



# Domino reactions between 3-(6-methylchromonyl)acrylonitrile and nucleophilic reagents

Magdy A. Ibrahim<sup>\*</sup>, Nasser M. El-Gohary

Department of Chemistry, Faculty of Education, Ain Shams University, Roxy, 11711, Cairo, Egypt



## ARTICLE INFO

### Article history:

Received 26 October 2017

Received in revised form

7 December 2017

Accepted 14 December 2017

Available online 16 December 2017

### Keywords:

3-(6-Methylchromonyl)acrylonitrile

RORC

Chromeno[4,3-*b*]pyridine

Benzonitrile

Benzophenone

Carbon nucleophiles

Cyclization

## ABSTRACT

The chemical reactivity of electron deficient chromone-linked acrylonitrile [3-(6-methylchromonyl)acrylonitrile (**1**)] was studied towards some active methylene nitriles and active methylene ketones. Reaction of compound **1** with malononitrile, cyanoacetamide, ethyl cyanoacetate, malononitrile dimer and acetoacetanilide afforded 5-cyanomethylchromeno[4,3-*b*]pyridines **2–4** and **9**. Compound **1** reacted with 1*H*-benzimidazol-2-ylacetonitrile producing pyrido[1,2-*a*]benzimidazole derivative **5**. Benzonitrile derivatives **6–8** were efficiently synthesized from the reaction of compound **1** with acetylacetone, ethyl acetoacetate and diethylmalonate. In these reactions a diversity of products has been synthesized through a domino process, including *Michael* addition, retro-*Michael* with  $\gamma$ -pyrone ring opening followed by different types of recyclization (RORC). Structures of the new synthesized products were deduced on the basis of their analytical and spectral data, and the reaction mechanisms are discussed.

© 2017 Elsevier Ltd. All rights reserved.

## 1. Introduction

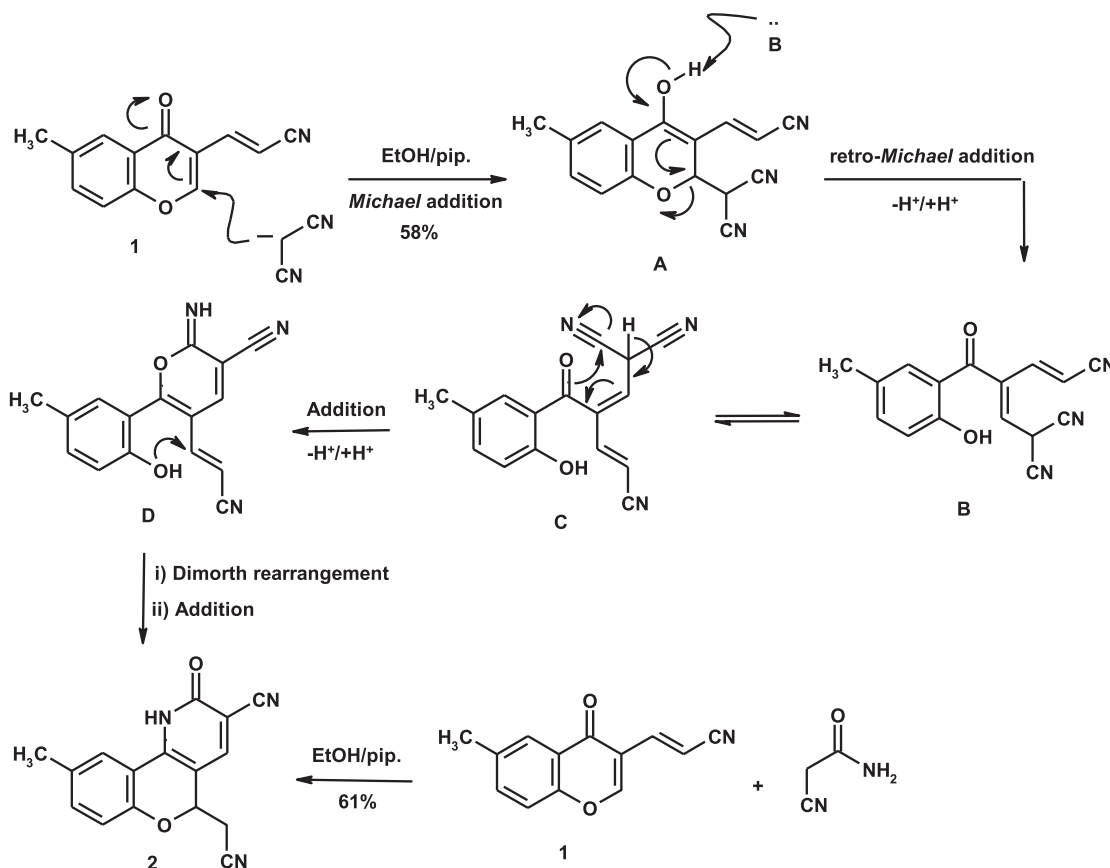
Chromones constitute one of the major classes of naturally occurring compounds.<sup>1–3</sup> Chromone derivatives have shown varied biological activities including anticancer,<sup>4–6</sup> neuroprotective,<sup>7</sup> HIV-inhibitory,<sup>8</sup> antimicrobial,<sup>9,10</sup> antiinflammatory<sup>11</sup> and antioxidant activity.<sup>12</sup> Recently, chromones were used in various optoelectronic applications.<sup>13–17</sup> The presence of an electron-withdrawing group at the 3-position of the chromone system changes the reactivity of the  $\gamma$ -pyrone ring with respect to nucleophiles, and provides a broad synthetic potential for the synthesis of 3-substituted chromones.<sup>18–22</sup> The diversity of properties of 3-substituted chromones is due to the fact that, they are highly reactive geminally activated push–pull enones.<sup>23</sup> The chemical reactivity of 3-substituted chromones is widely different depending on the nature of the functional group present at position 3 and the reaction conditions.<sup>24–31</sup> Our plan aimed to highlight the chemical transformations of an electron deficient chromone-linked acrylonitrile [namely: 3-(6-methylchromonyl)acrylonitrile] towards a variety of carbon nucleophiles under mild basic reaction conditions.

## 2. Results and discussion

The chemical transformations of an electron-deficient chromones containing multiple reactive centers [3-(6-methylchromonyl)acrylonitrile (**1**)] in domino reactions has not been fully investigated or used to synthesize heterocyclic compounds. The present work aimed to study the chemical transformations of 3-(6-methylchromonyl)acrylonitrile (**1**) towards some active methylene nitriles and active methylene ketones, under mild basic reaction conditions. Thus, treatment of chromonylacrylonitrile **1** with malononitrile in boiling ethanol containing few drops of piperidine afforded 5-(cyanomethyl)-9-methyl-2-oxo-1,5-dihydro-2*H*-chromeno[4,3-*b*]pyridine-3-carbonitrile (**2**) (Scheme 1). The same product (co-identical mp, mmp and spectral data) was also obtained from the reaction of chromonylacrylonitrile **1** with cyanoacetamide under the same reaction conditions. The reaction may proceed through domino process including nucleophilic addition of malononitrile at the C-2 position of the  $\gamma$ -pyrone ring (*Michael* addition; intermediate **A**) followed by retro-*Michael* with  $\gamma$ -pyrone ring opening (intermediate **B**). Free-rotation around the single bond (intermediate **C**) with nucleophilic addition at the cyano group produced intermediate **D**. Dimorph rearrangement with addition of the hydroxyl group onto the olefinic bond produced the final product **2** as depicted in Scheme 1. The IR

<sup>\*</sup> Corresponding author.

E-mail address: [magdy\\_ahmed@edu.asu.edu.eg](mailto:magdy_ahmed@edu.asu.edu.eg) (M.A. Ibrahim).



**Scheme 1.** Reaction of 3-(6-methylchromonyl)acrylonitrile (**1**) with malononitrile and cyanoacetamide.

spectrum of compound **2** showed characteristic absorption bands at  $\nu$  3231 (NH), 2252, 2218 (2 C $\equiv$ N), 1647 (C=O) and 1566  $\text{cm}^{-1}$  (C=C). Its  $^1\text{H}$  NMR spectrum showed characteristic doublet and triplet signals at  $\delta$  3.16 and 5.58 ppm attributed to CH<sub>2</sub>-CN and H-5, respectively, the spectrum also revealed two singlets at  $\delta$  7.96 and 8.12 ppm attributed to H-10 and H-4, respectively. Another two doublets were observed in the  $^1\text{H}$  NMR spectrum at  $\delta$  6.97 and 7.32 ppm assigned to H-7 and H-8, respectively. A D<sub>2</sub>O-exchangeable signal was observed at  $\delta$  12.71 ppm assigned to the NH proton. The  $^{13}\text{C}$  NMR spectrum of compound **2** showed characteristic signals at  $\delta$  23.2 and 71.4 ppm attributed to CH<sub>2</sub> and C-5, respectively. Furthermore, the structure of compound **2** was deduced from its mass spectrum which revealed the molecular ion peak at  $m/z$  277 and the base peak at  $m/z$  237; assigned to the molecular ion after loss of a CH<sub>2</sub>CN unit.

In the same manner, the reaction of chromonylacrylonitrile **1** with ethyl cyanoacetate and malononitrile dimer (2-aminoprop-1-ene-1,1,3-tricarbonitrile) afforded 5-(cyanomethyl)-9-methyl-2-oxo-2*H*,5*H*-pyrano[3,2-*c*]chromene-3-carbonitrile (**3**) and [3-cyano-5-(cyanomethyl)-9-methyl-1,5-dihydro-2*H*-chromeno[4,3-*b*]pyridin-2-ylidene]-propanedinitrile (**4**), respectively (Scheme 2). The IR spectrum of compound **3** showed characteristic absorption bands at  $\nu$  2249, 2220 (2C $\equiv$ N) and 1745  $\text{cm}^{-1}$  (OC=O), while that of compound **4** showed absorption bands at  $\nu$  3269 (NH), 2258, 2201 and 2195  $\text{cm}^{-1}$  (4C $\equiv$ N). The  $^1\text{H}$  NMR spectra of compounds **3** and **4** revealed characteristic doublet and triplet signals attributed to CH<sub>2</sub>CN and H-5 at  $\delta$  3.08/3.10 and 5.53/5.49 ppm, respectively. Also, H-4 was observed as a characteristic singlet at  $\delta$  8.15 and 7.79 ppm, respectively. The  $^1\text{H}$  NMR spectrum of compound **4** showed a D<sub>2</sub>O exchangeable signal assigned to NH at  $\delta$  5.41 ppm. The  $^{13}\text{C}$  NMR

spectra of compounds **3** and **4** showed characteristic signals at  $\delta$  20.9/20.4, 23.4/23.1 and 71.1/70.0 ppm assigned to CH<sub>3</sub>, CH<sub>2</sub> and C-5, respectively. The structure of compound **4** was further deduced from its mass spectrum which revealed the molecular ion peak at  $m/z$  325 and the base peak at  $m/z$  285 assigned to the molecular ion after loss of a CH<sub>2</sub>CN fragment.

The reaction of chromonylacrylonitrile **1** with 1*H*-benzimidazol-2-ylacetonitrile in boiling ethanol containing few drops of piperidine led to pyrido[1,2-*a*]benzimidazole-4-carbonitrile derivative **5** as shown in Scheme 3. The reaction may proceed through Michael addition (intermediate E) followed by  $\gamma$ -pyrone ring opening generating intermediate F which underwent free-rotation around the single bond (intermediate G) with concomitant cyclo-dehydration to produce the final product **5**, without addition of the OH group onto the olefinic bond. Compound **5** gave a red color with ferric chloride solution, indicating the presence of free phenolic OH group. The  $^1\text{H}$  NMR spectrum of compound **5** showed two characteristic doublets with the same coupling constant ( $J = 16.8$  Hz) at  $\delta$  6.61 and 7.01 ppm, indicating the presence of two olefinic protons in an *E*-configuration, confirming no addition of the hydroxyl group onto the olefinic bond. The  $^1\text{H}$  NMR spectrum also revealed two singlets at  $\delta$  7.22 and 8.86 ppm attributed to Ar-H<sub>phenolic</sub> and H-3, respectively, in addition to a broad D<sub>2</sub>O exchangeable signal attributed to phenolic OH proton at  $\delta$  9.91 ppm. The  $^{13}\text{C}$  NMR spectrum revealed characteristic signals at  $\delta$  19.9, 116.3 and 116.7 ppm attributed to CH<sub>3</sub> and 2C $\equiv$ N, respectively. The IR spectrum of compound **5** showed characteristic absorption bands at  $\nu$  3446 (OH), 3049 (CH<sub>arom.</sub>), 2923, 2880 (CH<sub>aliph.</sub>), 2242, 2218 (2 C $\equiv$ N), 1615 (C=N) and 1587  $\text{cm}^{-1}$  (C=C). The structure of compound **5** was further deduced from its mass spectrum which

Download English Version:

<https://daneshyari.com/en/article/7827825>

Download Persian Version:

<https://daneshyari.com/article/7827825>

[Daneshyari.com](https://daneshyari.com)