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REACTIVITY OF 4,9-DIMETHOXY-5-OXO-5*H*-FURO[3,2-*g*]-CHROMENE-6-CARBONITRILE TOWARDS SOME NITROGEN NUCLEOPHILIC REAGENTS

Magdy A. Ibrahim[a]* and Esam S. Allehyani[b]

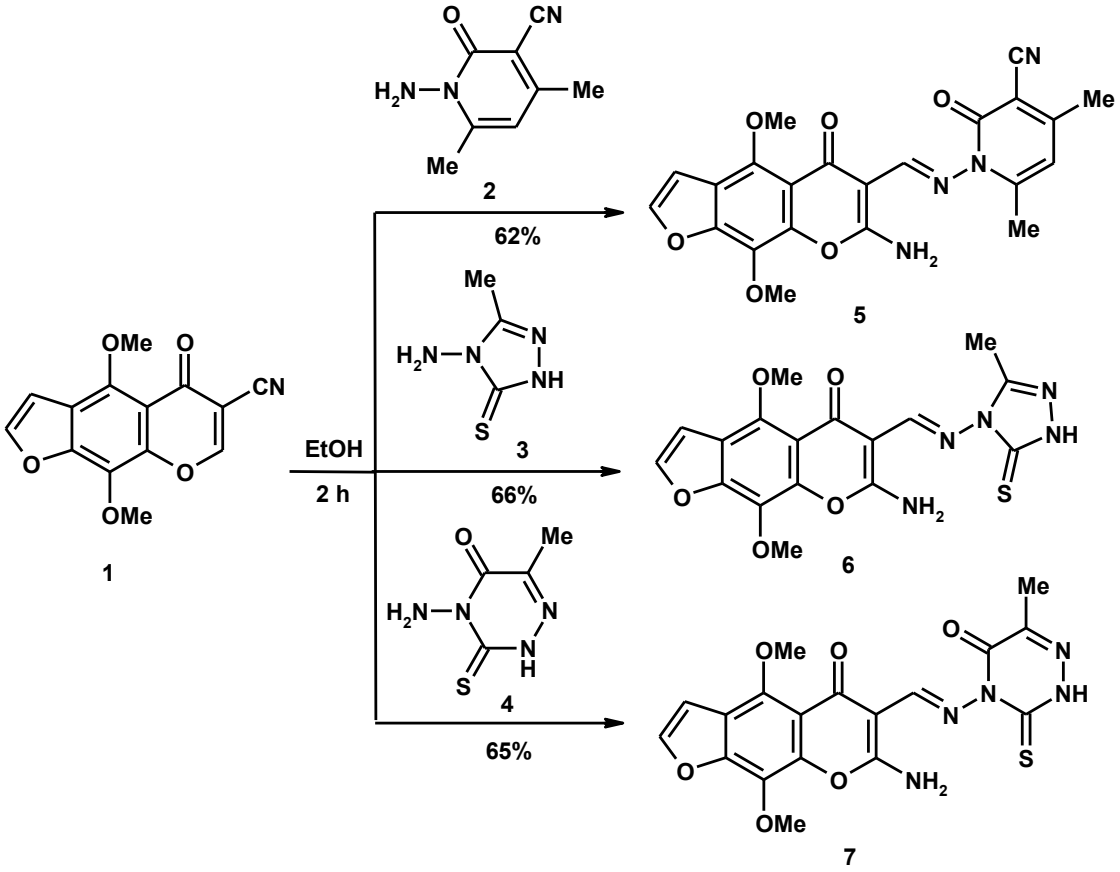
[a]Department of Chemistry, Faculty of Education, Ain Shams University, Cairo, Egypt
[b]Department of Chemistry, University College in Al-Jamoum, Umm Al-Qura University, Makkah, Saudi Arabia
*E-mail: magdy_ahmed1977@yahoo.com

Abstract – The chemical behavior of 4,9-dimethoxy-5-oxo-5*H*-furo[3,2-*g*]-chromene-6-carbonitrile (khellin-6-carbonitrile) (**1**) was examined towards a variety of nitrogen nucleophiles. Some novel Schiff bases **5-7** were prepared from reaction of carbonitrile **1** with some heterocyclic amines. Treatment of carbonitrile **1** with some hydrazine derivatives in boiling ethanol afforded pyrazole derivatives **8-13**. Khellin-6-carbonitrile (**1**) reacted with hydrazine hydrate and phenylhydrazine in acetic acid to afford angular heteroannulated furo[3`,2`:6,7]-chromeno[4,3-*c*]pyrazol-4(1*H*)-one derivatives **14** and **15**. Triazolo[1,5-*a*]pyrimidine **16** and pyrimido[1,2-*a*]benzimidazole **17** were synthesized through ring opening and recyclization reactions of compound **1** with 3-amino-1,2,4-triazole and 2-aminobenzimidazole, respectively. Reaction of compound **1** with guanidine and cyanoguanidine in ethanolic potassium hydroxide solution resulted in ring conversion giving the novel angular furo[3`,2`:6,7]chromeno[4,3-*d*]pyrimidin-5-ones **18** and **19**. The antimicrobial activity of the prepared compounds appeared distinguish activity against the selected microorganisms.

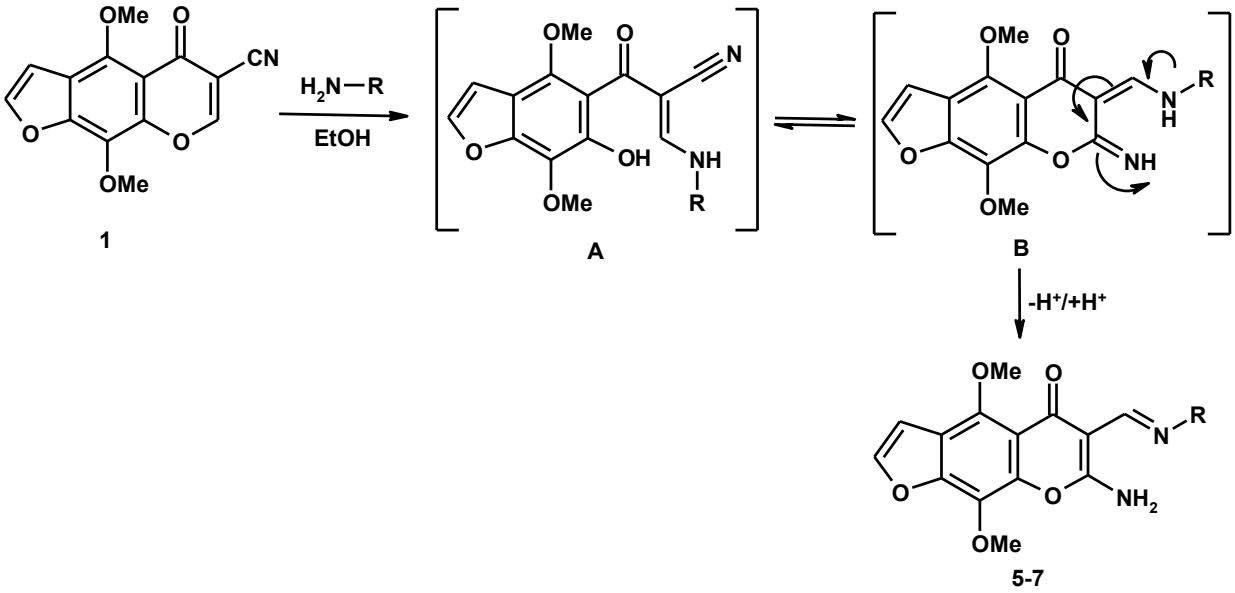
Khellin is a natural occurring furochromone and exists in the seeds of *Ammi visnaga* L.[1] Furochromones have attracted a great attention due to their various applications including analgesic,[2] anti-inflammatory,[3] anticonvulsant,[4] antitubercular,[5] anticancer,[6] and antimicrobial agents.[7] The optimized structures of some furo[3,2-*g*]chromenes were achieved by DFT-theoretical calculations.[8] There is a significant interest of

furo[3,2-*g*]chromene derivatives because of their variable properties including photosensitivity, photovoltaic, photoelectrical and photodiode applications.[9] Also, khellin showed high reactivity towards nucleophilic reactions due to the presence of electron deficient γ-pyrone ring system.[10] Basic hydrolysis of khellin using 10% potassium hydroxide solution afforded khellinone which upon Vielsmeier–Haack formylation gave 6-formylkhellin.[11] 4,9-Dimethoxy-5-oxo-5*H*-furo[3,2-*g*]chromene-6-carbonitrile (khellin-6-carbonitrile) (**1**)[12] represents an active substrate towards nucleophilic reagents due to the presence γ-pyrone ring which contain push-pull enone system as well as the cyano group.[13] The chemical transformations γ-pyrones having electron withdrawing cyano group at its 3 position were widely examined.[14] The present work is directed to examine the chemical reactivity of khellin-6-carbonitrile (**1**) towards a variety of nitrogen nucleophiles hoping to construct some novel furochromene and benzofuran derivatives and evaluate their antimicrobial activity.

Treatment of khellin-6-carbonitrile (**1**) with 1-amino-4,6-dimethyl-2-oxo-1,2-dihydropyridine-3-carbonitrile (**2**),[15] 4-amino-5-methyl-2,4-dihydro-3*H*-1,2,4-triazole-3-thione (**3**),[16] and 4-amino-6-methyl-3-thioxo-3,4-dihydro-1,2,4-triazin-5(2*H*)-one (**4**)[17] in boiling ethanol afforded the corresponding Schiff bases **5-7**, in which furo[3,2-*g*]chromene and nitrogen heterocyclic systems exist in one molecular frame (Scheme 1).[18] Formation of compounds **5-7** may proceed *via* nucleophilic attack at the more electron deficient center (C-7) with γ–pyrone ring opening (intermediate **A**) followed by nucleophilic addition of OH group onto the nitrile function with concomitant proton transfer to give the final products **5-7** as illustrated in Scheme 2. Characteristic singlet signals appeared in the ^{1}H NMR spectra of compounds **5-7** at δ 8.76, 8.94 and 8.99 ppm assignable to the azomethine protons. For compound **5** specific singlet attributed to H-4_{pyridine} appeared at δ 6.06 ppm, while the spectra of compounds **6** and **7** revealed upfield singlet at δ 2.08 and 2.18 ppm attributable to Me $_{\text{triazole}}$ and Me $_{\text{triazine}}$, respectively. The ^{13}C NMR spectra of compounds **5-7** showed downfield signal at δ 176.8, 177.1 and 176.6 ppm, corresponding to C=O of the γ-pyrone moiety. The mass spectra of compounds **5-7** recorded their parent ion peaks at *m/z* 434, 401 and 429, respectively. These parent peaks observed with low relative abundance (2, 4 and 3%) due to the weak nitrogen-nitrogen single bond which is rapidly cleaved producing 7-amino-4,9-dimethoxy-5-oxo-5*H*-furo[3,2-*g*]chromene-6-carbonitrile which appeared as the base peak in compounds **5-7**.[19]



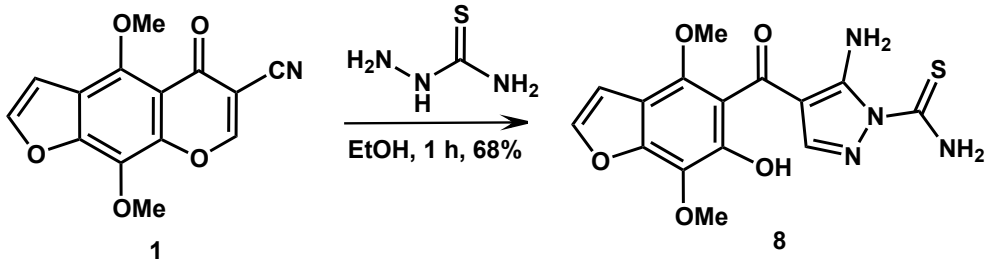
Scheme 1. Conversion of carbonitrile **1** into Schiff bases **5**-**7**



Scheme 2. The suggested mechanism for formation of Schiff bases **5**-**7**

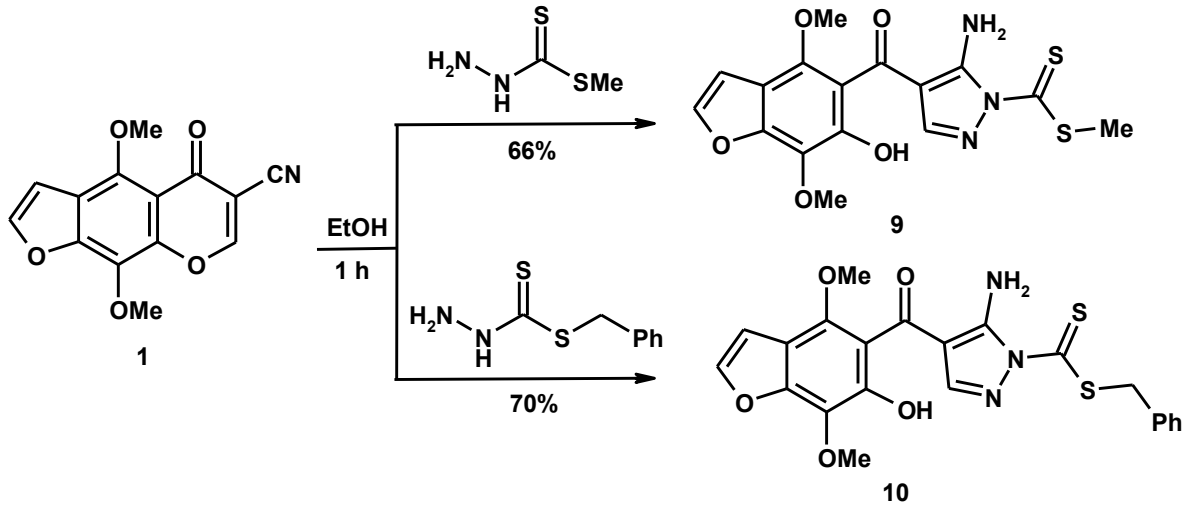
After that, treatment of khellin-6-carbonitrile (**1**) with thiosemicarbazide in boiling ethanol yielded pyrazole derivative **8** (Scheme 3).[20] Compound **8** presented dark red color with $FeCl_3$ solution; confirming the existence of free phenolic OH group. Characteristic absorption band observed in the IR

spectrum of compound **8** at $\tilde{\nu}$ 1636 cm^{-1}, attributable to $C{=}O_{benzoyl}$. Typical singlet assigned to $H\text{-}3_{pyrazole}$ detected in the ^1H NMR spectrum at δ 7.75 ppm, in addition to three D_2O-exchangeable signals at δ 7.65 (NH_2), 7.99 (NH_2) and 9.72 ppm (OH). The molecular ion peak recorded in the mass spectrum of compound **8** at *m/z* 362 that supports the suggested molecular weight (362.36).



Scheme 3. The suggested mechanism for formation of pyrazole derivative **8**

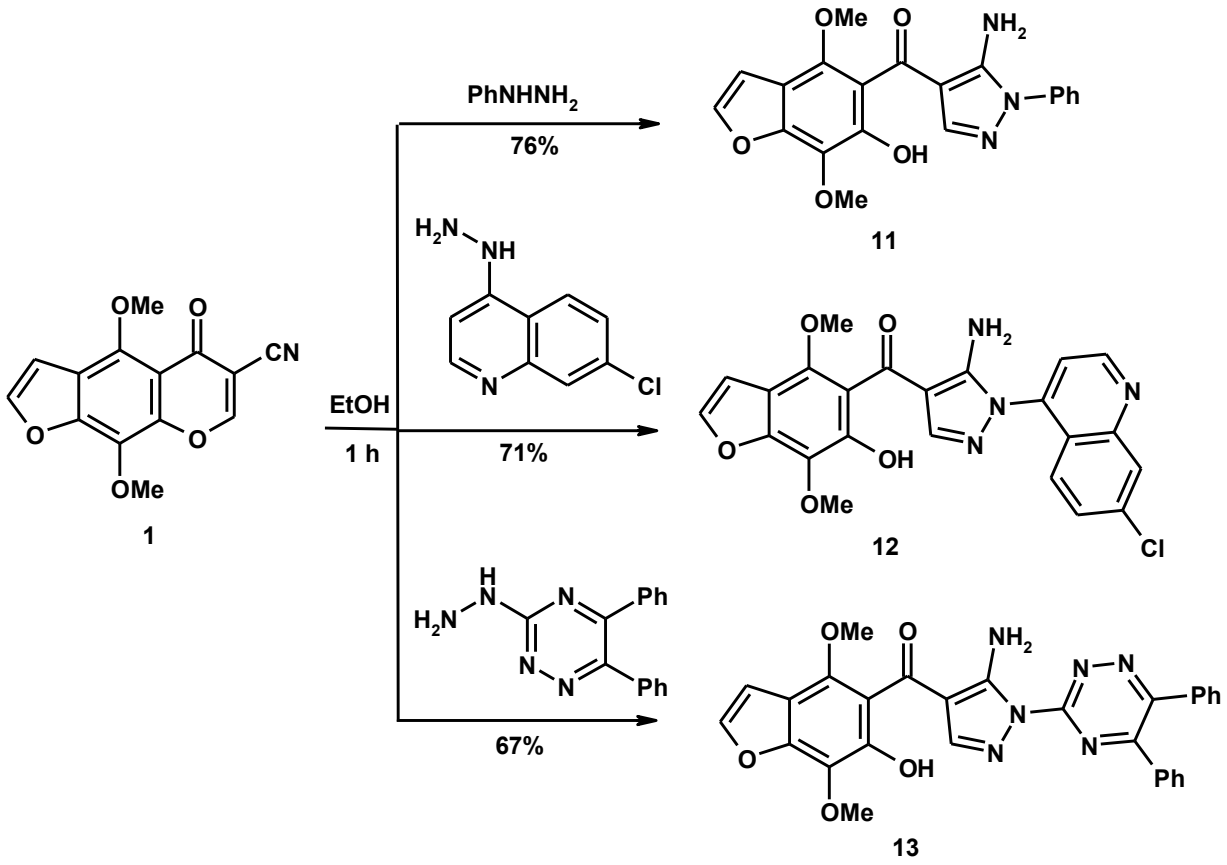
Similarly, pyrazole derivatives **9** and **10** were also obtained from boiling khellin-6-carbonitrile (**1**) with *S*-methyldithiocarbazate and *S*-benzyldithiocarbazate in ethanol (Scheme 4). Distinctive singlet attributed to $H\text{-}3_{pyrazole}$ appeared in the ^1H NMR spectra of compounds **9** and **10** at δ 7.78 and 7.72 ppm, respectively. The spectra also revealed D_2O exchangeable signal corresponding to the NH_2 protons at δ 8.87 and 8.94, respectively. Structures of compounds **9** and **10** were further confirmed from their mass spectra that recorded their parent ion peaks at *m/z* 393 and 469.



Scheme 4. Reaction of carbonitrile **1** with *S*-methyl/benzyldithiocarbazate

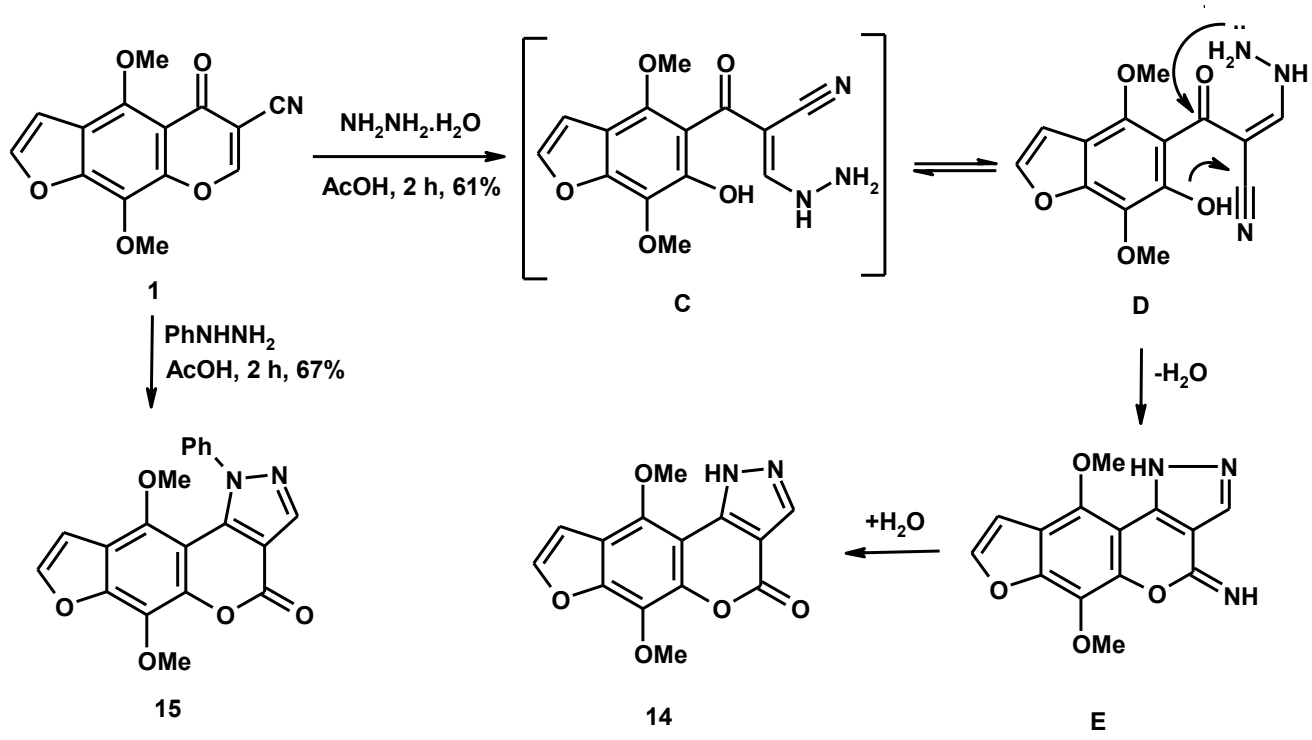
Also, phenylpyrazole **11**, quinolinylpyrazole **12** and triazinylpyrazole **13** were prepared from reacting khellin-6-carbonitrile (**1**) with phenylhydrazine, 7-chloro-4-hydrazinoquinoline[21] and 3-hydrazino-5,6-diphenyl-1,2,4-triazine[22] (Scheme 5). Compounds **11-13** gave red color with $FeCl_3$ solution. In the ^1H NMR spectra of compounds **11-13**, specific singlet attributed to $H\text{-}3_{pyrazole}$ appeared at δ 8.59, 8.56 and 8.63 ppm, respectively. In the IR spectra, characteristic absorption band attributable to

$C{=}O_{benzoyl}$ observed at $\tilde{\nu}$ 1634/1640//1637 cm^{-1}, respectively. The mass spectra of compounds **11-13** revealed their parent ion peaks at *m/z* 379, 464 and 534.



Scheme 5. Formation of phenyl/quinolinyl/triazinylpyrazole derivatives **11-13**

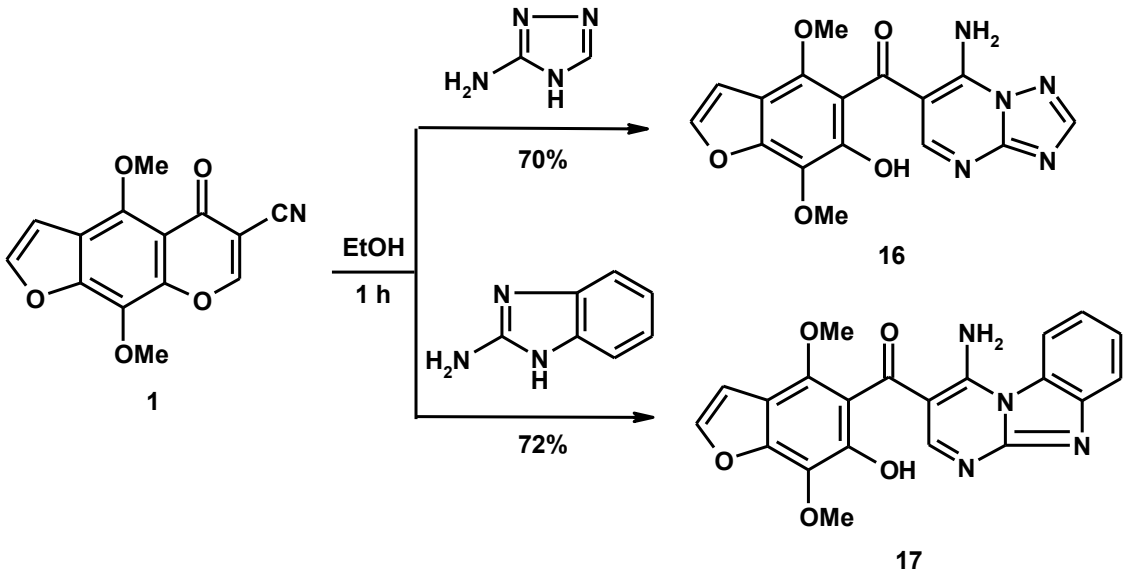
On the other hand, the chemical reactivity of khellin-6-carbonitrile (**1**) was studied towards hydrazine hydrate and phenylhydrazine in boiling acetic acid. Therefore, boiling compound **1** with hydrazine hydrate in acetic acid afforded 6,10-dimethoxyfuro[3`,2`:6,7]chromeno[4,3-*c*]pyrazol-4(1*H*)-one (**14**). The reaction occurs *via* nucleophilic attack at C-7 with γ-pyrone ring opening giving intermediate **C** which rotated around single bonds furnishing intermediate **D** which cyclized *via* cycloaddition and cyclocondensation yielding intermediate **E**. Hydrolysis of the latter intermediate under the reaction conditions afforded the final product **14** as depicted in Scheme 6. In the same manner, treating carbonitrile **1** with phenylhydrazine gave 6,10-dimethoxy-1-phenylfuro[3`,2`:6,7]chromeno[4,3-*c*]-pyrazol-4(1*H*)-one (**15**). The IR spectrum of compounds **14** and **15** showed typical absorption bands at $\tilde{\nu}$ 1708/1713 cm^{-1}, assigned to $C{=}O_{\alpha\text{-pyrone}}$. In the ^1H NMR spectra of compounds **14** and **15** typical singlet assignable to $H\text{-}3_{pyrazole}$ appeared at δ 8.40 and 8.47 ppm, in addition the spectrum of compound **14** revealed to D_2O-exchangeable signals at δ 14.36 attributed to NH proton. The molecular ion peaks were recorded in the mass spectra of compounds **14** and **15**, as the base peaks, at *m/z* 286 and 362 and confirm the suggested structures.



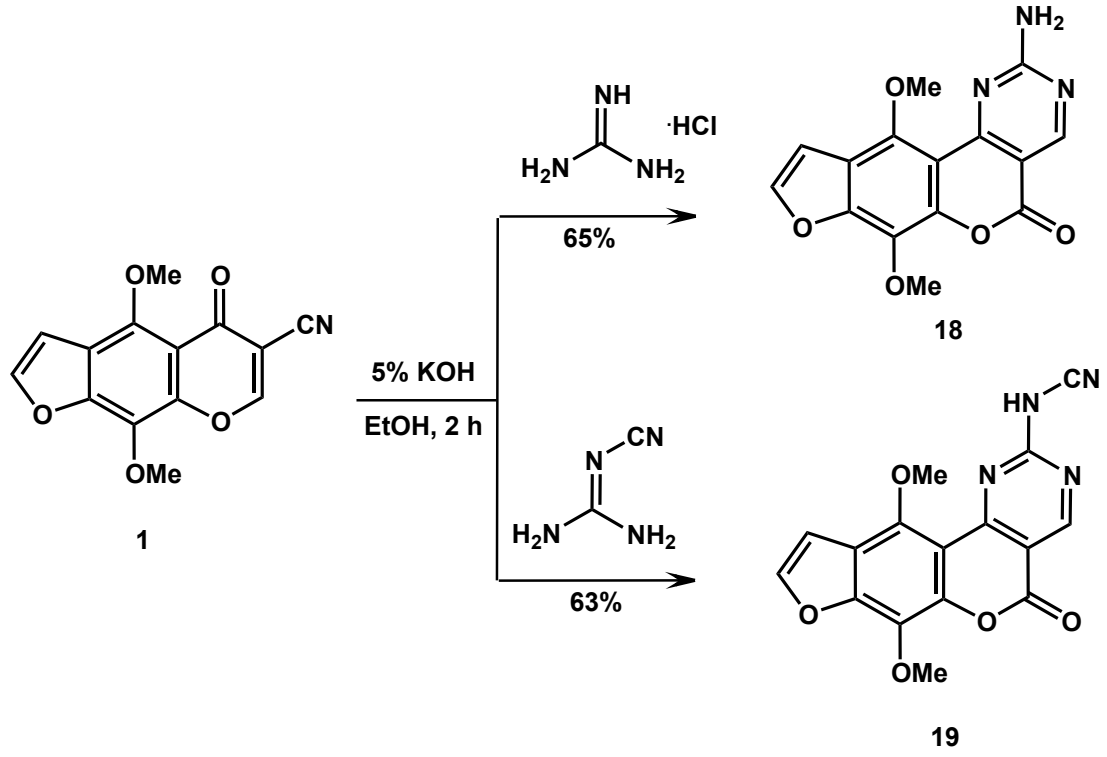
Scheme 6. Formation of furochromenopyrazoles **14** and **15**

Moreover, the reactivity of khellin-6-carbonitrile (**1**) was studied towards some 1,3-*N*,*N*-binucleophiles. Thus, boiling compound **1** with 3-amino-1,2,4-triazole and 2-aminobenzimidazole in absolute ethanol produced [1,2,4]triazolo[1,5-*a*]pyrimidine **16** and pyrimido[1,2-*a*]benzimidazole **17** linked 4,7-dimethoxy-6-hydroxy-1-benzofuran through a carbonyl group (Scheme 7).[23] The molecular ion peaks of compounds **16** and **17** were observed in their mass spectra at *m/z* 355 and 404 which approve the postulated formula weights $C_{16}H_{13}N_5O_5$ and $C_{21}H_{16}N_4O_5$, respectively. The ^{1}H NMR spectrum of compound **16** showed two specific singlet signals corresponding to H-5 and H-2 at δ 9.06 and 9.42 ppm, respectively, while specific singlet recorded in the ^{1}H NMR spectrum of compound **17** attributed to H-2 at δ 9.58 ppm.

After that, the conversion of khellin-6-carbonitrile (**1**) into furo[3`,2`:6,7]chromeno[4,3-*d*]-pyrimidin-5-ones **18** and **19**, was achieved through the ring opening ring closure (RORC) reactions of compound **1** with guanidine hydrochloride and cyanoguanidine in ethanolic potassium hydroxide solution (Scheme 8).[24] The $C{=}O_{\alpha\text{-pyrone}}$ observed in the IR spectra of compounds **18** and **19** at $\tilde{\nu}$ 1716 and 1702 cm^{-1}, respectively. The C≡N function appeared in the spectrum of compound **19** at 2206 cm^{-1}. The ^{1}H NMR spectra of compounds **18** and **19** presented characteristic singlet attributed to $H\text{-}4_{\text{pyrimidine}}$ at δ 8.97 and 8.92 ppm. The molecular ion peaks of compounds **18** and **19** were recorded in the mass spectrum at *m/z* 313 and 338, respectively.



Scheme 7. Formation of triazolo[1,5-*a*]pyrimidine **16** and pyrimido[1,2-*a*]benzimidazole **17**



Scheme 8. Formation of furochromenopyrimidines **18** and **19**

The antimicrobial activity of the new synthesized products was investigated against some selected microorganisms which are: Gram-positive bacteria [*Bacillus subtilis* (ATCC 6635) and *Staphylococcus aureus* (ATCC 25923)], Gram-negative bacteria [*Salmonella typhimurium* (ATCC 14028) and *Escherichia coli* (ATCC 25922)], yeast [*Candida albicans* (ATCC 10231)] and fungus strain [*Asperigillus fumigatus*]. The antimicrobial activities were determined using the standardized disc agar

diffusion method.[25] The inhibition zones, including the diameter of the disc (6 mm), was measure and listed in Table 1. The antimicrobial activity data presented in Table 1 was discussed as follows that:

[1] The measured compounds exhibited different inhibitory properties on the growing of the used microorganisms, and the inhibitory effects varies mostly between high and moderate activities.

[2] Compounds **6** and **7** recorded high activities against *Salmonella typhimurium* as Gram-negative bacteria*, Candida albicans* and *Asperigillus fumigatus* as the fungal strain and this may due to the combination of triazole and triazine rings with furo[3,2-g]chromene nucleus within the new molecules. Also, compounds **9** and **10** recorded high activities against *Escherichia coli*, *Candida albicans* and *Asperigillus fumigatus* microorganisms, and this may attributable to the existence of dithiolate function linked pyrazole nucleus with 4,7-dimethoxy-6-hydroxy-1-benzofuran moiety within the new molecules.

[3] Compounds **11**, **12** and **13** recorded high activities against both types of Gram-negative bacteria and this may due to the existence of pyrazole ring linked benzofuran moiety. Compound **13** also recorded high activity towards both types of Gram-positive bacteria as well as *Asperigillus fumigatus* and this may due to the existence of triazinylpyrazole linked benzofuran within the new molecules.

[4] Compounds **14** and **15** showed high activities against Gram-positive bacteria and may due to the fusion of pyrazole ring with furochromene moiety. While, compounds **16** and **17** recorded high activities against *Salmonella typhimurium* as Gram-negative bacteria

[5] Compounds **18** and **19** displayed high activities against all selected microorganisms and this may due to the fusion of pyrimidine moiety with furochromene moiety within the new molecules.

[6] The data depicted above presented that, some of the new products are of comparable activity with the reference drugs and may help as antimicrobial agents.

In conclusion, 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 nitrogen nucleophiles. A diversity of Schiff bases bearing 7-amino-4,9-dimethoxy-5-oxo-5*H*-furo[3,2-*g*]chromene moiety linked variable heterocyclic systems was efficiently synthesized from the reaction of compound **1** with certain heterocyclic amines. Some novel pyrazole derivatives linked 4,7-dimethoxy-6-hydroxy-1-benzofuran were synthesized from the reaction of compound **1** with hydrazine derivatives in boiling ethanol. Annulated furo[3`,2`:6,7]chromeno[4,3-*c*]-pyrazol-4(1*H*)-ones **14** and **15** were obtained from reaction of compound **1** with hydrazine hydrate and phenylhydrazine in boiling acetic acid. Ring opening ring and recyclization reactions of compound **1** with 3-amino-1,2,4-triazole and 2-aminobenzimidazole produced triazolo[1,5-*a*]pyrimidine **16** and pyrimido-[1,2-*a*]benzimidazole **17**, respectively. Chemical transformations of compound **1** with guanidine and cyanoguanidine resulted in ring conversion leading to furo[3`,2`:6,7]chromeno[4,3-*d*]pyrimidin-5-ones **18**

and **19**. The chemical transformations of 4,9-dimethoxy-5-oxo-5*H*-furo[3,2-*g*]chromene-6-carbonitrile (**1**) occur throughout a cascade process initiated by nucleophilic attack at C-7 with ring opening followed by different types of conversions depending on the nucleophile used and the reaction conditions

Table 1. *In vitro* antimicrobial evaluations of the prepared 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**			
	Staphylococus aureus		*Bacillus subtilis*		*Salmonella typhimurium*		*Escherichia coli*		*Candida albicans*		*Asperigillus fumigatus*	
	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	1000 μg/ml	500 μg/ml
5	16 I	12 I	17 I	13 I	15 I	10 I	19 I	12 I	19 I	14 I	17 I	10 I
6	21 I	17 I	18 I	12 I	**30 H**	**21 H**	20 I	14 I	**30 H**	**23 H**	**28 H**	**20 H**
7	22 I	16 I	20 I	15 I	**33 H**	**25 H**	23 I	16 I	**27 H**	**21 H**	**25 H**	**18 H**
8	17 I	11 I	19 I	12 I	20 I	13 I	18 I	12 I	22 I	16 I	19 I	14 I
9	19 I	13 I	17 I	10 I	19 I	13 I	**28 H**	**19 H**	**26 H**	**22 H**	**32 H**	**22 H**
10	15 I	10 I	13 I	9 I	16 I	11 I	**26 H**	**18 H**	**25 H**	**19 H**	**30 H**	**21 H**
11	16 I	12 I	18 I	12 I	**27 H**	**21 H**	**29 H**	**23 H**	16 I	12 I	16 I	12 I
12	17 I	10 I	14 I	9 I	**29 H**	**22 H**	**25 H**	**18 H**	15 I	10 I	18 I	13 I
13	**28 H**	**21 H**	**26 H**	**19 H**	**26 H**	**20 H**	**28 H**	**22 H**	17 I	11 I	**29 H**	**21 H**
14	**33 H**	**24 H**	**28 H**	**21 H**	19 I	14 I	18 I	12 I	20 I	12 I	18 I	13 I
15	**28 H**	**20 H**	**26 H**	**19 H**	21 I	15 I	16 I	10 I	14 I	10 I	20 I	15 I
16	18 I	13 I	19 I	14 I	**25 H**	**20 H**	16 I	11 I	21 I	16 I	17 I	12 I
17	15 I	10 I	21 I	15 I	**28 H**	**21 H**	15 I	11 I	17 I	13 I	19 I	15 I
18	**29 H**	**22 H**	**31 H**	**23 H**	**28 H**	**19 H**	**30 H**	**21 H**	**27 H**	**20 H**	**29 H**	**23 H**
19	**32 H**	**24 H**	**30 H**	**22 H**	**31 H**	**22 H**	**35 H**	**23 H**	**29 H**	**20 H**	**26 H**	**19H**
S	35	26	35	25	36	28	38	27	35	28	37	26

* Calculated from 3 values.

L = Low activity, I = Intermediate activity, H = High activity, S: Standard drug

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.

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 on 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 was 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 °C in the case of bacteria and for 48 h at 24 °C 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.[25]

1-{[(7-Amino-4,9-dimethoxy-5-oxo-5*H*-furo[3,2-*g*]chromen-6-yl)methylidene]amino}-4,6-dimethyl-2-oxo-1,2-dihydropyridine-3-carbonitrile (5). A mixture of compound **1** (0.54 g, 2 mmol) and 1-amino-4,6-dimethyl-2-oxo-1,2-dihydropyridine-3-carbonitrile (**2**) (0.33 g, 2 mmol) in absolute EtOH (20 mL) was heated under reflux for 2 h. The white crystals obtained during heating were filtered and crystallized from 2-PrOH, mp > 300 ºC, yield (0.54 g, 62%). IR (KBr, cm^{-1}): 3271, 3183 (NH_2), 3115 (CH_{furan}), 2951, 2917 ($CH_{aliph.}$), 2219 (C≡N), 1673 ($C{=}O_{pyridone}$), 1651 ($C{=}O_{\gamma\text{-}pyrone}$), 1610 (C=N), 1585 (C=C). ^{1}H NMR (DMSO, δ, 300 MHz): 2.27 (s, 3H, CH_3), 2.35 (s, 3H, CH_3), 3.84 (s, 3H, OCH_3), 3.91 (s, 3H, OCH_3), 6.06 (s, 1H, H-$4_{pyridine}$), 7.23 (d, 1H, *J*=2.1 Hz, H-3_{furan}), 7.92 (d, 1H, *J*=2.1 Hz, H-2_{furan}), 8.76 (s, 1H, CH=N), 9.52 (bs, 2H, NH_2 exchangeable with D_2O). ^{13}C NMR (DMSO-d_6, δ, 75 MHz): 19.3 (CH_3), 19.8 (CH_3), 58.5 (OCH_3), 59.6 (OCH_3), 87.4, 105.3, 109.2, 111.6, 113.2, 115.1, 116.2 (C≡N), 124.5, 133.6, 146.1, 147.4, 150.8, 152.6, 154.4, 155.2, 161.5, 167.9, 176.8. Mass spectrum (*m/z*, *I* %): 434 (M^+; 2), 287 (64), 286 (100), 258 (15), 228 (29), 216 (18), 191 (23), 177 (18), 147 (35), 118 (36), 102 (55), 77 (84), 65 (20). Anal. Calcd for $C_{22}H_{18}N_4O_6$ (434.40): C, 60.83; H, 4.18; N, 12.90%. Found: C, 60.52; H, 4.11; N, 12.85%.

7-Amino-4,9-dimethoxy-6-{([(3-methyl-5-thioxo-1,5-dihydro-4*H*-1,2,4-triazol-4-yl)imino]methyl}-5*H*-furo[3,2-g]chromen-5-one (6). A mixture of compound **1** (0.54 g, 2 mmol) and

4-amino-5-methyl-2,4-dihydro-3*H*-1,2,4-triazole-3-thione (**3**) (0.37 g, 2 mmol) in absolute EtOH (20 mL) was heated under reflux for 2 h. The pale yellow crystals deposited during heating were filtered and crystallized from MeOH, mp 258-259 ºC, yield (0.53 g, 66%). IR (KBr, cm^{-1}): 3342, 3219, 3178 (NH_2, NH), 3106 (CH_{furan}), 2956, 2922 ($CH_{aliph.}$), 1649 ($C=O_{\gamma\text{-pyrone}}$), 1612 (C=N), 1556 (C=C), 1236 (C=S). ^{1}H NMR (DMSO-d_6, δ, 300 MHz): 2.08 (s, 3H, CH_3), 3.92 (s, 3H, OCH_3), 3.99 (s, 3H, OCH_3), 7.12 (d, 1H, *J*=2.4 Hz, H-3_{furan}), 7.84 (d, 1H, *J*=2.4 Hz, H-2_{furan}), 8.94 (s, 1H, CH=N), 9.63 (bs, 2H, NH_2 exchangeable with D_2O), 11.96 (bs, 1H, NH exchangeable with D_2O). ^{13}C NMR (DMSO-d_6, δ, 75 MHz): 19.3 ($CH_{3\ triazole}$), 58.3 (OCH_3), 59.4 (OCH_3), 88.3, 105.2, 110.6, 111.9, 124.1, 145.8, 147.3, 150.4, 153.7, 154.6, 156.2, 167.4, 177.1, 184.3. Mass spectrum (*m/z*, *I* %): 401 (M^+; 4), 286 (100), 258 (36), 228 (30), 216 (41), 191 (26), 177 (14), 147 (9), 118 (12), 77 (30), 65 (26). Anal. Calcd for $C_{17}H_{15}N_5O_5S$ (401.39): C, 50.87; H, 3.77; N, 17.45; S, 7.99%. Found: C, 50.65; H, 3.49; N, 17.20; S, 7.87%.

4-{[(7-Amino-4,9-dimethoxy-5-oxo-5*H*-furo[3,2-*g*]chromen-6-yl)methylidene]amino}-6-methyl-3-thioxo-3,4-dihydro-1,2,4-triazin-5(2*H*)-one (7). A mixture of compound **1** (0.54 g, 2 mmol) and 4-amino-6-methyl-3-thioxo-3,4-dihydro-1,2,4-triazin-5(2*H*)-one (**4**) (0.32 g, 2 mmol) in absolute EtOH (20 mL) was heated under reflux for 2 h. The yellow crystals obtained during heating were filtered and crystallized from DMF/H_2O, mp 276-277 °C, yield (0.56 g, 65%). IR (KBr, cm^{-1}): 3426, 3277, 3158 (NH_2, NH), 1695 ($C=O_{triazine}$), 1656 ($C=O_{\gamma\text{-pyrone}}$), 1615 (C=N), 1562 (C=C), 1221 (C=S). ^{1}H NMR (DMSO-d_6, δ, 300 MHz): 2.18 (s, 3H, $CH_{3\ triazine}$), 3.89 (s, 3H, OCH_3), 3.96 (s, 3H, OCH_3), 7.11 (d, 1H, *J*=1.8 Hz, H-3_{furan}), 7.88 (d, 1H, *J*=1.8 Hz, H-2_{furan}), 8.99 (s, 1H, CH=N), 9.57 (bs, 2H, NH_2 exchangeable with D_2O), 13.51 (bs, 1H, $NH_{triazine}$ exchangeable with D_2O). ^{13}C NMR (DMSO-d_6, δ, 75 MHz): 17.5 ($CH_{3\ triazine}$), 58.6 (OCH_3), 59.9 (OCH_3), 87.9, 105.5, 110.7, 112.3, 124.1, 145.6, 147.3, 150.6, 152.8, 154.2, 155.4, 166.2, 168.1, 176.6, 185.2. Mass spectrum (*m/z*, *I* %): 429 (M^+; 3), 287 (71), 286 (100), 258 (42), 228 (24), 216 (14), 200 (15), 163 (32), 143 (11), 116 (22), 98 (9), 84 (54), 66 (19). Anal. Calcd for $C_{18}H_{15}N_5O_6S$ (429.41): C, 50.35; H, 3.52; N, 16.31; S, 7.47%. Found: C, 50.10; H, 3.31; N, 16.08; S, 7.22%.

5-Amino-4-[(4,7-dimethoxy-6-hydroxy-1-benzofuran-5-yl)carbonyl]-1*H*-pyrazole-1-carbothioamide (8). A mixture of compound **1** (0.54 g, 2 mmol) and thiosemicarbazide (0.18 g, 2 mmol) in absolute EtOH (20 mL) was heated under reflux for 1 h. The canary yellow crystals obtained during heating were filtered and crystallized from *n*-BuOH, mp 165-166 ºC, yield (0.49 g, 68%). IR (KBr, cm^{-1}): 3398, 3285, 3274, 3142 ($2NH_2$, OH), 3111 (CH_{furan}), 2962, 2931 ($CH_{aliph.}$), 1636 ($C=O_{benzoyl}$), 1579 (C=N), 1575 (C=C), 1236 (C=S). ^{1}H NMR (DMSO-d_6, δ, 300 MHz): 3.89 (s, 3H, OCH_3), 3.96 (s, 3H, OCH_3), 7.13 (d, 1H, *J*=1.8 Hz, H-3_{furan}), 7.65 (bs, 2H, NH_2 exchangeable with D_2O), 7.75 (s, 1H, H-$3_{pyrazole}$), 7.84 (d, 1H,

J=1.8 Hz, H-2_{furan}), 7.99 (bs, 2H, NH_2 exchangeable with D_2O), 9.72 (bs, 1H, OH exchangeable with D_2O). ^{13}C NMR (DMSO-d_6, δ, 75 MHz): 58.2 (OCH_3), 59.4 (OCH_3), 94.1, 102.1, 105.4, 110.9, 123.7, 132.4, 144.8, 146.7, 150.6, 152.2, 154.5, 182.1, 191.9. Mass spectrum (*m/z*, *I* %): 362 (M^+; 28), 302 (14), 287 (19), 220 (100), 205 (31), 191 (12), 163 (42), 147 (8), 102 (10), 77 (26), 66 (47). Anal. Calcd for $C_{15}H_{14}N_4O_5S$ (362.36): C, 49.72; H, 3.89; N, 15.46; S, 8.85%. Found: C, 49.55; H, 3.46; N, 15.11; S, 8.56%.

Methyl 5-amino-4-[(4,7-dimethoxy-6-hydroxy-1-benzofuran-5-yl)carbonyl]-1*H*-pyrazole-1-carbodithioate (9). A mixture of compound **1** (0.54 g, 2 mmol) and *S*-methyldithiocarbazate (0.24 g, 2 mmol) in absolute EtOH (20 mL) was heated under reflux for 1 h. The pale yellow crystals obtained after cooling were filtered and crystallized from MeOH, mp 212-213 ºC, yield (0.52 g, 66%). IR (KBr, cm^{-1}): 3387, 3295, 3175 (NH_2, OH), 2962, 2930 ($CH_{aliph.}$), 1634 ($C{=}O_{benzoyl}$), 1599 (C=N), 1554 (C=C), 1236 (C=S). ^1H NMR (DMSO-d_6, δ, 300 MHz): 2.63 (s, 3H, CH_3), 3.95 (s, 3H, OCH_3), 4.06 (s, 3H, OCH_3), 7.17 (d, 1H, *J*=1.8 Hz, H-3_{furan}), 7.78 (s, 1H, H-$3_{pyrazole}$), 7.93 (d, 1H, *J*=1.8 Hz, H-2_{furan}), 8.87 (bs, 2H, NH_2 exchangeable with D_2O), 10.79 (bs, 1H, OH exchangeable with D_2O). ^{13}C NMR (DMSO-d_6, δ, 75 MHz): 21.8 (CH_3), 58.5 (OCH_3), 59.6 (OCH_3), 93.7, 101.8, 105.2, 111.2, 124.1, 133.2, 144.4, 147.0, 151.3, 153.0, 154.4, 188.2, 192.6. Mass spectrum (*m/z*, *I* %): 393 (M^+; 37), 378 (8), 348 (17), 316 (12), 272 (49), 220 (34), 205 (100), 177 (23), 163 (9), 147 (34), 118 (6), 102 (11), 77 (20), 66 (37). Anal. Calcd for $C_{16}H_{15}N_3O_5S_2$ (393.44): C, 48.84; H, 3.84; N, 10.68; S, 16.30%. Found: C, 48.55; H, 3.60; N, 10.45; S, 16.13%.

Benzyl 5-amino-4-[(4,7-dimethoxy-6-hydroxy-1-benzofuran-5-yl)carbonyl]-1*H*-pyrazole-1-carbodithioate (10). A mixture of compound **1** (0.54 g, 2 mmol) and *S*-benzyldithiocarbazate (0.40 g, 2 mmol) in absolute EtOH (20 mL) was heated under reflux for 1 h. The white crystals obtained during heating were filtered and crystallized from EtOH, mp 198-199 ºC, yield (0.66 g, 70%). IR (KBr, cm^{-1}): 3415 (OH), 3341, 3274 (NH_2), 3102 (CH_{furan}), 3035 ($CH_{arom.}$), 2972, 2945 ($CH_{aliph.}$), 1631 ($C{=}O_{benzoyl}$), 1617 (C=N), 1584 (C=C), 1238 (C=S). ^1H NMR (DMSO-d_6, δ, 300 MHz): 3.91 (s, 3H, OCH_3), 4.03 (s, 3H, OCH_3), 4.43 (s, 2H, CH_2), 7.15 (d, 1H, *J*=1.8 Hz, H-3_{furan}), 7.28-7.43 (m, 5H, Ph-H), 7.72 (s, 1H, H-$3_{pyrazole}$), 7.96 (d, 1H, *J*=1.8 Hz, H-2_{furan}), 8.94 (bs, 2H, NH_2 exchangeable with D_2O), 10.36 (bs, 1H, OH exchangeable with D_2O). ^{13}C NMR (DMSO-d_6, δ, 75 MHz): 44.8 (CH_2), 58.1 (OCH_3), 59.0 (OCH_3), 93.8, 102.3, 105.8, 110.9, 123.8, 126.5, 128.7, 129.3, 132.7, 136.1, 145.2, 147.4, 150.8, 152.4, 155.1, 187.5, 193.1. Mass spectrum (*m/z*, *I* %): 469 (M^+; 40), 346 (12), 302 (16), 220 (51), 205 (100), 191 (45), 177 (17), 163 (9), 147 (8), 118 (11), 91 (100), 77 (16), 65 (12). Anal. Calcd for $C_{22}H_{19}N_3O_5S_2$ (469.53): C, 56.28; H, 4.08; N, 8.95; S, 13.66%. Found: C, 56.08; H, 4.00; N, 8.64; S, 13.41%.

5-(5-Amino-1-phenyl-1*H*-pyrazol-4-ylcarbonyl)-4,7-dimethoxy-6-hydroxy-1-benzofuran (11). A mixture of compound **1** (0.54 g, 2 mmol) and phenylhydrazine (0.22 g, 2 mmol) in absolute EtOH (20 mL) was heated under reflux for 1 h. The yellow crystals so formed after cooling were filtered and crystallized from MeOH, mp 265-266 ºC, yield (0.61 g, 76%). IR (KBr, cm^{-1}): 3431 (OH), 3374, 3249 (NH_2), 3121 (CH_{furan}), 3052 ($CH_{arom.}$), 2955, 2926 ($CH_{aliph.}$), 1634 ($C{=}O_{benzoyl}$), 1609 (C=N), 1572 (C=C). ^{1}H NMR (DMSO-d_6, δ, 300 MHz): 3.87 (s, 3H, OCH_3), 3.96 (s, 3H, OCH_3), 7.21 (d, 1H, *J*=2.1 Hz, H-3_{furan}), 7.36-7.54 (m, 5H, Ph-H), 7.91 (d, 1H, *J* = 2.1 Hz, H-2_{furan}), 8.59 (s, 1H, H-$3_{pyrazole}$), 9.85 (bs, 2H, NH_2 exchangeable with D_2O), 10.73 (bs, 1H, OH exchangeable with D_2O). ^{13}C NMR (DMSO-d_6, δ, 75 MHz): 58.8 (OCH_3), 59.8 (OCH_3), 94.3, 101.9, 105.3, 111.4, 122.8, 124.4, 126.8, 128.7, 138.3, 139.6, 145.4, 146.9, 150.3, 152.7, 154.1, 191.6. Mass spectrum (*m/z*, *I* %): 379 (M^+; 51), 364 (20), 349 (16), 312 (29), 220 (100), 205 (28), 191 (15), 177 (27), 162 (18), 135 (32), 118 (26), 77 (67), 66 (18). Anal. Calcd for $C_{20}H_{17}N_3O_5$ (379.37): C, 63.32; H, 4.52; N, 11.08%. Found: C, 63.13; H, 4.34; N, 10.85%.

5-[5-Amino-1-(7-chloroquinolin-4-yl)-1*H*-pyrazol-4-ylcarbonyl]-4,7-dimethoxy-6-hydroxy-1-benzofuran (12). A mixture of compound **1** (0.54 g, 2 mmol) and 7-chloro-4-hydrazinoquinoline (0.39 g, 2 mmol) in absolute EtOH (20 mL) was heated under reflux for 1 h. The orange crystals so formed during heating were filtered and crystallized from DMF/EtOH, mp 290-291 ºC, yield (0.66 g, 71%). IR (KBr, cm^{-1}): 3424, 3356 (NH_2, OH), 3113 (CH_{furan}), 3041 ($CH_{arom.}$), 2946, 2917 ($CH_{aliph.}$), 1640 ($C{=}O_{benzoyl}$), 1612 (C=N), 1574 (C=C). ^{1}H NMR (DMSO-d_6, δ, 300 MHz): 3.90 (s, 3H, OCH_3), 3.99 (s, 3H, OCH_3), 7.10 (d, 1H, *J*=2.1 Hz, H-3_{furan}), 7.34-7.41 (m, 2H, Ar-H), 7.81 (s, 1H, H-$8_{quinoline}$), 7.95 (d, 1H, *J*=2.1 Hz, H-2_{furan}), 8.56 (s, 1H, H-$3_{pyrazole}$), 8.73 (d, 1H, *J*=8.1 Hz, H-$3_{quinoline}$), 9.09 (d, 1H, *J*=8.1 Hz, H-$2_{quinoline}$), 9.42 (bs, 2H, NH_2 exchangeable with D_2O), 11.26 (bs, 1H, OH exchangeable with D_2O). ^{13}C NMR (DMSO-d_6, δ, 75 MHz): 58.6 (OCH_3), 59.5 (OCH_3), 95.1, 101.7, 105.7, 110.4, 113.5, 115.1, 123.5, 127.6, 129.2, 133.1, 135.4, 142.8, 145.0, 147.6, 148.2, 151.3, 152.6, 155.1, 158.3, 163.5, 192.6. Mass spectrum (*m/z*, *I* %): 464 (M^+; 26), 303 (16), 273 (52), 220 (100), 205 (62), 177 (15) 163 (42), 135 (22), 119 (12), 103 (16), 77 (33), 65 (15). Anal. Calcd for $C_{23}H_{17}ClN_4O_5$ (464.86): C, 59.43; H, 3.69; N, 12.05%. Found: C, 59.32; H, 3.35; N, 11.75%.

5-[5-Amino-1-(5,6-diphenyl-1,2,4-triazin-4-yl)-1*H*-pyrazol-4-ylcarbonyl]-4,7-dimethoxy-6-hydroxy-1-benzofuran (13). A mixture of compound **1** (0.54 g, 2 mmol) and 3-hydrazino-5,6-diphenyl-1,2,4-triazine (0.53 g, 2 mmol) in absolute EtOH (20 mL) was heated under reflux for 1 h. The yellow crystals so precipitated during heating were filtered and crystallized from DMF/MeOH to give compound **12**, mp > 300 ºC, yield (0.72 g, 67%). IR (KBr, cm^{-1}): 3412 (OH), 3326, 3296 (NH_2), 3118 (CH_{furan}), 3061 ($CH_{arom.}$), 2970, 2933 ($CH_{aliph.}$), 1637 ($C{=}O_{benzoyl}$), 1603 (C=N), 1586 (C=C). ^{1}H NMR (DMSO-d_6, δ,

300 MHz): 3.93 (s, 3H, OCH_3), 4.04 (s, 3H, OCH_3), 7.16 (d, 1H, *J*=1.8 Hz, H-3_{furan}), 7.34-7.65 (m, 12H, Ar-H), 7.87 (d, 1H, *J*=2.1 Hz, H-2_{furan}), 8.63 (s, 1H, H-$3_{pyrazole}$), 9.41 (bs, 1H, NH exchangeable with D_2O), 9.76 (bs, 1H, NH exchangeable with D_2O), 11.47 (bs, 1H, OH exchangeable with D_2O). Mass spectrum (*m/z*, *I* %): 534 (M^+; 39), 447 (8), 383 (15), 313 (39), 248 (7), 220 (100), 205 (76), 178 (44), 152 (18), 120 (30), 103 (19), 77 (22), 64 (81). Anal. Calcd for $C_{29}H_{22}N_6O_5$ (534.52): C, 65.16; H, 4.15; N, 15.72%. Found: C, 64.96; H, 3.89; N, 15.48%.

6,10-Dimethoxyfuro[3`,2`:6,7]chromeno[4,3-*c*]pyrazol-4(1*H*)-one (14). A mixture of compound **1** (0.54 g, 2 mmol) and hydrazine hydrate (0.10 g, 2 mmol) in AcOH (10 mL) was heated under reflux for 2 h. After cooling, the reaction mixture was poured onto crushed ice (~ 20 g). The solid so formed was filtered and crystallized from AcOH/H_2O to give compound **14** as white crystals, mp 201-202 °C, yield (0.35 g, 61%). IR (KBr, cm^{-1}): 3184 (NH), 3121 (CH_{furan}), 2958, 2921 ($CH_{aliph.}$), 1708 ($C{=}O_{\alpha\text{-pyrone}}$), 1624 (C=N), 1567 (C=C). ^{1}H NMR (DMSO-d_6, δ, 300 MHz): 3.93 (s, 3H, OCH_3), 4.02 (s, 3H, OCH_3), 7.22 (d, 1H, *J*=2.1 Hz, H-3_{furan}), 7.97 (d, 1H, *J*=2.1 Hz, H-2_{furan}), 8.40 (s, 1H, H-$3_{pyrazole}$), 14.36 (bs, 1H, NH exchangeable with D_2O). ^{13}C NMR (DMSO-d_6, δ, 75 MHz): 59.1 (OCH_3), 60.4 (OCH_3), 102.4, 106.2, 109.8, 114.6, 127.9, 141.8, 145.3, 146.9, 148.0, 150.6, 155.4, 158.3. Mass spectrum (*m/z*, *I* %): 286 (M^+; 100), 256 (63), 221 (72), 205 (36), 191 (10), 177 (13), 163 (9), 147 (11), 134 (9), 119 (22), 77 (39), 66 (12). Anal. Calcd for $C_{14}H_{10}N_2O_5$ (286.24): C, 58.74; H, 3.52; N, 9.79%. Found: C, 58.55; H, 3.30; N, 9.51%.

6,10-Dimethoxy-1-phenyl-furo[3`,2`:6,7]chromeno[4,3-*c*]pyrazol-4(1*H*)-one (15). A mixture of compound **1** (0.54 g, 2 mmol) and phenylhydrazine (0.22 g, 2 mmol) in AcOH (10 mL) was heated under reflux for 2 h. The while crystals deposited after cooling were filtered and crystallized from AcOH/H_2O, mp 233-234 °C, yield (0.48 g, 67%). IR (KBr, cm^{-1}): 3115 (CH_{furan}), 3041 ($CH_{arom.}$), 2971, 2942 ($CH_{aliph.}$), 1713 ($C{=}O_{\alpha\text{-pyrone}}$), 1618 (C=N), 1586 (C=C). ^{1}H NMR (DMSO-d_6, δ, 300 MHz): 3.87 (s, 3H, OCH_3), 3.94 (s, 3H, OCH_3), 7.18 (d, 1H, *J*=1.8 Hz, H-3_{furan}), 7.51-7.69 (m, 5H, Ph-H), 7.92 (d, 1H, *J*=1.8 Hz, H-2_{furan}), 8.47 (s, 1H, H-$3_{pyrazole}$). ^{13}C NMR (DMSO-d_6, δ, 75 MHz): 58.6 (OCH_3), 59.7 (OCH_3), 105.7, 110.2, 113.6, 115.1, 120.6, 126.3, 128.6, 129.7, 138.1, 140.1, 143.6, 145.7, 146.8, 147.6, 155.3, 158.8. Mass spectrum (*m/z*, *I* %): 362 (M^+; 100), 285 (46), 255 (18), 231 (26), 186 (20), 163 (52) 147 (32), 119 (13), 77 (71), 65 (24). Anal. Calcd for $C_{20}H_{14}N_2O_5$ (362.34): C, 66.30; H, 3.89; N, 7.73%. Found: C, 66.12; H, 3.53; N, 7.46%.

5-(7-Amino[1,2,4]triazolo[1,5-*a*]pyrimidin-6-ylcarbonyl)-4,7-dimethoxy-6-hydroxy-1-benzofuran (16). A mixture of carbonitrile **1** (0.54 g, 2 mmol) and 3-amino-1,2,4-triazole (0.17 g, 2 mmol) in absolute

EtOH (20 mL) was heated under reflux for 1 h. The pale yellow crystals obtained after cooling were filtered and crystallized from toluene, mp 280-281 ºC, yield (0.50 g, 70%). IR (KBr, cm^{-1}): 3412 (OH), 3306, 3248 (NH_2), 2947, 2910 ($CH_{aliph.}$), 1642 ($C{=}O_{benzoyl}$), 1619 (C=N), 1568 (C=C). ^{1}H NMR (DMSO-d_6, δ, 300 MHz): 3.89 (s, 3H, OCH_3), 3.98 (s, 3H, OCH_3), 7.25 (d, 1H, *J*=2.4 Hz, H-3_{furan}), 7.92 (d, 1H, *J*=2.4 Hz, H-2_{furan}), 9.06 (s, 1H, H-5), 9.42 (s, 1H, H-2), 10.76 (bs, 2H, NH_2 exchangeable with D_2O), 13.48 (bs, 1H, OH exchangeable with D_2O). ^{13}C NMR (DMSO-d_6, δ, 75 MHz): 58.2 (OCH_3), 59.3 (OCH_3), 100.2, 105.7, 109.5, 113.7, 122.8, 144.8, 146.8, 149.4, 152.6, 154.1, 154.8, 156.3, 159.6, 193.2. Mass spectrum (*m/z*, *I* %): 355 (M^+; 67), 340 (14), 325 (8), 310 (10), 220 (37), 205 (100), 191 (17), 177 (36), 163 (15), 133 (11), 119 (27), 84 (56), 77 (39), 66 (24). Anal. Calcd for $C_{16}H_{13}N_5O_5$ (355.30): C, 54.09; H, 3.69; N, 19.71%. Found: C, 53.80; H, 3.52; N, 19.47%.

5-(4-Aminopyrimido[1,2-*a*]benzimidazol-3-ylcarbonyl)-4,7-dimethoxy-6-hydroxy-1-benzofuran (17). A mixture of compound **1** (0.54 g, 2 mmol) and 2-aminobenzimidazole (0.26 g, 2 mmol) in absolute EtOH (20 mL) was heated under reflux for 1 h. The yellow crystals obtained during heating were filtered off and crystallized from DMF/EtOH, mp > 300 ºC, yield (0.58 g, 72%). IR (KBr, cm^{-1}): 3425 (OH), 3343, 3216 (NH_2), 1637 ($C{=}O_{benzoyl}$), 1623 (C=N), 1585 (C=C). ^{1}H NMR (DMSO-d_6, δ, 300 MHz): 3.93 (s, 3H, OCH_3), 4.07 (s, 3H, OCH_3), 7.13 (d, 1H, *J*=2.1 Hz, H-3_{furan}), 7.45-7.58 (m, 4H, Ar-H), 7.89 (d, 1H, *J*=2.1 Hz, H-2_{furan}), 9.58 (s, 1H, H-2), 10.69 (bs, 2H, NH_2 exchangeable with D_2O), 12.84 (bs, 1H, OH exchangeable with D_2O). Mass spectrum (*m/z*, *I* %): 404 (M^+; 29), 389 (14), 328 (22), 220 (100), 205 (65), 191 (7), 177 (42), 163 (21), 147 (14), 102 (40), 77 (72), 65 (33). Anal. Calcd for $C_{21}H_{16}N_4O_5$ (404.38): C, 62.37; H, 3.99; N, 13.86%. Found: C, 62.05; H, 3.70; N, 13.57%.

2-Amino-7,11-dimethoxy-5*H*-furo[3`,2`:6,7]chromeno[4,3-*d*]pyrimidin-5-one (18). To a solution of compound **1** (0.54 g, 2 mmol) in absolute EtOH (15 mL), guanidine hydrochloride (0.20 g, 2 mmol) in aqueous potassium hydroxide solution (5%, 10 mL) was added. The reaction mixture was heated under reflux for 2 h. After cooling, the reaction mixture was poured onto crushed ice (~ 20 g) and neutralized with conc. HCl. The white precipitate so formed was filtered and crystallized from AcOH to give compound **18**, mp > 300 ºC, yield (0.41 g, 65%). IR (KBr, cm^{-1}): 3387, 3379 (NH_2), 3107 (CH_{furan}), 2926, 2893 ($CH_{aliph.}$), 1716 ($C{=}O_{\alpha\text{-pyrone}}$), 1627 (C=N), 1601 (C=C). ^{1}H NMR (DMSO-d_6, δ, 300 MHz): 3.92 (s, 3H, OCH_3), 4.03 (s, 3H, OCH_3), 7.13 (d, 1H, *J*=1.8 Hz, H-3_{furan}), 7.84 (d, 1H, *J*=1.8 Hz, H-2_{furan}), 8.34 (bs, 2H, NH_2 exchangeable with D_2O), 8.97 (s, 1H, H-$4_{pyrimidine}$). ^{13}C NMR (DMSO-d_6, δ, 75 MHz): 58.9 (OCH_3), 59.7 (OCH_3), 105.3, 109.5, 112.8, 114.9, 127.3, 144.5, 146.1, 147.9, 153.6, 156.4, 157.7, 164.2, 167.6. Mass spectrum (*m/z*, *I* %): 313 (M^+; 100), 298 (25), 258 (42), 232 (15), 220 (27), 205 (38), 191 (13), 163 (8), 147 (24), 77 (16), 66 (43). Anal. Calcd for $C_{15}H_{11}N_3O_5$ (313.26): C, 57.51; H, 3.54; N, 13.41%. Found: C, 57.42; H, 3.30; N, 13.19%.

(7,11-Dimethoxy-5-oxo-5*H*-furo[3`,2`:6,7]chromeno[4,3-*d*]pyrimidin-2-yl)cyanamide (19). To a solution of compound **1** (0.54 g, 2 mmol) in absolute EtOH (15 mL), cyanoguanidine (0.18 g, 2 mmol) in aqueous potassium hydroxide solution (5%, 10 mL) was added. The reaction mixture was heated under reflux for 2 h. After cooling, the reaction mixture was poured onto crushed ice (~ 20 g) and neutralized with conc. HCl. The white precipitate so formed was filtered and crystallized from *n*-BuOH to give compound **19** as white crystals, mp > 300 ºC, yield (0.43 g, 63%). IR (KBr, cm^{-1}): 3367 (NH), 3114 (CH_{furan}), 2954, 2932 ($CH_{aliph.}$), 2206 (C≡N), 1702 ($C=O_{\alpha\text{-pyrone}}$), 1620 (C=N), 1597 (C=C). ^{1}H NMR (DMSO-d_6, δ, 300 MHz): 3.95 (s, 3H, OCH_3), 4.09 (s, 3H, OCH_3), 7.09 (d, 1H, *J*=2.1 Hz, H-3_{furan}), 7.91 (d, 1H, *J*=2.1 Hz, H-2_{furan}), 8.92 (s, 1H, H-$4_{pyrimidine}$), 10.42 (bs, H, NH exchangeable with D_2O). ^{13}C NMR (DMSO-d_6, δ, 75 MHz): 58.7 (OCH_3), 59.4 (OCH_3), 106.1, 110.3, 113.0, 115.2, 116.9 (C≡N), 125.2, 144.3, 145.9, 147.2, 153.4, 156.1, 158.7, 163.8, 166.3. Mass spectrum (*m/z*, *I* %): 338 (M^+; 100), 312 (22), 297 (10), 282 (51), 220 (36), 205 (19), 191 (26), 163 (14), 134 (23), 118 (39), 102 (42), 77 (28), 65 (13). Anal. Calcd for $C_{16}H_{10}N_4O_5$ (338.27): C, 56.81; H, 2.98; N, 16.56%. Found: C, 56.60; H, 2.72; N, 16.41%.

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