the wide range of applications for quinoline based analogues, many research groups have developed various methods for their synthesis by using a variety of catalysts like Cu/Pd,¹⁰ ruthenium,¹¹ Au¹², Brønsted acids,¹³ transition metals,¹⁴ Lewis acids,¹⁵ proline,¹⁶ molecular iodine,¹⁷ and ionic liquids¹⁸ in different conditions. Among them, one of the best protocol for the development of quinoline is Friedlander annulations which involves a condensation and cyclization reaction between a ketone possessing an active methylene group and an aromatic 2-aminoaldehyde or ketone. However, many of these methods suffered from expensiveness of catalyst, high reaction temperature, require more time to complete the reaction, low yields and hectic process to isolate the product. As part of our ongoing research in developing various synthetic methodologies for the preparation of heterocycles, herein we report, the synthesis of quinolines using PMA absorbed silica which is a recyclable and reusable catalyst. The catalyst PMA-Silica is known in the literature for a range of organic transformations.

MATERIALS AND METHODS

Melting points were recorded by using Buchi R-535 instrument and are uncorrected. NMR spectra were recorded on either a Bruker Advance 300 or Advance 400 spectrometer. Chemical shifts (d) are given in ppm using internal references or TMS as external reference for CDCl₃. Mass spectra were recorded on Finnigan MAT 1020 mass spectrometer operating at 70 eV.

Procedure for Preparation of PMA-Silica Catalyst: An equimolar amount of PMA and silica was taken in a 50 ml of round bottom flask then Dichloromethane in excess amount were added, and stirred for 20 minutes at room temperature, PMA silica supported catalyst was obtained as a free flowing powder after evaporation of dichloromethane at room temperature this powder dried at 120°C for 2 hr. and stored in desiccator over CaCl₂.

3.3. General Reaction Procedure: To a mixture of 2-Amino aryl ketones **1a** (1.0 mmol) and aliphatic ketones **2a** (1.1 mmol) in dichloroethane (5 mL), PMA-Silica (1 mol%) was added and the mixture was stirred at 40°C for 65 min. Reaction was monitored by thin layer chromatography (TLC) until total disappearance of the starting material. After completion of the reaction, the catalyst was recovered by filtration, then washed with dichloroethane and it is used for next reaction. The resulting mixture was evacuated by using rotary evaporator and the solid product was purified by column chromatography.

3.4. Selected Spectroscopic Data

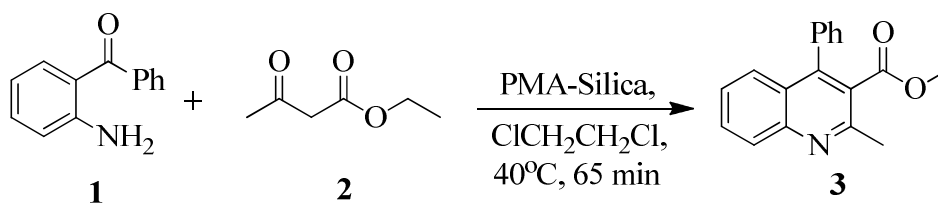
Ethyl 2-methyl-4-phenylquinoline-3-carboxylate (**3b**) : Solid. Melting range 98-99 °C. IR (KBr): 3030, 2960, 1700, 1605, 1568, 1482, 905 cm^{-1} . $^1\text{H NMR}$ (300 MHz CDCl_3) (δ/ppm): 1.30 (t, 3H, $J=7.0$ Hz), 2.80 (s, 3H), 4.20 (q, 2H, $J=7.0$ Hz), 7.30-7.60 (m, 6H) 7.75 (d, 1H, $J=8.1$ Hz), 7.80 (t, 1H, $J=7.9$ Hz), 8.10 (d, 1H, $J=8.1$ Hz). $^{13}\text{C NMR}$ (75 MHz, CDCl_3) (δ/ppm): 13.65, 23.32, 68.81, 96.14, 125.1, 126.1, 126.4, 127.8, 128.2, 129.1, 129.5, 135.7 (2C), 135.7, 145.7, 147.8, 153.6, 167.7. MS (ESI) m/z 291 ($M+1$); HRMS (ESI) calcd. For $\text{C}_{19}\text{H}_{17}\text{NO}_2$ ($M+1$) $^+$ 291.1259, Found 291.1254.

9-Methyl-1, 2, 3, 4-tetrahydroacridine (**3c**): Solid. Melting range. 75-77°C. IR (KBr): 2928, 1569, 1478, 1348, 1164, 1076, 939, 839, 819, 775, 752, 708, cm^{-1} . $^1\text{H NMR}$ (300 MHz CDCl_3) (δ/ppm): 1.55-1.65 (m, 4H), 2.55 (s, 3H), 2.90 (t, 2H, $J=7.6$ Hz), 3.10 (t, 2H, $J=7.6$ Hz), 7.40-7.95 (m, 4H). $^{13}\text{C NMR}$ (75 MHz, CDCl_3) (δ/ppm): 12.91, 22.36, 22.74, 26.53, 33.92, 122.75, 124.54, 126.61 (2C), 127.65, 128.43, 140.77, 145.44, 161.95. MS (ESI) m/z 198 (M^+); HRMS (ESI) calcd. For $\text{C}_{14}\text{H}_{15}\text{N}$ ($M+$) 197.1204, found 197.1207.

1-(6-Chloro-2-methyl-4-phenylquinolin-3-yl) ethanone (**3g**) : Solid. Melting range. 149-150°C. IR (KBr): 3029, 2960, 1701, 1606, 1567, 1481, 909, 602 cm^{-1} . $^1\text{H NMR}$ (300 MHz CDCl_3) (δ/ppm): 1.98 (s, 3H), 2.66 (s, 3H), 7.30-7.20 (m, 7H), 8.00 (d, 1H, $J=8.9$ Hz). $^{13}\text{C NMR}$ (75 MHz, CDCl_3) (δ/ppm): 23.58, 31.60, 124.71, 125.82, 128.83, 129.11, 129.84, 130.85, 132.27, 134.49, 135.46, 142.95, 145.86, 153.87 (2C), 204.91; MS (ESI) m/z 296 ($M+1$); HRMS (ESI) calcd. For $\text{C}_{19}\text{H}_{17}\text{NO}_2$ ($M+1$) $^+$ 295.0764; found: 295.0761.

RESULTS AND DISCUSSION

Initially, we have chosen (2-aminophenyl)(phenyl)methanone **1a** and ethyl 3-oxobutanoate **2a** as model substrates to establish the reaction conditions for this reaction and some experiments were performed to synthesize the corresponding quinoline **3a** (Table 1). We started our studies by dissolving the starting materials (2-aminophenyl)(phenyl)methanone **1a** (1.0 mmol) with ethyl 3-oxobutanoate **2a** (1.0 mmol) at room temperature for 2h, without catalyst. Under these conditions, no product **3a** was formed (Table 1, entry 1). In presence of PMA-Silica (1 mol%) catalyst, the same reaction gave the expected product in 54% yield. Excellent yields of product **3a** was achieved in a reaction carried out in 1,2-dichloroethane at 80°C using 1 mol% of catalyst in 65 min. When the amount of catalyst was raised to 2 mol%, no change in the yield of product **3a** was observed. Finally, the reaction was performed using 1 mol% of PMA-Silica at 40°C temperature for 65 min.



Scheme 1: Synthesis of Quinolines

In order to extend the scope of the reaction, the best conditions were employed in reactions of 2-Amino aryl ketones **1a-c** with other Aliphatic ketones **2a-d** with different patterns of substitution and the results are summarized in Table 2. Based on these results, this methodology is found to be very much suitable to synthesize various ketones. As it can be seen in Table 2 (Entries 1-5), our methodology is suitable to a range of substituted 2-Amino aryl ketones containing electron-withdrawing groups, affording excellent yields to desired products in all examples. In addition, the possibility of performing the reaction of 2-Amino aryl ketones **1a-e** with *o*-aliphatic ketones (**2b**) was also investigated (Table 2, entries 6-10). Using these substrates, a range of substituted quinolines were obtained in excellent yields using the phospho-molybdic acid absorbed on silica as catalyst under optimized reaction conditions.

Table 2. PMA-Silica promoted synthesis of quinolines from 2-amino aromatic carbonyl compounds

| Entry | 2-Amino aryl ketones (1) | Aliphatic ketones (2) | Product (3) | Time(min) | Yield(%) ^b |
|-------|--------------------------|-----------------------|-------------|-----------|-----------------------|
| (1) | | | | 65 | 98 |
| (2) | | | | 70 | 92 |
| (3) | | | | 70 | 94 |
| (4) | | | | 80 | 90 |
| (5) | | | | 70 | 92 |
| (6) | | | | 80 | 88 |
| (7) | | | | 59 | 89 |
| (8) | | | | 60 | 94 |
| (9) | | | | 74 | 90 |
| (10) | | | | 70 | 97 |

^aReaction conditions: 2-Amino aryl ketones (1.0 mmol), aliphatic ketones (1.1 mmol), PMA-Silica (5mol %), 1,2 Dichloroethane (5 mL); Nitrogen atmosphere was used. ^bIsolated yield.

Reused runs were carried out under similarly optimized conditions using 2-Amino aryl ketones react with aliphatic ketones and PMA-Silica catalyst (1 mol%) at 40°C in 10 mL of 1,2 dichloroethane. The catalyst showed excellent recoverability and reusability over 6 successive runs under the same conditions as the first run. The PMA-Silica

catalyst was found to be highly stable and reusable under the investigated conditions (up to 6 runs) without any significant loss of its catalytic activity (Table 3).

Table 3. Reuse of the PMA-Silica catalyst in the reaction of 2-Amino aryl ketones with Aliphatic ketone (2a)

| Run No. ^a | 1 | 2 | 3 | 4 | 5 | 6 |
|------------------------|----|----|----|----|----|----|
| Yield (%) ^b | 98 | 98 | 96 | 93 | 90 | 89 |

^a Reaction conditions: 2-Amino aryl ketones (5.0 mmol) and Aliphatic ketones (5.0 mmol), PMA-Silica (0.05 mmol, 0.165 g) in Dichloroethane (10 mL) at room temperature for 90 min. ^b Isolated yields.

CONCLUSION

In summary, we have developed PMA-Silica catalyzed synthesis of quinolines in excellent yields from 2-Amino aryl ketones and aliphatic ketones. Reactions could efficiently afford the target products after short reaction times. The reactions were carried in air with mild reaction conditions and required low loadings of the supported catalyst. The catalyst was found to be highly reusable for at least six reaction runs under the investigated conditions.

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