

HETEROCYCLES, Vol. 104, No. 4, 2022, pp. 707 - 722. © 2022 The Japan Institute of Heterocyclic Chemistry  
Received, 7th December, 2021, Accepted, 24th December, 2021, Published online, 11th January, 2022  
DOI: 10.3987/COM-21-14607

## NOVEL HETEROANNULATED CHROMENO[2,3-*b*]PYRIDINES AND RELATED COMPOUNDS USING 6-METHYLCHROMONE-3-CARBONITRILE

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**Abstract**– 6-Methylchromone-3-carbonitrile (**1**) was utilized as synthetic intermediate for construction of a diversity of annulated chromones. Heteroannulated chromeno[2,3-*b*]pyridines **2-8** were synthesized from reaction of carbonitrile **1** with some methylene active nitriles and cyclic active methylene ketones. Reaction of carbonitrile **1** with isomeric cyclohexanediones in 2:1 molar ratio gave three isomeric (*bis*chromeno)phenanthrolines. Applying Vilsmeier-Haack formylation on 8-methyl-1,2-dihydro-4*H*-chromeno[2,3-*b*]quinoline-4,6(3*H*)-dione (**11**) produced cyclic  $\beta$ -chloroaldehyde derivative **14** which upon condensation with benzylamine and *p*-toluidine afforded the corresponding Schiff bases. Condensation reactions of  $\beta$ -chloroaldehyde **14** with hydrazine hydrate and hydroxylamine hydrochloride produced the novel angularchromeno[2,3-*b*]pyrazolo[3,4-*f*]quinoline **17** and chromeno[2,3-*b*]isoxazolo[5,4-*f*]quinoline **18**, Structures of the new synthesized products were deduced based on their analytical and spectral data.

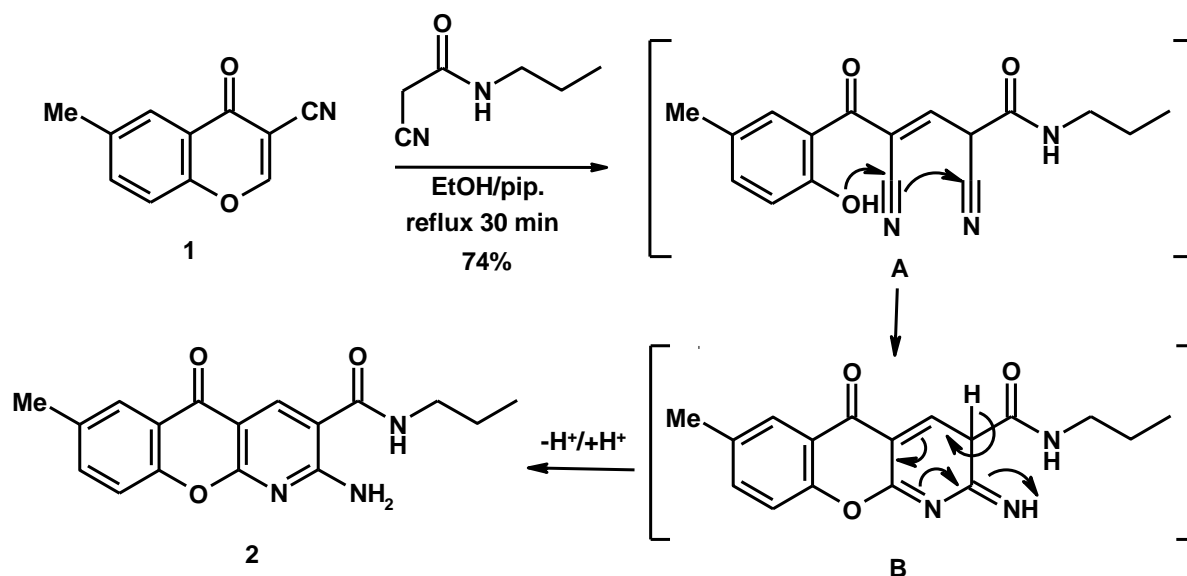
## INTRODUCTION

Chromone derivatives displayed various biological applications including anti-inflammatory,<sup>1</sup> antioxidant,<sup>2</sup> anti-HIV,<sup>3</sup> anticancer,<sup>4</sup> antibacterial,<sup>5</sup> antimicrobial,<sup>6</sup> antimalarial,<sup>7</sup> antibiotic,<sup>8</sup> antiproliferative,<sup>9</sup> neuroprotective,<sup>10</sup> as well as  $\alpha$ -glucosidase<sup>11</sup> and acetylcholinesterase inhibitors.<sup>12</sup> Chromones also used for treatment of Alzheimer's disease.<sup>13</sup> Due to their abundance in plants and their low mammalian toxicity, chromone derivatives are existing in large amounts in the diet of humans.<sup>14</sup> Electronic, optical, photoelectrical, photophysical, fluorescence studies as well as molecular docking and DFT calculations were performed for a diversity of chromones derivatives.<sup>15</sup> Chromones bearing an

electron withdrawing groups at position 3 appeared a variety of transformations upon treatment with nucleophilic reagents.<sup>16</sup> Chromone-3-carbonitriles gain the ability to undergo variable transformations related to  $\gamma$ -pyrone ring opening and heterocyclization.<sup>17</sup> Herein, we aimed to study the reactivity of 6-methylchromone-3-carbonitrile (**1**) towards some selected nucleophiles as well as construction of a diversity of annulated chromones.

## RESULTS AND DISCUSSION

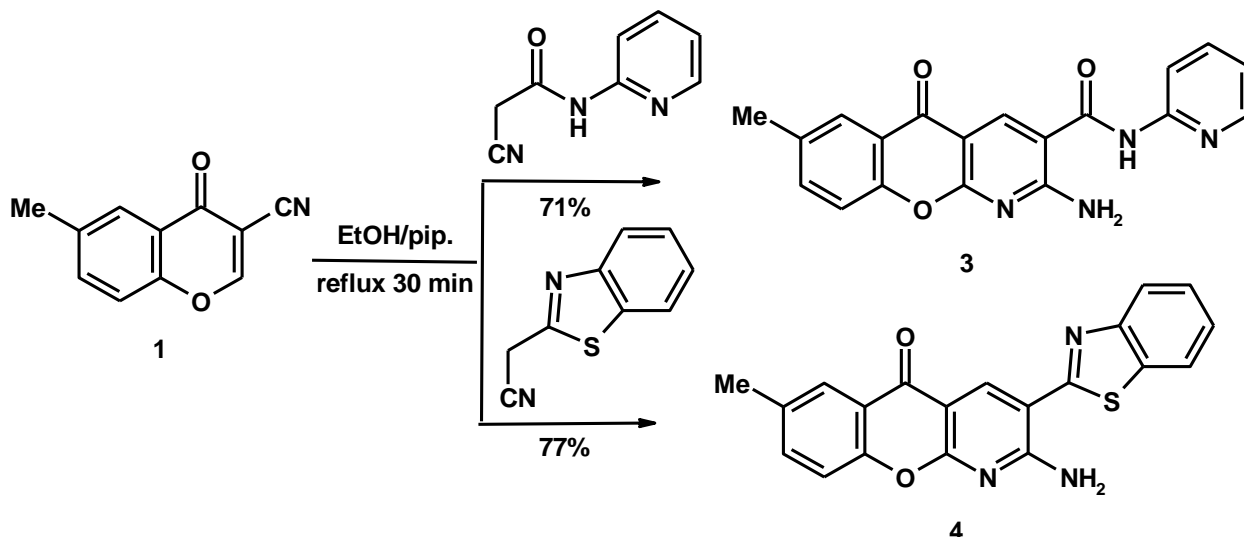
6-Methylchromone-3-carbonitrile (**1**) is a very active substrate towards nucleophilic reagents.<sup>17</sup> Firstly, the chemical behavior of carbonitrile **1** was examined towards some active methylene nitriles, under basic conditions. Reaction of carbonitrile **1** with 2-cyano-*N*-propylacetamide, in absolute ethanol containing piperidine, gave the corresponding 2-aminochromeno[2,3-*b*]pyridine-3-carboxamide **2** (Scheme 1). The reaction proceeds through nucleophilic attack at C-2 position of chromone moiety with  $\gamma$ -pyrone ring opening (intermediate **A**) followed by two consecutive cycloadditions into the nitrile groups (intermediate **B**) with concomitant proton transfer (Scheme 1). The <sup>1</sup>H NMR spectrum of compound **2** presented characteristic singlet attributed to H-4<sub>pyridine</sub> at  $\delta$  8.84 ppm. Its mass spectrum recorded the molecular ion peak at *m/z* 311 which agree well with the suggested molecular weight 311.34. The IR spectrum displayed characteristic absorption bands at  $\tilde{\nu}$  3414, 3332, 3246 (NH<sub>2</sub>, NH), 1672 (C=O<sub>amide</sub>), 1642 (C=O <sub>$\gamma$ -pyrone</sub>) and 1617 cm<sup>-1</sup> (C=N).



**Scheme 1.** Chemical transformation of carbonitrile **1** into chromeno[2,3-*b*]pyridine **2**

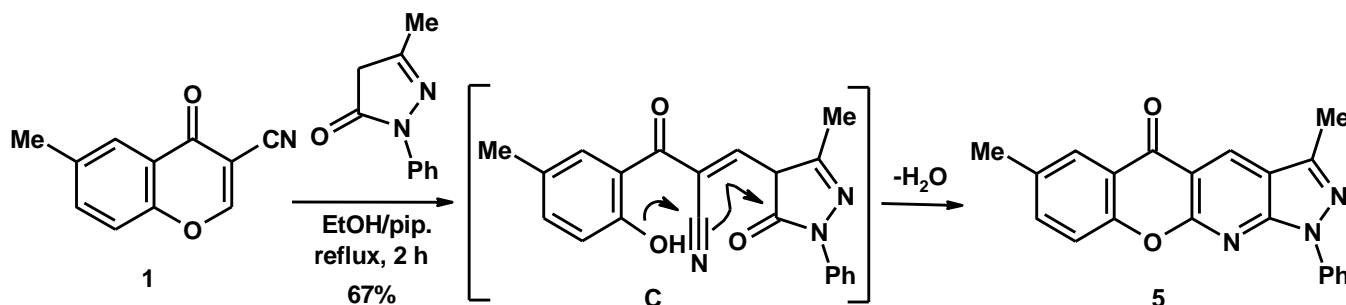
In a similar mechanism, reaction of carbonitrile **1** with 2-cyano-*N*-(pyridin-2-yl)acetamide and 1,3-benzothiazol-2-ylacetonitrile, in absolute ethanol containing piperidine, afforded the corresponding 3-substituted-2-aminochromeno[2,3-*b*]pyridines **3** and **4**, respectively (Scheme 2). Their <sup>1</sup>H NMR spectra

presented characteristic singlet signals attributed to H-4<sub>pyridine</sub> at  $\delta$  8.86 and 8.85, respectively. Structures **3** and **4** were further confirmed from their mass spectra that recorded their molecular ion peaks at  $m/z$  346 and 359 which agree well with the suggested molecular weights 346.34 and 359.40, respectively.



**Scheme 2.** Formation of 2-aminochromeno[2,3-*b*]pyridines **3** and **4**

Reaction of 6-methylchromone-3-carbonitrile (**1**) with 5-methyl-2-phenyl-2,4-dihydro-3*H*-pyrazol-3-one in boiling ethanol containing catalytic amount of piperidine as a basic catalyst produced heteroannulated chromeno[2,3-*b*]pyrazolo[4,3-*e*]pyridine derivative **5** (Scheme 3).<sup>18</sup> Formation of compound **5** occurs through  $\gamma$ -pyrone ring opening (intermediate **C**) followed by domino cycloaddition and cyclocondensation reactions. The <sup>1</sup>H NMR spectrum of compound **5** showed four characteristic singlets attributed to CH<sub>3</sub> pyrazole, CH<sub>3</sub> benzo, H-6 and H-4<sub>pyridine</sub> at  $\delta$  2.09, 2.37, 7.96 and 8.65 ppm, respectively. The mass spectrum recorded the molecular ion peak, as the base peak, at  $m/z$  341 which agrees with the formula weight (341.36) of the proposed structure. The IR spectrum of compound **5** showed typical absorption bands at  $\tilde{\nu}$  1659 and 1618 cm<sup>-1</sup>, assignable to C=O <sub>$\gamma$ -pyrone</sub> and C=N, respectively.

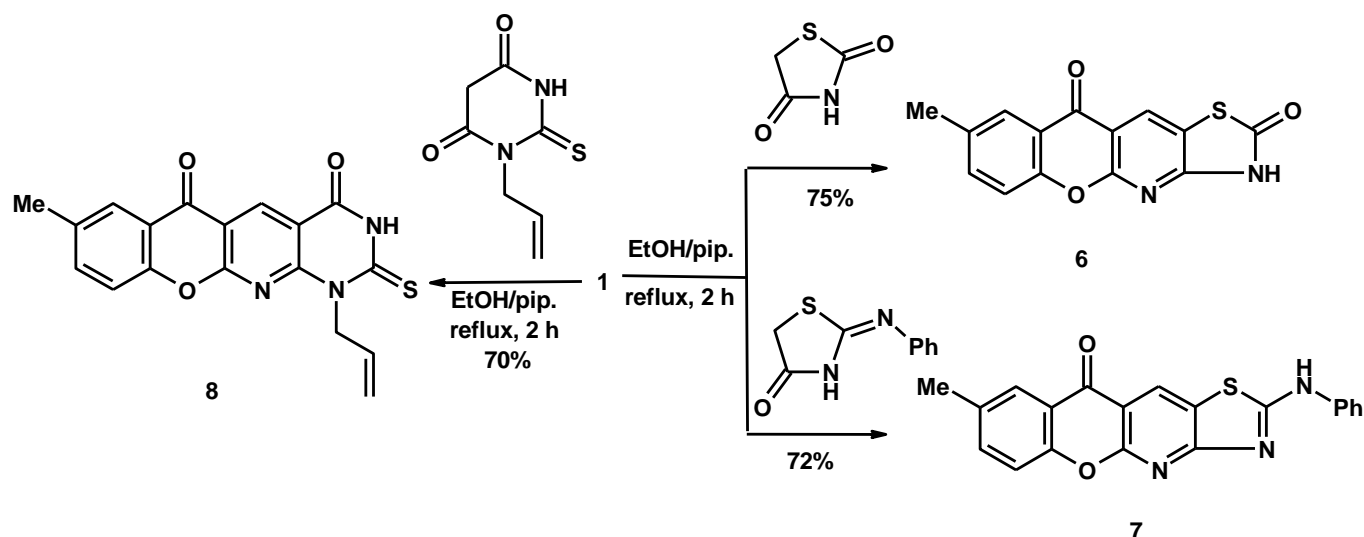


**Scheme 3.** Formation of heteroannulated chromeno[2,3-*b*]pyrazolo[4,3-*e*]pyridine **5**

In the same manner, reaction of carbonitrile **1** with thiazolidine-2,4-dione and 2-phenyliminothiazolidin-4-one, in boiling ethanol containing piperidine, afforded the tetracyclic chromeno[2,3-*b*][1,3]thiazolo-

[5,4-*e*]pyridines **6** and **7**, respectively (Scheme 4). Their  $^1\text{H}$  NMR spectra showed the pyridine ring proton as a specific singlet at  $\delta$  8.79 and 8.83 ppm, respectively. The IR spectra of compounds **6** and **7** displayed distinctive absorption bands attributed to  $\text{C}=\text{O}_{\gamma\text{-pyrone}}$  at  $\tilde{\nu}$  1655 and 1662  $\text{cm}^{-1}$ , in addition, the spectrum of compound **7** appeared the absorption band of  $\text{C}=\text{O}_{\text{thiazole}}$  at  $\tilde{\nu}$  1679  $\text{cm}^{-1}$ . The molecular weights of compounds **6** and **7** were further confirmed from their mass spectra which recorded the molecular ion peaks at  $m/z$  284 and 359.

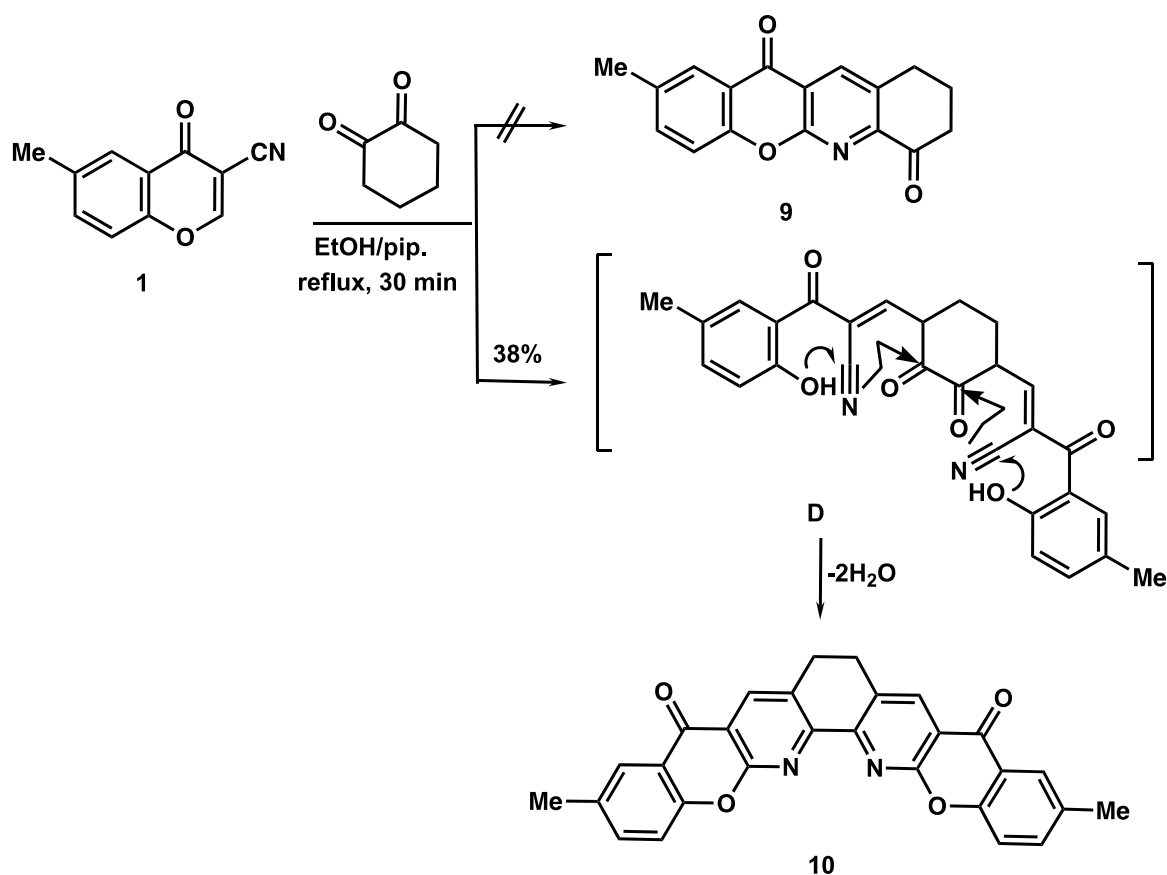
Further, carbonitrile **1** with 1-allyl-2-thioxodihydropyrimidine-4,6(1*H*,5*H*)-dione, in boiling ethanol containing piperidine, led to chromeno[3',2':5,6]pyrido[2,3-*d*]pyrimidine **8** (Scheme 4). Specific singlets appeared in the  $^1\text{H}$  NMR spectrum at  $\delta$  8.08 and 8.89 ppm, which attributed to H-7 and H-5, respectively. The IR spectrum of compound **8** showed distinctive absorption bands at  $\tilde{\nu}$  1696 ( $\text{C}=\text{O}_{\text{pyrimidine}}$ ), 1654 ( $\text{C}=\text{O}_{\gamma\text{-pyrone}}$ ), 1616 ( $\text{C}=\text{N}$ ) and 1228 ( $\text{C}=\text{S}$ )  $\text{cm}^{-1}$ . The molecular weight of compound **8** was further confirmed from its mass spectrum which recorded the molecular ion peak at  $m/z$  351.



**Scheme 4.** Formation of heteroannulated chromones **6-8**

The chemical behavior of 6-methylchromone-3-carbonitrile (**1**) was examined towards isomeric cyclohexanediones.<sup>19</sup> Therefore, reaction of carbonitrile **1** with cyclohexane-1,2-dione, in boiling ethanol containing piperidine, led to *bis*[1]chromeno[1,10]phenanthroline derivative **10** (Scheme 5). This reaction proceeds through ring opening of two molecules of carbonitrile **1** with one molecule of cyclohexane-1,2-dione furnishing intermediate **D** followed by consecutive cycloaddition and cyclodehydration reactions. The other expected product **9** (Mr 1:1) was ruled out from this reaction (Scheme 5). Structure of compound **10** was also confirmed from its mass spectrum which displayed the parent ion peak, as the base peak, at  $m/z$  446 which agrees with the assigned molecular formula ( $\text{C}_{28}\text{H}_{18}\text{N}_2\text{O}_4$ ). The  $^1\text{H}$  NMR spectrum of compound **10** showed specific singlet at  $\delta$  8.81 ppm attributed

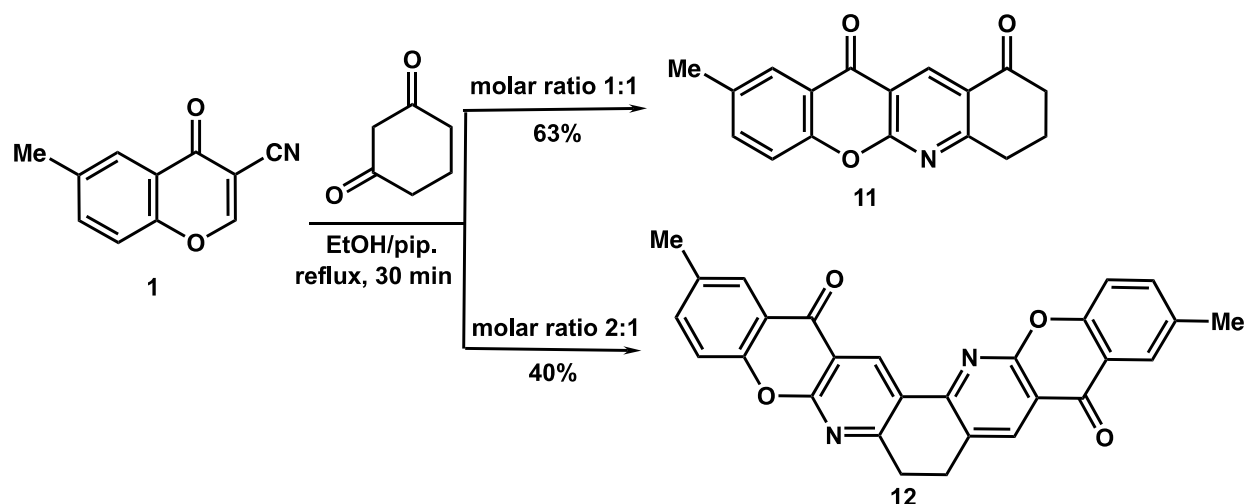
to H-4 of the pyridine rings. The IR spectrum showed distinctive absorption bands at  $\tilde{\nu}$  1666 ( $\text{C}=\text{O}_{\gamma\text{-pyrone}}$ ) and 1609 ( $\text{C}=\text{N}$ )  $\text{cm}^{-1}$



**Scheme 5.** Reaction of carbonitrile **1** with 1,2-cyclohexanedione

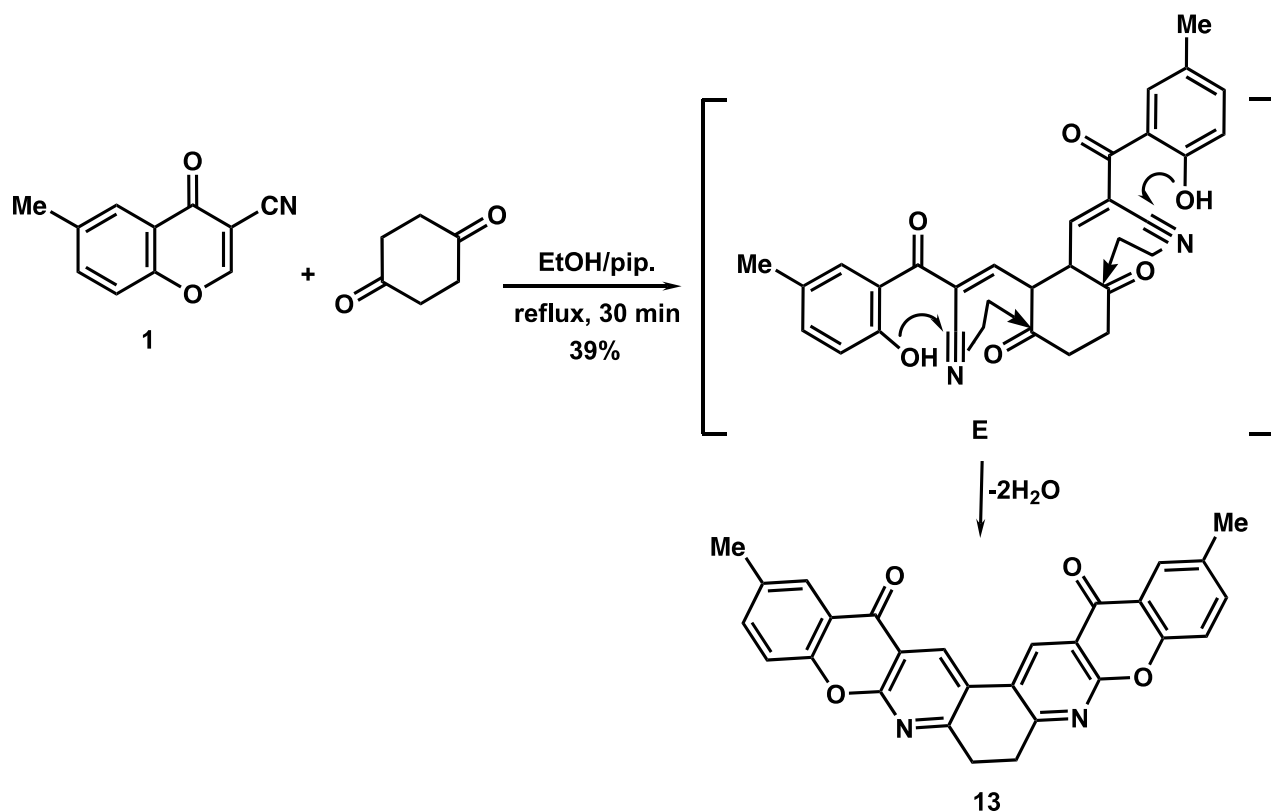
Moreover, reaction of carbonitrile **1** with 1,3-cyclohexanedione was considered under different molar ratios. Reaction of carbonitrile **1** with 1,3-cyclohexanedione (molar ratio 1:1) yielded chromenoquinoline derivative **11** (Scheme 6).<sup>20</sup> The <sup>1</sup>H NMR spectrum of compound **11** showed three triplet signals in the upfield region at  $\delta$  2.15, 2.71 and 3.16 ppm attributable to three CH<sub>2</sub> groups, as well as a distinctive singlet at  $\delta$  8.81 ppm assignable to H-4<sub>pyridine</sub>.

Repeating the previous reaction in 2:1 molar ratio (carbonitrile: 1,3-cyclohexanedione) gave heptacyclic (*bischromeno*)[1,7]phenanthroline **12** (Scheme 6). The mass spectrum of compound **12** appeared the molecular ion peak, as the base peak, at  $m/z$  446. The singlet signal characteristic for H-4 of the pyridine rings appeared in the <sup>1</sup>H NMR spectrum at  $\delta$  8.84 ppm



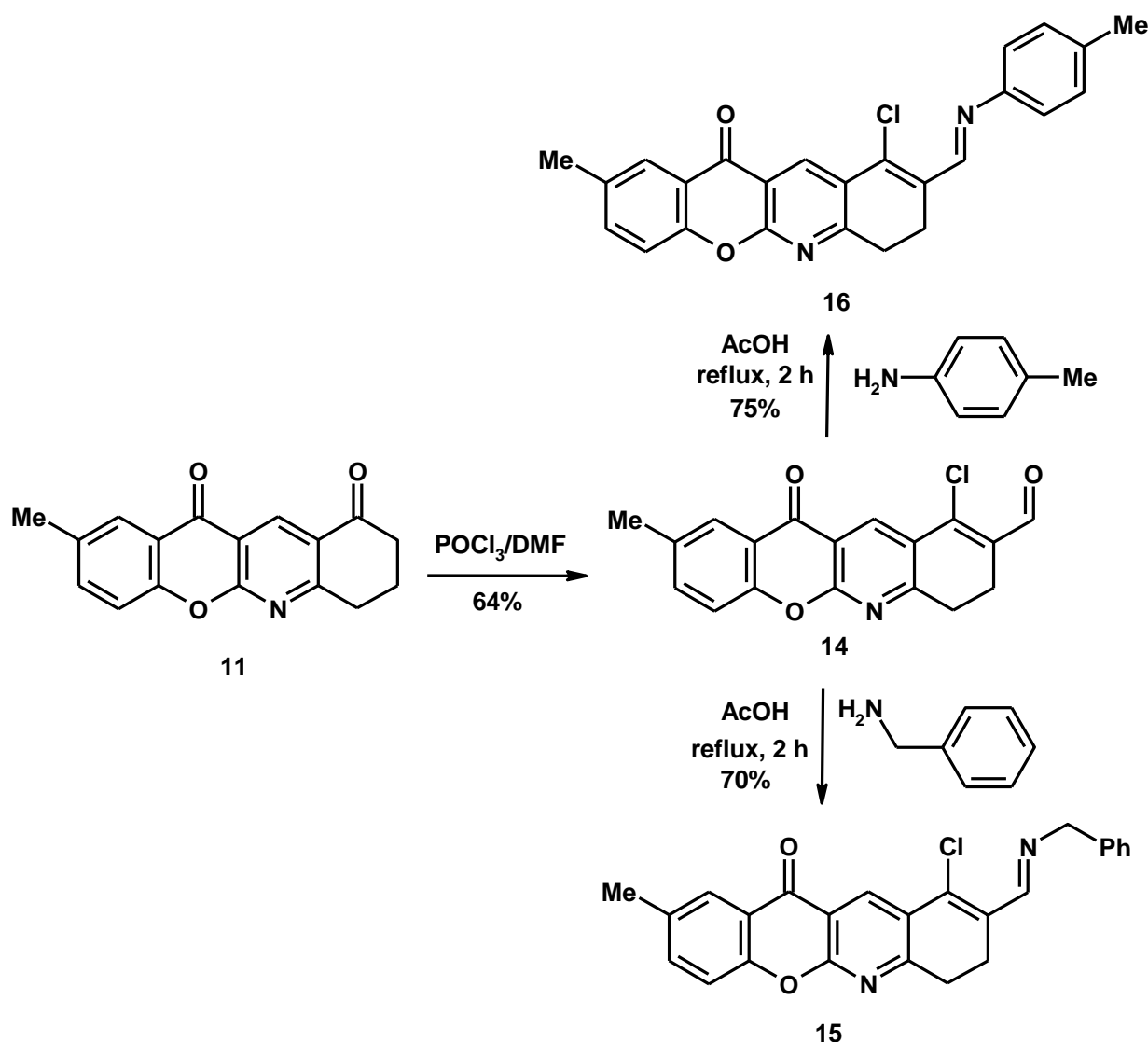
**Scheme 6.** Reaction of carbonitrile **1** with cyclohexane-1,3-dione at different molar ratios

As noticed with 1,2-cyclohexanedione, reaction of carbonitrile **1** with 1,4-cyclohexanedione, in boiling ethanol containing piperidine, gave heptacyclic (*bischromeno*)[4,7]phenanthroline derivative **13**, via non-isolable intermediate **E** (Scheme 7). The molecular ion peak appeared, as the base peak, at  $m/z$  446 and proves the suggested structure. In the  $^1\text{H}$  NMR spectrum, the singlet distinctive for H-4<sub>pyridine</sub> appeared at  $\delta$  8.88 ppm.



**Scheme 7.** Reaction of carbonitrile **1** with 1,4-cyclohexanedione

The presence of an active methylene group in compound **11** encourages us to apply Vilsmeier-Haack reaction on this compound.<sup>21</sup> Therefore, formylation of compound **11** using Vilsmeier-Haack reagent ( $\text{POCl}_3/\text{DMF}$ ) afforded the novel 1-chloro-9-methyl-11-oxo-3,4-dihydro-11*H*-chromeno[2,3-*b*]-quinoline-2-carboxaldehyde (**14**) (Scheme 8). The  $^1\text{H}$  NMR spectrum of compound **14** showed specific singlet signals at  $\delta$  10.81 ppm attributable to the aldehyde proton. The IR spectrum showed typical absorption bands at  $\tilde{\nu}$  1704 ( $\text{C}=\text{O}_{\text{aldehyde}}$ ) and 1646 ( $\text{C}=\text{O}_{\gamma\text{-pyrone}}$ )  $\text{cm}^{-1}$ . The mass spectrum represents a good evidence for the structure of  $\beta$ -chloroenaldehyde **14** which showed the molecular ion peak with the isotopic peak attributed to the presence of one chlorine atom as  $\text{M}^+/\text{M}+2$  at  $m/z$  325/327; in the expected relative abundance (24/8%).

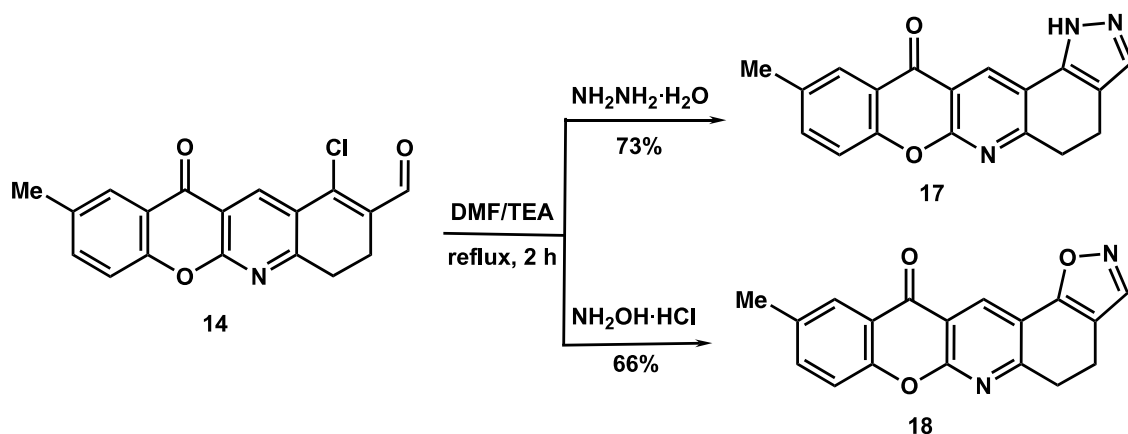


**Scheme 8.** Synthesis and condensation reactions of  $\beta$ -chloroenaldehyde **14**

The reactivity of cyclic  $\beta$ -chloroenaldehyde **14** was examined towards some primary amines. Therefore, boiling compound **14** with benzylamine and *p*-toluidine in acetic acid yielded the corresponding Schiff

bases **15** and **16**, respectively (Scheme 8). The IR spectra of compounds **15** and **16** showed the disappearance of the aldehyde function which observed in compound **14**. The mass spectra of compounds **15** and **16** recorded the parent ion peaks at  $m/z$  414/416 (relative abundance 48/16%) and 414/416 (relative abundance 59/20%) that confirms the existence of the chlorine atom in the products. The  $^1\text{H}$  NMR spectra of compounds **15** and **16** presented specific singlet attributable to the azomethine protons at  $\delta$  8.45 and 8.51 ppm, respectively.

After that, the behavior of  $\beta$ -chloroaldehyde **14** was investigated towards some binucleophilic reagents. Thus, treatment of compound **14** with hydrazine hydrate and hydroxylamine hydrochloride, in boiling DMF containing catalytic amount of triethylamine (TEA) yielded the novel angular chromeno[2,3-*b*]pyrazolo[3,4-*f*]quinoline **17** and chromeno[2,3-*b*]isoxazolo[5,4-*f*]quinoline **18**, respectively (Scheme 9). The mass spectra of compounds **17** and **18** verified the suggested structures and displayed the parent ion peaks at  $m/z$  303 and 304, that agree well with the proposed formula weights 303.31 and 304.30, respectively. The  $^1\text{H}$  NMR spectra of compounds **17** and **18** showed specific singlet assignable to the pyrazole ring proton (H-3) at  $\delta$  8.36 and 8.54 ppm, respectively.



**Scheme 9.** Reactions of  $\beta$ -chloroaldehyde **14** with some 1,2-binucleophiles

## CONCLUSION

6-Methylchromone-3-carbonitrile (**1**) was utilized as active precursor for construction of a diversity of heteroannulated systems containing chromeno[2,3-*b*]pyridine moiety. Reaction of carbonitrile **1** with some methylene active nitriles namely; 2-cyano-*N*-propylacetamide, 2-cyano-*N*-(pyridin-2-yl)acetamide and 1,3-benzothiazol-2-ylacetonitrile afforded 2-aminochromeno[2,3-*b*]pyridines **2-4**. Chromeno[2,3-*b*]pyrazolo[4,3-*e*]pyridine **5**, chromeno[2,3-*b*][1,3]thiazolo[5,4-*e*]pyridines **6, 7** and chromeno[3',2':5,6]-pyrido[2,3-*d*]pyrimidine **8** were synthesized from ring opening ring closure (RORC) reactions of carbonitrile **1** with 5-methyl-2-phenyl-2,4-dihydro-3*H*-pyrazol-3-one, thiazolidine-2,4-dione and 2-phenyliminothiazolidin-4-one and 1-allyl-2-thioxodihydropyrimidine-4,6(1*H*,5*H*)-dione. Three isomeric



(*bis*chromeno)phenanthrolines were efficiently synthesized from reaction of carbonitrile **1** with isomeric cyclohexanediones in 2:1 molar ratio. Reaction of carbonitrile **1** with 1,3-cyclohexanedione in 1:1 molar ratio afforded 8-methyl-1,2-dihydro-4*H*-chromeno[2,3-*b*]quinoline-4,6(3*H*)-dione **11** which upon Vilsmeier-Haack formylation afforded the novel  $\beta$ -chloroaldehyde derivative **14**. Reaction of compound **14** with benzylamine and *p*-toluidine afforded the corresponding Schiff bases. Condensation reactions of compound **14** with hydrazine hydrate and hydroxylamine gave the novel angular chromeno[2,3-*b*]pyrazolo[3,4-*f*]quinoline **17** and chromeno[2,3-*b*]isoxazolo[5,4-*f*]quinoline **18**.

## EXPERIMENTAL

Melting points were determined on a digital Stuart SMP3 apparatus. Infrared spectra were measured on FTIR Nicolet IS10 spectrophotometer (cm<sup>-1</sup>), using KBr disks. <sup>1</sup>H NMR (300 MHz) and <sup>13</sup>C NMR (75 MHz) spectra were measured on Mercury-300BB, using DMSO-*d*<sub>6</sub> as a solvent and TMS ( $\delta$ , ppm) as the internal standard. Mass spectra were obtained using GC-2010 Shimadzu Gas chromatography instrument mass spectrometer (70 eV). Elemental microanalyses were performed on a Perkin-Elmer CHN-2400 analyzer. 6-Methylchromene-3-carbonitrile (**1**) was prepared according to literature method.<sup>22</sup>

**2-Amino-7-methyl-5-oxo-*N*-propyl-5*H*-chromeno[2,3-*b*]pyridine-3-carboxamide (2).** A mixture of carbonitrile **1** (0.56 g, 3 mmol) and 2-cyano-*N*-propylacetamide (0.48 g, 3 mmol), in absolute EtOH (20 mL) containing piperidine (0.1 mL), was heated under reflux for 30 min. The white crystals obtained after cooling were filtered and crystallized from EtOH, mp 191-192 °C, yield (0.69 g, 74%). IR (KBr, cm<sup>-1</sup>)  $\nu$ : 3414, 3332, 3246 (NH<sub>2</sub>, NH), 3048 (CH<sub>arom.</sub>), 2974, 2927, 2889 (CH<sub>aliph.</sub>), 1672 (C=O<sub>amide</sub>), 1642 (C=O<sub>pyrone</sub>), 1617 (C=N), 1579 (C=C). <sup>1</sup>H NMR (300 MHz, DMSO-*d*<sub>6</sub>)  $\delta$ : 0.97 (t, 3H, *J*=6.9 Hz, CH<sub>3</sub>), 1.07-1.23 (m, 2H, CH<sub>2</sub>), 2.14 (t, 3H, *J*=6.6 Hz, CH<sub>2</sub>), 2.32 (s, 3H, CH<sub>3</sub>), 7.28 (d, 1H, *J*= 7.2 Hz, H-9), 7.53 (d, 1H, *J*= 7.2 Hz, H-8), 7.92 (s, 1H, H-6), 8.84 (s, 1H, H-4<sub>pyridine</sub>), 9.68 (bs, 2H, NH<sub>2</sub> exchangeable with D<sub>2</sub>O), 10.37 (br, 1H, NH exchangeable with D<sub>2</sub>O). <sup>13</sup>C NMR (75 MHz, DMSO-*d*<sub>6</sub>,  $\delta$ ): 12.4, 20.9, 22.6, 37.7, 104.8, 108.4, 118.6, 121.7, 126.7, 129.4, 132.1, 142.7, 150.8, 154.3, 159.6, 168.2, 175.8. Mass spectrum, *m/z* (*I*<sub>r</sub>%): 311 (20), 253 (100), 225 (37), 210 (18), 157 (6), 135 (52), 120 (29), 77 (17), 64 (8). Anal. Calcd for C<sub>17</sub>H<sub>17</sub>N<sub>3</sub>O<sub>3</sub> (311.34): C, 65.58; H, 5.50; N, 13.50%. Found: C, 65.46; H, 5.34 N, 13.29%.

**2-Amino-7-methyl-5-oxo-*N*-(pyridin-2-yl)-5*H*-chromeno[2,3-*b*]pyridine-3-carboxamide (3).** A mixture of carbonitrile **1** (0.56 g, 3 mmol) and 2-cyano-*N*-(pyridin-2-yl)acetamide (0.52 g, 3 mmol), in absolute EtOH (20 mL) containing piperidine (0.1 mL), was heated under reflux for 30 min. The white crystals obtained during heating were filtered and crystallized from DMF/H<sub>2</sub>O, mp 272-273 °C, yield (0.74 g, 71%). IR (KBr, cm<sup>-1</sup>)  $\nu$ : 3432, 3357, 3259 (NH<sub>2</sub>, NH), 3067 (CH<sub>arom.</sub>), 1669 (C=O<sub>amide</sub>), 1645

(C=O<sub>γ</sub>-pyrone), 1611 (C=N), 1582 (C=C). <sup>1</sup>H NMR (300 MHz, DMSO-*d*<sub>6</sub>) δ: 2.31 (s, 3H, CH<sub>3</sub>), 7.31-7.60 (m, 6H, Ar-H), 7.96 (s, 1H, H-9), 8.86 (s, 1H, H-4<sub>pyridine</sub>), 9.83 (bs, 2H, NH<sub>2</sub> exchangeable with D<sub>2</sub>O), 10.82 (br, 1H, NH exchangeable with D<sub>2</sub>O). <sup>13</sup>C NMR (75 MHz, DMSO-*d*<sub>6</sub>) δ: 21.1, 104.7, 109.1, 112.3, 114.8, 118.8, 120.3, 122.8, 126.5, 127.2, 129.0, 132.7, 135.8, 143.9, 150.6, 154.9, 159.2, 169.4, 176.1. Mass spectrum, *m/z* (*I*<sub>r</sub>%): 346 (100), 318 (91), 239 (54), 181 (12), 135 (42), 120 (38), 78 (15), 64 (17). Anal. Calcd for C<sub>19</sub>H<sub>14</sub>N<sub>4</sub>O<sub>3</sub> (346.34): C, 65.89; H, 4.07; N, 16.18%. Found: C, 65.76; H, 3.85; N, 16.12%.

**2-Amino-3-(1,3-benzothiazol-2-yl)-7-methyl-5H-chromeno[2,3-*b*]pyridin-5-one (4).** A mixture of carbonitrile **1** (0.56 g, 3 mmol) and 1,3-benzothiazol-2-ylacetonitrile (0.52 g, 3 mmol), in absolute EtOH (20 mL) containing piperidine (0.1 mL), was heated under reflux for 30 min. The yellow crystals obtained during heating were filtered off and crystallized from DMF/EtOH, mp > 300 °C, yield (0.83 g, 77%). IR (KBr, cm<sup>-1</sup>) v: 3406, 3312 (NH<sub>2</sub>), 3039 (CH<sub>arom.</sub>), 1657 (C=O<sub>γ</sub>-pyrone), 1619 (C=N), 1574 (C=C). <sup>1</sup>H NMR (300 MHz, DMSO-*d*<sub>6</sub>) δ: 2.37 (s, 3H, CH<sub>3</sub>), 7.26-7.59 (m, 5H, Ar-H and H-9), 7.58 (d, 1H, *J* = 7.8 Hz, H-8), 8.02 (s, 1H, H-6), 8.85 (s, 1H, H-4<sub>pyridine</sub>), 9.23 (br, 2H, NH<sub>2</sub> exchangeable with D<sub>2</sub>O). Mass spectrum, *m/z* (*I*<sub>r</sub>%): 359 (64), 331 (100), 223 (32), 181 (8), 157 (11), 135 (51), 120 (31), 77 (28), 64 (10). Anal. Calcd for C<sub>20</sub>H<sub>13</sub>N<sub>3</sub>O<sub>2</sub>S (359.40): C, 66.84; H, 3.65; N, 11.69; S, 8.92%. Found: C, 66.61; H, 3.40; N, 11.33; S, 8.67%.

**3,7-Dimethyl-1-phenylchromeno[2,3-*b*]pyrazolo[4,3-*e*]pyridin-5(1H)-one (5).** A mixture of carbonitrile **1** (0.56 g, 3 mmol) and 5-methyl-2-phenyl-2,4-dihydro-3H-pyrazol-3-one (0.52 g, 3 mmol) in absolute EtOH (20 mL) containing piperidine (0.1 mL), was heated under reflux for 2 h. The orange crystals obtained after cooling were filtered and crystallized from DMF/H<sub>2</sub>O, mp 206-207 °C, yield (0.46 g, 67%). IR (KBr, cm<sup>-1</sup>) v: 3081 (CH<sub>arom.</sub>), 2962, 2913 (CH<sub>aliph.</sub>), 1659 (C=O<sub>γ</sub>-pyrone), 1618 (C=N), 1592 (C=C). <sup>1</sup>H NMR (300 MHz, DMSO-*d*<sub>6</sub>) δ: 2.09 (s, 3H, CH<sub>3</sub>), 2.37 (s, 3H, CH<sub>3</sub>), 6.75-6.98 (m, 5H, Ph-H), 7.59 (d, 1H, *J* = 7.5 Hz, H-9), 7.76 (d, 1H, *J* = 7.5 Hz, H-8), 7.96 (s, 1H, H-6), 8.65 (s, 1H, H-4<sub>pyridine</sub>). Mass spectrum, *m/z* (*I*<sub>r</sub>%): 341 (100), 264 (46), 236 (38), 195 (13), 181 (8), 135 (49), 120 (18), 77 (14), 64 (7). Anal. Calcd for C<sub>21</sub>H<sub>15</sub>N<sub>3</sub>O<sub>2</sub> (341.36): C, 73.89; H, 4.43; N, 12.31%. Found: C, 73.71; H, 4.35; N, 12.11%.

**8-Methylchromeno[2,3-*b*][1,3]thiazolo[5,4-*e*]pyridine-2,10(3H,10H)-dione (6).** A mixture of carbonitrile **1** (0.56 g, 3 mmol) and 1,3-thiazolidin-4-one (0.35 g, 3 mmol) in absolute EtOH (20 mL) containing piperidine (0.1 mL), was heated under reflux for 2 h. The yellow crystals obtained during heating were filtered and crystallized from AcOH/H<sub>2</sub>O, mp 275-276 °C, yield (0.64 g, 75%). IR (KBr, cm<sup>-1</sup>) v: 3352 (NH), 3045 (CH<sub>arom.</sub>), 2934, 2889 (CH<sub>aliph.</sub>), 1679 (C=O<sub>thiazole</sub>), 1655 (C=O<sub>γ</sub>-pyrone), 1613 (C=N), 1576 (C=C). <sup>1</sup>H NMR (300 MHz, DMSO-*d*<sub>6</sub>) δ: 2.32 (s, 3H, CH<sub>3</sub>), 6.93-7.35 (m, 6H, Ph-H and H-6), 7.52 (d, 1H, *J* = 7.5 Hz, H-7), 7.92 (s, 1H, H-9), 8.79 (s, 1H, H-4<sub>pyridine</sub>), 11.63 (bs, 1H, NH

exchangeable with D<sub>2</sub>O). <sup>13</sup>C NMR (75 MHz, DMSO-*d*<sub>6</sub>) δ: 20.5, 113.6, 114.7, 119.2, 122.8, 127.1, 129.7, 132.6, 138.4, 149.7, 152.3, 154.7, 169.3, 176.1. Mass spectrum, *m/z* (*I*<sub>r</sub>%): 284 (37), 256 (100), 224 (9), 196 (26), 135 (59), 120 (32), 77 (19), 64 (10). Anal. Calcd for C<sub>14</sub>H<sub>8</sub>N<sub>2</sub>O<sub>3</sub>S (284.29): C, 59.15; H, 2.84; N, 9.85; S, 11.28%. Found: C, 58.88; H, 2.71; N, 9.60; S, 11.03%.

**2-Anilino-8-methylchromeno[2,3-*b*][1,3]thiazolo[5,4-*e*]pyridin-10(10*H*)-one (7).** A mixture of carbonitrile **1** (0.56 g, 3 mmol) and 2-(phenylimino)-1,3-thiazolidin-4-one (0.58 g, 3 mmol) in absolute EtOH (20 mL) and piperidine (0.1 mL) was heated under reflux for 2 h. The pale brown crystals obtained during heating were filtered and recrystallized from AcOH, mp > 300 °C, yield (0.78 g, 72%). IR (KBr, cm<sup>-1</sup>) ν: 3382 (NH), 3061 (CH<sub>arom.</sub>), 2945, 2895 (CH<sub>aliph.</sub>), 1662 (C=O<sub>γ-pyrone</sub>), 1610 (C=N), 1583 (C=C). <sup>1</sup>H NMR (300 MHz, DMSO-*d*<sub>6</sub>) δ: 2.36 (s, 3H, CH<sub>3</sub>), 6.93-7.24 (m, 5H, Ph-H), 7.39 (d, 1H, *J* = 7.8 Hz, H-6), 7.57 (d, 1H, *J* = 7.8 Hz, H-7), 7.97 (s, 1H, H-9), 8.83 (s, 1H, H-4<sub>pyridine</sub>), 9.68 (bs, 1H, NH exchangeable with D<sub>2</sub>O). <sup>13</sup>C NMR (75 MHz, DMSO-*d*<sub>6</sub>) δ: 20.8, 112.9, 114.2, 117.4, 119.6, 120.1, 123.1, 126.8, 128.0, 130.2, 133.3, 136.7, 138.9, 144.5, 149.3, 151.5, 155.2, 176.4. Mass spectrum, *m/z* (*I*<sub>r</sub>%): 359 (27), 267 (41), 239 (15), 213 (8), 181 (13), 135 (42), 120 (33), 92 (72), 77 (100), 64 (28). Anal. Calcd for C<sub>20</sub>H<sub>13</sub>N<sub>3</sub>O<sub>2</sub>S (359.40): C, 66.84; H, 3.65; N, 11.69; S, 8.92%. Found: C, 66.58; H, 3.35; N, 11.40; S, 8.80%.

**1-Allyl-8-methyl-2-thioxo-2*H*-chromeno[3',2':5,6]pyrido[2,3-*d*]pyrimidine-4,6(1*H*,3*H*)-dione (8).** A mixture of carbonitrile **1** (0.56 g, 3 mmol) and 1-allyl-2-thioxodihydropyrimidine-4,6(1*H*,5*H*)-dione (0.55 g, 3 mmol) in absolute EtOH (20 mL) containing piperidine (0.1 mL), was heated under reflux for 2 h. The yellow crystals obtained during heating were filtered and crystallized from DMF/H<sub>2</sub>O, mp 280-281 °C, yield (0.49 g, 70%). IR (KBr, cm<sup>-1</sup>) ν: 3232 (NH), 3044 (CH<sub>arom.</sub>), 2979, 2942 (CH<sub>aliph.</sub>), 1696 (C=O<sub>pyrimidine</sub>), 1654 (C=O<sub>γ-pyrone</sub>), 1616 (C=N), 1579 (C=C), 1228 (C=S). <sup>1</sup>H NMR (300 MHz, DMSO-*d*<sub>6</sub>) δ: 2.33 (s, 3H, CH<sub>3</sub>), 3.10 (d, 2H, *J*=6.3 Hz, NCH<sub>2</sub>), 4.96 (d, 2H, *J*=6.6 Hz, CH<sub>2</sub> olefinic), 5.79-5.83 (m, 1H, CH<sub>olefinic</sub>), 7.49 (d, 1H, *J* = 7.2 Hz, H-10), 7.81 (d, 1H, *J* = 7.2 Hz, H-9), 8.08 (s, 1H, H-7), 8.89 (s, 1H, H-5), 11.26 (bs, 1H, NH exchangeable with D<sub>2</sub>O). <sup>13</sup>C NMR (75 MHz, DMSO-*d*<sub>6</sub>) δ: 20.5, 36.7, 88.2, 98.3, 112.2, 115.3, 116.4, 117.6, 123.6, 124.3, 128.9, 133.1, 137.2, 152.9, 157.9, 160.7, 162.5, 168.4. Mass spectrum, *m/z* (*I*<sub>r</sub>%): 351 (100), 323 (75), 295 (47), 255 (39), 211 (15), 135 (35), 120 (46), 77 (42), 64 (21). Anal. Calcd for C<sub>18</sub>H<sub>13</sub>N<sub>3</sub>O<sub>3</sub>S (351.38): C, 61.53; H, 3.73; N, 11.96; S, 9.13%. Found: C, 61.30; H, 3.65; N, 11.74; S, 9.02%.

**7,8-Dihydro-3,12-dimethyl-bis[1]chromeno[2,3-*b*:3',2'-*J*][1,10]phenanthroline-5,10-(5*H*,10*H*)-dione (10).** A mixture of carbonitrile **1** (0.56 g, 3 mmol) and 1,2-cyclohexanedione (0.34 g, 3 mmol), in absolute EtOH (20 mL) containing piperidine (0.1 mL), was heated at reflux for 30 min. The pale-yellow crystals obtained during heating were filtered and crystallized from DMF, mp > 300 °C, yield (0.51 g, 38%). IR (KBr, cm<sup>-1</sup>) ν: 3018 (CH<sub>arom.</sub>), 2952, 2906 (CH<sub>aliph.</sub>), 1666 (C=O<sub>γ-pyrone</sub>), 1609 (C=N), 1544

(C=C). <sup>1</sup>H-NMR (300 MHz, DMSO-*d*<sub>6</sub>) δ: 2.01 (s, 4H, 2CH<sub>2</sub>), 2.34 (s, 6H, 2CH<sub>3</sub>), 7.57 (d, 2H, *J* = 8.1 Hz, Ar-H), 7.76 (d, 2H, *J* = 8.1 Hz, Ar-H), 7.94 (s, 2H, H-4 and H-11), 8.81 (s, 2H, 2H-4<sub>pyridine</sub>). Mass spectrum, *m/z* (*I*<sub>r</sub>%): 446 (100). Anal. Calcd for C<sub>28</sub>H<sub>18</sub>N<sub>2</sub>O<sub>4</sub> (446.45): C, 75.33; H, 4.06; N, 6.27%. Found: C, 75.25; H, 4.02; N, 6.10%.

**8-Methyl-1, 2-dihydro-4H-chromeno[2,3-*b*]quinoline-4,6(3H)-dione (11).** A mixture of carbonitrile **1** (0.55 g, 3 mmol) and cyclohexane-1,3-dione (0.34 g, 3 mmol) in absolute EtOH (20 mL) containing piperidine (0.1 mL) was heated under reflux for 30 min. The white crystals obtained during heating were filtered and recrystallized from EtOH, mp 256-257 °C, yield (0.53 g, 63%). IR (KBr, cm<sup>-1</sup>) ν: 3051 (CH<sub>arom.</sub>), 2943, 2925, 2849 (CH<sub>aliph.</sub>), 1689 (C=O<sub>quinolinone</sub>), 1663 (C=O<sub>γ-pyrone</sub>), 1618 (C=N), 1589 (C=C). <sup>1</sup>H NMR (300 MHz, DMSO-*d*<sub>6</sub>) δ: 2.17 (t, 2H, *J* = 6.3 Hz, CH<sub>2</sub>), 2.44 (s, 3H, CH<sub>3</sub>), 2.72 (t, 2H, *J* = 6.3 Hz, CH<sub>2</sub>), 3.16 (t, 2H, *J* = 7.2 Hz, CH<sub>2</sub>), 7.57 (d, 1H, *J* = 8.4 Hz, H-10), 7.71 (d, 1H, *J* = 8.1 Hz, H-9), 7.91 (s, 1H, H-7), 8.80 (s, 1H, H-5). <sup>13</sup>C NMR (75 MHz, DMSO-*d*<sub>6</sub>) δ: 20.2 (CH<sub>3</sub>), 20.7 (C-2), 32.3 (C-1), 37.6 (C-3), 114.9 (C-5a), 118.3 (C-6a), 120.6, 125.3, 125.9, 134.9, 135.5, 137.3, 153.0, 160.6, 169.3, 176.1 (C-6 as C=O), 195.6 (C-4 as C=O). Mass spectrum, *m/z* (*I*<sub>r</sub>%): 279 (70), 251 (100), 223 (21), 166 (17), 118 (10), 105 (8), 77 (18), 63 (14). Anal. Calcd for C<sub>17</sub>H<sub>13</sub>NO<sub>3</sub> (279.29): C, 73.11; H, 4.69; N, 5.02%. Found: C, 73.10; H, 4.65; N, 4.93%.

**7,8-Dihydro-3,11-dimethyl-5H,15H-bis[1]chromeno[2,3-*b*:2',3'-*J*][1,7]phenanthroline-5,15-dione (12).** A mixture of carbonitrile **1** (0.56 g, 3 mmol) and 1,3-cyclohexanedione (0.17 g, 1.5 mmol), in absolute EtOH (20 mL) containing piperidine (0.1 mL), was heated at reflux for 30 min. The pale-yellow crystals obtained during heating were filtered and crystallized from DMF, mp > 300 °C, yield (0.54 g, 40%). IR (KBr, cm<sup>-1</sup>) ν: 3065 (CH<sub>arom.</sub>), 2928, 2892 (CH<sub>aliph.</sub>), 1670 (C=O<sub>γ-pyrone</sub>), 1610 (C=N), 1576 (C=C). <sup>1</sup>H NMR (300 MHz, DMSO-*d*<sub>6</sub>) δ: 2.07 (s, 4H, 2CH<sub>2</sub>), 2.30 (s, 6H, 2CH<sub>3</sub>), 7.49 (d, 2H, *J* = 7.8 Hz, Ar-H), 7.72 (d, 2H, *J* = 7.8 Hz, Ar-H), 7.97 (s, 2H, H-4 and H-11), 8.84 (s, 2H, 2H-4<sub>pyridine</sub>). Mass spectrum, *m/z* (*I*<sub>r</sub>%): 446 (100). Anal. Calcd for C<sub>28</sub>H<sub>18</sub>N<sub>2</sub>O<sub>4</sub> (446.45): C, 75.33; H, 4.06; N, 6.27%. Found: C, 75.19; H, 3.97; N, 6.06%.

**7,8-Dihydro-2,13-dimethyl-bis[1]chromeno[3,2-*b*:2',3'-*J*][4,7]phenanthroline-15,18-(15H,18H)-dione (13).** A mixture of carbonitrile **1** (0.56 g, 3 mmol) and 1,4-cyclohexanedione (0.34 g, 3 mmol), in absolute EtOH (20 mL) containing piperidine (0.1 mL), was heated at reflux for 30 min. The pale-yellow crystals obtained during heating were filtered and crystallized from DMF, mp > 300 °C, yield (0.52 g, 39%). IR (KBr, cm<sup>-1</sup>) ν: 3065 (CH<sub>arom.</sub>), 2939, 2885 (CH<sub>aliph.</sub>), 1662 (C=O<sub>γ-pyrone</sub>), 1613 (C=N), 1582 (C=C). <sup>1</sup>H NMR (300 MHz, DMSO-*d*<sub>6</sub>) δ: 2.10 (s, 4H, 2CH<sub>2</sub>), 2.32 (s, 6H, 2CH<sub>3</sub>), 7.53 (d, 2H, *J* = 7.5 Hz, Ar-H), 7.75 (d, 2H, *J* = 7.5 Hz, Ar-H), 8.02 (s, 2H, H-1 and H-14), 8.88 (s, 2H, 2H-4<sub>pyridine</sub>). Mass spectrum, *m/z* (*I*<sub>r</sub>%): 446 (100). Anal. Calcd for C<sub>28</sub>H<sub>18</sub>N<sub>2</sub>O<sub>4</sub> (446.45): C, 75.33; H, 4.06; N, 6.27%. Found: C, 75.22; H, 3.91; N, 6.12%.

**1-Chloro-9-methyl-11-oxo-3,4-dihydro-11H-chromeno[2,3-b]quinoline-2-carboxaldehyde (14).**

Phosphoryl chloride (14 mL, 15 mmol) was added drop-wise to a stirred cold DMF (30 mL) in an ice-bath, then the mixture was stirred at room temperature for 30 min. A solution of compound **11** (1.12 g, 4 mmol) in DMF (10 mL) was added dropwise with continuous stirring. After completion of addition, the reaction mixture was left overnight and poured onto crushed ice (*ca.* 50 g). The pale-yellow solid so formed was filtered, air dried, and crystallized from 2-propanol as pale-yellow crystals, mp 284-285 °C, yield (0.83 g, 64%). IR (KBr,  $\text{cm}^{-1}$ )  $\nu$ : 3035 ( $\text{CH}_{\text{arom.}}$ ), 1704 ( $\text{C}=\text{O}_{\text{aldehyde}}$ ), 1646 ( $\text{C}=\text{O}_{\gamma\text{-pyrone}}$ ), 1608 ( $\text{C}=\text{N}$ ), 1582 ( $\text{C}=\text{C}$ ).  $^1\text{H}$  NMR (300 MHz,  $\text{DMSO-}d_6$ )  $\delta$ : 2.02 (t, 2H,  $J=6.3$  Hz,  $\text{CH}_2$ ), 2.13 (t, 2H,  $J=6.3$  Hz,  $\text{CH}_2$ ), 2.30 (s, 3H,  $\text{CH}_3$ ), 7.58 (d, 1H,  $J=7.8$  Hz, H-7), 7.79 (d, 1H,  $J=7.8$  Hz, H-8), 8.02 (s, 1H, H-10), 8.91 (s, 1H, H-4<sub>pyridine</sub>), 10.81 (s, 1H, CHO).  $^{13}\text{C}$  NMR (75 MHz,  $\text{DMSO-}d_6$ )  $\delta$ : 20.8 ( $\text{CH}_3$ ), 23.6 ( $\text{CH}_2$ ), 27.4 ( $\text{CH}_2$ ), 113.7, 120.3, 122.8, 124.8, 126.3, 129.0, 131.2, 137.6, 140.1, 146.6, 150.2, 158.9, 163.2, 175.8 ( $\text{C}=\text{O}_{\gamma\text{-pyrone}}$ ), 185.8 ( $\text{CH}=\text{O}$ ). Mass spectrum,  $m/z$  ( $I_r\%$ ): 325/327 (24/8), 297/299 (100/33), 269/271 (42/14), 234 (15), 135 (52), 120 (42), 77 (32), 64 (16). Anal. Calcd for  $\text{C}_{18}\text{H}_{12}\text{ClNO}_3$  (325.75): C, 66.37; H, 3.71; N, 4.30%. Found: C, 66.16; H, 3.50; N, 4.15%.

**2-[(Benzylimino)methyl]-1-chloro-3,4-dihydro-9-methyl-11H-chromeno[2,3-b]quinolin-11-one (15).**

A mixture of compound **14** (0.70 g, 2 mmol) and benzylamine (0.22 g, 0.2 mL, 2 mmol) in acetic acid (10 mL) was heated under reflux for 2 h. The yellow crystals obtained after cooling were filtered and crystallized from toluene, mp 265-266 °C, yield (0.58 g, 70%). IR (KBr,  $\text{cm}^{-1}$ )  $\nu$ : 3049 ( $\text{CH}_{\text{arom.}}$ ), 2931, 2894 ( $\text{CH}_{\text{aliph.}}$ ), 1650 ( $\text{C}=\text{O}_{\gamma\text{-pyrone}}$ ), 1611 ( $\text{C}=\text{N}$ ), 1574 ( $\text{C}=\text{C}$ ).  $^1\text{H}$  NMR (300 MHz,  $\text{DMSO-}d_6$ )  $\delta$ : 2.00 (t, 2H,  $J=6.6$  Hz,  $\text{CH}_2$ ), 2.14 (t, 2H,  $J=6.6$  Hz,  $\text{CH}_2$ ), 2.30 (s, 3H,  $\text{CH}_3$ ), 3.61 (s, 2H,  $\text{CH}_2$ ), 6.98-7.21 (m, 5H, Ph-H), 7.54 (d, 1H,  $J=7.2$  Hz, H-7), 7.78 (d, 1H,  $J=7.2$  Hz, H-8), 7.96 (s, 1H, H-10), 8.45 (s, 1H,  $\text{CH}=\text{N}$ ), 8.82 (s, 1H, H-4<sub>pyridine</sub>).  $^{13}\text{C}$  NMR (75 MHz,  $\text{DMSO-}d_6$ )  $\delta$ : 20.6 ( $\text{CH}_3$ ), 23.7 ( $\text{CH}_2$ ), 27.8 ( $\text{CH}_2$ ), 54.3 ( $\text{NCH}_2$ ), 120.7, 122.9, 124.8, 126.9, 127.3, 127.9, 128.4, 129.2, 131.2, 133.6, 134.7, 136.9, 139.3, 141.2, 149.3, 157.4, 161.4, 164.6 ( $\text{C}=\text{N}$ ), 176.3 ( $\text{C}=\text{O}_{\gamma\text{-pyrone}}$ ). Mass spectrum,  $m/z$  ( $I_r\%$ ): 414/416 (48/16), 323/325 (15/5), 295/297 (24/8), 268/270 (12/4), 233 (17), 205 (14), 150 (8), 135 (60), 120 (48), 91 (100), 77 (19), 64 (10). Anal. Calcd for  $\text{C}_{25}\text{H}_{19}\text{ClN}_2\text{O}_2$  (414.88): C, 72.37; H, 4.62; N, 6.75%. Found: C, 72.17; H, 4.35; N, 6.60%.

**1-Chloro-2-[(4-methylphenyl)imino]methyl]-3,4-dihydro-9-methyl-11H-chromeno[2,3-b]-**

**quinolin-11-one (16).** A mixture of compound **14** (0.70 g, 2 mmol) and *p*-toluidine (0.22 g, 2 mmol) in acetic acid (10 mL) was heated under reflux for 2 h. The pale-yellow crystals obtained after cooling were filtered and recrystallized from AcOH, mp 290-291 °C, yield (0.62 g, 75%). IR (KBr,  $\text{cm}^{-1}$ )  $\nu$ : 3056 ( $\text{CH}_{\text{arom.}}$ ), 2946, 2908 ( $\text{CH}_{\text{aliph.}}$ ), 1653 ( $\text{C}=\text{O}_{\gamma\text{-pyrone}}$ ), 1608 ( $\text{C}=\text{N}$ ), 1569 ( $\text{C}=\text{C}$ ).  $^1\text{H}$  NMR (300 MHz,  $\text{DMSO-}d_6$ )  $\delta$ : 2.05 (t, 2H,  $J=6.3$  Hz,  $\text{CH}_2$ ), 2.19 (t, 2H,  $J=6.3$  Hz,  $\text{CH}_2$ ), 2.33 (s, 3H,  $\text{CH}_3$ ), 2.42 (s, 3H,  $\text{CH}_3$ ), 7.19 (d, 2H,  $J=8.1$  Hz, Ar-H), 7.47 (d, 1H,  $J=7.5$  Hz, H-7), 7.61 (d, 1H,  $J=7.5$  Hz, H-8), 7.82 (d,

2H,  $J = 8.1$  Hz, Ar-H), 7.96 (s, 1H, H-10), 8.51 (s, 1H, CH=N), 8.87 (s, 1H, H-4<sub>pyridine</sub>). <sup>13</sup>C NMR (75 MHz, DMSO-*d*<sub>6</sub>)  $\delta$ : 21.1 (CH<sub>3</sub>), 23.9 (CH<sub>3</sub>), 23.5 (CH<sub>2</sub>), 27.9 (CH<sub>2</sub>), 114.0, 119.9, 122.3, 123.8, 124.6, 126.9, 128.5, 129.9, 130.5, 131.8, 134.7, 139.5, 140.8, 143.1, 148.6, 156.8, 161.3, 165.3 (C=N), 176.3 (C=O <sub>$\gamma$</sub> -pyrone). Mass spectrum,  $m/z$  ( $I_r\%$ ): 414/416 (59/20), 386/388 (42/14), 269/271 (18/6), 234 (11), 210 (6), 176 (8), 135 (32), 120 (36), 117 (100), 91 (16), 77 (22), 64 (8). Anal. Calcd for C<sub>25</sub>H<sub>19</sub>ClN<sub>2</sub>O<sub>2</sub> (414.88): C, 72.37; H, 4.62; N, 6.75%. Found: C, 72.09; H, 4.43; N, 6.46%.

**4,5-Dihydro-10-methyl-1H-chromeno[2,3-*b*]pyrazolo[3,4-*f*]quinoline (17).** A mixture of compound **14** (0.70 g, 2 mmol) and hydrazine hydrate (0.1 g, 0.1 mL, 2 mmol) in DMF (10 mL) containing TEA (0.1 mL) was heated under reflux for 2 h. The white crystals obtained after cooling were filtered and crystallized from toluene, mp > 300 °C, yield (0.45 g, 73%). IR (KBr, cm<sup>-1</sup>)  $\nu$ : 3241 (NH), 3035 (CH<sub>arom.</sub>), 2938, 2916 (CH<sub>aliph.</sub>), 1649 (C=O <sub>$\gamma$</sub> -pyrone), 1613 (C=N), 1579 (C=C). <sup>1</sup>H NMR (300 MHz, DMSO-*d*<sub>6</sub>)  $\delta$ : 2.01 (t, 2H,  $J = 6.1$  Hz, CH<sub>2</sub>), 2.12 (t, 2H,  $J = 6.1$  Hz, CH<sub>2</sub>), 2.31 (s, 3H, CH<sub>3</sub>), 7.52 (d, 1H,  $J = 8.1$  Hz, H-8), 7.86 (d, 1H,  $J = 8.1$  Hz, H-9), 7.99 (s, 1H, H-11), 8.36 (s, 1H, H-3<sub>pyrazole</sub>), 8.79 (s, 1H, H-4<sub>pyridine</sub>). <sup>13</sup>C NMR (75 MHz, DMSO-*d*<sub>6</sub>)  $\delta$ : 21.0 (CH<sub>3</sub>), 24.4 (CH<sub>2</sub>), 28.6 (CH<sub>2</sub>), 113.7, 118.1, 119.0, 120.5, 123.6, 127.6, 129.2, 132.3, 135.4, 138.9, 143.2, 150.6, 155.8, 159.5, 176.5 (C=O as  $\gamma$ -pyrone). Mass spectrum,  $m/z$  ( $I_r\%$ ): 303 (100), 275 (69), 268 (43), 229 (26), 175 (13), 135 (36), 120 (21), 77 (16), 64 (9). Anal. Calcd for C<sub>18</sub>H<sub>13</sub>N<sub>3</sub>O<sub>2</sub> (303.31): C, 71.28; H, 4.32; N, 13.85%. Found: C, 71.13; H, 4.17; N, 13.55%.

**4,5-Dihydro-10-methyl-12H-chromeno[2,3-*b*]isoxazolo[5,4-*f*]quinolin-12-one (18).** To a solution of compound **14** (0.70 g, 2 mmol) in DMF (10 mL) containing TEA (0.1 mL), hydroxylamine hydrochloride (0.14 g, 2 mmol) in distilled water (5 mL) was added and the reaction mixture was heated under reflux for 2 h. The pale-yellow crystals obtained after cooling were filtered and crystallized from DMF/EtOH, mp 260-261 °C, yield (0.40 g, 66%). IR (KBr, cm<sup>-1</sup>)  $\nu$ : 3052 (CH<sub>arom.</sub>), 2965, 2925 (CH<sub>aliph.</sub>), 1658 (C=O <sub>$\gamma$</sub> -pyrone), 1616 (C=N), 1586 (C=C). <sup>1</sup>H NMR (300 MHz, DMSO-*d*<sub>6</sub>)  $\delta$ : 1.98 (t, 2H,  $J = 6.3$  Hz, CH<sub>2</sub>), 2.13 (t, 2H,  $J = 6.3$  Hz, CH<sub>2</sub>), 2.29 (s, 3H, CH<sub>3</sub>), 7.55 (d, 1H,  $J = 7.5$  Hz, H-8), 7.84 (d, 1H,  $J = 7.5$  Hz, H-9), 8.03 (s, 1H, H-11), 8.54 (s, 1H, H-3<sub>isoxazole</sub>), 8.83 (s, 1H, H-4<sub>pyridine</sub>). <sup>13</sup>C NMR (75 MHz, DMSO-*d*<sub>6</sub>)  $\delta$ : 21.4 (CH<sub>3</sub>), 24.2 (CH<sub>2</sub>), 28.3 (CH<sub>2</sub>), 103.2, 112.8, 119.7, 122.6, 125.4, 127.9, 129.9, 132.2, 138.4, 149.6, 151.2, 156.5, 159.8, 167.0, 175.5 (C=O <sub>$\gamma$</sub> -pyrone). Mass spectrum,  $m/z$  ( $I_r\%$ ): 304 (100), 249 (64), 209 (17), 195 (16), 150 (10), 135 (37), 120 (58), 77 (63), 64 (34). Anal. Calcd for C<sub>18</sub>H<sub>12</sub>N<sub>2</sub>O<sub>3</sub> (304.30): C, 71.05; H, 3.97; N, 9.21%. Found: C, 70.88; H, 3.62; N, 9.04%.

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