International Journal of Engineering and Technical Research (IJETR)
ISSN: 2321-0869, Volume-2, Issue-3, March 2014

# New approach for the synthesis of chromeno[*b*] pyrazolo[*f*] quinolinone compounds

**Hossein Dianat, Alireza Nazif, Saeid Salimi**

***Abstract*— A series of chromeno[*b*]pyrazolo[*f*]quinolinone derivatives has been synthesized via one-pot cyclocondensation of 3*H*-chromene-2,4-dione, aromatic aldehydes and 5-aminoindazole utilizing silica supported ionic liquid [pmim]$HSO_{4SiO2}$ in $CH_3CN$ under reflux condition.**

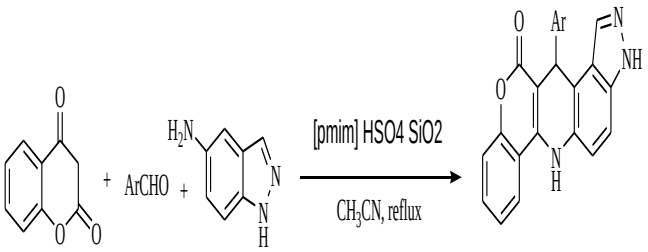
***Index Terms*— Pyrazolopyrimido[4,5-*b*] quinolineone, One-pot, synthesis.**

## I. INTRODUCTION

The first multi-component reaction (MCR) was reported by Strecker in 1850 for the synthesis of amino acids [1]. In recent years, multi-component reactions (MCRs) have occupied an important part in modern synthetic organic chemistry due to their valued features such as convergence, productivity, facile execution, and generally high yield of products [2-4]. Recently, we have reported several MCRs on the synthesis of indenoquinolinones [5], pyranoindoles [6], phenanthroimidazoles [7].

Pyrazoles are known for various biological activities, e.g. pyrazolo[3,4-*b*]quinolines as potential antiviral [8], antimalarial [9], lowering of serum cholesterol [10], pyrazolo[3,4-*c*]pyrazoles are useful for the treatment of esophageal and gastrointestinal mucosa injury [11], brain injury [11,12] and also as immunostimulatory, antianginal [13] and antitumor agents [13]. Pyrazolo[3,4-*f*] quinoline derivatives are a novel class of immunostimulant with potent in vivo effects in a murine infection model [14,15].

The ionic liquids are readily recycled and tunable to specific chemical tasks. One type is Brø nsted acidic task-specific ionic liquids. Among these ionic liquids possessing $HSO_4$ as a counteranion finds a broad application in organic synthesis, acting as both a solvent and a catalyst [16]. Recently, immobilization processes involving acidic ionic liquids on solid supports have been designed [17-19]. In this paper, The synthesis of tetrahydrochromeno[4,3-*b*]pyrazolo[4,3-*f*]quinolin-12-one derivatives has been reported (Scheme 1).




**Scheme 1**

## II. EXPERIMENTAL

### A. General

[pmim]$HSO_{4\ SiO2}$ (extent of labeling 0.25 mmol/gr loading) was prepared according to the literature [20].

***General procedure for synthesis of chromeno[4,3-b]pyrazolo[4,3-f]quinolinone derivatives***

In a round bottom flask purged by nitrogen gas already, a mixture of 3*H*-chromene-2,4-dione (1 mmol), aromatic aldehydes (1 mmol) and 5-aminoindazole (1mmol), in the presence of ionic liquid catalyst (0.15 mmol) was stirred under reflux condition in dried acetonitrile. The progress of the reactions were monitored by TLC (ethylacetate:*n*-hexane 1:5). Upon the completion of the reaction, the heterogeneous catalyst was separated from the mixture. After cooling to room temperature, the resulting precipitate was filtered off and washed with water. The solid was dried and crystallized from $H_2O$:EtOH (1:4) to obtain the pure desired product in high to excellent yield. The representative spectral data for the selected products are as follows:

**4b**: IR: (KBr, *v*, $cm^{-1}$): 3375, 3218, 1670, 1561, 1475, 1387, 1277, 1159, 1044. $^1$H NMR (100 MHz,DMSO-$d_6$) : $\delta$ 12.60 (s, 1H, NH), 9.82 (s, 1H, NH), 8.28 (d, 1H, *J* = 7.4 Hz, ArH), 8.08-7.95 (m, 3H, ArH), 7.60-7.35 (m, 7H, ArH), 5.53 (s, 1H, CH). Anal. Calcd. for $C_{23}H_{14}N_4O_4$: C, 67.31; H, 3.44; N, 13.65%. Found: C, 66.28; H, 3.37; N, 13.54 %.

**4e**: IR: (KBr, *v*, $cm^{-1}$): 3412, 3265, 1666, 1522, 1452, 1240, 1166, 1071. $^1$H NMR (100 MHz,DMSO-$d_6$) : $\delta$ 12.75 (s, 1H, NH), 10.15 (s, 1H, NH), 8.22 (d, 1H, *J* = 8.2 Hz, ArH), 8.00 (s, 1H, ArH), 7.65-7.45 (m, 4H, ArH), 7.40-7.27 (m, 3H, ArH), 6.82 (d, 2H, *J* = 8.4 Hz, ArH), 5.64 (s, 1H, CH), 3.62 (s, 3H, OMe). Anal. Calcd. for $C_{24}H_{17}N_3O_3$: C, 72.90; H, 4.33; N, 10.63; Found: C, 70.83; H, 4.22; N, 10.55 %.

Manuscript received March 20, 2014.

**Hossein Dianat**, Department of Chemistry, Sarvestan Branch, Islamic Azad University, Sarvestan, Iran
**Alireza Nazif**, Sarvestan Branch, Islamic Azad University, Sarvestan, Iran
**Saeid Salimi**, Sarvestan Branch, Islamic Azad University, Sarvestan, Iran

**4g**: IR: (KBr, *v*, $cm^{-1}$): 3357, 3282, 1668, 1562, 1473, 1414, 1263, 1121, 1065. $^1H$ NMR (100 MHz,DMSO-$d_6$): $\delta$ 12.88 (s, 1H, NH), 10.15 (s, 1H, NH), 8.37 (d, 1H, $J$ = 7.6 Hz, ArH), 8.22 (s, 1H, ArH), 7.55-7.22 (m, 6H, ArH), 7.15-6.95 (m, 3H, ArH), 5.90 (s, 1H, CH). Anal. Calcd. for $C_{27}H_{17}N_3O_2S$: C, 72.47; H, 3.83; N, 9.39%; Found: C, 70.33; H, 3.71; N, 9.30 %.

**4h**: IR: (KBr, *v*, $cm^{-1}$): 3345, 3188, 1662, 1645, 1524, 1447, 1255, 1155, 1036. $^1H$ NMR (100 MHz,DMSO-$d_6$): $\delta$ 12.75 (s, 1H, NH), 9.80 (s, 1H, NH), 8.18 (d, 1H, $J$ = 6.8 Hz, ArH), 8.03 (s, 1H, ArH), 7.60-7.40 (m, 4H, ArH), 7.40–7.25 (m, 5H, ArH), 5.52 (s, 1H, CH). Anal. Calcd. for $C_{23}H_{14}BrN_3O_2$: C, 62.18; H, 3.18; N, 9.46%. Found: C, 60.16; H, 3.10; N, 9.36 %.

## III. RESULTS AND DISCUSSION

Choosing an appropriate solvent is of crucial importance for successful synthesis. To optimize the reaction solvent, the reaction of 4-nitrobenzaldehyde, 3*H*-chromene-2,4-dione, and 5-aminoindazole was carried out in different organic solvents such as toluene, benzene, ethylacetate, 1,2-dichloroethane, acetonitrilr and DMF at reflux condition. The results are summarized in Table 1. It was shown that the reactions in refluxing acetonitrile afforded the best results. Polar solvents such as 1,2-dichloroethane and DMF afforded good results. Therefore, acetonitrile was chosen as the best solvent for the subsequent reactions. In addition, the catalyst, could efficiently catalyze the multicomponent reactions and as illustrated in Table 2, a various series of chromeno[4,3-*b*]pyrazolo[4,3-*f*]quinolin-12-one derivatives were synthesized in high to excellent yields.

**Table 1**. Influence of solvent on the reaction efficiency

| Solvent | Toluene | Benzene | DMF | EtOAc | $C_2H_4Cl_2$ | $CH_3CN$ |
|---|---|---|---|---|---|---|
| Isolated Yield[a] | 74 | 58 | 81 | 70 | 80 | 90 |

a) All the reactions were carried out at reflux condition for 8 h. Reaction conditions: 4-nitrobenzaldehyde (1.0 equiv), 3*H*-chromene-2,4-dione (1.0 equiv), and 5-aminoindazole (1.0 equiv), catalyst (0.15 equiv).

With the intention of providing more diversity to the chromeno[4,3-*b*]pyrazolo[4,3-*f*]quinolin-12-one structure, various aldehydes were examined and the reactions of aryl aldehydes, in combination with 3*H*-chromene-2,4-dione and 5-aminoindazole were tried out. The results revealed that this protocol could be applied to aromatic aldehydes with either electron-withdrawing as well as electron-donating groups (Table 2).

**Table 2.** Results on the synthesis of chromeno[4,3-*b*]pyrazolo[4,3-*f*]quinolinones

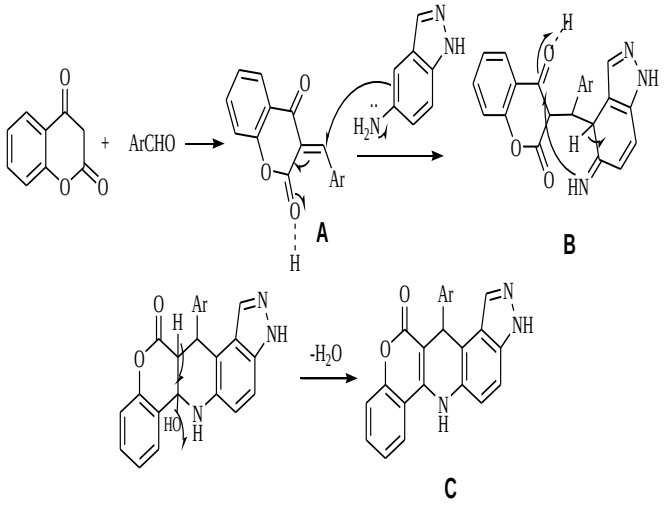
| Entry[a,b] | Ar | Product | Yield(%)[a] |
|---|---|---|---|
| 1 | $C_6H_5$ | **4a** | 90 |
| 2 | 4-$NO_2$-$C_6H_4$ | **4b** | 90 |
| 3 | 3-$NO_2$-$C_6H_4$ | **4c** | 88 |
| 4 | 4-$CH_3$-$C_6H_4$ | **4d** | 86 |
| 5 | 4-$CH_3O$-$C_6H_4$ | **4e** | 85 |
| 6 | 4-$NMe_2C_6H_4$ | **4f** | 82 |
| 7 | 2-Thienyl | **4g** | 84 |
| 8 | 4-Br-$C_6H_4$ | **4h** | 90 |

a ) Isolated yields. b) Reaction conditions: 1.0 equiv. of 5-aminoindazole, 1.0 equiv. of aldehyde, 1.0 equiv. of 3*H*-chromene-2,4-dione, 10 mol% of Ti catalyst, 5 mL of $CH_3CN$ as solvent and reflux condition for 6h.

The possible mechanism is likely involves a sequence reaction of condensation, addition, cyclization, and dehydration (Scheme 2). First, the condensation between aromatic aldehyde and 3*H*-chromene-2,4-dione leads to formation of intermediate **A**; Michael-type addition of 5-aminoindazole to **A** provides **B**, which upon intermolecular cyclization and dehydration furnishes the corresponding chromeno[4,3-*b*]pyrazolo[4,3-*f*]quinolinone product **C**.

## IV. CONCLUSION

In conclusion, the synthesis of a series of 13-(aryl)-3,6,12,13-tetrahydrochromeno[4,3-*b*]pyrazolo[4,3-*f*]quinolin-12-ones through an efficient one-pot multicomponent approach is described.




**Scheme 2**

## REFERENCES

[1] A. Strecker, *Liebigs Ann. Chem*. **1850**, 75, 27.
[2] M. Lei, L. Ma, L. Hu, *Monatsh. Chem*., **2010**, 141, 1005.
[3] J. N. Tan, M. Lia, Y. Gu, *Green Chem*., **2010**, 12, 908.
[4] M. Lei, L. Ma, L. Hu, *Tetrahedron Lett*., **2010**, 51, 4746.
[5] S. Damavandi, R. Sandaroos, *Heterocycl. Commun*., **2011**, 17, 121.
[6] S. Damavandi, R. Sandaroos, *Heterocycl. Commun*., **2011**, 17, 125.
[7] S. Damavandi, *Heterocycl. Commun*., **2011**, 17, 79.
[8] P. Smirnoff, R. R. Crenshaw. *Antimicrob. Agents Chemother*. **1977**, 11, 571.
[9] R. G. J. H. Stein, *J Med Chem*., **1970**, 13, 153.
[10] W. S. Salim, M. Shakir. *Chem Abstr*, **1994**, 120, 280314.
[11] C. Palmer, J. Towfighi, R. L. Roberts, D. F. Heitjan. *Pediatr Res*., **1993**; 33:1; Chem Abstr.**1993**, 118, 247476.
[12] M. Marzi, P. Minetti, P. Foresta, M. O. Tinti, *Chem Abstr*., **1993**, 118, 60136.
[13] A. S. Bell, N. K. Terrett, *Chem Abstr*, **1993**, 119, 95549.
[14] E. C. Taylor, H. Patel, H. Kumar. *Tetrahedron* **1992**, 48, 8089.
[15] Blecha F, Vet Med, 1990, 231.
[16] Wang, W.; Cheng, W.; Shao, L.; Yang, J. *Catal. Lett.* **2008**, 121 (1-2), 77-80.
[17] Qiao, K.; Hagiwara, H.; Yokoyama, C. *J. Mol. Catal. A: Chem*. **2006**, 246, 65-69.
[18] Sugimura, R.; Qiao, K.; Tomida, D.; Yokoyama, C. *Catal. Commun*. **2007**, 8 (5):770-772.
[19] Wasserscheid, P.; Welton, T (**2007**). Ionic Liquids in Synthesis. 2nd edn. Wiley-VCH, Weinheim
[20] Chrobok, A.; Baj, S.; Pudło, W.; Jarzebski, A. *Appl. Catal. A: Gen*. **2009**, 366 (1), 22-28.