

## Montmorillonite K10 clay an efficient catalyst for one pot synthesis of polyhydroquinoline

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**Abstract:** The synthesis of polyhydroquinoline derivatives via Hantzsch condensation is excellent route. Herein we report four component coupling reaction of aldehydes, dimedone, ethyl acetoacetate and ammonium acetate in the presence of Montmorillonite K10 clay heterogeneous catalyst under solvent free condition. Present protocol provides an efficient route for the synthesis of polyhydroquinolines.

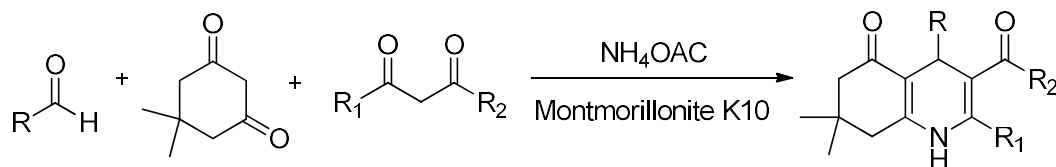
**Keywords:** Aldehyde; Dimedone; Montmorillonite K10, Hantzsch reaction.

### 1. Introduction

4 Substituted 1,4 dihydropyridine (1,4-DHP) nucleus is a fertile source of biologically important molecules possessing various important pharmacological properties such as vasodilator, antihypertensive, bronchodilator antithrombotic, hepto-protective, antitumor, antimutagenic, geroprotective and antidiabetic agents<sup>1-4</sup>. From recent studies 1-4 DHP shows several medicinal applications which include neuroprotectant and platelet anti-aggregatory activity, in addition cerebral antiischemic activity in the treatment in the of Alzheimer's disease<sup>5-7</sup>. An efficient Hantzsch condensation polyhydroquinoline derivatives via a four-component coupling reaction of aldehydes, dimedone, ethyl acetoacetate and ammonium acetate in the presence of  $\text{HClO}_4\text{-SiO}_2$  under solvent free conditions at 90°C temperature<sup>8</sup>.  $\text{Yb}(\text{OTf})_3$  promoted one pot synthesis of polyhydroquinoline derivatives via Hantzsch reaction of aldehydes, dimedone, ethyl acetoacetate and ammonium acetate at ambient temperature in excellent yield<sup>9</sup>. Photocatalytic oxidation of 1,4 dihydropyridine to pyridine has been extensively investigated<sup>10</sup>. Here in the present work, developed new efficient method for synthesis of polyhydroquinoline using *Montmorillonite K10*.

### 2. Material and methods:

A mixture of aldehyde (1mmol), dimedone (1mmol), ethyl acetoacetate (1mmol), ammonium acetate (1.5mmol), Montmorillonite K10 (wt %) were refluxed under methanol as solvent. The reaction was confirmed by thin layer chromatography; the reaction mixture was separated from catalyst by simple filtration. The filtrate is poured on crushed ice to obtain the solid product. The pure product was obtained by further recrystallization using absolute alcohol.



**Table:** Montmorillonite K10 catalyzed synthesis of polyhydroquinolines derivatives.

Entry	R	R1	R2	Time (min.)	Product	Yield	Melting point (°C) Observed	Melting point (°C) Reported
1	C <sub>6</sub> H <sub>5</sub>	CH <sub>3</sub>	OEt	20	2a	85	203-204	202-204 <sup>9</sup>
2	4-F-C <sub>6</sub> H <sub>4</sub>	CH <sub>3</sub>	OEt	22	2b	82	185-186	184-186 <sup>9</sup>
3	4-OCH <sub>3</sub> -C <sub>6</sub> H <sub>4</sub>	CH <sub>3</sub>	OEt	24	2c	84	256-257	257-259 <sup>9</sup>
4	4-CH <sub>3</sub> -C <sub>6</sub> H <sub>4</sub>	CH <sub>3</sub>	OEt	21	2d	80	261-262	260-261 <sup>9</sup>
5	3-NO <sub>2</sub> -C <sub>6</sub> H <sub>4</sub>	CH <sub>3</sub>	OEt	22	2e	82	178-179	177-178 <sup>10</sup>

The structure of the product was determined from their spectroscopic (UV, IR, NMR, Mass) data.

### 3. Spectroscopic data:

#### Ethyl-1,4,7,8-tetrahydro-2,7,7-trimethyl-4-(4-fluorophenyl)-5(6*H*)-oxoquinolin-3-carboxylate

**(2b).** Yellow solid, mp 185-186 °C. IR (KBr): 3292, 2959, 1696, 1649, 1608, 1487, 1380, 1219, 1025, 764 cm<sup>-1</sup>. <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>): δ = 0.92 (s, 3H, CH<sub>3</sub>), 1.07 (s, 3H, CH<sub>3</sub>), 1.18 (t, *J* = 7.3 Hz, 3H, CH<sub>3</sub>), 2.13-2.25 (m, 4H, 2 × CH<sub>2</sub>), 2.38 (s, 3H, CH<sub>3</sub>), 4.05 (q, *J* = 7.33 Hz, 2H, CH<sub>2</sub>), 5.02 (s, 1H, CH), 5.8 (s, 1H, NH), 6.85-6.89 (m, 2H, ArH), 7.23-7.27 (m, 2H, ArH). <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>) δ 14.1, 18.2, 26.4, 29.0, 32.1, 35.2, 50.1, 50.3, 59.0, 103.4, 110.0, 114.2, 114.3, 114.4, 129.0, 129.1, 144.1, 145.1, 149.4, 169.8, 194.2. LCMS: *m/z* = 356 (M-H)<sup>-</sup>. Anal. Calcd for C<sub>21</sub>H<sub>24</sub>NO<sub>3</sub>F: C, 70.58; H, 6.72; N, 3.92; F, 5.32. Found: C, 70.52; H, 6.79; N, 3.87; F, 5.28.

#### Ethyl-1,4,7,8-tetrahydro-2,7,7-trimethyl-4-(4-methoxyphenyl)-5(6*H*)-oxoquinolin-3-carboxylate

**(2c).** Yellow solid, mp 256-257 °C. IR (KBr): 3276, 2956, 1703, 1648, 1606, 1496, 1381, 1215, 1031, 765 cm<sup>-1</sup>. <sup>1</sup>H NMR (200 MHz, CDCl<sub>3</sub> + DMSO-d<sub>6</sub>): δ = 0.95 (s, 3H, CH<sub>3</sub>), 1.09 (s, 3H, CH<sub>3</sub>), 1.21 (t, *J* = 7.2 Hz, 3H, CH<sub>3</sub>), 2.01-2.10 (m, 4H, 2 × CH<sub>2</sub>), 2.30 (s, 3H, CH<sub>3</sub>), 3.70 (s, 3H OCH<sub>3</sub>), 4.00 (q, *J* = 7.2 Hz, 2H, CH<sub>2</sub>), 4.80 (s, 1H, CH), 6.65 (d, *J* = 7.3 Hz, 2H, ArH), 7.10 (d, *J* = 7.3 Hz, 2H, ArH), 8.65 (s, 1H, NH). <sup>13</sup>C NMR (75 MHz, DMSO-d<sub>6</sub>) δ 14.1, 18.2, 26.4, 29.1, 32.1, 34.7, 50.2, 50.5, 54.8, 58.9, 103.2, 110.1, 113.0, 113.1, 128.2, 128.3, 139.8, 144.6, 149.1, 157.2, 166.9, 194.2. LCMS: *m/z* = 368 (M-H)<sup>-</sup>. Anal. Calcd for C<sub>22</sub>H<sub>27</sub>NO<sub>4</sub>: C, 71.54; H, 7.31; N, 3.79; Found: C, 71.59; H, 7.35; N, 3.84.

Table2.

Effect of temperature and amount of catalyst on the reaction<sup>a</sup>

Entry	Amount of catalyst (wt%)	Temp (°C)	Time (min)	Yield of <b>2a</b> %
1	10	70	30	75
2	20	50	40	70
3	20	80	80	60
4	20	85	120	40
5	5	30	100	30

<sup>a</sup>all reactions are conducted using methanol as a solvent

#### 4. Result and Discussion:

The classical method for the preparation of polyhydroquinoline derivatives involves the reaction of aldehyde with ethyl acetoacetate and ammonia, in acetic acid or in refluxing in alcohol without catalyst. However, this method suffers from several drawbacks such as long reaction time, excess of organic solvent and lower product yield<sup>11</sup>. All the starting materials in the ratio of 1:1:1:1 mixture of aldehyde, dimedone, ethyl acetoacetate and ammonium acetate catalyzed by 10% mol weight Montmorillonite K10 catalyst is a green protocol.

#### 5. Conclusion:

In conclusion, we reported Montmorillonite K10 recyclable and reusable green catalyst for Hantzsch reaction. Some of the efficient feature for this method such as simplicity of the experiment, mild reaction condition, high yield, short reaction time and easy work up. Hence such simple and lucidness makes this method attractive for the synthesis of polyhydroquinoline derivatives.

#### References:

- 1] Godfraid, T.; Miller, R.; Wibo, M. *Pharmacol. Rev.* **1986**, 38, 321.
- 2] Sausins, A.; Duburs, G. *Heterocycles* **1988**, 27, 269.
- 3] Mager, P. P.; Coburn, R. A.; Solo, A. J.; Triggler, D. J.; Rothe, H. *Drug Design Discovery* **1992**, 8, 273.
- 4] Mannhold, R.; Jablonka, B.; Voigdt, W.; Schoenafinger, K.; Schraivan, K. *Eur. J. Med. Chem.* **1992**, 27, 229.
- 5] Klusa, V. *Drugs Fut.* **1995**, 20, 135.
- 6] Bretzel, R. G.; Bollen, C. C.; Maeser, E.; Federlin, K. F. *Am. J. Kidney. Dis.* **1993**, 21, 53.
- 7] Bretzel, R. G.; Bollen, C. C.; Maeser, E.; Federlin, K. F. *Drugs Fut.* **1992**, 17, 465.
- 8] M. Maheswara, V. Siddaiah, *ARKIVOC* **2006** (II) 201-206.
- 9] L.M. Wang, j. Sheng, *Tetrahedron*, **2005**, 61, 1539-1543.

- 10] Sainani, J. B.; Shah, A. C.; Arya, V. P. *Indian J. Chem, Sect B* **1994**, 33, 526.  
11] Mohammad Ziarani.; Ghodsi. *Iran. J. Chem. Chem. Eng.* **2010**, 29, 2