HETEROCYCLES, Vol. 100, No. 8, pp. -. © 2020 The Japan Institute of Heterocyclic Chemistry
Received, 4th May, 2020, Accepted, 24th June, 2020, Published online, 30th June, 2020
DOI: 10.3987/COM-20-14273

CHEMICAL TRANSFORMATIONS WITH 4,9-DIMETHOXY-5-OXO-5*H*-FURO[3,2-*g*]CHROMENE-6-CARBONITRILE: CONSTRUCTION AND ANTIMICROBIAL EVALUATION OF THE NOVEL HETEROANNULATED FUROCHROMENOPYRIDINES

Magdy A. Ibrahim,[a]* Sami A. Al-Harbi,[b] and Esam S. Allehyani[b]

[a]Department of Chemistry, Faculty of Education, Ain Shams University, Cairo, Egypt.

[b]Department of Chemistry, University College in Al-Jamoum, Umm Al-Qura University, Makkah, Saudi Arabia
*E-mail: magdy_ahmed1977@yahoo.com

Abstract – The chemical reactivity of 4,9-dimethoxy-5-oxo-5*H*-furo[3,2-*g*]-chromene-6-carbonitrile (**1**) was studied towards a variety of active methylene nitriles namely; malononitrile, cyanoacetamide, *N*-phenylcyanoacetamide, (phenylthio)acetonitrile, ethyl cyanoacetate and benzothiazol-2-ylacetonitrile producing the novel annulated furo[3`,2`:6,7]chromeno[2,3-*b*]pyridines. Reactions of carbonitrile **1** with malononitrile dimer, cyanoacetohydrazide and 1*H*-benzimidazol-2-ylacetonitrile showed different behavior giving the novel angular heteroannulated furochromenes **10, 11** and **13**, respectively. A series of novel furo[3``,2``:6`,7`]chromeno[3`,2`:5,6]pyrido[2,3-*d*]pyrimidines were also synthesized. The proposed mechanisms for the different synthetic pathways were also discussed. The prepared compounds were screened in *vitro* for their antimicrobial activity and some of them showed notable activity against the tested microorganisms. Structures of the synthesized products were confirmed based on their analytical and spectral data.

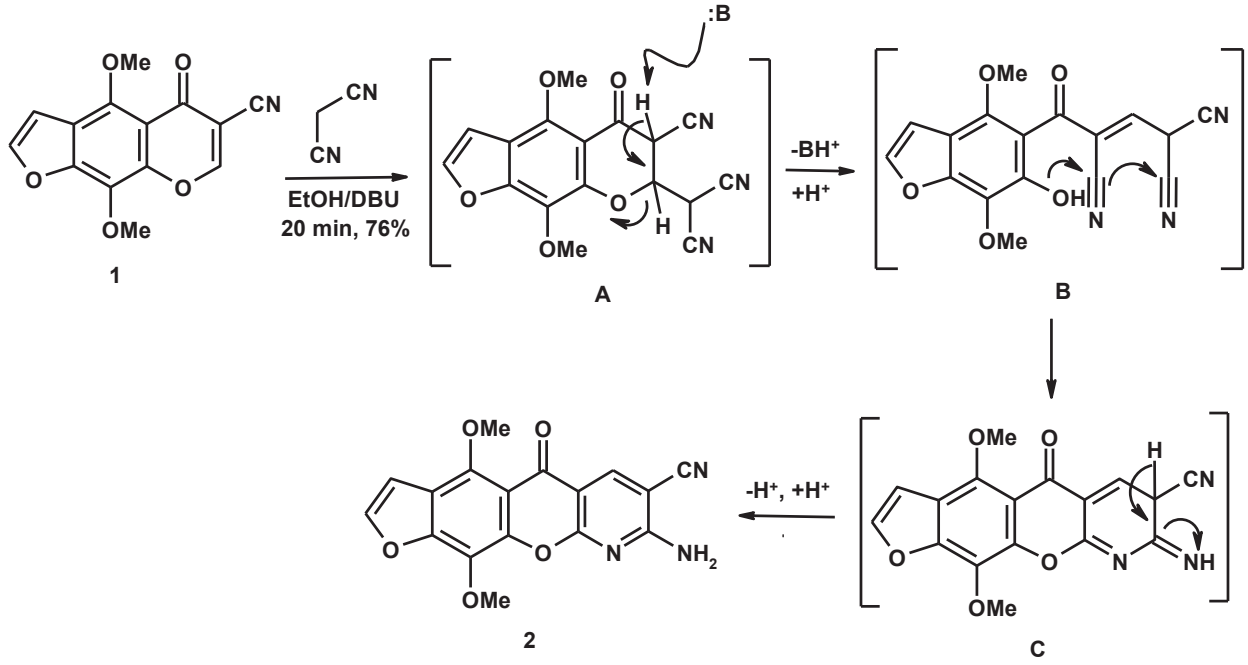
INTRODUCTION

The naturally occurring furochromones (khellin and visnagin) are extracted from the fruits and seeds of *Ammi visnaga* L.,[1] which represents one of the dietary plants used for treatment of urolithiasis, hypertriglyceridemia,[2] as well as prevention of kidney stones.[3] Furochromones are broadly used as

anticancer,[4] anticonvulsant,[5] anti-inflammatory, analgesic,[6] antitubercular,[7] and antimicrobial agents,[8] DFT-theoretical calculations were applied to determine the optimized geometries of some furo[3,2-*g*]-chromenes.[9] Photoelectrical, photosensitivity, photovoltaic, photodiode, electronic spectra, solvatochromic computational and molecular docking studies were performed on a range of furo[3,2-*g*]chromene derivatives.[10] The chemical reactivity of fused γ-pyrone bearing nitrile function at its 3-position was extensively studied.[11] The present work aimed to study the chemical transformations of 4,9-dimethoxy-5-oxo-5*H*-furo[3,2-*g*]chromene-6-carbonitrile (khellin-6-carbonitrile) (**1**)[12] with a variety of active methylene nitriles, bearing –CH_2-CN moiety, hoping to construct the novel heteroannulated furo[3`,2`:6,7]chromeno[2,3-*b*]pyridines and furo[3``,2``:6`,7`]chromeno[3`,2`:5,6]pyrido[2,3-*d*]-pyrimidines and evaluated their antimicrobial inhibitory effects.

RESULTS AND DISCUSSION

Reaction of 4,9-dimethoxy-5-oxo-5*H*-furo[3,2-*g*]chromene-6-carbonitrile (**1**) with malononitrile in absolute ethanol containing 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU), as a basic catalyst, afforded 8-amino-4,11-dimethoxy-5-oxo-5*H*-furo[3`,2`:6,7]chromeno[2,3-*b*]pyridine-7-carbonitrile (**2**) in 76% yield.[13] Compound **2** may be synthesized *via Michael* addition of malononitrile at C-7 leading to intermediate **A** which underwent retro-*Michael* reaction with concomitant ring opening to give open-chain intermediate **B**. Intermediate **B** underwent two consecutive cycloaddition reactions generating intermediate **C** which underwent proton transfer producing the final product **2** as described in Scheme 1. The chemical transformation of carbonitrile **1** into furochromenopyridine **2** can be regarded as a domino "*Michael*/retro-*Michael*/nitrile additions" reactions. Characteristic absorption bands appeared in the IR spectrum of compound **2** at 3363, 3329 (NH_2), 2222 (C≡N), 1651 ($C{=}O_{\gamma\text{-pyrone}}$) and 1608 cm^{-1} (C=N). In the ^1H NMR spectrum definite singlet appeared at δ 8.65 assigned to $H\text{-}4_{pyridine}$, D_2O-exchangeable signal observed at δ 8.40 attributed to NH_2 protons. The ^{13}C NMR spectrum of compound **2** showed characteristic signals attributed to C≡N and $C{=}O_{\gamma\text{-pyrone}}$ at δ 116.6 and 177.4 ppm, respectively. Structure of the product **2** was further established based on the mass spectrum which recorded the molecular ion peak, as the base peak, at *m/z* 337 corresponding to its formula weight (337.29).



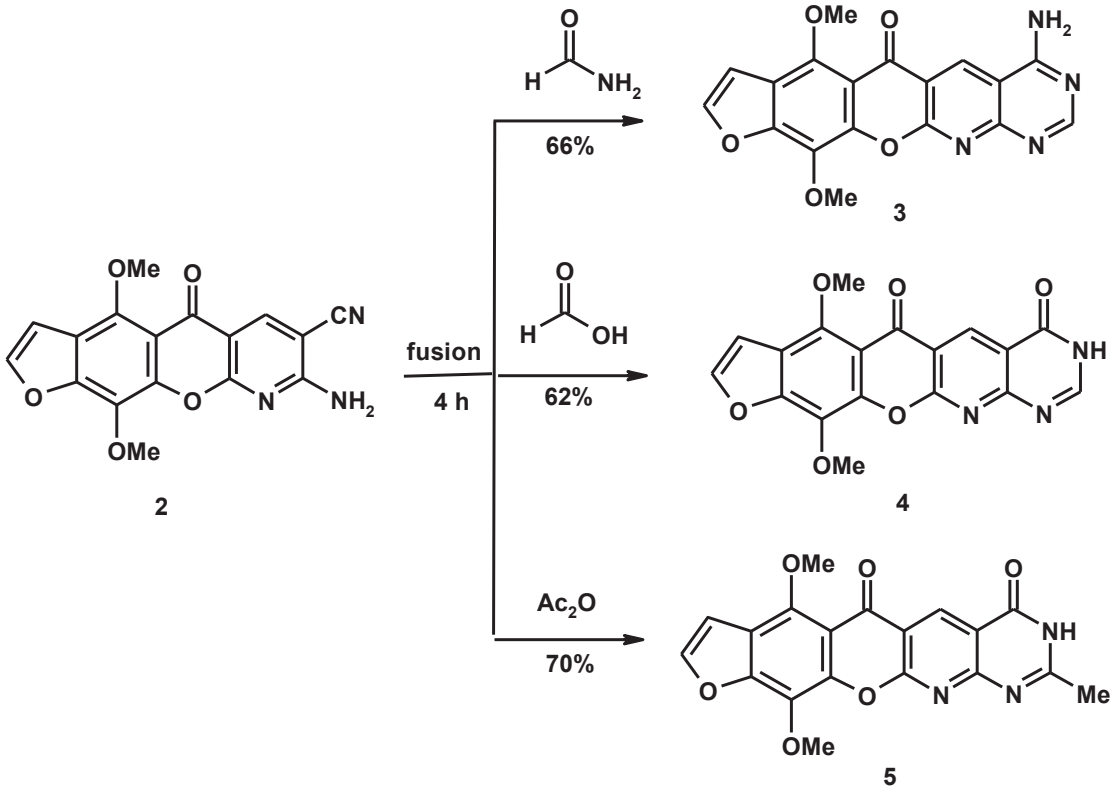
Scheme 1. Formation of furo[3`,2`:6,7]chromeno[2,3-*b*]pyridine-7-carbonitrile **2**

The presence of amino and cyano groups adjacent to each other in compound **2** may be consider as a good precursor for construction of pyrimidine nucleus fused furochromenopyridine moiety.[14] Consequently, reaction of compound **2** with formamide under fusion conditions afforded 7-amino-4,13-dimethoxyfuro-[3``,2``:6`,7`]chromeno[3`,2`:5,6]pyrido[2,3-*d*]pyrimidin-5-one (**3**) (Scheme 2). Specific absorption bands observed in the IR spectrum at 3344, 3260 (NH_2), 1653 ($C=O_{\gamma\text{-pyrone}}$) and 1611 cm^{-1} (C=N). In the ^1H NMR spectrum of compound **3** two singlet signals appeared at δ 8.57 and 9.26 assigned to $H\text{-}4_{pyridine}$ and $H\text{-}2_{pyrimidine}$, respectively, in addition to an exchangeable signal at δ 8.23 attributed to NH_2 protons. The molecular ion peak of compound **3** appeared in the mass spectrum at *m/z* 364 corresponding to its formula weight (364.31).

Moreover, fusion of compound **2** with formic acid afforded 4,13-dimethoxy-5*H*-furo[3``,2``:6`,7`]-chromeno[3`,2`:5,6]pyrido[2,3-*d*]pyrimidine-5,7(8*H*)-dione (**4**) (Scheme 2). The IR spectrum of compound **4** showed characteristic absorption bands at 3395 (NH), 1681 ($C=O_{pyrimidinone}$), 1655 ($C=O_{\gamma\text{-pyrone}}$) and 1613 cm^{-1}(C=N). The ^1H NMR spectrum showed two characteristic singlet signals at δ 8.61 and 9.04 attributed to $H\text{-}4_{pyridine}$, and $H\text{-}2_{pyrimidine}$, respectively, in addition to an exchangeable signal at δ 11.67 ppm attributed to NH proton. The parent ion peak recorded in mass spectrum at *m/z* 365 which approves the suggested molecular formula ($C_{18}H_{11}N_3O_6$).

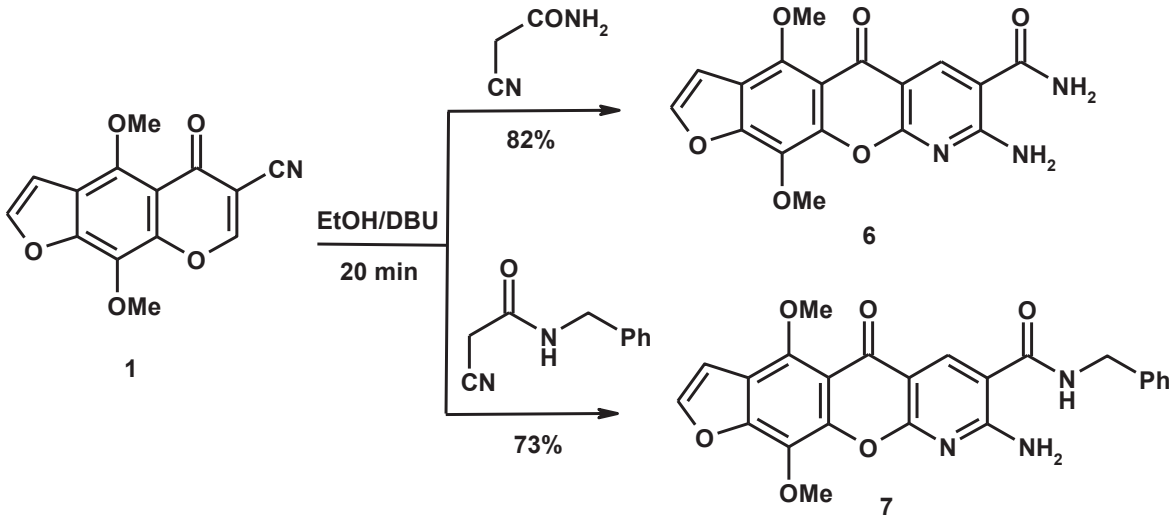
Further, refluxing compound **2** with acetic anhydride produced furo[3``,2``:6`,7`]chromeno[3`,2`:5,6]-pyrido[2,3-*d*]pyrimidine-5,7(8*H*)-dione **5** (Scheme 2). The IR spectrum of compound **5** showed characteristic absorption bands at 1695 ($C=O_{pyrimidinone}$), 1657 ($C=O_{\gamma\text{-pyrone}}$) and 1615 cm^{-1}(C=N). Two distinctive singlet signals appeared in the ^1H NMR spectrum at δ 2.17 and 8.48 attributed to CH_3 and H-

$4_{pyridine}$, respectively. Structure of compound **5** was further deduced from its mass spectrum which revealed the molecular ion peak at *m/z* 379 and confirms the proposed structure. The ^{13}C NMR spectrum of compound **5** appeared specific signal assignable to Me and $C{=}O_{\gamma\text{-pyrone}}$ at δ 22.8 and 177.5 ppm, respectively.



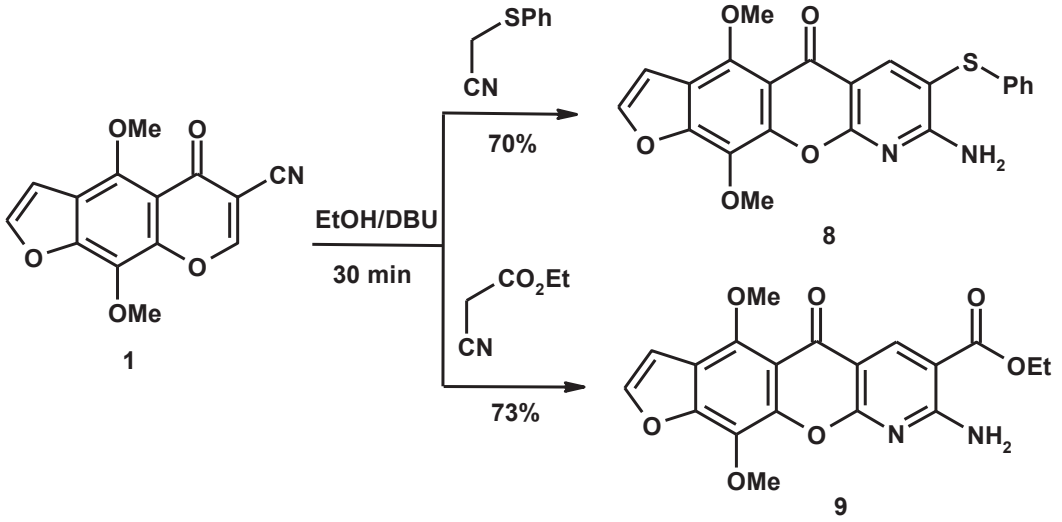
Scheme 2. Formation of furo[3``,2``:6`,7`]chromeno[3`,2`:5,6]pyrido[2,3-*d*]pyrimidines **3-5**

After that, ring opening ring closure (RORC) reactions of furo[3,2-*g*]chromene-6-carbonitrile**1** with cyanoacetamide and *N*-benzylcyanoacetamide, in boiling ethanol containing DBU, afforded furo[3`,2`:6,7]chromeno[2,3-*b*]pyridines **6** and **7**, respectively (Scheme 3). Formation of compounds **3** and **4** also occur through γ-pyrone ring opening followed by recyclization as happened in Scheme 1. The IR spectra of compounds **6** and **7** presented characteristic absorption bands at 1673/1669 ($C{=}O_{amide}$), 1650/1655 ($C{=}O_{\gamma\text{-pyrone}}$) and 1613/1609 cm^{-1} (C=N), respectively. The ^1H NMR spectra showed specific singlet corresponds to $H\text{-}4_{pyridine}$ at δ 8.68 and 8.51 for compounds **6** and **7**, respectively. The spectrum of compound **7** showed characteristic doublet exchanged to singlet in D_2O assigned to CH_2 protons at δ 4.48 ppm. Furthermore, the mass spectra for compounds **6** and **7** revealed their molecular ion peaks at *m/z* 355 and 445 that agree well with their formula weights 355.30 and 445.42, respectively.



Scheme 3. Formation of furo[3`,2`:6,7]chromeno[2,3-*b*]pyridines **6** and **7**

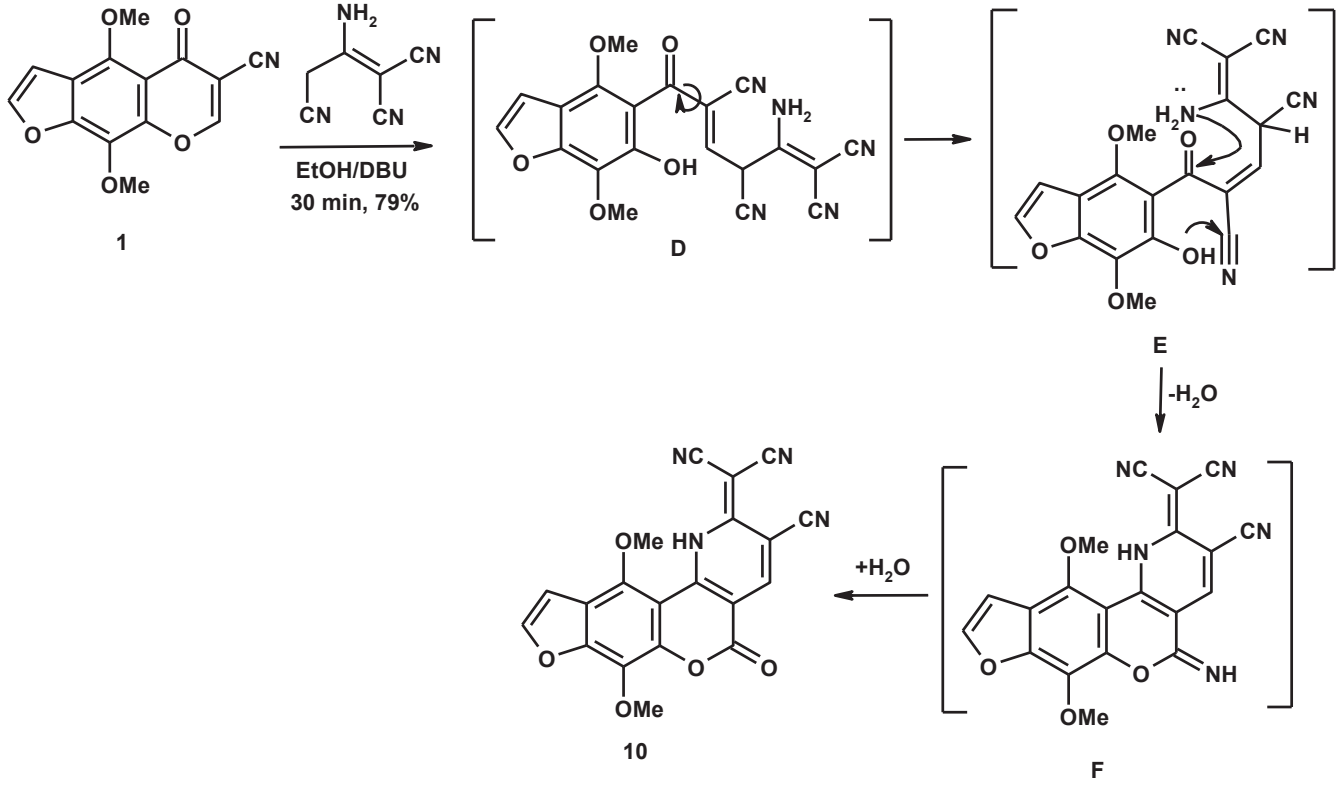
Moreover, the chemical transformation of carbonitrile **1** with (phenylthio)acetonitrile and ethyl cyanoacetate, in boiling ethanol containing DBU, yielded 8-amino-7-substituted-furo[3`,2`:6,7]chromeno-[2,3-*b*]pyridines **8** and **9**, respectively (Scheme 4). The ^{1}H NMR spectrum of compounds **8** and **9** showed singlet signals attributed to H-4$_{pyridine}$ at δ 8.57 and 8.64, respectively. The mass spectra for compounds **8** and **9** revealed their molecular ion peaks at *m/z* 420 and 384 that agree well with their formula weights of $C_{22}H_{16}N_2O_5S$ and $C_{19}H_{16}N_2O_7$, respectively.



Scheme 4. Reaction of carbonitrile **1** with (phenylthio)acetonitrile and ethyl cyanoacetate

On the other hand, treatment of carbonitrile **1** with malononitrile dimer (2-aminoprop-1-ene-1,1,3-tricarbonitrile) showed different behavior than the above active methylene nitrile producing the novel 7-cyano-4,11-dimethoxy-9-oxo-5,9-dihydro-6*H*-furo[3`,2`:6,7]chromeno[4,3-*b*]pyridin-6-ylidene)propane-dinitrile (**10**) (Scheme 5).[27] Formation of compound **10** occurs through a domino process including

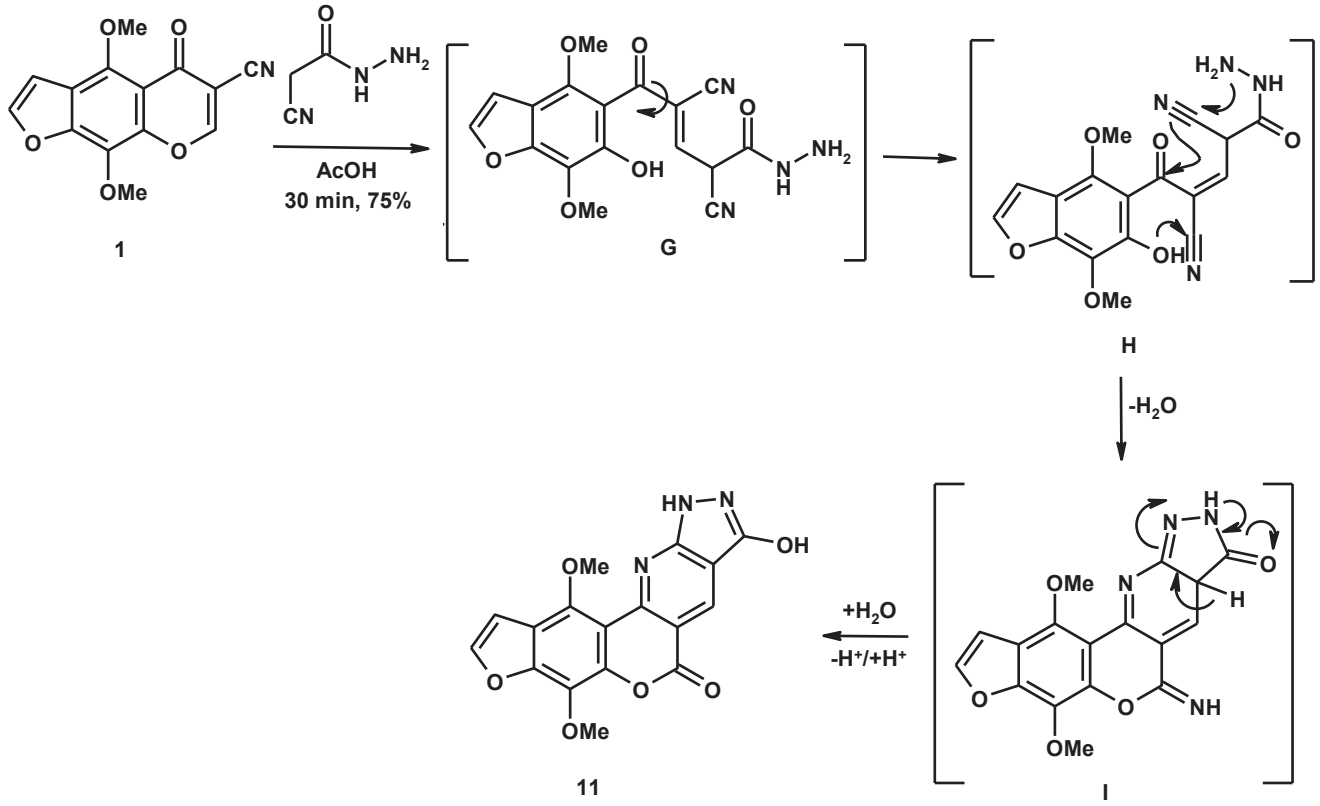
deprotonation of malononitrile dimer and nucleophilic attack at C-7 position with γ-pyrone ring opening, producing intermediate **E**, followed by free rotation around the single bond leading to intermediate **F**. Cycloaddition and cyclodehydration reactions of the latter intermediate yielded intermediate **G** which hydrolyzed to produce the final product **10** as depicted in Scheme 5. The IR spectrum of compound **10** showed characteristic absorption bands at 3414 (NH), 2221, 2196, 2178 (3C≡N), 1717 ($C=O_{\alpha-pyrone}$), 1627 ($C=C_{exocyclic}$) and 1602 cm^{-1} (C=C). Its ^1H NMR spectrum showed characteristic singlet at δ 8.40 ppm attributed to $H\text{-}4_{pyridine}$, in addition to D_2O-exchangeable signal assigned to NH proton at δ 11.86 ppm. The mass spectrum is a good evidence for the formation of compound **10**; which revealed the molecular ion peak, as the base peak, at *m/z* 386 and confirms the suggested structure.



Scheme 5. Formation of furo[3`,2`:6,7]chromeno[4,3-*b*]pyridine derivative **10**

Fascinatingly, reaction of carbonitrile **1** with cyanoacetohydrazide in boiling acetic acid proceed through a domino process leading to heteroannulated furo[3`,2`:6,7]chromeno[4,3-*b*]pyrazolo[4,3-*e*]pyridin-10(6*H*)-one derivative **11** (Scheme 6).[12] Under these reaction conditions, cyanoacetohydrazide acted as carbon nucleophile and the reaction initially proceeds *via* nucleophilic attack at C-7 position with γ-pyrone ring opening to produce intermediate **G**, which underwent free rotation producing intermediate **H**. Cycloaddition and cyclodehydration reactions of the later intermediate led to intermediate **I**, which hydrolyzed under the reaction conditions to give the final product **11** as illustrated in Scheme 6. The IR spectrum of compound **11** showed characteristic absorption bands at 3354 (OH), 3312 (NH), 1708 ($C=O_{\alpha}$-

$_{pyrone}$) and 1623 cm^{-1} (C=N). The ^{1}H NMR spectrum of compound **11** revealed singlet signal at δ 8.73 assigned to H-$4_{pyridine}$, in addition to broad exchangeable signal at δ 11.47 (NH) and 12.89 (OH) ppm. The mass spectrum is a strong evidence for elucidation of structure of compound **11** which revealed the molecular ion peak at *m/z* 353, as the base peak, and agrees well with the formula weight of $C_{17}H_{11}N_3O_6$.

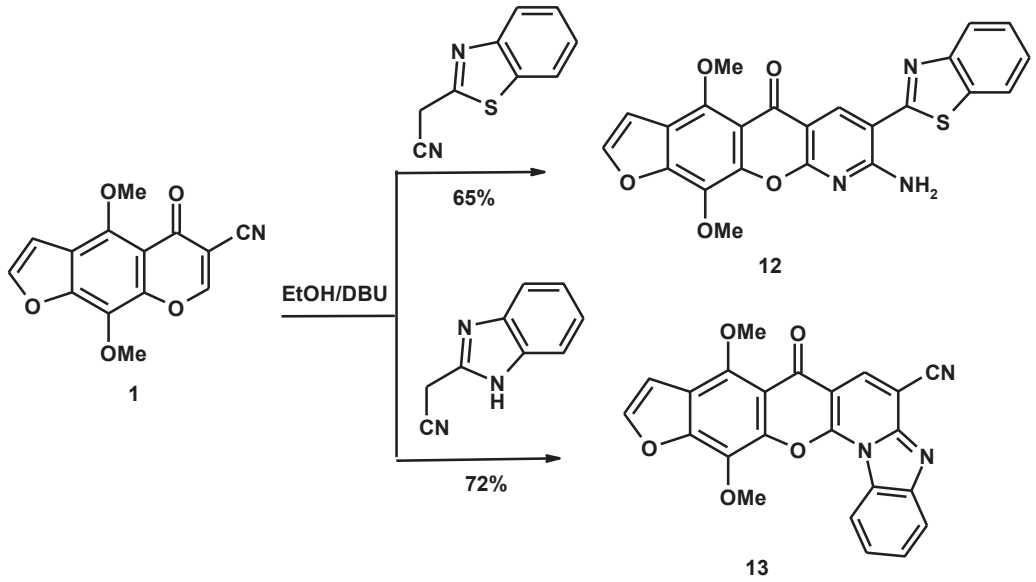


Scheme 6. Formation of furochromenopyrazolopyridine derivative **11**

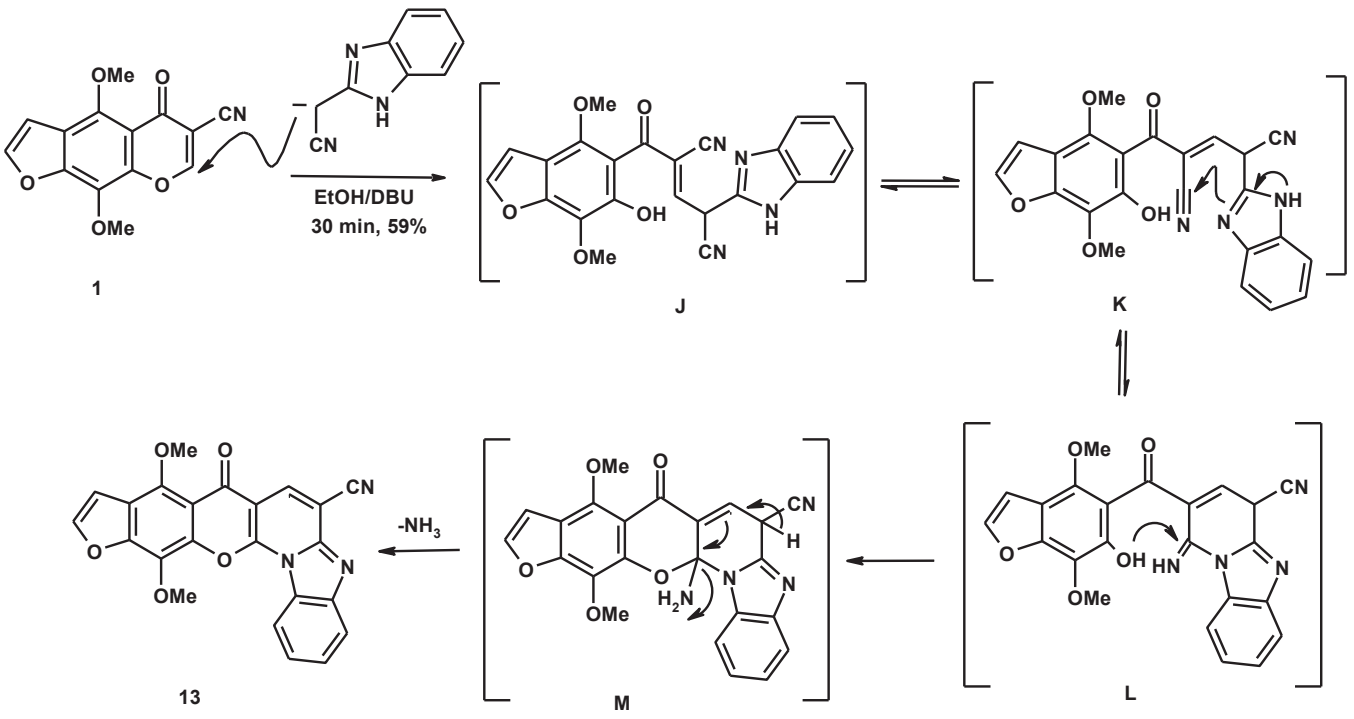
On the other hand, the chemical behavior of carbonitrile **1** was studied towards 1,3-benzothiazol-2-ylacetonitrile and 1*H*-benzimidazol-2-ylacetonitrile. Refluxing carbonitrile **1** with 1,3-benzothiazol-2-ylacetonitrile, in absolute ethanol containing DBU, gave 8-amino-7-(1,3-benzothiazol-2-yl)-4,11-dimethoxy-5-oxo-5*H*-furo[3`,2`:6,7]chromeno[2,3-*b*]pyridine (**12**) (Scheme 7). Specific singlet appeared in the ^{1}H NMR spectrum of compound **12** at δ 8.65 ppm attributed to H-$4_{pyridine}$.

Under the previous recation conditions, 1*H*-benzimidazol-2-ylacetonitrile showed different behavior upon treatment with carbonitrile **1** producing the novel angular furochromenopyridobenzimidazole derivative **13** (Scheme 7). The suggested mechanism for the formation of compound **13** is depicted in Scheme 8. The reaction proceed *via* nucleophilic attack of the deprotonated 1*H*-benzimidazol-2-ylacetonitrile at C-7 of carbonitrile **1** with ring opening giving intermediate **J** which rotated to intermediate **K** with nucleophilic addition of NH group into the nitrile function (intermediate **L**) followed by cycloaddition

(intermediate **M**) with removal of ammonia (Scheme 8).



Scheme 7. Formation of heteroannulated furochromenopyridine derivatives **12** and **13**



Scheme 8. The suggested mechanism for the formation of compound **13**

ANTIMICROBIAL EVALUATION

The standardized disc agar diffusion method[16] was followed to determine the antimicrobial activity of the prepared compounds against the sensitive microorganisms which are: Gram-positive bacteria *Staphylococcus aureus* (ATCC25923) and *Bacillus subtilis* (ATCC6635), Gram-negative bacteria

Escherichia coli (ATCC 25922) and *Salmonella typhimurium* (ATCC 14028), yeast *Candida albicans* (ATCC 10231) and fungus *Asperigillus fumigatus*. The antimicrobial activities were determined by measuring the inhibition zones, including the diameter of the disc (6 mm) as shown in Table 1. The data of the antimicrobial activity presented in Table 1 reported that:

[1] The antimicrobial activities of the synthesized compounds are variable towards the selected microorganisms.

[2] The novel series of furochromenopyridopyrimidines **3**-**5** appeared high inhibitory effects towards the two types of Gram-positive bacteria, *Escherichia coli* as Gram-positive bacteria and the fungus, *Asperigillus fumigatus*.

[3] The novel angular heterocycles systems **10** and **11** showed notable inhibitory effects towards all types of the used microorganisms.

[4] Compound **8** revealed high inhibitory effects towards some microorganisms; *Bacillus subtilis*, *Escherichia coli* and *Asperigillus fumigatus*. While, compound **12** showed high activity towards the selected Gram-positive bacteria; *Staphylococcus aureus* and *Bacillus subtilis*.

[5] The polyfused furochromenopyridobenzimidazole **13** recorded high activity against the selected Gram-negative bacteria, yeast and fungus strains.

[6] The high antimicrobial inhibitory effects of some of the synthesized compounds against certain microorganisms, may attribute to the presence of multi-fused heterocyclic systems namely furochromenopyridines and furochromenopyridopyrimidines within the molecules.

[7] The above results appeared that, some of the prepared compounds recorded high activity as comparable with the reference drugs and may serve as antimicrobial agents.

Table 1. In *vitro* antimicrobial activities of the synthesized compounds at 500 and 1000 μg/mL by disc diffusion assay

Compd. No.	Mean* of zone diameter(mm)											
	Gram - positive bacteria				Gram - negative bacteria				Yeasts and Fungi			
	Staphylococcus aureus		*Bacillus subtilis*		*Salmonella typhimurium*		*Escherichia coli*		*Candida albicans*		*Asperigillus fumigatus*	
	1000 μg/ml	500μg/ml	1000 μg/ml	500 μg/ml	1000 μg/ml	500 μg/ml	1000 μg/ml	500 μg/ml	1000 μg/ml	500 μg/ml	1000 μg/ml	500 μg/ml
2	16 I	12 I	9 L	6 L	14 I	8 L	16 I	12 I	13 I	9 L	15 I	10 I
3	**28 H**	**21 H**	**26 H**	**22 H**	17 I	13 I	**16 H**	**20 H**	20 I	13 I	**25 H**	**19 H**
4	**30 H**	**23 H**	**25 H**	**20 H**	19 I	14 I	**16 H**	**20 H**	15 I	8 L	**28 H**	**21 H**
5	**29 H**	**20 H**	**30 H**	**21 H**	19 I	13 I	**25 H**	**19 H**	15 I	11 I	**26 H**	**20 H**
6	18 I	13 I	12 I	9 I	18 I	11 I	17 I	13 I	19 I	14 I	18 I	13 I
7	12 I	8 L	11 L	7 L	15 I	9 L	16 I	11 I	18 I	11 I	17 I	11 I
8	19 I	12 I	**16 H**	**20 H**	13 I	8 L	**29 H**	**22 H**	17 I	11 I	**27 H**	**19 H**
9	18 I	13 I	21 I	15 I	20 I	14 I	19 I	12 I	22 I	15 I	**31 H**	**25 H**
10	**26 H**	**20 H**	**29 H**	**19 H**	**31 H**	**23 H**	**28 H**	**20 H**	**26 H**	**20 H**	**27 H**	**20 H**
11	**29 H**	**22 H**	**32 H**	**20 H**	**28 H**	**19 H**	**26 H**	**19 H**	**31 H**	**22 H**	**29 H**	**21 H**
12	**28 H**	**20 H**	**25 H**	**18 H**	19 I	16 I	20 I	15 I	16 I	11 I	19 I	14 I
13	16 I	9 I	14 I	11 I	**26 H**	**20 H**	**27 H**	**21 H**	**25 H**	**19 H**	**28 H**	**20 H**
S	35	26	35	25	36	28	38	27	35	28	37	26

* Calculated from 3 values.
S: Standard drug, H = High activity, I = Intermediate activity, L = Low activity,
S: Standard drug such as Chloramphencol in the case of Gram-positive bacteria, Cephalothinin the case of Gram-negative bacteria and cycloheximide in the case of yeast and fungi.

CONCLUSIONS

In conclusion, a novel series of linear and angular heteroannulated furo[3,2-*g*]chromenes and related compounds were efficiently synthesized from ring opening ring closure reactions of the electron deficient 4,9-dimethoxy-5-oxo-5*H*-furo[3,2-*g*]chromene-6-carbonitrile (**1**) with some active methylene compounds. These transformations occur throughout a cascade process including '*Michael*/retro-*Michael*/nitrile addition/heterocyclization' reactions. A diversity of linear furo[3`,2`:6,7]chromeno[2,3-*b*]pyridines and furo[3``,2``:6`,7`]chromeno[3`,2`:5,6]pyrido[2,3-*d*]pyrimidines were efficiently synthesized. Some novel angular heteroannulated furochromenopyrimidines were synthesized from the reaction of carbonitrile **1** with malononitrile dimer, cyanoacetohydrazide and 1*H*-benzimidazol-2-ylacetonitrile.

EXPERIMENTAL

General. 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 osn Mercury-300BB, using DMSO-d_6 as a solvent and TMS (δ) 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. The purity of the synthesized compounds were tested using TLC. 4,9-Dimethoxy-5-oxo-5*H*-furo[3,2-*g*]chromene-6-carbonitrile (**1**) was prepared according to literature.[12]

Biological method. The test for the antimicrobial activity was performed on medium potato dextrose agar (PDA) which contained infusion of 200 g potatoes, 6 g dextrose and 15 g agar. Uniform size filter paper disks (6 mm diameter, 3 disks per compound) were impregnated by equal volume (10 μL) from the concentrations of 500 and 1000 μg/mL dissolved compounds in dimethylformamide (DMF) and carefully placed on inoculated agar surface. After incubation for 36 h at 27 ºC in the case of bacteria and for 48 h at 24 ºC in the case of fungi. The obtained results were recorded for each tested compound as average diameter of inhibition zones of the bacteria and fungus around the disks in mm at the concentrations 500 and 1000 μg/mL.[16]

8-Amino-4,11-dimethoxy-5-oxo-5*H*-furo[3`,2`:6,7]chromeno[2,3-*b*]pyridine-7-carbonitrile (2). A mixture of carbonitrile **1** (0.54 g, 2 mmol) and malononitrile (0.13 g, 2 mmol) in absolute EtOH (20 mL) containing DBU (0.1 mL) was heated under reflux for 20 min. The yellow crystals obtained during heating were filtered and crystallized from DMF/H_2O, mp 244-245 ºC, yield (0.51 g, 76%). IR (KBr, cm^{-1}): 3363, 3329 (NH_2), 3100 (CH_{furan}), 3023 ($CH_{arom.}$), 2966, 2943 ($CH_{aliph.}$) 2222 (C≡N), 1651 ($C{=}O_{\gamma\text{-pyrone}}$), 1608 (C=N), 1589 (C=C). ^{1}H NMR (DMSO-d_6, δ, 300 MHz): 3.85 (s, 3H, OCH_3), 3.93 (s, 3H, OCH_3), 7.27 (d, 1H, *J*=1.8 Hz, H-3_{furan}), 7.89 (d, 1H, *J*=1.8 Hz, H-2_{furan}), 8.40 (bs, 2H, NH_2 exchangeable with D_2O), 8.65 (s, 1H, H-6). ^{13}C NMR (DMSO-d_6, δ, 75 MHz): 58.1 (OCH_3), 59.0 (OCH_3), 100.3, 105.8, 106.2, 108.0, 109.3, 116.6, 128.4, 139.7, 144.2, 146.4, 147,6, 150.7, 162.8, 164 9, 177.4. Mass spectrum (*m/z*, *I*%): 337 (M^+; 100), 309 (39), 279 (32), 253 (68), 230 (8), 202 (13), 187 (27), 118 (54), 80 (22), 64 (21). Anal. Calcd for $C_{17}H_{11}N_3O_5$ (337.29): C, 60.54; H, 3.29; N, 12.46%. Found: C, 60.39; H, 3.11; N, 12.30%.

7-Amino-4,13-dimethoxy-furo[3``,2``:6`,7`]chromeno[3`,2`:5,6]pyrido[2,3-*d*]pyrimidin-5-one (3). A mixture of compound **2** (0.67 g, 2 mmol) and formamide (10 mL) was heated under reflux for 4 h. The solid obtained after cooling was filtered, washed with cooled EtOH and crystallized from DMF/H_2O to give compound **3** as pale yellow crystals, mp 261-262 ºC, yield (0.48 g, 66%). IR (KBr, cm^{-1}): 3344, 3260

(NH_2), 3106 (CH_{furan}), 3029 ($CH_{arom.}$), 2973, 2936 ($CH_{aliph.}$), 1653 ($C=O_{\gamma\text{-pyrone}}$), 1611 (C=N), 1593 (C=C). ^{1}H NMR (DMSO-d_6, δ, 300 MHz): 3.88 (s, 3H, OCH_3), 3.96 (s, 3H, OCH_3), 7.15 (d, 1H, *J*=2.1 Hz, H-3_{furan}), 7.91 (d, 1H, *J*=2.1 Hz, H-2_{furan}), 8.23 (bs, 2H, NH_2 exchangeable with D_2O), 8.57 (s, 1H, H-6), 9.26 (s, 1H, H-9). ^{13}C NMR (DMSO-d_6, δ, 75 MHz): 58.3 (OCH_3), 59.4 (OCH_3), 105.4, 106.6, 108.4, 114.2, 117.9, 128.2, 139.3, 140.6, 144.8, 146.9, 151.4, 156.8, 157.5, 159.2, 162.1, 177.4. Mass spectrum (*m/z*, *I*%): 364 (M^+; 35), 336 (100), 306 (52), 291 (9), 264 (17), 216 (41), 205 (18), 177 (27), 118 (69), 102 (23), 64 (15). Anal. Calcd for $C_{18}H_{12}N_4O_5$ (364.31): C, 59.34; H, 3.32; N, 15.38%. Found: C, 59.21; H, 3.08; N, 15.14%.

4,13-Dimethoxy-5*H*-furo[3``,2``:6`,7`]chromeno[3`,2`:5,6]pyrido[2,3-*d*]pyrimidine-5,7(8*H*)dione (4). A mixture of compound **2** (0.67 g, 2 mmol) and formic acid (10 mL) was heated under reflux for 4 h. The solid obtained after cooling was filtered, washed with cooled EtOH and crystallized from DMF to give compound **4** as yellow crystals, mp > 300 ºC, yield (0.45 g, 62%). IR (KBr, cm^{-1}): 3395 (NH), 3113 (CH_{furan}), 3026 ($CH_{arom.}$), 2956, 2924 ($CH_{aliph.}$), 1681 ($C=O_{pyrimidinone}$), 1655 ($C=O_{\gamma\text{-pyrone}}$), 1613 (C=N), 1594 (C=C). ^{1}H NMR (DMSO-d_6, δ, 300 MHz): 3.82 (s, 3H, OCH_3), 3.95 (s, 3H, OCH_3), 7.18 (d, 1H, *J*=1.8 Hz, H-3_{furan}), 7.86 (d, 1H, *J*=1.8 Hz, H-2_{furan}), 8.61 (s, 1H, H-6), 9.04 (s, 1H, H-9), 11.67 (bs, 1H, NHexchangeable with D_2O). ^{13}C NMR (DMSO-d_6, δ, 75 MHz): 58.2 (OCH_3), 59.3 (OCH_3), 105.7, 106.9, 109.4, 114.3, 117.5, 128.0, 140.1, 144.6, 145.8, 147.3, 151.5, 154.6, 156.4, 160.7, 162.8, 177.7. Mass spectrum (*m/z*, *I*%): 365 (M^+; 13), 337 (62), 309 (100), 278 (33), 205 (14), 188 (9), 205 (18), 148 (55), 104 (10), 102 (8), 64 (17). Anal. Calcd for $C_{18}H_{11}N_3O_6$ (365.29): C, 59.18; H, 3.04; N, 11.50%. Found: C, 58.90; H, 2.85; N, 11.33%.

4,13-Dimethoxy-9-methyl-5*H*-furo[3``,2``:6`,7`]chromeno[3`,2`:5,6]pyrido[2,3-*d*]pyrimidine-5,7(8*H*)-dione (5). A mixture of compound **2** (0.67 g, 2mmol) and acetic anhydride (10 mL) was heated under reflux for 4 h. After cooling, the reaction mixture was poured onto crushed ice. The solid so formed was filtered, washed with water and crystallized from AcOH to give compound **5** as yellow crystals, mp 299-300 ºC, yield (0.55 g, 70%). IR (KBr, cm^{-1}): 3414 (NH), 3105 (CH_{furan}), 3058 ($CH_{arom.}$), 2942, 2911 ($CH_{aliph.}$), 1695 ($C=O_{pyrimidinone}$), 1657 ($C=O_{\gamma\text{-pyrone}}$), 1615 (C=N), 1577 (C=C). ^{1}H NMR (DMSO-d_6, δ, 300 MHz): 2.17 (s, 3H, CH_3), 3.91 (s, 3H, OCH_3), 4.06 (s, 3H, OCH_3), 7.21 (d, 1H, *J*=1.8 Hz, H-3_{furan}), 7.99 (d, 1H, *J*=1.8 Hz, H-2_{furan}), 8.48 (s, 1H, H-6), 11.34 (bs, 1H, NH exchangeable with D_2O). ^{13}C NMR (DMSO-d_6, δ, 75 MHz): 22.8 (CH_3), 58.4 (OCH_3), 59.2 (OCH_3), 105.4, 107.3, 110.1, 114.4, 117.3, 128.3, 140.6, 144.2, 145.9, 147.7, 151.3, 154.0, 156.8, 161.3, 163.5, 177.5. Mass spectrum (*m/z*, *I*%): 379 (M^+; 24), 351 (100), 293 (71), 242 (46), 228 (31), 187 (21), 143 (16), 119 (11), 77 (34), 65 (13). Anal. Calcd for $C_{19}H_{13}N_3O_6$ (379.32): C, 60.16; H, 3.45; N, 11.08%. Found: C, 59.80; H, 3.24; N, 10.85%.

8-Amino-4,11-dimethoxy-5-oxo-5*H*-furo[3`,2`:6,7]chromeno[2,3-*b*]pyridine-7-carboxamide (6). A mixture of carbonitrile **1** (0.54 g, 2 mmol) and cyanoacetamide (0.17 g, 2 mmol) in absolute EtOH (20 mL) containing DBU (0.1 mL) was heated under reflux for 20 min. The yellow crystals obtained during heating were filtered and crystallized from DMF/EtOH, mp 279-280 ºC, yield (0.58 g, 82%). IR (KBr, cm^{-1}): 3391, 3340, 3286, 3160 ($2NH_2$), 3115 (CH_{furan}), 3030 ($CH_{arom.}$), 2963, 2921 ($CH_{aliph.}$), 1673 ($C{=}O_{amide}$), 1650 ($C{=}O_{\gamma\text{-pyrone}}$), 1613 (C=N), 1578 (C=C). ^{1}H NMR (DMSO-d_6, δ, 300 MHz): 3.93 (s, 3H, OCH_3), 4.05 (s, 3H, OCH_3), 7.22 (d, 1H, *J*=1.8 Hz, H-3_{furan}), 7.95 (d, 1H, *J*=1.8 Hz, H-2_{furan}), 8.68 (s, 1H, H-6), 9.47 (bs, 2H, NH_2 exchangeable with D_2O), 10.68 (bs, 2H, NH_2 exchangeable with D_2O). ^{13}C NMR (DMSO-d_6, δ, 75 MHz): 58.3 (OCH_3), 59.1 (OCH_3), 105.4, 107.0, 108.6, 110.3, 114.6, 128.3, 140.1, 144.7, 146.3, 147.4, 151.8, 156.9, 163.7, 167.7, 177.5. Mass spectrum (*m/z*, *I*%): 355 (M^+; 62), 399 (100), 311 (51), 281 (15), 235 (17), 216 (28) 177 (9), 143 (20), 119 (17), 77 (62), 65 (19). Anal. Calcd for $C_{17}H_{13}N_3O_6$ (355.30): C, 57.47; H, 3.69; N, 11.83%. Found: C, 57.30; H, 3.42; N, 11.51%.

8-Amino-*N*-benzyl-4,11-dimethoxy-5-oxo-5*H*-furo[3`,2`:6,7]chromeno[2,3-*b*]pyridine-7-carboxamide (7). A mixture of carbonitrile **1** (0.54 g, 2 mmol) and *N*-benzyl-2-cyanoacetamide (0.37 g, 2 mmol) in absolute EtOH (20 mL) containing DBU (0.1 mL) was heated under reflux for 20 min. The yellow crystals obtained during heating were filtered and crystallized from DMF/H_2O, mp > 300 ºC, yield (0.65 g, 73%). IR (KBr, cm^{-1}): 3375, 3288, 3210 (NH_2, NH), 3111 (CH_{furan}), 3046 ($CH_{arom.}$), 2970, 2938 ($CH_{aliph.}$), 1669 ($C{=}O_{amide}$), 1655 ($C{=}O_{\gamma\text{-pyrone}}$), 1609 (C=N), 1585 (C=C). ^{1}H NMR (DMSO-d_6, δ, 300 MHz): 3.87 (s, 3H, OCH_3), 3.96 (s, 3H, OCH_3), 4.48 (d, 2H, CH_2 exchanged to singlet with D_2O), 7.14 (d, 1H, *J*=2.4 Hz, H-3_{furan}), 7.36-7.53 (m, 5H, Ph-H), 7.95 (d, 1H, *J*=2.4 Hz, H-2_{furan}), 8.51 (s, 1H, H-6), 8.90 (bs, 2H, NH_2 exchangeable with D_2O), 10.73 (bs, 1H, NH exchangeable with D_2O). ^{13}C NMR (DMSO-d_6, δ, 75 MHz): 44.8 (CH_2), 58.8 (OCH_3), 59.6 (OCH_3), 105.6, 107.2, 108.7, 110.6, 114.2, 120.2, 125.7, 127.3, 128.6, 130.4, 136.2, 140.3, 144.5, 145.8, 147.4, 151.6, 157.3,167.3, 178.0. Mass spectrum (*m/z*, *I*%): 445 (M^+; 29), 417 (21), 311 (61), 281 (32), 253 (74), 205 (37) 163 (30), 118 (44), 106 (100), 92 (67), 77 (26), 65 (10). Anal. Calcd for $C_{24}H_{19}N_3O_6$ (445.42): C, 64.72; H, 4.30; N, 9.43%. Found: C, 64.67; H, 4.17; N, 9.22%.

8-Amino-4,11-dimethoxy-7-phenylthio-5-oxo-5*H*-furo[3`,2`:6,7]chromeno[2,3-*b*]pyridine-7-carboxamide (8). A mixture of carbonitrile **1** (0.54 g, 2 mmol) and (phenylthio)acetonitrile (0.32 g, 0.26 mL, 2 mmol) in absolute EtOH (30 mL) containing DBU (0.1 mL) was heated under reflux for 30 min. The paleyellow crystals obtained after cooling were filtered and crystallized from EtOH, mp 265-266 ºC, yield (0.53 g, 70%). IR (KBr, cm^{-1}): 3385, 3298 (NH_2), 3117 (CH_{furan}), 3020 ($CH_{arom.}$), 2959, 2923 ($CH_{aliph.}$), 1647 ($C{=}O_{\gamma\text{-pyrone}}$), 1610 (C=N), 1576 (C=C). ^{1}H NMR (DMSO-d_6, δ, 300 MHz): 3.91 (s, 3H, OCH_3),

4.03 (s, 3H, OCH_3), 7.19 (d, 1H, *J*=2.1 Hz, H-3_{furan}), 7.29-7.47 (m, 5H, Ph-H), 7.90 (d, 1H, *J*=2.1 Hz, H-2_{furan}), 8.57 (s, 1H, H-6), 8.82 (bs, 2H, NH_2 exchangeable with D_2O). ^{13}C NMR (DMSO-d_6, δ, 75 MHz): 57.7 (OCH_3), 58.7 (OCH_3), 105.3, 106.7, 108.0, 114.4, 114.9, 123.6, 128.3, 129.7, 130.5, 131.8, 136.4, 140.9, 143.9, 146.2, 151.8, 156.0, 164.2, 177.4. Mass spectrum (*m/z*, *I*%): 420 (M^+; 38), 392 (23), 283 (78), 253 (18), 220 (60), 205 (26) 191 (15), 163 (8), 109 (11), 77 (100), 65 (42). Anal. Calcd for $C_{22}H_{16}N_2O_5S$ (420.44): C, 62.85; H, 3.84; N, 6.66; S, 7.63%. Found: C, 62.60; H, 3.58; N, 6.42; S, 7.60%.

Ethyl 8-Amino-4,11-dimethoxy-5-oxo-5*H*-furo[3`,2`:6,7]chromeno[2,3-*b*]pyridine-7-carboxylate (9). A mixture of carbonitrile **1** (0.54 g, 3 mmol) and ethyl cyanoacetate (0.23 g, 0.24 mL, 2 mmol) in absolute EtOH (20 mL) containing DBU (0.1 mL) was heated under reflux for 30 min. The white crystals obtained after cooling were filtered and crystallized from MeOH, mp 243-244 ºC, yield (0.56 g, 73%). IR (KBr, cm^{-1}): 3369, 3272 (NH_2), 3107 (CH_{furan}), 3036 ($CH_{arom.}$), 2982, 2946 ($CH_{aliph.}$), 1686 ($C{=}O_{ester}$), 1658 ($C{=}O_{\gamma\text{-pyrone}}$), 1608 (C=N), 1592 (C=C). ^1H NMR (DMSO-d_6, δ, 300 MHz): 1.36 (t, 3H, *J*=6.9 Hz, CH_3), 3.96 (s, 3H, OCH_3), 4.08 (s, 3H, OCH_3), 4.39 (q, 2H, *J*= 6.9 Hz, CH_2), 7.11 (d, 1H, *J*=2.1 Hz, H-3_{furan}), 7.89 (d, 1H, *J*=2.1 Hz, H-2_{furan}), 8.64 (s, 1H, H-6), 8.91 (bs, 2H, NH_2 exchangeable with D_2O). ^{13}C NMR (DMSO-d_6, δ, 75 MHz): 14.3 (CH_2), 58.1 (OCH_3), 58.9 (OCH_3), 61.7 (CH_3), 104.9, 105.9, 106.7, 108.6, 114.7, 128.1, 140.6, 142.8, 145.8, 147.4, 152.2, 157.7, 162.9, 166.5, 177.8. Mass spectrum (*m/z*, *I*%): 384 (M^+; 53), 339 (100), 311 (46), 281 (39), 266 (24), 224 (5), 187 (12), 144 (9),118 (34), 102 (16), 77 (36), 65 (61). Anal. Calcd for $C_{19}H_{16}N_2O_7$ (384.34): C, 59.38; H, 4.20; N, 7.29%. Found: C, 59.22; H, 4.00; N, 6.98%.

7-Cyano-4,11-dimethoxy-9-oxo-5,9-dihydro-6*H*-furo[3`,2`:6,7]chromeno[4,3-*b*]pyridin-6-ylidene)-propanedinitrile (10). A mixture of carbonitrile **1** (0.54 g, 2 mmol) and malononitrile dimmer (2-aminoprop-1-ene-1,1,3-tricarbonitrile) (0.27 g, 2 mmol) in absolute EtOH (20 mL) containing DBU (0.1 mL) was heated under reflux for 30 min. The orange crystals formed during heating were filtered and recrystallized from DMF, mp 290-291 ºC, yield (0.59 g, 79%). IR (KBr, cm^{-1}): 3414 (NH), 3119 (CH_{furan}), 3064 ($CH_{arom.}$), 2953, 2925 ($CH_{aliph.}$), 2221, 2196, 2178 (3C≡N), 1717 ($C{=}O_{\alpha\text{–pyrone}}$), 1627 ($C{=}C_{exocyclic}$), 1602 (C=C). ^1H NMR (DMSO-d_6, δ, 300 MHz): 3.89 (s, 3H, OCH_3), 4.13 (s, 3H, OCH_3), 7.16 (d, 1H, *J*=2.1 Hz, H-3_{furan}), 7.84 (d, 1H, *J*=2.1 Hz, H-2_{furan}), 8.40 (s, 1H, H-8), 11.86 (s, 1H, NH exchangeable with D_2O). ^{13}C NMR (DMSO-d_6, δ, 75 MHz): 45.1 $C(CN)_2$, 58.3 (OCH_3), 59.5 (OCH_3), 96.4, 104.7, 108.6, 112.7, 114.3, 116.2, 116,7, 116.9, 133.3, 142.5, 144.4, 147.6, 148.9, 152.4, 158.5, 168.8, 173.2. Mass spectrum (*m/z*, *I*%): 386 (M^+; 100), 356 (32), 280 (21), 254 (15), 212 (9), 184 (30), 152 (34), 103 (47), 77 (56), 64 (20). Anal. Calcd for $C_{20}H_{10}N_4O_5$ (386.32): C, 62.18; H, 2.61; N, 14.50%. Found: C,

61.84; H, 2.30; N, 14.36%.

8-Hydroxy-4,12-dimethoxyfuro[3`,2`:6,7]chromeno[4,3-*b*]pyrazolo[4,3-e]pyridin-10(6*H*)-one (11). A mixture of carbonitrile **1** (0.54 g, 2 mmol) and cyanoacetohydrazide (0.20 g, 2 mmol) in AcOH (10 mL) was heated under reflux for 30 min. The pale yellow crystals obtained after cooling was filtered and crystallized from AcOH, mp > 300 ºC, yield (0.53 g, 75%). IR (KBr, cm^{-1}): 3354 (OH), 3312 (NH), 3102 (CH_{furan}), 3051 ($CH_{arom.}$), 2959, 2928 ($CH_{aliph.}$), 1708 ($C=O_{\alpha\text{-pyrone}}$), 1623 (C=N), 1601 (C=C). ^{1}H NMR (DMSO-d_6, δ, 300 MHz): 3.80 (s, 3H, OCH_3), 4.01 (s, 3H, OCH_3), 7.20 (d, 1H, *J*=1.8 Hz, H-3_{furan}), 7.84 (d, 1H, *J*=1.8 Hz, H-2_{furan}), 8.73 (s, 1H, H-9), 11.47 (s, 1H, NH exchangeable with D_2O), 12.89 (s, 1H, OH exchangeable with D_2O). ^{13}C NMR (DMSO-d_6, δ, 75 MHz): 58.6 (OCH_3), 59.8 (OCH_3), 99.8, 105.6, 112.3, 115.5, 117.4, 128.4, 136.5, 144.9, 146.1, 147.8, 148.9, 151.7 159.5, 187.8, 196.7. Mass spectrum (*m/z*, *I*%): 353 (M^+; 100), 323 (48), 306 (26), 280 (51), 220 (73), 205 (34), 191 (16), 177 (9), 147 (13), 118 (27), 77 (83), 64 (15). Anal. Calcd for $C_{17}H_{11}N_3O_6$ (353.29): C, 57.80; H, 3.14; N, 11.89%. Found: C, 57.58; H, 2.91; N, 11.67%.

8-Amino-7-(1,3-benzothiazol-2-yl)-4,11-dimethoxy-5-oxo-5*H*-furo[3`,2`:6,7]chromeno[2,3-*b*]pyridine (12). A mixture of carbonitrile **1** (0.54 g, 2 mmol) and 1,3-benzothiazol-2-ylacetonitrile (0.35 g, 2 mmol), in absolute EtOH (20 mL) containing DBU (0.1 mL), was heated under reflux for 30 min. The canary yellow crystals obtained during heating were filtered and crystallized from DMF/H_2O to give compound **12**, mp > 320 ºC, yield (0.58 g, 65%). IR (KBr, cm^{-1}): 3373, 3287 (NH_2), 3113 (CH_{furan}), 3036 ($CH_{arom.}$), 2946, 2916 ($CH_{aliph.}$), 1661 ($C=O_{\gamma\text{-pyrone}}$), 1626 (C=N), 1578 (C=C). ^{1}H NMR (DMSO-d_6, δ, 300 MHz): 3.81 (s, 3H, OCH_3), 3.98 (s, 3H, OCH_3), 7.14 (d, 1H, *J*=1.8 Hz, H-3_{furan}), 7.25-7.46 (m, 4H, Ph-H), 7.89 (d, 1H, *J*=1.8 Hz, H-2_{furan}), 8.65 (s, 1H, H-6), 9.25 (bs, 2H, NH_2 exchangeable with D_2O).^{13}C NMR (DMSO-d_6, δ, 75 MHz): 58.7 (OCH_3), 59.9 (OCH_3), 105.2, 106.8, 107.5, 108.4, 112.9, 114.2, 121.7, 122.6, 125.4, 126.3, 128.7, 135.3, 140.7, 142.6, 147.5, 150.8, 152.0, 153.6, 157.0, 158.6, 178.2. Mass spectrum (*m/z*, *I*%): 445 (M^+; 25), 415 (18), 387 (41), 253 (13), 205 (22), 187 (100), 147 (49), 118 (18), 77 (53), 64 (29). Anal. Calcd for $C_{23}H_{15}N_3O_5S$ (445.45): C, 62.02; H, 3.39; N, 9.43; S, 7.20%. Found: C, 61.75; H, 3.19; N, 9.22; S, 7.03%.

4,14-Dimethoxy-5-oxo-5*H*-furo[3``,2``:6`,7`]chromeno[3`,2`:5,6]pyrido[1,2-*a*]benzimidazole-7carbonitrile (13). A mixture of carbonitrile **1** (0.54 g, 2 mmol) and 1*H*-benzimidazol-2-ylacetonitrile (0.31 g, 2 mmol), in absolute EtOH (20 mL) containing DBU (0.1 mL), was heated under reflux for 20 min. The yellow crystals obtained during heating were filtered and crystallized from DMF, mp > 320 ºC, yield (0.59 g, 72%). IR (KBr, cm^{-1}): 3121 (CH_{furan}), 3052 ($CH_{arom.}$), 2952, 2928 ($CH_{aliph.}$), 2225 (C≡N), 1666 ($C=O_{\gamma\text{-pyrone}}$), 1621 (C=N), 1582 (C=C). ^{1}H NMR (DMSO-d_6, δ, 300 MHz): 3.83 (s, 3H, OCH_3), 3.95 (s,

3H, OCH_3), 7.11 (d, 1H, *J*=2.1 Hz, H-3_{furan}), 7.27-7.51 (m, 4H, Ph-H), 7.92 (d, 1H, *J*=2.1 Hz, H-2_{furan}), 8.43 (s, 1H, H-6).Mass spectrum (*m/z*, *I*%): 411 (M^+; 100), 383 (76), 353 (32), 242 (83), 205 (51), 118 (24), 77 (19), 64 (8). Anal. Calcd for $C_{23}H_{13}N_3O_5$ (411.37): C, 67.15; H, 3.19; N, 10.21%. Found: C, 66.86; H, 3.01; N, 9.88%.

REFERENCES

1. A. A. Abu-Hashem and M. El-Shazly, *Eur. J. Med. Chem.*, 2015, **90**, 633.
2. N. Khalil, M. Bishr, S. Desouky, and O. Salama, *Molecules*, 2020, **25**, 301; A. S. Bhagavathula, A. J. M. Al-Khatib, A. A. Elnour, N. M. Al Kalbani, and A. Shehab. *Pharm. Res.*, 2014, **7**, 397.
3. M. C. Nirumand, M. Hajialyani, R. Rahimi, M. H. Farzaei, S. Zingue, S. M. Nabavi, and A. Bishayee, *Int. J. Mol. Sci.*, 2018, **19**, 765.
4. I. F. Zaeid, A. M. Nasef, N. M. Fawzy, A. M. Soliman, and M. M. E-Baroudy, *Int. J. Pharm. Sci. Rev. Res.*, 2015, **30**, 306; K. M. Amin, Y. M. Syam, M. Anwar, H. I. Ali, T. M. Abdel-Ghani, and A. M. Serry, *Bioorg*. *Chem*., 2018, **76**, 487.
5. F. A. Ragab, N. A. El-Sayed, A. A. M. Eissa, and A. M. El Kerdawy, *Chem. Pharm. Bull.*, 2010, **58**, 1148.
6. M. Ghate and M. V. Kulkarni, *Indian. J. Chem.*, 2005, **44B**, 1674; M. S. Frasinyuk, S. V. Gorelov, S. P. Bondarenko, and V. P.Khilya, *Chem. Heterocycl. Compd.*, 2009, **45**, 1261.
7. S. V. Laxmi, Y. T. Reddy, B. S. Kuarm, P. N. Reddy, P. A. Crooks, and B. Rajitha, *Bioorg. Med. Chem. Lett.*, 2011, **21**, 4329.
8. H. Regaila, A. Gohar, and G. Abdel Sadek, *Egypt. J. Pharm. Sci.*, 1988, **29**, 343.
9. I. O. Akchurin, A. I. Yakhutina, A. Y. Bochkov, N. P. Solovjova, M. G. Medvedev, and V. F. Traven, *J. Mol. Struct.*, 2018, **1160**, 215; M. A. Ibrahim, S. Abdel Halim, N. Roushdy, A. A. M. Farag, and N. M. El-Gohary, *Opt. Mater*., 2017, **73**, 290.
10. N. Roushdy, A. A. M. Farag, M. A. Ibrahim, S. Abdel Halim, and N. M. El-Gohary, *Optik*, 2019, **178**, 1163; A. A. M. Farag, M. A. Ibrahim, S. Abdel Halim, N. Roushdy, and N. M. El-Gohary, *J. Mol. Struct.*, 2018, **1156**, 516; M. A. Ibrahim, S. Abdel Halim, N. Roushdy, A. A. M. Farag, and N. M. El-Gohary, *Optik*, 2018, **166**, 294; C. V. Maridevarmath, L. Naik, V. S. Negalurmath, M. Basanagouda, and G. H. Malimath, *Chem. Data Collect*., 2019, **21**, 100221; C. V. Maridevarmath, L. Naik, V. S. Negalurmath, M. Basanagouda, and G. H. Malimath, *J. Mol. Struct.*, 2019, **1188**, 142; D. Coskun, B. Gunduz, and M. F. Coskun, *J. Mol. Struct.*, 2019, **1178**, 261.
11. A. Badran, M. A. Ibrahim, and Y. A. Alnamer, *Tetrahedron*, 2018, **74**, 4119; M. A. Ibrahim, N. M. El-Gohary, and S. Said, Heterocycles, 2018, **96**, 690; M. A. Ibrahim, A. Badran, and S. H. Hashiem, *J. Heterocycl. Chem.*, 2018, **55**, 2844; M. A. Ibrahim and A. M. El-Kazak *J. Heterocycl. Chem.*,

2019, **56**, 1075.

12. F. Eiden and J. Schünemzinn, *Arch. Pharm.*, 1983, **316**, 201.
13. M. A. Ibrahim, *Synth. Commun*., 2009, **39**, 3527.
14. M. A. Ibrahim, N. M. El-Gohary, S. S. Ibrahim, and S. Said *Chem. Heterocycl. Compd*, 2015, **50**, 1624.
15. S. Abdel Halim and M. A. Ibrahim *J. Heterocycl. Chem.*, 2019, **56**, 2542.
16. J. C. Gould and J. M. Bowie, *Edinb. Med. J.*, 1952, **59**, 198; A. Singh, R. Latita, R. Dhakarey, and G. Saxena, *J. Indian Chem. Soc*., 1996, **73**, 339.