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**Short Communication**

# Two component reaction for the synthesis of Quinolines in the presence of γ-$Al_2O_3$ and Cu/ZnO nanoparticles

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**ABSTRACT**

Two-component reaction of 2-aminobenzophenones with acetylenic esters in the presence of γ-$Al_2O_3$ and Cu/ZnO as suitable heterogeneous catalysts has been studied. Nano γ-$Al_2O_3$ and Cu/ZnO showed high activities when used as surface catalysts for the synthesis of quinoline derivatives. After completion of the reaction, the catalyst was recovered and reused several times under the same reaction conditions.

**Keywords:** *Nano γ-$Al_2O_3$; Nano Cu/ZnO; Acetylenic esters; Quinoline; 2-Aminobenzophenones.*

## INTRODUCTION

The application of nanocatalysts has been an emerging strategy for the preparation of organic species. In this method new molecules can be synthesized under moderate conditions. Inorganic nanomaterials such as metal and metal oxide nanoparticles have very interesting applications as active absorbents [1-7]. Also, they can be used as surface catalysts for the synthesis of organic compounds because their surface exhibit both Lewis acid and Lewis base character [8]. As the size of a catalyst decreases, the surface to volume ratio will be increased [9]. Due to these properties, various organic transformations have been reported on the surface of nanocatalysts [10-11]. Nano metal oxides such as $TiO_2$, CaO, $Al_2O_3$ and Cu/ZnO have been investigated by many researchers to carry out organic reactions [12-14].

## EXPERIMENTAL

$^1$HNMR spectra were recorded on BRUCKER DRX-500 AVANCE spectrometer at 400.13 MHz with $CDCl_3$ as solvent. IR spectra were recorded on a Shimadzu IR-470 spectrometer. Melting points were measured by a thermo scientific apparatus.

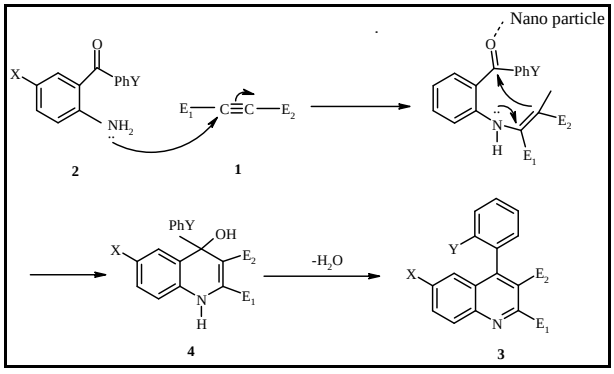
$^1$HNMR spectra were recorded on BRUCKER DRX-500 AVANCE spectrometer at 400.13 MHz with $CDCl_3$ as solvent. IR spectra were recorded on a Shimadzu IR-470 spectrometer. Melting points were measured by a thermo scientific apparatus. The nano catalysts were purchased from the NANOPAC Persia company, Iran. TLC was carried out on Fluka Silica gel TLC-cards. All other reagents and solvents were used as received from commercial suppliers.

***General procedure for the preparation of 4-arylquinolines (exemplified by 3a)***

To a magnetically stirred solution of 2-amino benzophenone (2 mmol) and dimethyl acetylenedicarboxylate (2 mmol) in EtOAc (5 ml) was added nano $Al_2O_3$ (5 mol %). The reaction mixture was refluxed for 3 h. The reaction progress was monitored by TLC. Then, the solid product was filtered and the nano catalyst was removed by centrifuge and pure product 3a was obtained as pure crystal. The nanocatalyst was recovered to be reused several times with slight decrease in activity. The structure of the product was confirmed by melting point, IR and $^1$HNMR spectra. The results were compared with authentic samples.

***Characterization***

The reaction mechanism has been shown in Scheme 1. The initial attack of nucleophilic amine to the acetylenic ester leads to the formation of intermediate 4 on the surface of nano catalyst which can act as lewis acid to increase the electrophilicity of the carbonyl group of 2-aminobenzophenone [15-17]. Then, the product 3 is formed by water removing under reflux condition (Scheme 1).




**Scheme. 1.** Mechanism of the synthesis of quinolines

We monitored the solvent effect, temperature dependency and the amount of different nanocatalyst during the time of completion of the reaction. To study the optimized condition of the reaction parameters, the reaction between 2-amino benzophenone and DMAD was chosen as the model reaction. The effect of different solvents was monitored and the excellent results were obtained when the reaction has been carried out in EtOAc. The temperature monitoring showed that the best temperature for this reaction is the reflux condition for 3 hour. Also, when the reaction was scaled up to 5 mol% of nanocatalyst, the highest yield was achieved (Table 1).

**Table 1.** Effect of various solvents on the yield of dimethyl 4-phenyl-2, 3-quinolinedicarboxylate (3a) in the presence of nano $Al_2O_3$ (Method A) and nano Cu/ZnO (Method B)

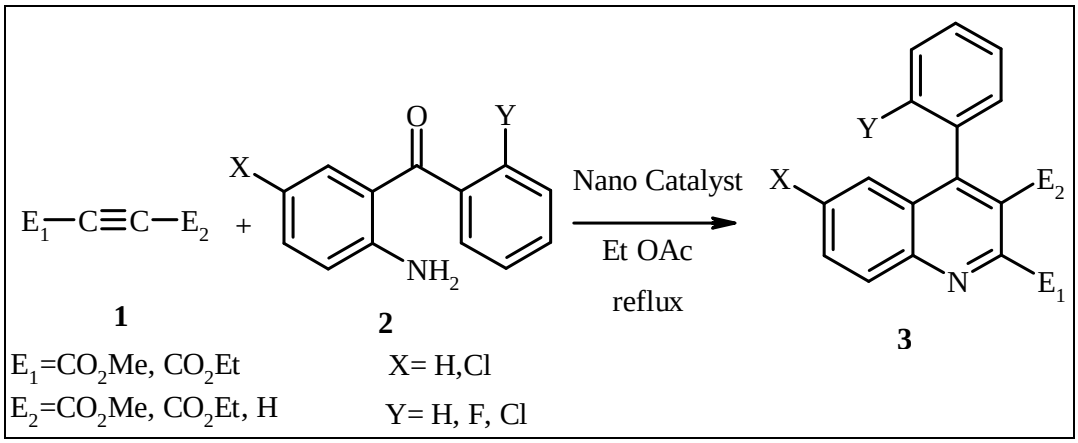
| Entry | Solvent | Time (h) | Method A /Yield (%) | Method B /Yield (%) |
|---|---|---|---|---|
| 1 | Dichloromethane | 10 | 35 | 20 |
| 2 | Chloroform | 8 | 47 | 28 |
| 3 | Acetone | 7 | 66 | 40 |
| 4 | Toluene | 5 | 70 | 65 |
| 5 | Ethyl acetate | 3 | 88 | 92 |

Conditions: Method A (5 mol%, reflux), Method B (5 mol%, reflux)

## RESULTS AND DISCUSSION

Synthesis of 4-arylquinolines *via* a three-component reaction of acetylenic esters and 2-amino benzophenone derivatives in the presence of triphenylphosphine has been reported previously in our lab [15, 17]. In our continuous efforts to optimize the reaction conditions for the synthesis of quinoline derivatives, the catalytic activities of nano $Al_2O_3$ and nano Cu/ZnO have been investigated in the two-component reaction of 2-amino benzophenones and acetylenic esters (Scheme 2).

The yields of the reactions show that nano $Al_2O_3$ and Cu/ZnO catalyze these reactions efficiently. The results show that by using nano Cu/ZnO, higher yields of the products can be obtained (Table 2).




**Scheme. 2.** Synthesis of quinolines in the presense of γ-$Al_2O_3$ and Cu/ZnO nanoparticles

**Table 2.** Synthesis of 4-arylquinolines 3a-l in EtOAc using nano $Al_2O_3$ (Method A) and nano Cu/ZnO (Method B) as catalysts

| product | $E_1$ | $E_2$ | X | Y | Yield (%) | |
|---|---|---|---|---|---|---|
| | | | | | Method A | Method B |
| **3a** | $CO_2Me$ | $CO_2Me$ | H | H | 88 | 92 |
| **3b** | $CO_2Et$ | $CO_2Et$ | H | H | 86 | 90 |
| **3c** | H | $CO_2Me$ | H | H | 90 | 95 |
| **3d** | H | $CO_2Et$ | H | H | 85 | 89 |
| **3e** | $CO_2Me$ | $CO_2Me$ | Cl | H | 83 | 85 |
| **3f** | $CO_2Et$ | $CO_2Et$ | Cl | H | 90 | 92 |
| **3g** | H | $CO_2Me$ | Cl | H | 69 | 70 |
| **3h** | H | $CO_2Et$ | Cl | H | 74 | 75 |
| **3i** | $CO_2Me$ | $CO_2Me$ | Cl | Cl | 76 | 80 |
| **3j** | $CO_2Et$ | $CO_2Et$ | Cl | Cl | 89 | 90 |
| **3k** | $CO_2Me$ | $CO_2Me$ | Cl | F | 94 | 95 |
| **3l** | $CO_2Et$ | $CO_2Et$ | Cl | F | 94 | 95 |

Conditions: Method A (5 mol%, reflux), Method B (5 mol%, reflux)

## CONCLUSIONS

In conclusion, we studied an efficient procedure for the synthesis of quinoline derivatives on the surface of two nanoparticles γ-$Al_2O_3$ and Cu/ZnO as advantageous heterogeneous nanocatalyst. The method offers ease of the work-up, high yields of products and short reaction times.

### *Spectroscopic data*

- **Dimethyl4-phenyl-2,3-quinolinedicarboxylate (3a)**

White powder; yield: 90 %, m.p. 123-125 ˚C. IR (KBr) ($\upsilon_{max}$, $cm^{-1}$): 3050 ($C_{sp2}$-H), 2995

($C_{sp3}$-H), 1725 (CO); $^1$H NMR (400.13, $CDCl_3$): $\delta_H$ 3.61(s, 3H, OCH) ,4.04 (s, 3H, OCH), 7.34 (dd, $^3J_{HH}$ = 6.4 Hz, $^3J_{HH}$ = 2.0 Hz, 2H, 2CH) 7.47 (d, $^3J_{HH}$ = 2.0 Hz, 2H, 2CH), 7.48 (t,$^3J_{HH}$ = 6.4 Hz, 1H , CH), 7.55 (t,$^3J_{HH}$ = 7.7 Hz, 1H, CH), 7.62 (d, $^3J_{HH}$ = 7.7 Hz , 1H, CH), 7.79 (ddd, $^3J_{HH}$ = 8.5 Hz , $^3J_{HH}$ = 7.7 Hz, $^4J_{HH}$ = 1.4 Hz, 1H, CH), 8.3 (d, $^3J_{HH}$ = 8.5 Hz ,1 H, CH)

- **Diethyl 4-phenyl-2,3-quinolinedicarboxylate (3b)**

White powder; yield: 87 %, m.p. 95-97 ˚C. IR (KBr) ($\upsilon_{max}$, $cm^{-1}$): 3030 ($C_{sp2}$-H), 2985 ($C_{sp3}$-H), 1728(CO); $^1$H NMR (400.13, $CDCl_3$): $\delta_H$ 0.96 (t, $^3J_{HH}$ = 7.1 Hz, H, $CH_3$ ), 1.43(t, $^3J_{HH}$ = 7.1 Hz, 3H, $CH_3$), 4.06(q, $^3J_{HH}$ = 7.1 Hz, 2H, $OCH_2$), 4.50(q, $^3J_{HH}$ = 7.1 Hz, 2H), 7.33 (dd, $^3J_{HH}$ = 6.5 Hz, $^3J_{HH}$ = 2.2 Hz, 2H, 2CH), 7.45 (d, $^3J_{HH}$ = 2.2 Hz, 2H, 2CH), 7.46 (t,$^3J_{HH}$ = 6.5 Hz, 1H , CH), 7.53 (t,$^3J_{HH}$ = 7.8 Hz, 1H, CH), 7.59 (d, $^3J_{HH}$ = 7.8 Hz, 1H, CH), 7.79 (ddd, $^3J_{HH}$ = 8.5 Hz , $^3J_{HH}$ = 7.8 Hz, $^4J_{HH}$ = 1.4 Hz, 1H, CH), 8.29 (d, $^3J_{HH}$ = 8.5 Hz , 1 H, CH)

- **Methyl 4-phenyl-2-quinoline carboxylate (3c)**

White powder; yield: 60 %, m.p. 101-103 ˚C. IR (KBr) ($\upsilon_{max}$, $cm^{-1}$): 3010 ($C_{sp2}$-H), 2995 ($C_{sp3}$-H), 1725 (CO)

- **Ethyl 4-phenyl-2-quinolinecarboxylate (3d)**

White powder; yield: 65 %, m.p. 125-127 ˚C. IR (KBr) ($\upsilon_{max}$, $cm^{-1}$): 3045 ($C_{sp2}$-H), 2985 ($C_{sp3}$-H), 1724 (CO)

- **Dimethyl 6-chloro-4-phenyl-2,3-quinolinedicarboxylate (3e)**

White powder; yield: 80 %, m.p. 158-160 ˚C. IR (KBr) ($\upsilon_{max}$, $cm^{-1}$): 3074 ($C_{sp2}$-H), 2958 ($C_{sp3}$-H), 1732 and 1729 (CO)

- **Diethyl 6-chloro-4-phenyl-2,3-quinolinedicarboxylate (3f)**

White powder; yield: 90 %, m.p. 165-167 ˚C. IR (KBr) ($\upsilon_{max}$, $cm^{-1}$): 3075 ($C_{sp2}$-H), 2988 ($C_{sp3}$-H), 1739 and 1724 (CO)

- **Methyl 6-chloro-4-phenyl-2-quinolinecarboxylate (3g)**

White powder; yield: 70 %, m.p. 177-179 ˚C. IR (KBr) ($\upsilon_{max}$, $cm^{-1}$): 3054 ($C_{sp2}$-H), 2998 ($C_{sp3}$-H), 1719 (CO)

- **Ethyl 6-chloro-4-phenyl-2-quinolinecarboxylate (3h)**

Yellow powder; yield: 75 %, m.p. 172-174 ˚C. IR (KBr) ($\upsilon_{max}$, $cm^{-1}$): 3064 ($C_{sp2}$-H), 2983 ($C_{sp3}$-H), 1729 (CO)

- **Dimethyl 6-chloro-4-(2-chlorophenyl)-2,3-quinolinedicarboxylate (3i)**

Yellow powder; yield: 74 %, mp 190-192 ˚C. IR (KBr) ($\upsilon_{max}$, $cm^{-1}$): 3070 ($C_{sp2}$-H), 2985 ($C_{sp3}$-H), 1729 and 1720 (CO)

- **Diethyl 6-chloro-4-(2-chlorophenyl)-2,3-quinolinedicarboxtlate (3j)**

White powder; yield: 87 %, mp 127-129 ˚C. IR (KBr) ($\upsilon_{max}$, $cm^{-1}$): 3074 ($C_{sp2}$-H), 2983 ($C_{sp3}$-H), 1729 and 1724 (CO)

- **Dimethyl 6-chloro-4-(2-fluorophenyl)-2,3-quinolinedicarboxylate (3k)**

White powder; yield: 92 %, mp 210-212 ˚C. IR (KBr) ($\upsilon_{max}$, $cm^{-1}$): 3079 ($C_{sp2}$-H), 2953 ($C_{sp3}$-H), 1729 and 1718 (CO)

- **Diethyl 6-chloro-4-(2-fluorophenyl)-2,3-quinolinedicarboxylate (3l)**

White powder; yield: 95 %, mp 135-137 ˚C. IR (KBr) ($\upsilon_{max}$, $cm^{-1}$): 3084 ($C_{sp2}$-H), 2983 ($C_{sp3}$-H), 1729 and 1719 (CO)

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