Est. 1984

ORIENTAL JOURNAL OF CHEMISTRY
An International Open Free Access, Peer Reviewed Research Journal
www.orientjchem.org

ISSN: 0970-020 X
CODEN: OJCHEG
2014, Vol. 30, No. (3):
Pg. 1361-1364

# An Efficient Method for the One-pot, Three-Component Synthesis of 3,4-Dihydropyrano[*c*]chromenes Catalyzed by Nano $Al_2O_3$

**ALIREZA MONTAGHAMI and NASER MONTAZERI***

Department of Chemistry, Tonekabon Branch, Islamic Azad University, Tonekabon, Iran.
*Corresponding author E-mail: Montazer1350@gmail.com

http://dx.doi.org/10.13005/ojc/300355

(Received: May 21, 2014; Accepted: June 17, 2014)

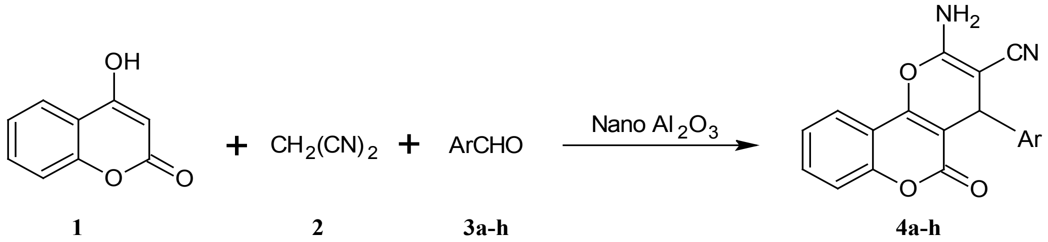
## ABSTRACT

Nano $Al_2O_3$ efficiently catalyzed the one-pot, three-component reaction of 4-hydroxycoumarin, aromatic aldehydes and malononitrile to yield 3,4-dihydropyrano[*c*]chromene derivatives in high yields. The features of this procedure are mild, reaction conditions, short reaction time and operational simplicity.

**Keywords:** Nano $Al_2O_3$, 3,4-Dihydropyrano[*c*]chromene,
4-Hydroxycoumarin, Malononitrile, Aromatic aldehydes.

## INTRODUCTION

4*H*-Chromene and its derivatives have been studied due to a variety of chemical and biological significance[1]. The importance of chromenes as biologically active compounds includes their use as emetic[2], anti-HIV[3], anti-tumor[4], anti-cancer[1], anti-coagulant[1], anti-alzheimer[5], anti-bacterial[6], anti-malaria[7], diuretic[8], spasmolytic[9], anti-leukemic[10,11], anti-anaphylactic activities[12]. Moreover, chromene derivatives such as 3,4-dihydropyrano[*c*] chromenes are of importance as they have various industrial, pharmaceutical and biological applications[13]. Therefore, the development of new and efficient methodologies for the synthesis of 3,4-dihydropyrano[*c*]chromenes will be interesting in both synthetic organic and medicinal chemistry. 3,4-Dihydropyrano[*c*] chromene derivatives are generally synthesized via one-pot reaction of an aryl aldehydes, malononitrile and 4-hydroxycoumarin in the presence of several catalysts such as sodium dodecyl sulfate (SDS)[14], DBU[15], morpholine[16], piperidine[17], $K_2CO_3$ under microwave irradiation[18], sulfonic acid functionalized silica ($SiO_2PrSO_3H$)[19], trisodium citrate[20], silica gel[21], inorganic-organic hybrid magnetic nanocatalyst[22], nano ZnO[23], $KAl(SO_4)_2.12H_2O$[24], TBAB[25], TMGT[26], MgO[27], diammonium hydrogen phosphate[28] and heteropoly acids[29]. However, in spite of their potential utility, some difficulties still exist, such as expensive or toxic reagent. Therefore, the development of new, simple and cheap methods for the synthesis of 3,4-dihydropyrano[*c*] chromene derivatives is of main importance. In continuation of our efforts to develop novel synthetic routes using solid catalysts in organic reactions[30], and due to our interest in the synthesis of heterocyclic compounds[31], herein, we wish to report an efficient synthesis of 3,4-dihydropyrano[*c*] chromenes by cyclocondensation reaction of 4-hydroxycoumarin, aryl aldehydes and malononitrile using nano $Al_2O_3$ as a solid catalyst (Scheme 1).



**Scheme 1: Synthesis of 3,4- dihydropyrano[*c*]chromene by nano $Al_2O_3$**

## EXPERIMENTAL

All of the chemical material used in this work purchased from Fluka or Merk and without further purification. Melting points were recorded on an Electrothermal type 9100 melting point apparatus. The IR spectra were obtained on a 4300 Shimadzu spectrophotometer in KBr disks. The $^1H$ NMR (500 MHz) spectra were recorded on a Bruker-Ac-500 spectrophotometer.

### General procedure for the synthesis of 3,4-dihydropyrano[*c*]chromenes (4a-h).

A solution of 4-hydroxycoumarin 1(1 mmol), malononitrile 2(1.5 mmol), an aromatic aldehydes 3a-h(1 mmol) and nano $Al_2O_3$ (25 mol% based on 4-hydroxycoumarin) in EtOH (5 mL) was stirred at room temperature for 5h. The progress of the reaction was monitored by TLC. After completion of the reaction, boiling ethanol (20 mL) was added and catalyst was filtrated. The filtrate was concentrated to give the solid product that washed with water, and recrystallized in the ethanol to give pure products (4a-h). The structures of the products were confirmed by $^1H$ NMR, IR spectroscopies and comparison with authentic samples prepared by reported methods.

## RESULTS AND DISCUSSION

In order to optimize the reaction conditions, including solvents and temperature, the reaction was conducted under various conditions and the results are listed in Table 1. In an optimized reaction conditions, 4-hydroxycoumarin (1 mmol), malononitrile (1.5 mmol), and 3-nitrobenz aldehyde (1 mmol) in ethanol (5 mL) was mixed in the presence of nano $Al_2O_3$ (25 mol%) as catalyst for 5h. The reaction proceeds very cleanly at room temperature and was free of side products. After completion of the reaction (monitored by TLC), a simple workup affords the products in high yields (Scheme 1). Among the solvents tested, the reaction in $H_2O$, $CH_3CN$ and $CHCl_3$ using 25 mol% of the catalyst gave a moderate yield of the desired product at room temperature. However in the EtOH relatively high yield of product is obtained at room temperature after 5h. Without catalyst, in refluxing EtOH, $H_2O$, $CHCl_3$ and $CH_3CN$ or at room temperature in this solvents the reaction times are prolonged and the yields are poor. In the solvent-free conditions, even in the presence of 35 mol% of the catalyst at room temperature, 60 °C, 70 °C, 80 °C and 90 °C, the yields are moderate. The results are summarized in Table 1. We also evaluated the amount of nano $Al_2O_3$ required for this transformation. It was found that the yield of product was affected by the catalyst amount. Increasing the amount of the catalyst up to 25 mol% in the EtOH at room temperature increased the yield of the product. Further increase in the catalyst amount did not increase the yield noticeably.

In order to show generality and scope of this new protocol, we used various substituted aromatic aldehydes and the results obtained are summarized in Table 2. In all cases, aromatic aldehydes with substitutes carrying either electron-donating or electron- withdrawing group reacted successfully and gave the expected products in high yields. The type of aldehyde had no significant effect on the reaction.

**Table 1: Effect of nano $Al_2O_3$ amount on the model reaction[a]**

| Entry | Catalyst (mol%) | Solvent | Condition | Time (h) | Yield (y)[b] |
|---|---|---|---|---|---|
| 1 | - | EtOH | Reflux | | 18 |
| 2 | - | $H_2O$ | Reflux | | 15 |
| 3 | - | $CHCl_3$ | Reflux | | 12 |
| 4 | - | $CH_3CN$ | Reflux | | 12 |
| 5 | - | EtOH | r.t | | - |
| 6 | - | $H_2O$ | r.t | | - |
| 7 | - | $CHCl_3$ | r.t | | - |
| 8 | - | $CH_3CN$ | r.t | | - |
| 9 | 35 | - | r.t | | 45 |
| 10 | 35 | - | 60 °C | | 43 |
| 11 | 35 | - | 70 °C | | 40 |
| 12 | 35 | - | 80 °C | | 35 |
| 13 | 35 | - | 90 °C | | 32 |
| 14 | 20 | EtOH | r.t | | 72 |
| 15 | 25 | EtOH | r.t | | 88 |
| 16 | 30 | EtOH | r.t | | 85 |
| 17 | 35 | EtOH | r.t | | 82 |
| 18 | 25 | $H_2O$ | r.t | | 65 |
| 19 | 25 | $CHCl_3$ | r.t | | 55 |
| 20 | 25 | $CH_3CN$ | r.t | | 45 |
| 21 | 25 | EtOH | Reflux | | 85 |
| 22 | 25 | $H_2O$ | Reflux | | 70 |
| 23 | 25 | $CHCl_3$ | Reflux | | 68 |
| 24 | 25 | $CH_3CN$ | Reflux | | 65 |

[a] 4-Hydroxycoumarin (1mmol), 3-nitrobenzaldehyde (1 mmol) and malononitrile (1.5 mmol). [b] Isolated yields.

**Table 2: Synthesis of 3,4-dihydropyrano[*c*]chromenes (4a-h)[a]**

| Entry | Ar | Product | Yield(%)[b] | m.p(°C) | |
|---|---|---|---|---|---|
| | | | | Found | Reported |
| 1 | $3\text{-}NO_2C_6H_4$ | 4a | 88 | 260-261 | 257-258 [22] |
| 2 | $4\text{-}ClC_6H_4$ | 4b | 80 | 263-265 | 260-262 [15] |
| 3 | $3\text{-}ClC_6H_4$ | 4c | 75 | 245-247 | 242-243 [15] |
| 4 | $C_6H_5$ | 4d | 84 | 259-260 | 256-258 [15] |
| 5 | $4\text{-}NO_2C_6H_4$ | 4e | 89 | 263-265 | 259-261 [21] |
| 6 | $4\text{-}MeOC_6H_4$ | 4f | 82 | 247-248 | 248-250 [15] |
| 7 | $4\text{-}MeC_6H_4$ | 4g | 77 | 250-252 | 253-255 [15] |
| 8 | $3\text{-}MeOC_6H_4$ | 4h | 87 | 246-248 | 242-244 [19] |

[a] 1 mmol 4-hydroxycoumarin, 1 mmol 3-nitrobenzaldehyde, 1.5 mmol malononitrite and 25 mol% nano $Al_2O_3$ in the EtOH after 5h. [b] Isolated yields.

## CONCLUSIONS

In conclusion we have successfully demonstrated the catalytic activity of nano $Al_2O_3$ in the synthesis of 3,4-dihydropyrano[*c*]chromene derivatives. Easy simple work-up and high yields of products are some advantages on this method.

## ACKNOWLEDGMENTS

We gratefully acknowledgments the financial support of this research by Islamic Azad University, Tonekabon Branch.

## REFERENCES

1. Foye, W. O. Principidi Chimica Farmaceutica Piccin- Padova, Italy, **1991**.
2. Cannon, J. G.; Khonji, R. R. *J. Med. Chem.* **1975**, 18, 110-112.
3. Tanabe, A.; Nakashima, H.; Yoshida, O.; Yamamoto, N.; Tenmyo, O; Oki, T. *J. Antibiot*. **1988**, 41, 1708-1710.
4. Shijay, G.; Cheng, H. T.; Chi, T.; Ching-Fa, Y. *Tetrahedron* **2008**, 64, 9143-9149.
5. Bayer, T. A.; Schafer, S.; Breyh, H.; Breyhan, O.; Wirths, C.; Treiber, G. A. *Clin Neuropathol*. **2006**, 25, 163-171.
6. Morgan, L. R.; Jursic, B. S.; Hooper, C. L.; Neumann, D. M.; Thangaraj, K.; Leblance, B. *Bioorg. Med. Chem. Lett.* **2002**, 12, 3407-3411.
7. Bolognese, A.; Correale, G.; Manfra, M.; Levecchia, A.; Mazzoni, O.; novellino, E.; Lacolla, P.; Sanna, G.; Loddo, R. *J. Med. Chem.* **2004**, 47, 849-858.
8. Hafez, E. A. A.; Elnaghi, M. H.; Elagamey, A. G. A.; El-Taweel, F. M. A. A. *Heterocycles*. **1987**, 26, 903-907.
9. Ellis, G. P. *The Chemistry of Heterocyclic Compounds*. In Chromenes; Chromenes, and Chromenes; Weissberger; Taylor, A.; Eds, E. C.; John Wiley; NewYork. **1977**.
10. Beagley, P.; Blackic, M. A. L.; Chibale, K.; Clarkson, C.; Meijboom, R.; Moss, J. R.; Smith, P.; Su, H. *Dalton Trans*. **2003**, 3046-3051.
11. Fokialakis, n.; Magiatis, P.; Chinou, L.; Mitaka, S.; Tillequin, F. *Chem. Pharm. Bull.* **2002**, 50, 413-414.
12. Biot, O.; Blampain, G.; Blampain, G.; Blampain, P.; Georges, A. F.; Abessolo, H.; Dive, D.; Lebibi, J. *J. Med. Chem.* **1997**, 40, 3715-3718.
13. Konkoy, C. S.; Fick, D. B.; Cai, S. X.; Lan, N. C.; Keana, J. F. W.; PCT Int. Appl. Wo 0075123, 2000; *Chem. Abstr.* **2001**, 134, 293130.
14. Mehrabi, H.; Abusaidi, H. *J. Iran. Chem. Soc.* **2010**, 7, 890-894.
15. Khurana, J. M.; Nand, B.; Saluja, P. *Tetrahedron* **2010**, 66, 5637-5641.
16. Heravi, M. M.; Zaheri, M.; Mohammadi, N. *Chin. J. Chem.* **2011**, 29, 1163-1166.
17. Shaker, R. M. R. *Pharmazie*. **1996**, 51, 148-151.
18. Kidwai, M.; Saxena, S. *Synth. Commun.* **2006**, 36, 2737-2742.
19. Mohammadi ziarani, G.; Badiei, A.; Azizi, M.; Zarabadi, P. *Iran. J. Chem. Chem. Eng.* **2011**, 2, 59-65.
20. Zheng, J.; Yi-Qun, Li. *Scholars Res. Libr*. **2011**, 2, 381-388.
21. Prasanna, T. S. R.; Mohana Raju, K. *J. Korean Chem. Soc.* **2011**, 4, 662-665.
22. Khoobi, M.; Mamani, L.; Rezazadeh, F.; Zareie, Z.; Foroumadi, A.; Ramazani, A.; Shafiee, A. *J. Mol. Cat. A: Chem.* **2012**, 359, 74-80.
23. Paul, S.; Bhattacharyya, P.; Das, A. R. *Tetrahedron Lett.* **2011**, 52, 4636-4641.
24. Karimi, A. R.; Sedaghatpour, F. *Synthesis.* **2010**, 1731-1735.
25. Khurana, J. M.; Kumar, S. *Tetrahedron Lett.* **2009**, 50, 4125-4127.
26. Shaabani, A.; Samadi, S.; Badri, Z.; Rahmati, A. *Catal. Lett.* **2005**, 104, 39-43.
27. Seifi, M.; Sheibani, H. *Catal. Lett.* **2008**, 126, 275-279.
28. Abdolmohammadi, S.; Balalaie, S. *Tetrahedron Lett.* **2007**, 48, 3299-3303.
29. Heravi, M. M.; Sadjadi, S.; Haj, N. M.; Oskooie, H. A.; Bamoharram, F. F. *Catal. Commun.* **2009**, 10, 1643-1646.
30. Montazeri, N.; Rad-Moghadam, K. *Chine Chem. Lett.* **2008,** 19, 1143-1146.
31. Montazeri, N.; Pourshamsian, K.; Khoddadi, M.; Khddadi, K. *Oriental J. Chem*. **2011,** 27, 1023-1027.