



# COPPER-NICKEL TARTARATES COMPOSITES: A REUSABLE AND GREEN CATALYSTS FOR THE SYNTHESIS OF QUINOLINES AND DIHYDROPYRIMIDINES DERIVATIVES

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A series of Cu-Ni tartarate composites at various compositions is prepared and used as green catalyst for the synthesis of quinoline and dihydropyrimidine derivatives. Time required for the completion of reaction using such new catalyst is comparatively less and affording high percentage yield of products.

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precursor of 8-hydroxy quinoline which is a versatile chelating agent and precursor to pesticides. Oxidation of quinoline affords quinolinic acid, a precursor to herbicide sold under the name "Assert". These compounds were synthesized by different methods reported using various catalysts.<sup>7-17</sup>

## INTRODUCTION

A wide range of organic reactions take place only in presence of suitable catalyst under suitable conditions. Different organic reactions have been reported using various heterogeneous catalysts such as synthesis of spirochromenes and spiroacridines,<sup>1</sup> and 3,4-dihydropyrimidinones<sup>2</sup> using ammonium chloride. A novel method is reported for the synthesized 3,4,5-trisubstituted furan-2(5H)-ones by the three component reaction between aldehyde, amine and diethyl acetylene dicarboxylate using  $\beta$ -cyclodextrin supramolecule and  $\text{SnCl}_2 \cdot 2\text{H}_2\text{O}$  as catalyst respectively.<sup>3-4</sup>

Several natural products possessing interesting biological activities containing the dihydropyrimidine-5-carboxylate core have recently been isolated. An electron donating group at *para* position of the aromatic aldehydes readily gives dihydropyrimidines (DHPMS) as compare to electron withdrawing groups.

Biginelli reaction was invented for the synthesis of pyrimido[4,5-d]pyrimidine via one-pot condensation of 1,3 diketone, urea and aldehydes. Recently, the modification of Biginelli reaction is reported using catalyst  $\text{KHSO}_4$ <sup>5</sup> and other basic catalysts.<sup>6</sup>

Quinoline derivatives also called 1-azanaphthalene or benzo[b] pyridine received increasing attention due to their wide biological and pharmacological activities. These derivatives belongs to important heterocyclic compounds that constitute core structure of many naturally occurring substance that have interesting biological & pharmaceutical properties like anti-malarial, anti-inflammatory, anti-microbial, anti-cancer, anti-HIV, etc. It is used as a principal

Previously, we have synthesized and characterized mixed metal oxalate and tartarate complexes.<sup>18-19</sup> Present investigation focuses on the synthesis of quinoline and dihydropyrimidine derivatives using different composition of copper nickel tartarates  $[\text{Cu}_x\text{Ni}_{1-x} (\text{C}_4\text{H}_4\text{O}_6)] \cdot \text{H}_2\text{O}$  as catalysts.

## Experimental

All chemicals used were of analytical grade and used without further purifications. Copper-Nickel tartarates with different composition ( $x = 0.2$  to  $1.0$ ) were prepared and characterized by the methods and techniques reported earlier.<sup>18-19</sup>

### Synthesis of quinolines

In a 50 mL round bottom flask, to a mixture of substituted anilines (1 mol) and ethylacetoacetate (1 mol) 5 mol % catalyst in ethanol (15 mL) was added. The reaction mixture was refluxed at 120 °C for appropriate time. After completion of reaction (confirmed by TLC), the reaction mixture was diluted with cold water. The separated solid product was filtered on suction pump, washed several times with cold water. The crude product was recrystallized from ethanol solvent. The product formation was confirmed on the basis of melting point and spectral data analysis. Using the same procedure other derivatives has been also prepared and confirmed by spectral analysis.

### Synthesis of dihydropyrimidines

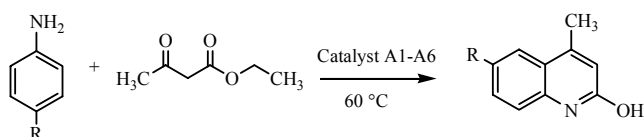
In a typical procedure, to a mixture of 1.10 mL of benzaldehyde (1 mol), 1.30 mL of ethylacetoacetate (1 mol),

0.9 g of urea (1 mol) and catalytic amount of Cu-Ni tartarate composites (six different weight proportions) was refluxed for 4 to 4.30 h. It was cooled to room temperature and poured onto ice cold water. The separated solid product was filtered and recrystallized using ethanol solvent. Above experimental procedure of dihydropyrimidines synthesis is repeated for the synthesis of other derivatives confirmed on the basis of melting points and spectral analysis.

## Results and discussion

In continuation of our earlier work, various quinolines have been synthesized by the cyclocondensation of aromatic amines with different 1,3 diketone using Cu-Ni-Tartarate composites as a catalyst (Scheme 1).

The reaction time and the yield of product of the reaction of substituted aniline with ethyl acetoacetate are given in table 1.

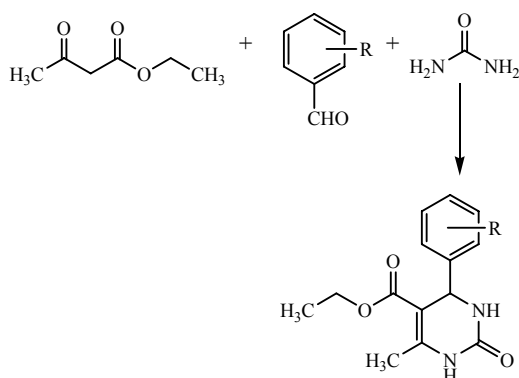


Scheme 1. Synthesis of quinolines.

Table 1. Synthesis of substituted quinolines.

S. No.	R	Time (Min)	Yield (%)
1	H	20	90
2	Cl	10	89
3	Br	15	90
4	NO <sub>2</sub>	25	91
5	OMe	15	87
6	Me	18	82

Synthesis of Biginelli dihydropyrimidines and their derivatives has been carried out by the condensation of 1,3 diketone, urea and aldehydes using Cu-Ni-Tartarate composites as a catalyst (Scheme-2).



Scheme 2. Synthesis of Biginelli dihydropyrimidines.

The reaction time and the yield of products of the reaction of different aromatic aldehydes with ethyl acetoacetate are given in Table 2.

Table 2. Synthesis of Biginelli dihydropyrimidines.

S. No.	Ar	Time, h	Yield	m. p., °C
1	C <sub>6</sub> H <sub>5</sub>	1.30	92 %	205-207
2	4-OHC <sub>6</sub> H <sub>4</sub>	1.35	94 %	221-222
3	4-OCH <sub>3</sub> C <sub>6</sub> H <sub>4</sub>	1	92 %	198-200
4	4-OH-3-OCH <sub>3</sub> C <sub>6</sub> H <sub>3</sub>	1.45	91 %	257-259
5	3,4-(OCH <sub>3</sub> ) <sub>2</sub> C <sub>6</sub> H <sub>3</sub>	1.15	88 %	172-173
6	4-NO <sub>2</sub> C <sub>6</sub> H <sub>4</sub>	1	87 %	209-211
7	4-ClC <sub>6</sub> H <sub>4</sub>	1.2	92 %	211-213
8	4-BrC <sub>6</sub> H <sub>4</sub>	1.5	92 %	212-214
9	3-NO <sub>2</sub> C <sub>6</sub> H <sub>4</sub>	1.2	90 %	208-201
10	2-ClC <sub>6</sub> H <sub>4</sub>	1.2	94 %	213-215
11	2-Furyl	1.2	89 %	208-210

It is observed that Cu-Ni tartarates composites behave as suitable catalyst in the synthesis of quinoline and dihydropyrimidine derivatives. During synthesis of quinolines and dihydropyrimidines, the time required for completion of reaction using new catalyst is comparatively less. Percentage yield of products are slightly higher in presence of new catalyst for the synthesis of quinolines and dihydropyrimidines. These composites have active centre present in the structure and behave like Lewis acid, hence show a powerful catalytic activity toward synthesis of quinoline and dihydropyrimidine derivatives. Moreover, the catalyst is reusable, thus used several time in reactions without losing their efficiency.

It is further noted that new catalyst having higher percentage of Cu/Ni-tartarate is remarkably more active for the synthesis of quinolines (Table 3 and Table 4). The catalytic activity of A1 Cu/Ni-tartarate can be explained on the basis of more active centers and more surface area present as compare to other catalysts. Activity of new catalysts also depends on temperature. As the reaction temperature changes from room temperature up to 60 °C, the time required for completion of reaction is reduced and yield of product quinolines also increases to certain extent.

Similarly, new catalyst having more percent of Ni/Cu-tartarate is remarkably more active for the synthesis of dihydropyrimidines (Table 5 and Table 6). The catalytic activity of A4 Ni/Cu-tartarate may be explained on the basis of more active centers and more surface area present as compare to other catalyst. Activity of new catalysts also depends on temperature. As the reaction temperature changes from room temperature upto 80 °C, it is observed that the time required for completion of reaction is less and also yield of product dihydropyrimidines increases to certain extent. This temperature effect is due to the fact that, at higher temperature available kinetic energy is more than that of room temperature. It is observed that electron donating group at *para* position readily gives DHPMS as compare to electron withdrawing groups at respective positions of aromatic aldehydes.

**Table 3.** Time required for completion and yield of Quinoline using new catalysts.

Catalyst	Time of	% Yield
InCl <sub>3</sub> (Control)	125	75
A1 - Cu(0.8)Ni(0.2) (C <sub>4</sub> H <sub>4</sub> O <sub>6</sub> ).x H <sub>2</sub> O	30	81
A2 - Cu(0.6)Ni(0.4) (C <sub>4</sub> H <sub>4</sub> O <sub>6</sub> ).x H <sub>2</sub> O	28	86
A3 - Cu(0.4)Ni(0.6) (C <sub>4</sub> H <sub>4</sub> O <sub>6</sub> ).x H <sub>2</sub> O	25	91
A4 - Cu(0.2)Ni(0.6) (C <sub>4</sub> H <sub>4</sub> O <sub>6</sub> ).x H <sub>2</sub> O	40	78
A5 - Cu(C <sub>4</sub> H <sub>4</sub> O <sub>6</sub> ).x H <sub>2</sub> O	45	80
A6 - Cu(0.1) (C <sub>4</sub> H <sub>4</sub> O <sub>6</sub> ). x H <sub>2</sub> O	47	77

**Table 4.** Effect of reaction temperature on the yield of quinoline using catalyst A3.

S. No.	Reaction	Time for	% Yield
1	23 °C	25 min	26
2	75 °C	25 min	71
3	100 °C	25 min	82
4	120 °C	25 min	91

**Table 5.** Time required for completion and yield of dihydropyrimidines using new catalysts.

Catalyst	Time of	%
Conc. HCl (Control)	4 to 4.30	70
A1 - Cu(0.8)Ni(0.2)(C <sub>4</sub> H <sub>4</sub> O <sub>6</sub> ).x H <sub>2</sub> O	3.00 to 3.30	72
A2 - Cu(0.6)Ni(0.4) (C <sub>4</sub> H <sub>4</sub> O <sub>6</sub> ).x H <sub>2</sub> O	3.15 to 3.30	69
A3 - Cu(0.4)Ni(0.6) (C <sub>4</sub> H <sub>4</sub> O <sub>6</sub> ).x H <sub>2</sub> O	2.30 to 2.45	73
A4 - Cu(0.2)Ni(0.6) (C <sub>4</sub> H <sub>4</sub> O <sub>6</sub> ).x H <sub>2</sub> O	1.30 to 2.00	84
A5 - Cu(C <sub>4</sub> H <sub>4</sub> O <sub>6</sub> ).x H <sub>2</sub> O	1.30 to 2.00	65
A6 - Cu(0.1) (C <sub>4</sub> H <sub>4</sub> O <sub>6</sub> ). x H <sub>2</sub> O	1.30 to 2.00	75

**Table 6.** Effect of reaction-temperature during synthesis of Dihydropyrimidine derivative using catalyst A4.

S. No.	Reaction	Time of completion	% Yield
1	23 °C	50 min	56
2	45 °C	40 min	68
3	60 °C	30 min	79
4	80 °C	30 min	87

#### Characterization of quinoline and dihydropyrimidine derivatives

4-Methyl-2-hydroxyquinolines (Entry 1, Table 1): <sup>1</sup>H NMR (400 MHz, DMSO-d<sub>6</sub>): δ ppm 2.41 (s, 3H, C<sub>4</sub>-CH<sub>3</sub>), 6.21 (s, 1H, C<sub>3</sub>-H), 7.35-8.18 (m, 4H, Ar-H), 11.68 (s, 1H, NH). IR (KBr) cm<sup>-1</sup> 1334, 1512, 2478, 3403.

4-Methyl-6-bromo-2-hydroxyquinolines (Entry 3, Table 1): <sup>1</sup>H NMR (400 MHz, DMSO-d<sub>6</sub>): δ ppm 2.43 (s, 3H, C<sub>4</sub>-CH<sub>3</sub>), 6.22 (s, 1H, C<sub>3</sub>-H), 7.35-8.26 (m, 3H, Ar-H), 11.65 (s, 1H, NH). IR (KBr) cm<sup>-1</sup> 1338, 1510, 2485, 3408.

4,6-Dimethyl-2-hydroxyquinolines (Entry 6, Table 1): <sup>1</sup>H NMR (400 MHz, DMSO-d<sub>6</sub>): δ ppm 2.42 (s, 3H, C<sub>4</sub>-CH<sub>3</sub>), 2.44 (s, 3H, C<sub>6</sub>-CH<sub>3</sub>), 6.23 (s, 1H, C<sub>3</sub>-H), 7.36-8.21 (m, 3H, Ar-H), 11.65 (s, 1H, NH). IR (KBr) cm<sup>-1</sup> 1338, 1510, 2485, 2864, 3415.

5-Ethoxycarbonyl-6-methyl-4-(4-hydroxyphenyl)-3, 4-dihydropyrimidine-2(1H)-one (Entry 2, Table 2): m.p. 221-222 °C; <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>): δ ppm 1.6 (t, 3H), 1.9 (s, 3H), 4.65 (q, 2H), 5.05 (s, 1H), 5.8 (s, 2H), 5.5 (s, 1H), 6.6 (d, 2H), 7.05 (d, 2H); <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>): δ ppm 23.123, 24.011, 29.726, 50.001, 62.584, 117.356, 121.814, 127.645, 136.015, 145.143, 153.468, 169.542; IR (KBr) cm<sup>-1</sup> 3383, 3236, 2920, 1627, 1516, 1447.

5-Ethoxycarbonyl-6-methyl-4-(4-methoxyphenyl)-3, 4-dihydropyrimidine-2(1H)-one (Entry 3, Table 7): m.p. 198-200 °C; <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>): δ ppm 1.15 (t, 3H), 2.29 (s, 3H), 3.72 (s, 3H), 4.05 (q, 2H), 5.28 (s, 1H), 6.20 (brs, 1H, NH), 6.84 (d, 2H), 7.21 (d, 2H), 8.75 (brs, 1H, NH); <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>): δ ppm 14.404, 16.742, 55.47, 60.18, 67.301, 101.723, 114.154, 128.039, 136.494, 146.399, 154.021, 159.421, 165.365; IR (KBr) cm<sup>-1</sup> 3276, 3112, 2979, 2826, 1614, 1512, 1720, 1653, 1463, 1082, 842.

#### Conclusion

A new approach for the synthesis of quinolines and dihydropyrimidines has been developed using new Cu-Ni tartarate composites catalysts.

#### References

- Dabiri M., Bahramnejad M., Baghbanzadeh M., *Tetrahedron*. **2009**, *65* (45), 9443-9447.
- Shaabani A., Bazgir A., Teimouri F., *Tetrahedron Lett.* **2003**, *44*(4), 857-859.
- Murthy S. N., Madhav B., Kumar A. V., Rao K. R., Nageswar Y. V. D., *Tetrahedron*. **2009**, *65*(27), 5251-5256.
- Nagarapu L., Kumar U. N., Upendra P., Bantu R., *Synth. Comm.* **2012**, *42*(14), 2139-2148.
- Shi F., Jia R., Zhang X., et al., *Synthesis*. **2007**, *18*, 2782-2790.
- Sharma P., Rane N., Gurrum V. K., *Bioorg. Med. Chem. Lett.* **2004**, *14*, 4185-4190.
- Kidwai, Mazaahir B., Vikas M., Neeraj K. B., Divya., *Indian J. Chem.*, **2009**, *48B* (5), 746-748.
- Mehdi A., Mohammad M., Sharareh B., Long-Guan Z., Mehdi R.N., *Tetrahedron Lett.*, **2010**, *51*, 27-29.
- Manas C., Ajanta M., Sulakshana K., Ratna M., Kenichiro N., Athina G. and Pitta E., *ARKIVOC*. **2010**, *11*, 265-290.
- Tian L., Xian X. Y., Jiang H Y., Chao J., Yu S. W., Hui J. Z., Zi F. M., Wei D. Y., *Chinese Chemical Letters*, **2011**, 253-255.
- Revanasiddappa B. C., Subrahmanyam E. V. S., Satyanarayana D., John Thomas, *Int. J. Chem. Techn Res.*, **2009**, *1* (4), 1100-1104.
- Swenson R. E., Sowin T. J., Zhang H. Q., *J. Org. Chem.* **2002**, *67*, 9182-9185.
- Cho C. K., Hooh B., Shim S.C., *J. Heterocycl. Chem.* **1999**, *36*, 1175-1178.
- Makioka Y., Shindo T., Taniguchi Y., Takaki K., Fujiwara Y., *Synthesis*. **1995**, 801-806.
- Sangu K., Fuchibe K., Akiyama T., *Org. Lett.* **2004**, *6*, 353-355.
- Crousse B., Begue J. P., Bonnet-Delpon D., *Tetrahedron Lett.* **1998**, *39*, 5765-5768.
- Crousse B., Begue J. P., Bonnet-Delpon D., *J. Org. Chem.* **2000**, *65*, 5009-5013.

<sup>18</sup>Pawar S. S., Patil C. S., Tadke V. B., Vhankate S. M., Dhanmane S. A., Pathade G. R. and Pawar R. P., *Int J Pharm Sci Res.* **2014**, *5(4)*, 1557-65.

<sup>19</sup>Vhankate S. M., Pawar S. S., Dhanmane S. A., Dhavale N. S., Fulzele K., Patil C. S., Pawar R. P. and Tadke V. B., *SRTMU's Res. J. Sci.* **2013**, *2(1)*, 88 – 100.

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