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

Magdy A. Ibrahim* and Al-Shimaa Badran

Department of Chemistry, Faculty of Education, Ain Shams University, Cairo, Egypt.
*E-mail: magdy_ahmed1977@yahoo.com

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 β-chloroenaldehyde derivative **14** which upon condensation with benzylamine and *p*-toluidine afforded the corresponding Schiff bases. Condensation reactions of β-chloroenaldehyde **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*]isoxazo-lo[5,4-*f*]-quinoline **18**, Structures of the new synthesized products were deduced based on their analytical and spectral data.

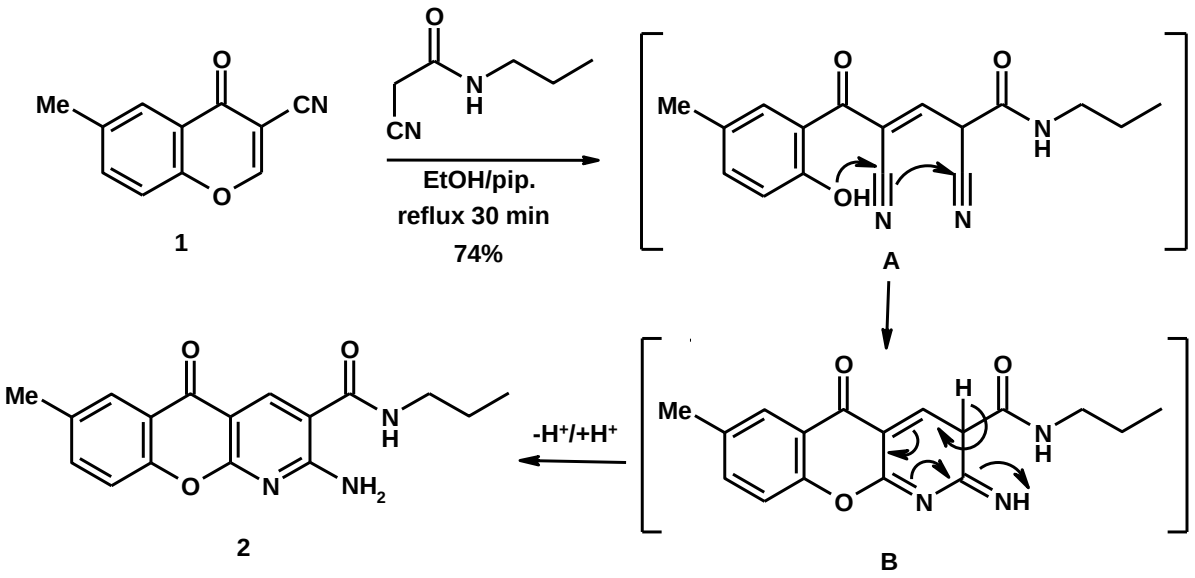
INTRODUCTION

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

electron withdrawing groups at position 3 appeared a variety of transformations upon treatment with nucleophilic reagents.[16] Chromone-3-carbonitriles gain the ability to undergo variable transformations related to γ-pyrone ring opening and heterocyclization.[17] 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

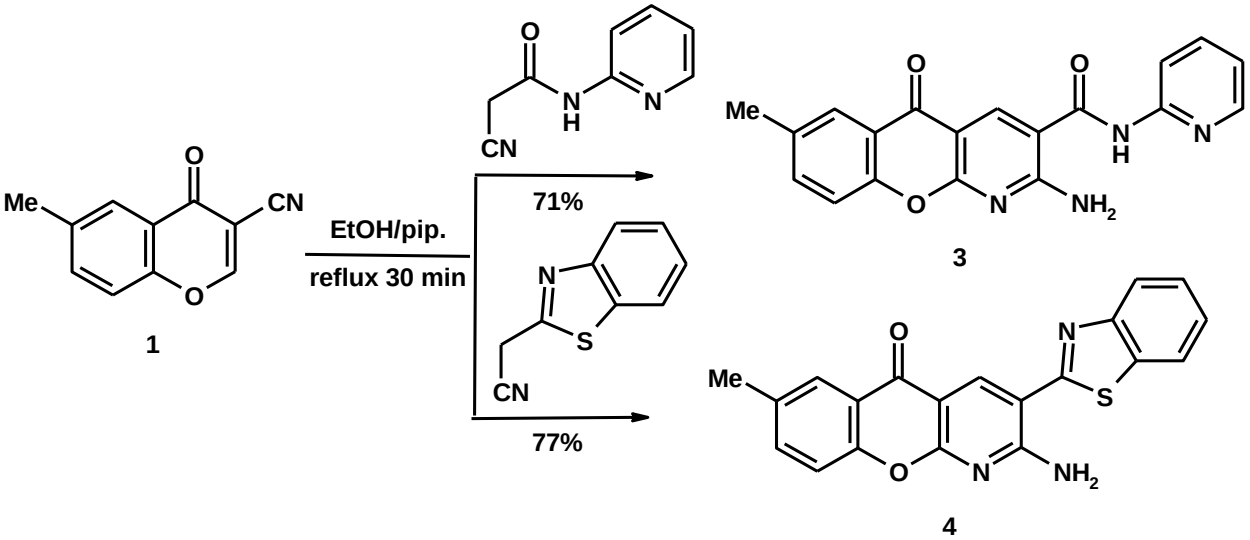
6-Methylchromone-3-carbonitrile (**1**) is a very active substrate towards nucleophilic reagents.[17] Firstly, the chemical behavior of carbonitrile **1** was examined towards some active methylene nitriles, under basic conditions. Reaction of carbonitrile **1** with 2-cyano-*N*-propylacetamide, in absolute 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 γ-pyrone ring opening (intermediate **A**) followed by two consecutive cycloadditions into the nitrile groups (intermediate **B**) with concomitant proton transfer (Scheme 1). The ^{1}H NMR spectrum of compound **2** presented characteristic singlet attributed to H-4$_{pyridine}$ at δ 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_2, NH), 1672 (C=O$_{amide}$), 1642 (C=O$_{\gamma\text{-pyrone}}$) and 1617 cm^{-1} (C=N).



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

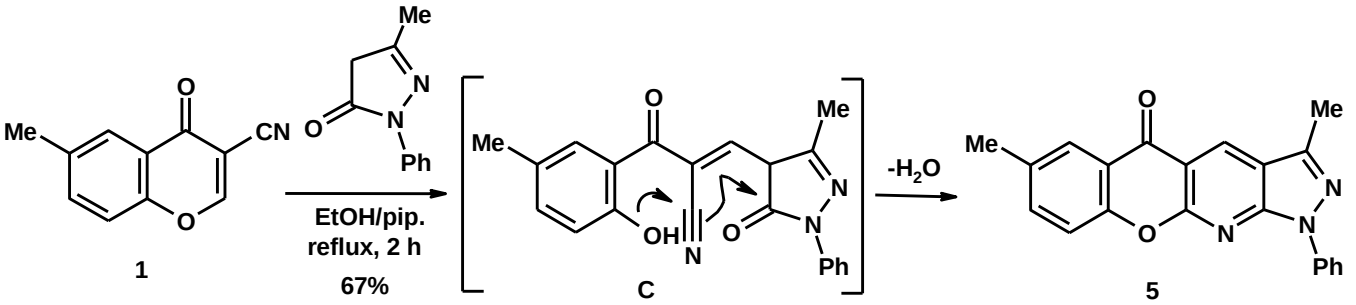
In a similar mechanism, reaction of carbonitrile **1** with 2-cyano-*N*-(pyridin-2-yl)acetamide and 1,3-benzothiazol-2-ylacetonitrile, in absolute ethanol containing piperidine, afforded the corresponding 3-substituted-2-aminochromeno[2,3-*b*]pyridines **3** and **4**, respectively (Scheme 2). Their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

presented characteristic singlet signals attributed to H-$4_{pyridine}$ at δ 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).[18] Formation of compound **5** occurs through γ-pyrone ring opening (intermediate **C**) followed by domino cycloaddition and cyclocondensation reactions. The ^{1}H NMR spectrum of compound **5** showed four characteristic singlets attributed to $CH_{3\ pyrazole}$, $CH_{3\ benzo}$, H-6 and H-$4_{pyridine}$ at δ 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^{-1}, assignable to C=$O_{\gamma\text{-pyrone}}$ and C=N, respectively.

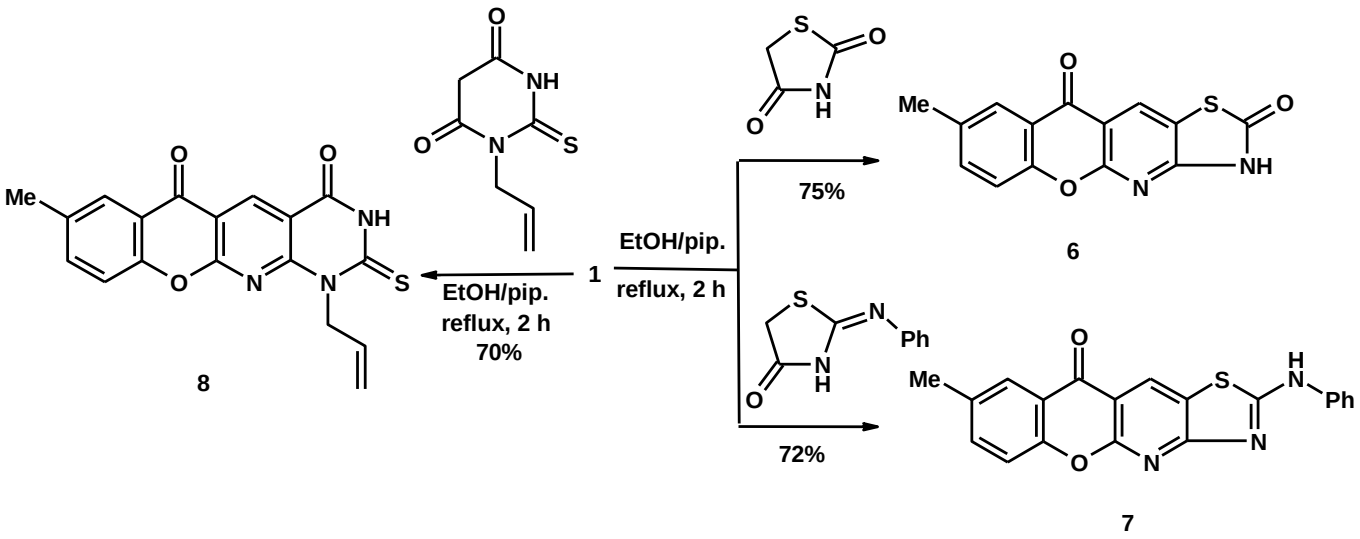


Scheme 3. Formation of heteroannulated chromeno[2,3-*b*]pyrazolo[4,3-*e*]pyridine **5**

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}H NMR spectra showed the pyridine ring proton as a specific singlet at δ 8.79 and 8.83 ppm, respectively. The IR spectra of compounds **6** and **7** displayed distinctive absorption bands attributed to C=O$_{\gamma\text{-pyrone}}$ at $\tilde{\nu}$ 1655 and 1662 cm^{-1}, in addition, the spectrum of compound **7** appeared the absorption band of C=O$_{\text{thiazole}}$ at $\tilde{\nu}$ 1679 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.

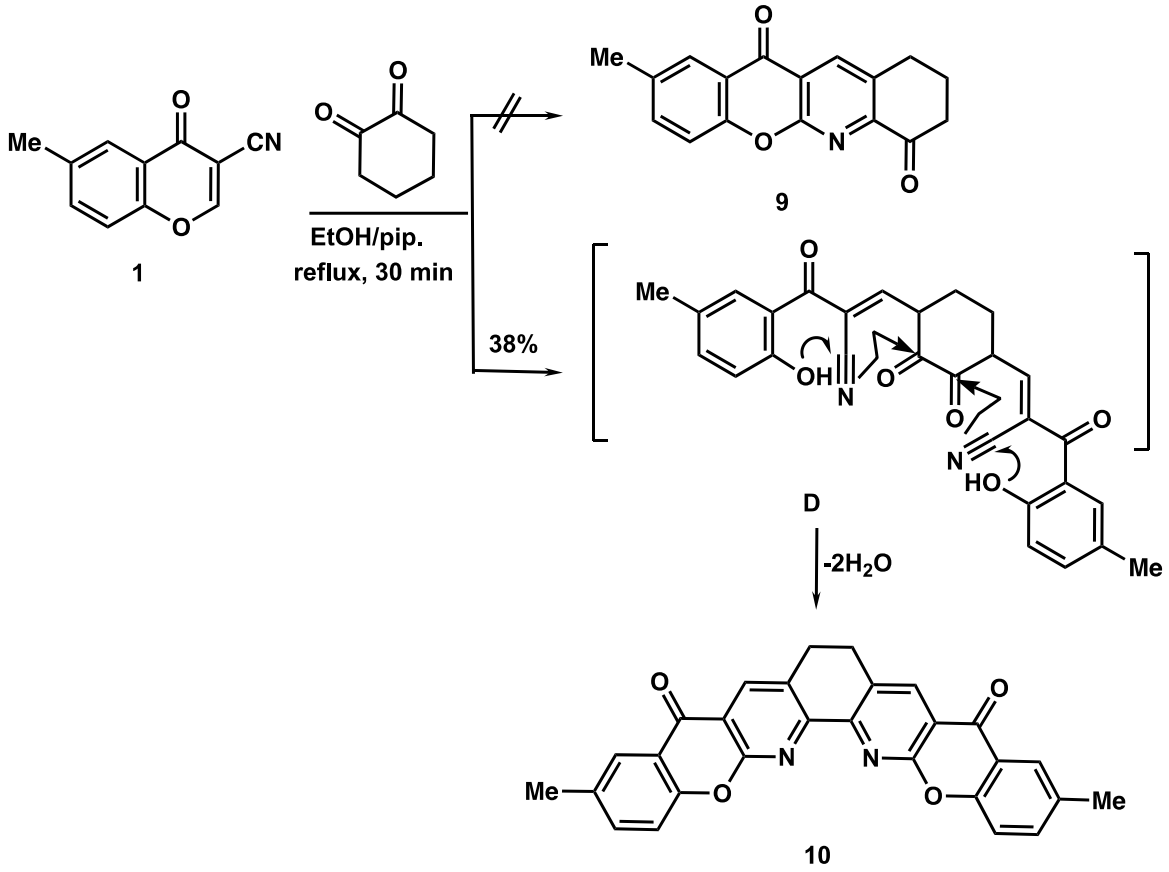
Further, carbonitrile **1** with 1-allyl-2-thioxodihydropyrimidine-4,6(1*H*,5*H*)-dione, in boiling ethanol containing piperidine, led to chromeno[3`,2`:5,6]pyrido[2,3-*d*]pyrimidine **8** (Scheme 4). Specific singlets appeared in the ^{1}H NMR spectrum at δ 8.08 and 8.89 ppm, which attributed to H-7 and H-5, respectively. The IR spectrum of compound **8** showed distinctive absorption bands at $\tilde{\nu}$ 1696 (C=O$_{\text{pyrimidine}}$), 1654 (C=O$_{\gamma\text{-pyrone}}$), 1616 (C=N) and 1228 (C=S) 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.[19] 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 will the assigned molecular formula ($C_{28}H_{18}N_2O_4$). The ^{1}H NMR spectrum of compound **10** showed specific singlet at δ 8.81 ppm attributed

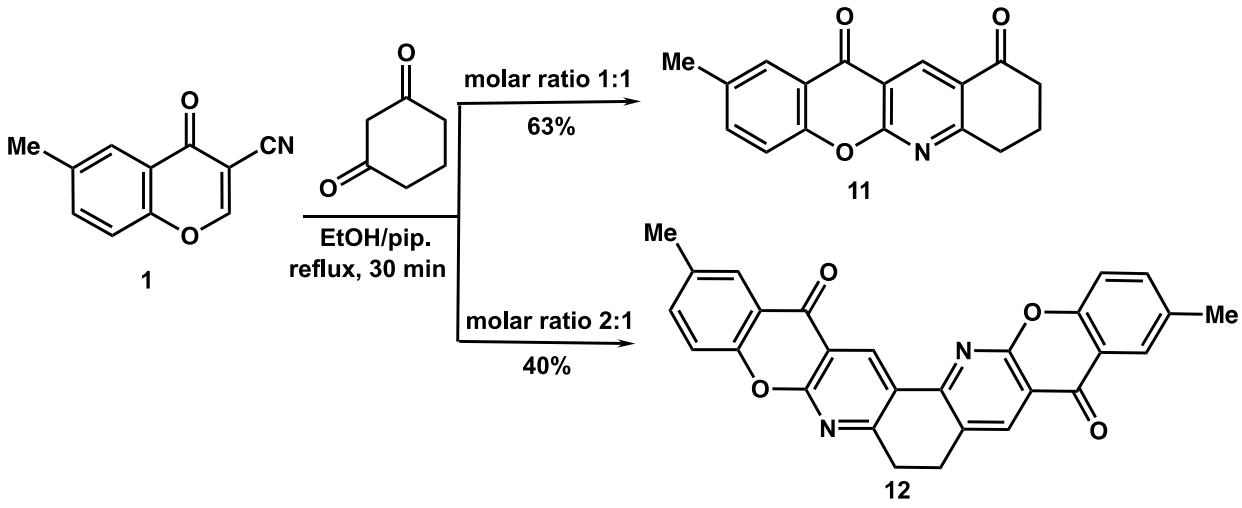
to H-4 of the pyridine rings. The IR spectrum showed distinctive absorption bands at $\tilde{\nu}$ 1666 ($C{=}O_{\gamma\text{-pyrone}}$) and 1609 (C=N) cm^{-1}



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

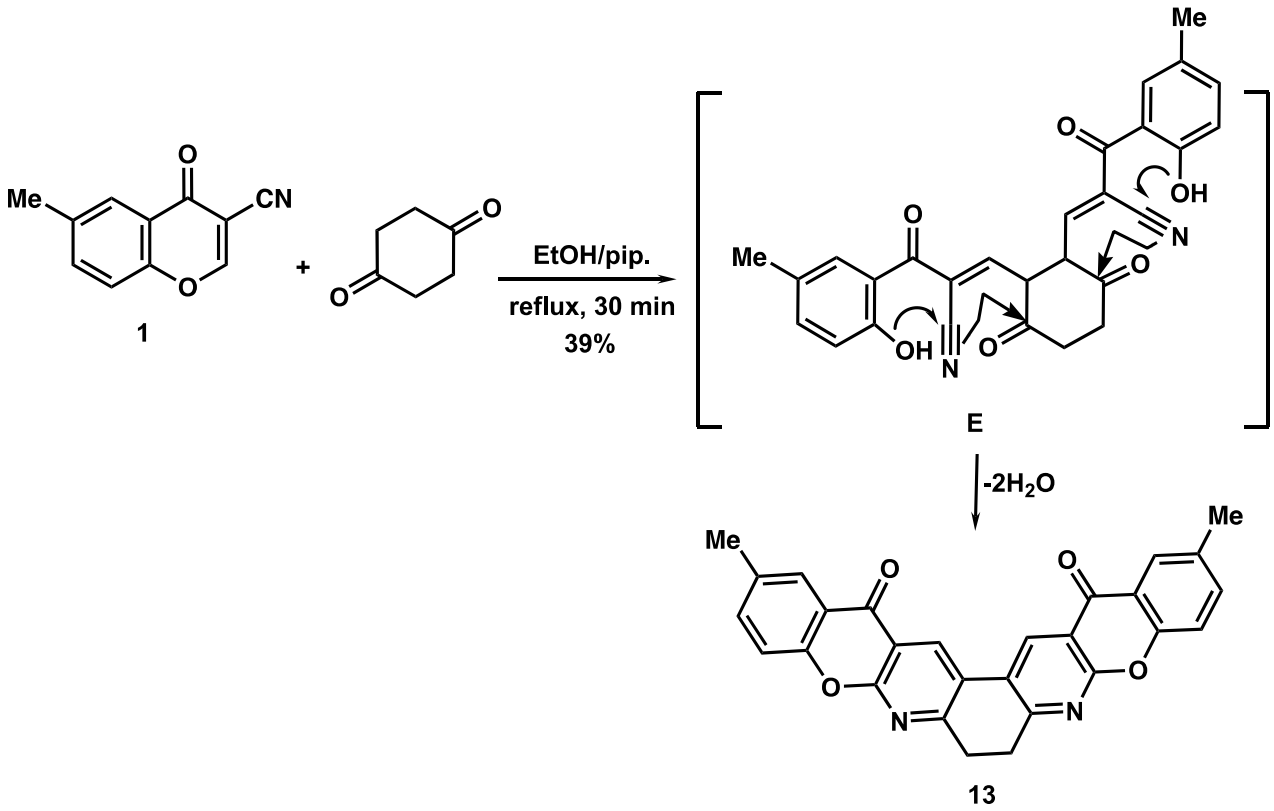
Moreover, reaction of carbonitrile **1** with 1,3-cyclohexanedione was considered under different molar ratios. Reaction of carbonitrile **1** with 1,3-cycloheaxnedione (molar ratio 1:1) yielded chromenoquinoline derivative **11** (Scheme 6).[20] The ^{1}H NMR spectrum of compound **11** showed three triplet signals in the upfield region at δ 2.15, 2.71 and 3.16 ppm attributable to three CH_2 groups, as well as a distinctive singlet at δ 8.81 ppm assignable to $H\text{-}4_{pyridine}$.

Repeating the previous reaction in 2:1 molar ratio (carbonitrile: 1,3-cyclohexanedione) gave heptacyclic (*bis*chromeno)[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 ^{1}H NMR spectrum at δ 8.84 ppm



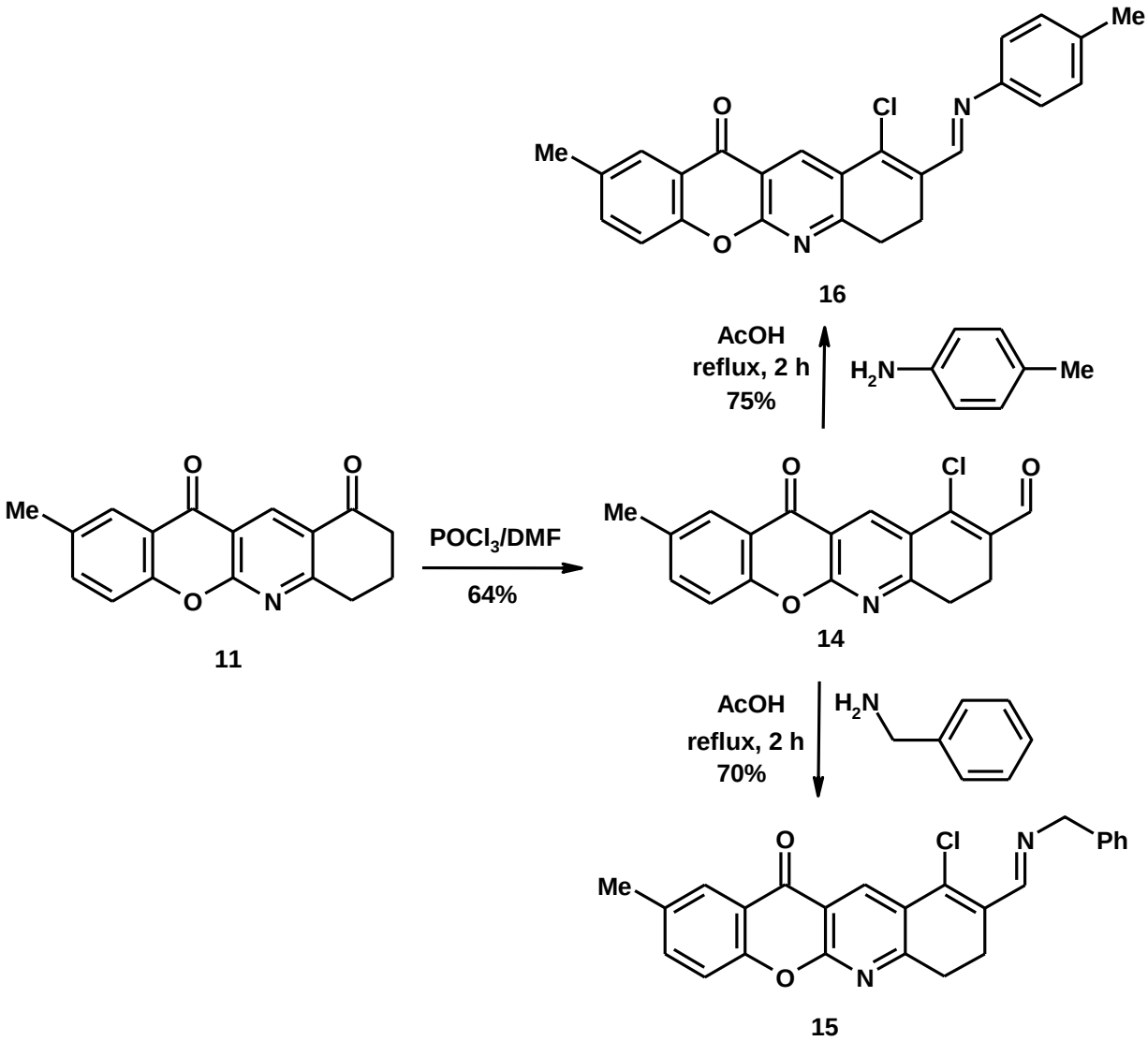
Scheme 6. Reaction of carbonitrile **1** with cyclohexane-1,3-dione at different molar ratios

As noticed with 1,2-cyclohexanedione, reaction of carbonitrile **1** with 1,4-cyclohexanedione, in boiling ethanol containing piperidine, gave heptacyclic (*bis*chromeno)[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}H NMR spectrum, the singlet signal distinctive for H-4$_{pyridine}$ appeared at δ 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.[21] Therefore, formylation of compound **11** using Vilsmeier-Haack reagent ($POCl_3$/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}H NMR spectrum of compound **14** showed specific singlet signals at δ 10.81 ppm attributable to the aldehyde proton. The IR spectrum showed typical absorption bands at $\tilde{\nu}$ 1704 ($C{=}O_{aldehyde}$) and 1646 ($C{=}O_{\gamma\text{-pyrone}}$) cm^{-1}. The mass spectrum represents a good evidence for the structure of β-chloroenaldehyde **14** which showed the molecular ion peak with the isotopic peak attributed to the presence of one chlorine atom as M^+/M+2 at *m/z* 325/327; in the expected relative abundance (24/8%).

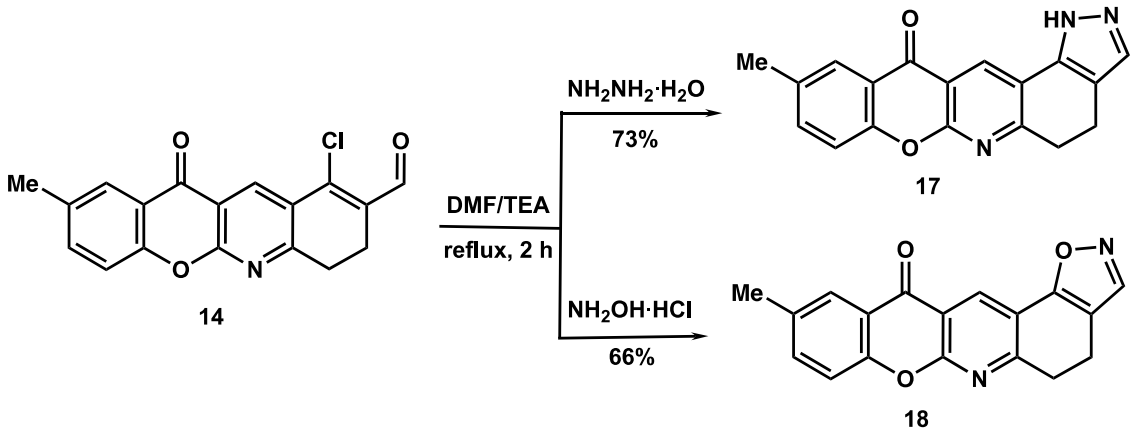


Scheme 8. Synthesis and condensation reactions of β-chloroenaldehyde **14**

The reactivity of cyclic β-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}H NMR spectra of compounds **15** and **16** presented specific singlet attributable to the azomethine protons at δ 8.45 and 8.51 ppm, respectively.

After that, the behavior of β-chloroenaldehyde **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}H NMR spectra of compounds **17** and **18** showed specific singlet assignable to the pyrazole ring proton (H-3) at δ 8.36 and 8.54 ppm, respectively.



Scheme 9. Reactions of β-chloroenaldehyde **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 β-chloroenaldehyde 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^{-1}), using KBr disks. ^{1}H NMR (300 MHz) and ^{13}C NMR (75 MHz) spectra were measured on Mercury-300BB, using DMSO-d_6 as a solvent and TMS (δ, 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.[22]

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 ºC, yield (0.69 g, 74%). IR (KBr, cm^{-1}) ν: 3414, 3332, 3246 (NH_2, NH), 3048 ($CH_{arom.}$), 2974, 2927, 2889 ($CH_{aliph.}$), 1672 ($C{=}O_{amide}$), 1642 ($C{=}O_{\gamma\text{-pyrone}}$), 1617 (C=N), 1579 (C=C). ^{1}H NMR (300 MHz, DMSO-d_6) δ: 0.97 (t, 3H, *J*=6.9 Hz, CH_3), 1.07-1.23 (m, 2H, CH_2), 2.14 (t, 3H, *J*=6.6 Hz, CH_2), 2.32 (s, 3H, CH_3), 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-$4_{pyridine}$), 9.68 (bs, 2H, NH_2 exchangeable with D_2O), 10.37 (br, 1H, NH exchangeable with D_2O). ^{13}C NMR (75 MHz, DMSO-d_6, δ): 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_r%): 311 (20), 253 (100), 225 (37), 210 (18), 157 (6), 135 (52), 120 (29), 77 (17), 64 (8). Anal. Calcd for $C_{17}H_{17}N_3O_3$ (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_2O, mp 272-273 ºC, yield (0.74 g, 71%). IR (KBr, cm^{-1}) ν: 3432, 3357, 3259 (NH_2, NH), 3067 ($CH_{arom.}$), 1669 ($C{=}O_{amide}$), 1645

(C=$O_{\gamma\text{-pyrone}}$), 1611 (C=N), 1582 (C=C). ^{1}H NMR (300 MHz, DMSO-d_6) δ: 2.31 (s, 3H, CH_3), 7.31-7.60 (m, 6H, Ar-H), 7.96 (s, 1H, H-9), 8.86 (s, 1H, H-4$_{pyridine}$), 9.83 (bs, 2H, NH_2 exchangeable with D_2O), 10.82 (br, 1H, NH exchangeable with D_2O). ^{13}C NMR (75 MHz, DMSO-d_6) 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_r%): 346 (100), 318 (91), 239 (54), 181 (12), 135 (42), 120 (38), 78 (15), 64 (17). Anal. Calcd for $C_{19}H_{14}N_4O_3$ (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-5*H*-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 ºC, yield (0.83 g, 77%). IR (KBr, cm^{-1}) ν: 3406, 3312 (NH_2), 3039 ($CH_{arom.}$), 1657 (C=$O_{\gamma\text{-pyrone}}$), 1619 (C=N), 1574 (C=C). ^{1}H NMR (300 MHz, DMSO-d_6) δ: 2.37 (s, 3H, CH_3), 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$_{pyridine}$), 9.23 (br, 2H, NH_2 exchangeable with D_2O). Mass spectrum, *m/z* (I_r%): 359 (64), 331 (100), 223 (32), 181 (8), 157 (11), 135 (51), 120 (31), 77 (28), 64 (10). Anal. Calcd for $C_{20}H_{13}N_3O_2S$ (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(1*H*)-one (5). A mixture of carbonitrile **1** (0.56 g, 3 mmol) and 5-methyl-2-phenyl-2,4-dihydro-3*H*-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_2O, mp 206-207 ºC, yield (0.46 g, 67%). IR (KBr, cm^{-1}) ν: 3081 ($CH_{arom.}$), 2962, 2913 ($CH_{aliph.}$), 1659 (C=$O_{\gamma\text{-pyrone}}$), 1618 (C=N), 1592 (C=C). ^{1}H NMR (300 MHz, DMSO-d_6) δ: 2.09 (s, 3H, CH_3), 2.37 (s, 3H, CH_3), 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$_{pyridine}$). Mass spectrum, *m/z* (I_r%): 341 (100), 264 (46), 236 (38), 195 (13), 181 (8), 135 (49), 120 (18), 77 (14), 64 (7). Anal. Calcd for $C_{21}H_{15}N_3O_2$ (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(3*H*,10*H*)-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_2O, mp 275-276 ºC, yield (0.64 g, 75%). IR (KBr, cm^{-1}) ν: 3352 (NH), 3045 ($CH_{arom.}$), 2934, 2889 ($CH_{aliph.}$), 1679 (C=$O_{thiazole}$), 1655 (C=$O_{\gamma\text{-pyrone}}$), 1613 (C=N), 1576 (C=C). ^{1}H NMR (300 MHz, DMSO-d_6) δ: 2.32 (s, 3H, CH_3), 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$_{pyridine}$), 11.63 (bs, 1H, NH

exchangeable with D_2O). ^{13}C NMR (75 MHz, DMSO-d_6) 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_r%): 284 (37), 256 (100), 224 (9), 196 (26), 135 (59), 120 (32), 77 (19), 64 (10). Anal. Calcd for $C_{14}H_8N_2O_3S$ (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 ºC, yield (0.78 g, 72%). IR (KBr, cm^{-1}) ν: 3382 (NH), 3061 ($CH_{arom.}$), 2945, 2895 ($CH_{aliph.}$), 1662 ($C=O_{\gamma\text{-pyrone}}$), 1610 (C=N), 1583 (C=C). ^1H NMR (300 MHz, DMSO-d_6) δ: 2.36 (s, 3H, CH_3), 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-$4_{pyridine}$), 9.68 (bs, 1H, NH exchangeable with D_2O). ^{13}C NMR (75 MHz, DMSO-d_6) 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_r%): 359 (27), 267 (41), 239 (15), 213 (8), 181 (13), 135 (42), 120 (33), 92 (72), 77 (100), 64 (28). Anal. Calcd for $C_{20}H_{13}N_3O_2S$ (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_2O, mp 280-281 ºC, yield (0.49 g, 70%). IR (KBr, cm^{-1}) ν: 3232 (NH), 3044 ($CH_{arom.}$), 2979, 2942 ($CH_{aliph.}$), 1696 ($C=O_{pyrimidine}$), 1654 ($C=O_{\gamma\text{-pyrone}}$), 1616 (C=N), 1579 (C=C), 1228 (C=S). ^1H NMR (300 MHz, DMSO-d_6) δ: 2.33 (s, 3H, CH_3), 3.10 (d, 2H, *J*=6.3 Hz, *N*CH_2), 4.96 (d, 2H, *J*=6.6 Hz, $CH_{2\ olefinic}$), 5.79-5.83 (m, 1H, $CH_{olefinic}$), 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_2O). ^{13}C NMR (75 MHz, DMSO-d_6) 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_r%): 351 (100), 323 (75), 295 (47), 255 (39), 211 (15), 135 (35), 120 (46), 77 (42), 64 (21). Anal. Calcd for $C_{18}H_{13}N_3O_3S$ (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 ºC, yield (0.51 g, 38%). IR (KBr, cm^{-1}) ν: 3018 ($CH_{arom.}$), 2952, 2906 ($CH_{aliph.}$), 1666 ($C=O_{\gamma\text{-pyrone}}$), 1609 (C=N), 1544

(C=C). ^{1}H-NMR (300 MHz, DMSO-d_6) δ: 2.01 (s, 4H, 2CH_2), 2.34 (s, 6H, 2CH_3), 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$_{pyridine}$). Mass spectrum, *m/z* (*I*$_r$%): 446 (100). Anal. Calcd for $C_{28}H_{18}N_2O_4$ (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-4*H*-chromeno[2,3-*b*]quinoline-4,6(3*H*)-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 ºC, yield (0.53 g, 63%). IR (KBr, cm^{-1}) ν: 3051 ($CH_{arom.}$), 2943, 2925, 2849 ($CH_{aliph.}$), 1689 ($C{=}O_{quinolinone}$), 1663 ($C{=}O_{\gamma\text{-pyrone}}$), 1618 (C=N), 1589 (C=C). ^{1}H NMR (300 MHz, DMSO-d_6) δ: 2.17 (t, 2H, *J*= 6.3 Hz, CH_2), 2.44 (s, 3H, CH_3), 2.72 (t, 2H, *J*= 6.3 Hz, CH_2), 3.16 (t, 2H, *J*= 7.2 Hz, CH_2), 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). ^{13}C NMR (75 MHz, DMSO-d_6) δ: 20.2 (CH_3), 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*$_r$%): 279 (70), 251 (100), 223 (21), 166 (17), 118 (10), 105 (8), 77 (18), 63 (14). Anal. Calcd for $C_{17}H_{13}NO_3$ (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-5*H*,15*H*-*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 ºC, yield (0.54 g, 40%). IR (KBr, cm^{-1}) ν: 3065 ($CH_{arom.}$), 2928, 2892 ($CH_{aliph.}$), 1670 ($C{=}O_{\gamma\text{-pyrone}}$), 1610 (C=N), 1576 (C=C). ^{1}H NMR (300 MHz, DMSO-d_6) δ: 2.07 (s, 4H, 2CH_2), 2.30 (s, 6H, 2CH_3), 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$_{pyridine}$). Mass spectrum, *m/z* (*I*$_r$%): 446 (100). Anal. Calcd for $C_{28}H_{18}N_2O_4$ (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-(15*H*,18*H*)-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 ºC, yield (0.52 g, 39%). IR (KBr, cm^{-1}) ν: 3065 ($CH_{arom.}$), 2939, 2885 ($CH_{aliph.}$), 1662 ($C{=}O_{\gamma\text{-pyrone}}$), 1613 (C=N), 1582 (C=C). ^{1}H NMR (300 MHz, DMSO-d_6) δ: 2.10 (s, 4H, 2CH_2), 2.32 (s, 6H, 2CH_3), 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$_{pyridine}$). Mass spectrum, *m/z* (*I*$_r$%): 446 (100). Anal. Calcd for $C_{28}H_{18}N_2O_4$ (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-11*H*-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 ºC, yield (0.83 g, 64%). IR (KBr, cm^{-1}) ν: 3035 ($CH_{arom.}$), 1704 ($C=O_{aldehyde}$), 1646 ($C=O_{\gamma\text{-pyrone}}$), 1608 (C=N), 1582 (C=C). ^{1}H NMR (300 MHz, DMSO-d_6) δ: 2.02 (t, 2H, *J*=6.3 Hz, CH_2), 2.13 (t, 2H, *J*=6.3 Hz, CH_2), 2.30 (s, 3H, 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-$4_{pyridine}$), 10.81 (s, 1H, CHO). ^{13}C NMR (75 MHz, DMSO-d_6) δ: 20.8 (CH_3), 23.6 (CH_2), 27.4 (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 ($C=O_{\gamma\text{-pyrone}}$), 185.8 (CH=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 $C_{18}H_{12}ClNO_3$ (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-11*H*-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 ºC, yield (0.58 g, 70%). IR (KBr, cm^{-1}) ν: 3049 ($CH_{arom.}$), 2931, 2894 ($CH_{aliph.}$), 1650 ($C=O_{\gamma\text{-pyrone}}$), 1611 (C=N), 1574 (C=C). ^{1}H NMR (300 MHz, DMSO-d_6) δ: 2.00 (t, 2H, *J*= 6.6 Hz, CH_2), 2.14 (t, 2H, *J*= 6.6 Hz, CH_2), 2.30 (s, 3H, CH_3), 3.61 (s, 2H, 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, CH=N), 8.82 (s, 1H, H-$4_{pyridine}$). ^{13}C NMR (75 MHz, DMSO-d_6) δ: 20.6 (CH_3), 23.7 (CH_2), 27.8 (CH_2), 54.3 (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 (C=N), 176.3 ($C=O_{\gamma\text{-pyrone}}$). 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 $C_{25}H_{19}ClN_2O_2$ (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-11*H*-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 ºC, yield (0.62 g, 75%). IR (KBr, cm^{-1}) ν: 3056 ($CH_{arom.}$), 2946, 2908 ($CH_{aliph.}$), 1653 ($C=O_{\gamma\text{-pyrone}}$), 1608 (C=N), 1569 (C=C). ^{1}H NMR (300 MHz, DMSO-d_6) δ: 2.05 (t, 2H, *J*= 6.3 Hz, CH_2), 2.19 (t, 2H, *J*= 6.3 Hz, CH_2), 2.33 (s, 3H, CH_3), 2.42 (s, 3H, 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$_{pyridine}$). ^{13}C NMR (75 MHz, DMSO-d_6) δ: 21.1 (CH_3), 23.9 (CH_3), 23.5 (CH_2), 27.9 (CH_2), 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$_{γ\text{-pyrone}}$). 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 $C_{25}H_{19}ClN_2O_2$ (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-1*H*-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 ºC, yield (0.45 g, 73%). IR (KBr, cm^{-1}) ν: 3241 (NH), 3035 (CH$_{arom.}$), 2938, 2916 (CH$_{aliph.}$), 1649 (C=O$_{γ\text{-pyrone}}$), 1613 (C=N), 1579 (C=C). ^{1}H NMR (300 MHz, DMSO-d_6) δ: 2.01 (t, 2H, *J*= 6.1 Hz, CH_2), 2.12 (t, 2H, *J*= 6.1 Hz, CH_2), 2.31 (s, 3H, CH_3), 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$_{pyrazole}$), 8.79 (s, 1H, H-4$_{pyridine}$). ^{13}C NMR (75 MHz, DMSO-d_6) δ: 21.0 (CH_3), 24.4 (CH_2), 28.6 (CH_2), 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 γ-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 $C_{18}H_{13}N_3O_2$ (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-12*H*-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 ºC, yield (0.40 g, 66%). IR (KBr, cm^{-1}) ν: 3052 (CH$_{arom.}$), 2965, 2925 (CH$_{aliph.}$), 1658 (C=O$_{γ\text{-pyrone}}$), 1616 (C=N), 1586 (C=C). ^{1}H NMR (300 MHz, DMSO-d_6) δ: 1.98 (t, 2H, *J*= 6.3 Hz, CH_2), 2.13 (t, 2H, *J*= 6.3 Hz, CH_2), 2.29 (s, 3H, CH_3), 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$_{isoxazole}$), 8.83 (s, 1H, H-4$_{pyridine}$). ^{13}C NMR (75 MHz, DMSO-d_6) δ: 21.4 (CH_3), 24.2 (CH_2), 28.3 (CH_2), 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$_{γ\text{-pyrone}}$). 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 $C_{18}H_{12}N_2O_3$ (304.30): C, 71.05; H, 3.97; N, 9.21%. Found: C, 70.88; H, 3.62; N, 9.04%.

REFERENCES

1. Y. Liu, X. Yu, W. Zhang, T. Wang, B. Jiang, H. Tang, Q. Su, and Y. Fu, *Bioorg. Chem.*, 2020, **101**, 104030; H.-X. Huo, Y.-F. Gu, H. Sun, Y.-F. Zhang, W.-J. Liu, Z.-X. Zhu, S.-P. Shi, Y.-L. Song, H.-W. Jin, Y.-F. Zhao, P.-F. Tu, and J. Li, *Fitoterapia*, 2017, **118**, 49.

2. J. E. Philip, S. A. Antony, S. J. Eeettinilkunnathil, M. R. P. Kurup, and M. P. Velayudhan, *Inorg. Chim. Acta*, 2018, **469**, 87.
3. T. Zhou, Q. Shi, C.-H. Chen, H. Zhu, L. Huang, P. Ho, and K.-H. Lee, *Bioorg. Med. Chem.*, 2010, **18**, 6678.
4. A. Kantankar, Y. J. Rao, G. Mallikarjun, Y. Hemasri, and R. R. Kethiri, *J. Mol. Struct.*, 2021, **1239**, 130502; Y. Duan, Y. Jiang, F. Guo, L. Chen, L. Xu, W. Zhang, and B. Liu, *Fitoterapia*, 2019, **135**, 114; E. Venkateswararao, V. K. Sharma, M. Manickam, J. Yun, and S.-H. Jung, *Bioorg. Med. Chem. Lett.*, 2014, **24**, 5256.
5. K. S. Babu, T. H. Babu, P. V. Srinivas, K. H. Kishore, U. S. N. Murthy, and J. M. Rao, *Bioorg. Med. Chem. Lett.*, 2006, **16**, 221.
6. M. A. Ibrahim and N. M. El-Gohary, *Heterocycles*, 2021, **102**, 489.
7. P. Lerdsirisuk, C. Maicheen, and J. Ungwitayatorn, *Bioorg. Chem.*, 2014, **57**, 142.
8. U. Albrecht, M. Lalk, and P. Langer, *Bioorg. Med. Chem.*, 2005, **13**, 1531.
9. Y. Saito, Y. Taniguchi, S. Hirazawa, Y. Miura, H. Tsurimoto, T. Nakayoshi, A. Oda, E. Hamel, K. Yamashita, M. Goto, and K. Nakagawa-Goto, *Eur. J. Med. Chem.*, 2021, **222**, 113578.
10. R. Larget, B. Lockhart, P. Renard, and M. Largeron, *Bioorg. Med. Chem. Lett.*, 2000, **10**, 835.
11. C. Mi, J. Yuan, M. Zhu, L. Yang, Y. Wei, H. Wang, W. Long, W. Mei, and H. Dai, *Phytochemistry*, 2021, **181**, 112578; G. Wang, M. Chen, J. Wang, Y. Peng, L. Li, Z. Xie, B. Deng, S. Chen, and W. Li, *Bioorg. Med. Chem. Lett.*, 2017, **27**, 2957.
12. G. Liao, W.-L. Mei, F.-D. Kong, W. Li, J.-Z. Yuan, and H.-F. Dai, *Phytochemistry*, 2017, **139**, 98.
13. S. Abdpour, L. Jalili-Baleh, H. Nadri, H. Forootanfar, S. N. A. Bukhari, A. Ramazani, S. E. S. Ebrahimi, A. Foroumadi, and M. Khoobi, *Bioorg. Chem.*, 2021, **110**, 104750; F. Li, J.-J. Wu, J. Wang, X.-L. Yang, P. Cai, Q.-H. Liu, L.-Y. Kong, and X.-B. Wang, *Bioorg. Med. Chem.*, 2017, **25**, 3815.
14. P. Valenti, A. Rampa, R. Budriesi, A. Bisi, and A. Chiarini, *Bioorg. Med. Chem.*, 2000, **6**, 803.
15. M. A. Ibrahim, A. A. M. Farag, N. Roushdy, and N. M. El-Gohary, *J. Mol. Struct.*, 2016, **1105**, 370; M. A. Ibrahim, S. Abdel Halim, N. Roushdy, A. A. M. Farag, and N. M. El-Gohary, *Opt. Mater.*, 2017, **73**, 290; S. Abdel Halim, M. A. Ibrahim, N. Roushdy, A. A. M. Farag, Y. Gabr, and S. Said, *Mater. Chem. Phys.*, 2018, **217**, 403; A. Mohammadi, B. Khalili, and A. S. Haghayegh, *Spectrochim. Acta, Part A*, 2019, **222**, 117193; A. Y. Chumak, Y. O. Denysieva, O. O. Kolomoitsev, V. M. Kotlyar, E. H. Shvets, and A. O. Doroshenko, *J. Luminescence*, 2020, **223**, 117206; A. A. M. Farag, N. Roushdy, N. M. El-Gohary, S. Abdel Halim, and M. A. Ibrahim, *Appl. Sur. Sci.*, 2019, **467-468**, 1226; M. A. Rohman, P. Baruah, S. O. Yesylevskyy, and S. Mitra, *Chem. Phys.*, 2019, **517**, 67.
16. M. A. Ibrahim, T. E. Ali, M. A. El-Kazak, and A. M. Mohamed, *J. Heterocycl. Chem.*, 2015, **52**,

815; M. A.Ibrahim and T. E. Ali, *Turk. J. Chem.*, 2015, **39**, 412; M. A. Ibrahim and N. M. El-Gohary, *Tetrahedron*, 2018, **74**, 512; M. Y. Kornev, D. S. Tishin, and V. Y. Sosnovskikh, *Mendeleev Commun.*, 2019, **29**, 67; M. Y. Kornev, D. S. Tishin, D. L. Obydennov, and V. Y. Sosnovskikh, *Mendeleev Commun.*, 2020, **30**, 233; A. Badran, M. A. Ibrahim, and A. Ahmed, *Synth. Commun.*, 2021, **51**, 1868; S. H. Hashiem, M. A. Ibrahim, A. Badran, N. M. El-Gohary, and H. A. Allimony, *Heterocycles*, 2021, **102**, 1011.

17. C. K. Ghosh and S. K. Karak, *J. Heterocycl. Chem.*, 2005, **42**, 1035; M. A. Ibrahim and N. M. El-Gohary, *J. Heterocycl. Chem.*, 2016, **53**, 859; M. A. Ibrahim, N. M. El-Gohary, S. S. Ibrahim, and S. Said, *Chem. Heterocycl. Compd.*, 2015, **50**, 1624; T. Zarganes-Tzitzikas, M. A. Terzidis, J. Stephanidou-Stephanatou, C. A. Tsoleridis, and G. E. Kostakis, *J. Org. Chem.*, 2011, **76**, 9008.
18. M. A. Ibrahim and A. M. El-Kazak, *J. Heterocycl. Chem.*, 2019, **56**, 1075.
19. M. A. Ibrahim and N. M. El-Gohary, *J. Heterocycl. Chem.*, 2016, **53**, 1091.
20. A. A. M. Farag, N. Roushdy, S. Abdel Halim, N. M. El-Gohary, M. A. Ibrahim, and S. Said, *Spectrochim. Acta, Part A*, 2018, **191**, 478.
21. A. M. El-Kazak, N. M. El-Gohary, A. Badran, and M. A. Ibrahim, *Tetrahedron*, 2019, **75**, 3923.
22. U. Petersen and H. Heitzer, *Liebigs Ann. Chem.*, 1976, **9**, 1659.