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CONSTRUCTION AND BIOLOGICAL EVALUATIONS OF SOME NOVEL CHROMENO[2,3-*b*]PYRIDINES AND CHROMENO[2,3-*b*]-QUINOLINES USING 6-METHYLCHROMONE-3-CARBONITRILE

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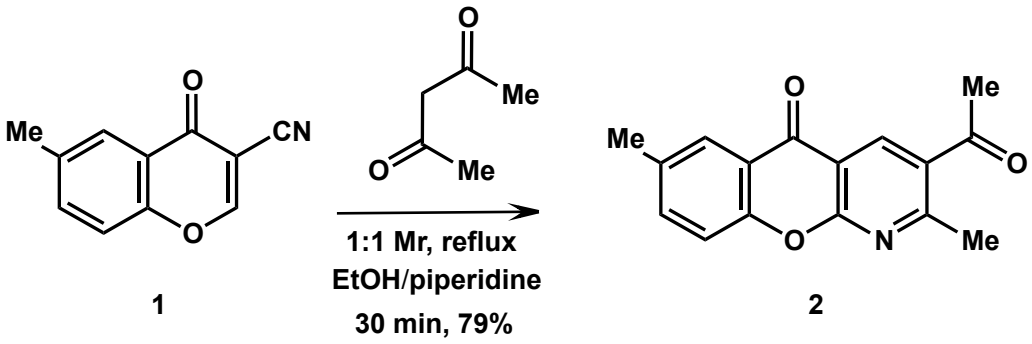
Abstract – Reaction of 6-methylchromone-3-carbonitrile (**1**) with acetylacetone under basic conditions afforded 3-acetyl-2,7-dimethyl-5*H*-chromeno[2,3-*b*]-pyridin-5-one (**2**) which utilized as a starting substrate. Condensation of compound **2** with a variety of amines and hydrazines produced chromeno[2,3-*b*]-pyridines linked variable compounds in the same molecular frame. Condensation reaction of compound **2** with variable carbon nucleophilic reagents namely; malononitrile, ethyl cyanoacetate, malononitrile dimer, 1*H*-benzimidazol-2-ylacetonitrile and dimedone produced heteroannulated chromeno[2,3-*b*]-quinolines **18**-**22**. The synthesized compounds were screened in *vitro* for their antimicrobial activity and revealed remarkable inhibitory effects against the selected microorganisms. Structures of the newly synthesized products have been deduced upon the help of elemental analysis and spectral data (IR, ^{1}H NMR, ^{13}C NMR and mass spectra).

Chromones are chemically active compounds and displayed variable chemical transformations upon treatment with nucleophilic reagents.[1] The ring-opening/ring-closure (RORC) reactions are well known for substituted chromones.[2] Chromones possess a wide range of biological applications including anticancer,[3] antitumor,[4] anti-HIV,[5] antioxidant,[6] anti-inflammatory[7] and antimicrobial activities.[8] Optical, photoelectrical, photophysical, fluorescence and electronic spectral studies as well as molecular docking and DFT calculations were performed for a variety of chromone derivatives.[9] The present work aimed to synthesize and study the chemical reactivity of 3-acetyl-2,7-dimethyl-5*H*-chromeno[2,3-*b*]pyridin-5-one (**2**) towards some nitrogen and carbon nucleophiles hoping to construct some novel chromeno[2,3-*b*]-pyridines and chromeno[2,3-*b*]quinolines and examine their antimicrobial activities.

Treatment of 6-methylchromone-3-carbonitrile (**1**) with acetylacetone in boiling ethanol containing piperidine afforded 3-acetyl-2,7-dimethyl-5*H*-chromeno[2,3-*b*]pyridin-5-one (**2**) (Scheme 1).[10]

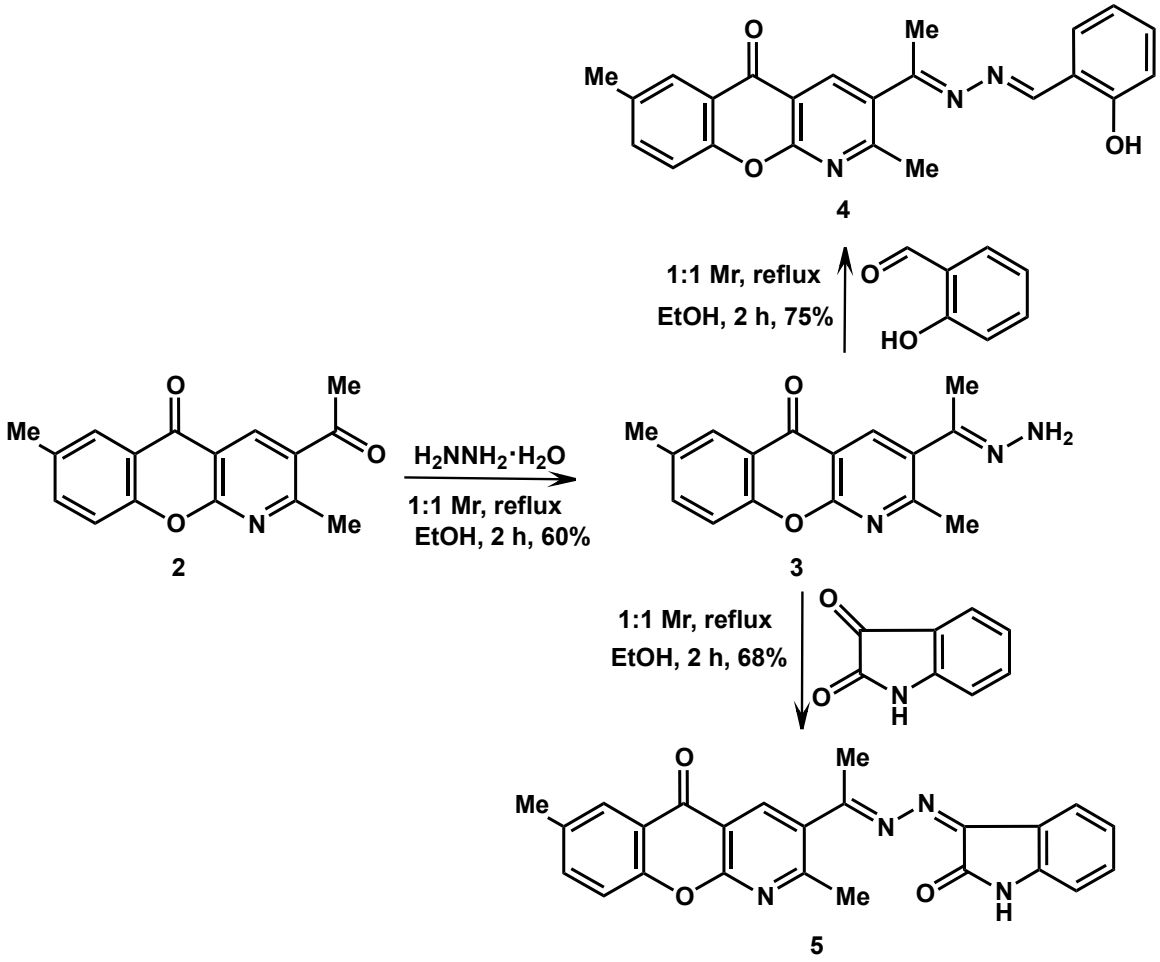


Scheme 1. Synthesis of 3-acetyl-2,7-dimethyl-5*H*-chromeno[2,3-*b*]pyridin-5-one (**2**)

Compound **2** was utilized as a starting material and its chemical behavior was studied towards a variety of nucleophilic reagents. Reaction of compound **2** with hydrazine hydrate in 1:1 molar ratio (Mr), afforded the corresponding hydrazone **3** (Scheme 2). The geometrical structure of compound **3** expected to be *E* isomer in which the amino group oriented away from the methyl group to avoid the steric hindrance. The IR spectrum of compound **3** showed the disappearance of ($C=O_{acetyl}$) absorption band which was observed at 1685 cm^{-1} in the IR spectrum of compound **2**, also, new absorption bands attributable to NH_2 group appeared at wavenumber 3378 and 3250 cm^{-1}.

The free NH_2 group in compound **3** was subjected to condensation reactions with some carbonyl compounds. Therefore, treatment of hydrazone **3** with salicylaldehyde in boiling ethanol yielded the unsymmetrical hydrazone **4** (Scheme 2). In the ^1H NMR spectrum of compound **4**, characteristic singlet signal assignable to CH=N was observed at δ 9.02, also D_2O-exchangeable signal attributable to OH appeared at chemical shift (δ) 11.06 ppm.

In the same manner, condensation of hydrazone **3** with isatine (1*H*-indole-2,3-dione) yielded the unsymmetrical hydrazone **5** (Scheme 2). The IR spectrum of compound **5** showed characteristic absorption bands at 3352 (NH), 1683 ($C=O_{indole}$), 1652 ($C=O_{\gamma\text{-pyrone}}$) and 1608 cm^{-1} (C=N). In the mass spectrum of compound **5**, the molecular ion peak was recorded at *m/z* 410 which agrees well with the suggested molecular formula weight (410.44).

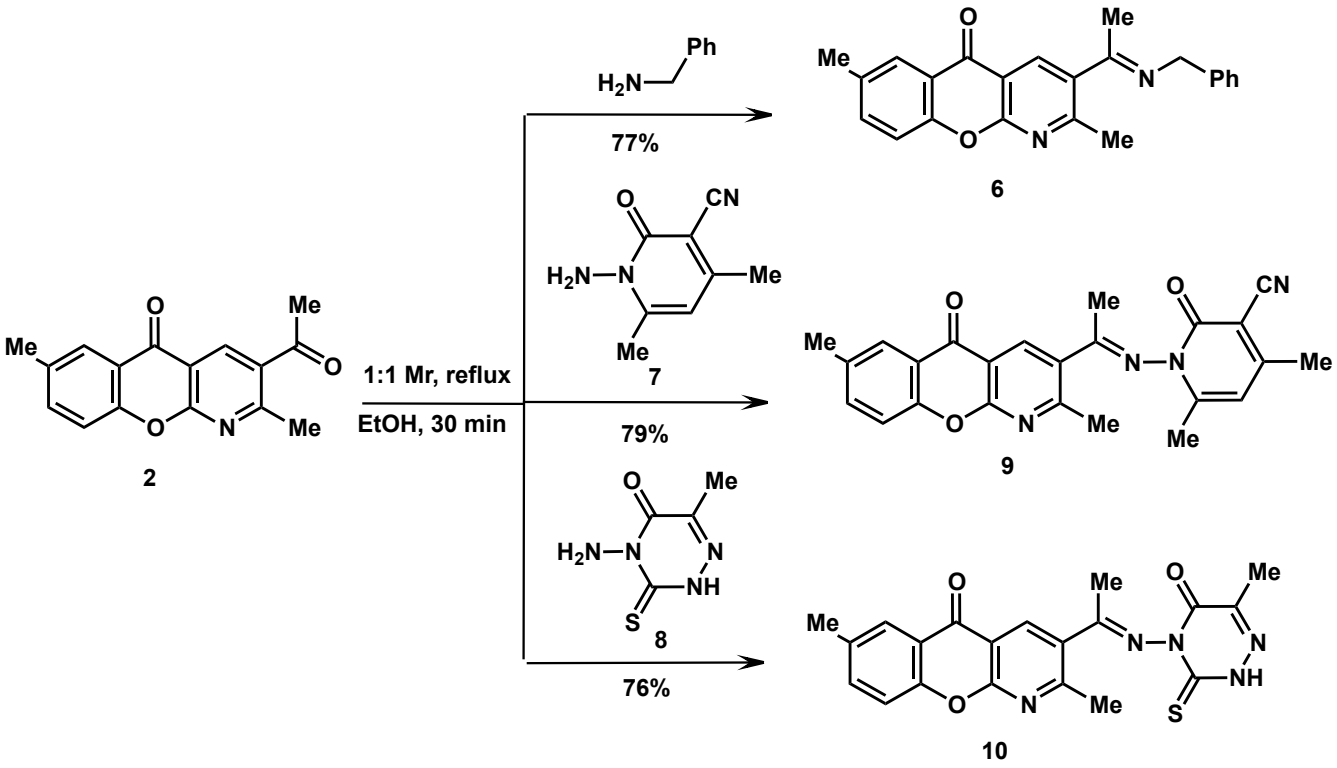


Scheme 2. Formation of hydrazones **3**-**5**

Treating acetyl derivative **2** with benzylamine in boiling ethanol gave the corresponding Schiff base **6** (Scheme 3). Its ^{1}H NMR spectrum showed distinctive singlet signals assignable to CH_2, H-6 and H-4 at δ 4.70, 7.92 and 8.79 ppm, respectively.

Similarly, simple condensation of compound **2** with 1-amino-4,6-dimethyl-2-oxo-1,2-dihydropyridine-3-carbonitrile (**7**)[11] and 4-amino-6-methyl-3-thioxo-3,4-dihydro-1,2,4-triazin-5(2*H*)-one (**8**)[12] produced the corresponding hydrazones **9** and **10**, in which the chromeno[2,3-*b*]pyridine moiety linked pyridine and triazine nuclei, respectively (Scheme 3). The IR spectrum of compound **9** showed specific absorption bands at 2219 (C≡N), 1684 ($C=O_{pyridone}$) and 1653 cm^{-1} ($C=O_{\gamma\text{-pyrone}}$). Its ^{1}H NMR spectrum showed five upfield singlet signals assignable to five methyl groups at δ 2.28, 2.37, 2.43, 2.68 and 2.72 ppm, in addition to specific singlet signals at δ 6.92 and 8.90 attributed to H-$5_{pyridone}$ and H-$4_{pyridine}$, respectively. The IR spectrum of compound **10** showed absorption bands at 1684 ($C=O_{triazinone}$), 1663 ($C=O_{\gamma\text{-pyrone}}$) and 1617 cm^{-1} (C=N). The ^{1}H NMR spectrum of compound **10** showed specific singlet at δ 2.15 ppm corresponding to $CH_{3\ triazine}$, in addition to D_2O-exchangeable signal δ 13.74 ppm ($NH_{triazine}$). In the ^{13}C NMR spectrum of compound **10**, four signals assignable to the four methyl carbons appeared in the

upfield region at δ 17.0, 20.7, 25.5 and 29.9 ppm. The mass spectra of compounds **9** and **10** recorded their molecular ion peaks at *m/z* 412 and 407, respectively, and support the identity of the structures.



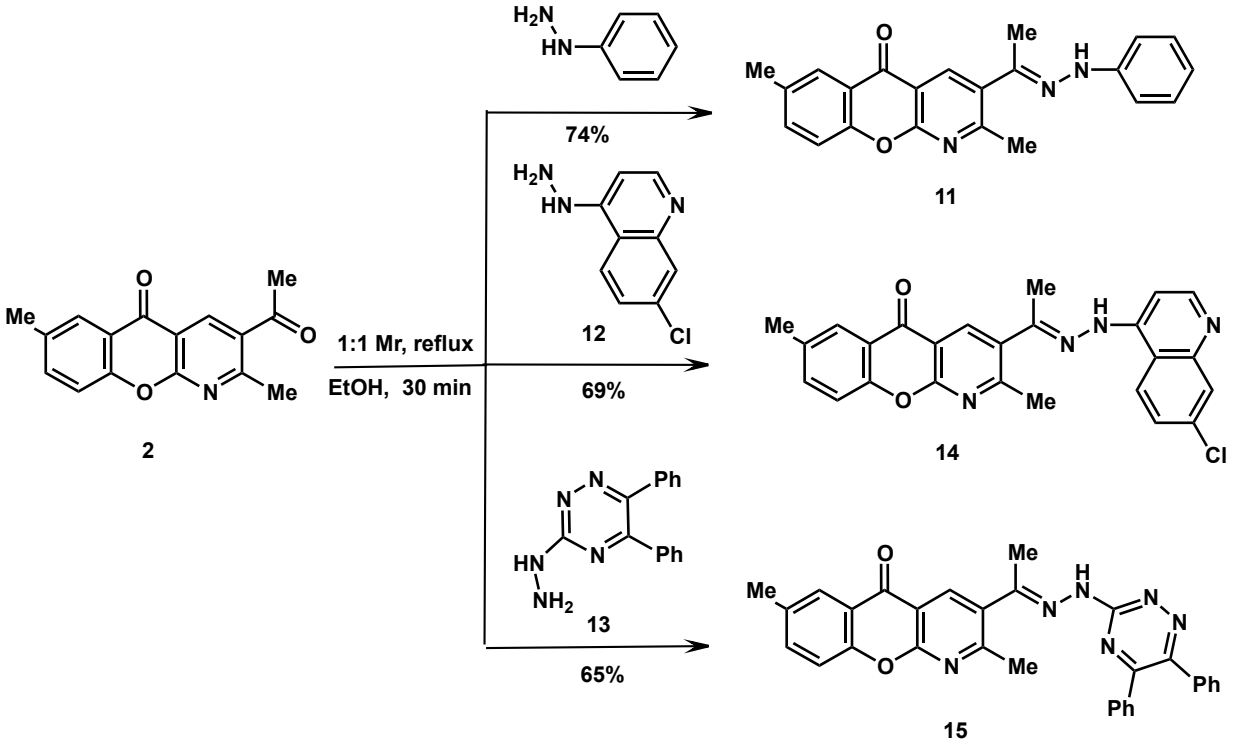
Scheme 3. Formation of Schiff bases of chromenopyridines **6**, **9** and **10**

Next, the chemical reactivity of compound **2** was studied toward some hydrazine derivatives. Thus, condensation of compound **2** with phenylhydrazine in boiling ethanol afforded the corresponding hydrazone **11** (Scheme 4). The IR spectrum of compound **11** showed characteristic absorption bands at 3248 (NH), 1641 ($C=O_{\gamma\text{-pyrone}}$) and 1606 cm^{-1} (C=N). The mass spectrum of compound **11** recorded the molecular ion peak at *m/z* 357 and confirms the proposed structure.

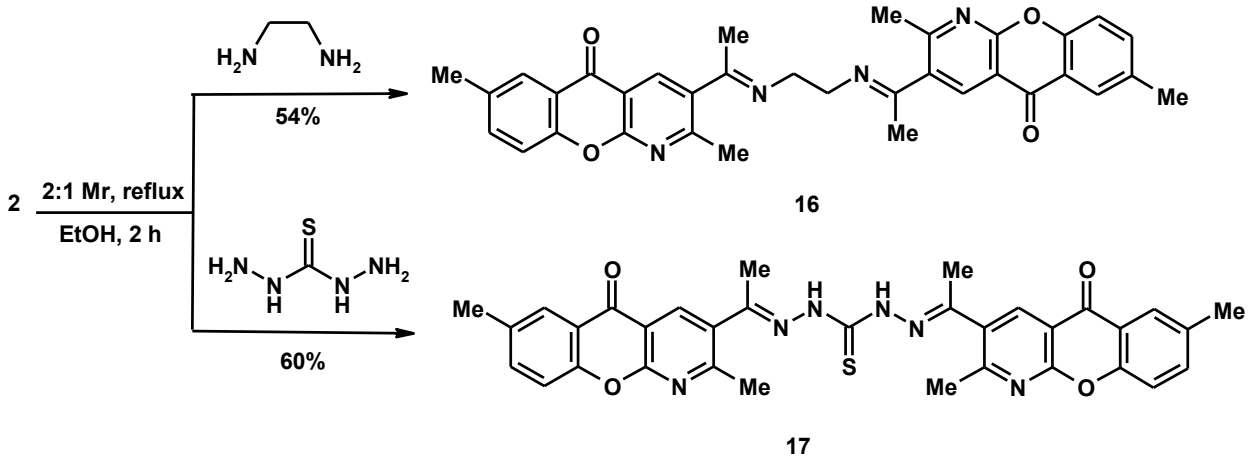
Also, condensation of compound **2** with 7-chloro-4-hydrazinoquinoline (**12**)[13] and 3-hydrazino-5,6-diphenyl-1,2,4-triazine (**13**)[14] produced chromeno[2,3-*b*]pyridines **14** and **15**, linked quinoline and triazine nuclei, respectively (Scheme 4). The ^1H NMR spectrum of compound **14** revealed characteristic singlet signals at δ 7.81 ($H\text{-}8_{quinoline}$), 7.85 (H-6), 9.13 ($H\text{-}4_{pyridine}$). While, the ^1H NMR spectrum of compound **15** showed singlet signals typical to H-6 and H-4 at δ 7.95 and 8.51 ppm, respectively. In the mass spectra of compounds **14** and **15**, the parent ion peaks observed at *m/z* 442 and 512, respectively.

Moreover, treating compound **2** with ethylenediamine in 2:1 molar ratio in boiling ethanol afforded the *bis* condensate **16** (Scheme 5). Specific absorption bands appeared in the IR spectrum of compound **16** at 1667 and 1618 cm^{-1} assignable $C=O_{\gamma\text{-pyrone}}$ and C=N, respectively. The molecular ion peak was recorded in the mass spectrum at *m/z* 558 which consent with its formula weight (558.64).

Also, treatment of compound **2** with thiocarbohydrazide, in boiling ethanol, gave *N*",*N*"'-*bis*-thiocarbohydrazone derivative **17** (Scheme 5). The parent ion peak was observed in the mass spectrum at *m/z* 604 which agrees with its suggested molecular formula ($C_{33}H_{28}N_6O_4S$).



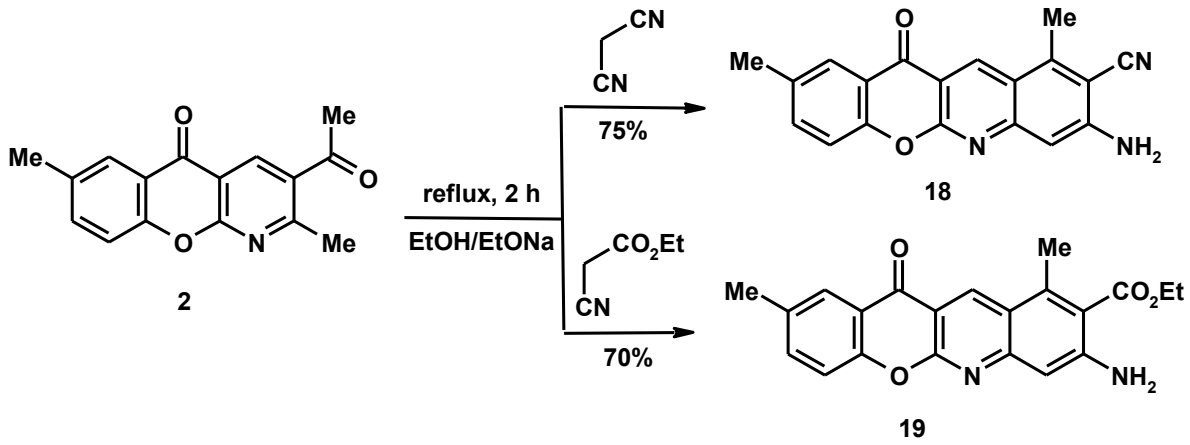
Scheme 4. Formation of hydrazone derivatives of chromenopyridines **11**, **14** and **15**



Scheme 5. Formation of *bis*-chromenopyridines **16** and **17**

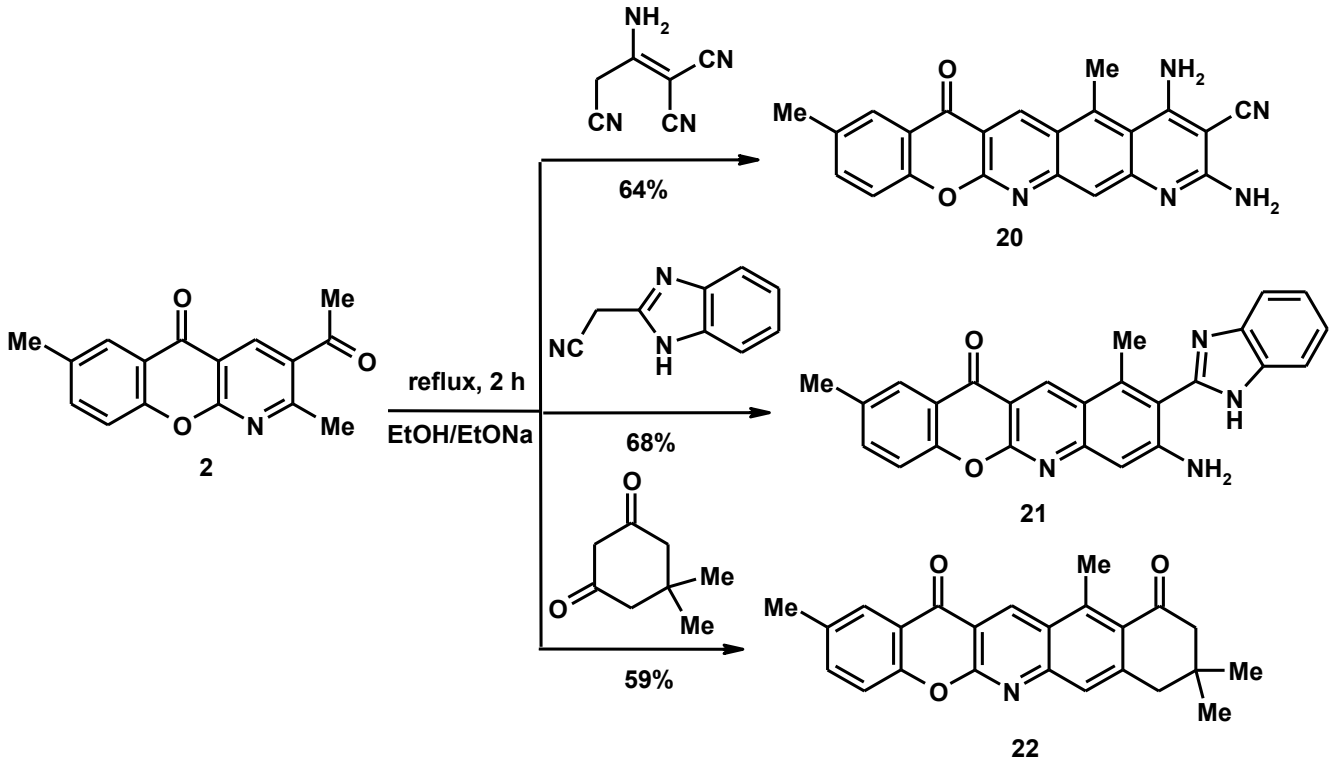
Then, the chemical reactivity of compound **2** was studied towards some carbon nucleophiles. Therefore, reaction of compound **2** with malononitrile and ethyl cyanoacetate in sodium ethoxide solution afforded chromeno[2,3-*b*]quinoline-2-carbonitrile **18** and chromeno[2,3-*b*]quinoline-2-carboxylate **19**, respectively

(Scheme 6). The reaction proceeds through condensation of the active methylene group with the carbonyl function followed by cyclization of the generated anion into the cyano function. The IR spectrum of compound **18** showed specific absorption bands at 3381, 3325, 3242 (NH_2), 2222 (C≡N) and 1652 cm^{-1} ($C{=}O_{\gamma\text{-pyrone}}$). Its ^1H NMR spectrum showed characteristic singlets at δ 7.29, 7.85 and 8.59 ppm attributed to H-4, H-10 and H-12, respectively. The spectrum also revealed an exchangeable signal at δ 8.11 ppm attributed to NH_2 protons. The mass spectrum of compound **18** revealed the molecular ion peak at *m/z* 315 which consent with the formula weight (315.10). The IR spectrum of compound **19** showed absorption bands at 3275, 3165 (NH_2), 1698 ($C{=}O_{ester}$) and 1669 cm^{-1} ($C{=}O_{\gamma\text{-pyrone}}$). Its ^1H NMR spectrum showed the ethoxycarbonyl protons as triplet and quartet signals at δ 1.34 and 4.32 ppm, in addition to characteristic singlet singlets at δ 7.85, 7.95 and 8.76 ppm attributed to H-4, H-10 and H-12, respectively. The mass spectrum of compound **19** showed the molecular ion peak at *m/z* 362 and confirms the structure.



Scheme 6. Formation of chromeno[2,3-*b*]quinoline derivatives **18** and **19**

Under the same reaction conditions, treatment of compound **2** with malononitrile dimer (2-aminoprop-1-ene-1,1,3-tricarbonitrile) and 1*H*-benzimidazol-2-ylacetonitrile afforded chromeno-[2,3-6`,5`]pyrido[2,3-*g*]quinoline **20** and chromeno[2,3-*b*]quinoline **21**, respectively (Scheme 7). The IR spectrum of compound **20** showed characteristic absorption bands at 3354, 3325, 3219, 3176 ($2NH_2$), 2224 (C≡N), 1635 cm^{-1} ($C{=}O_{\gamma\text{-pyrone}}$). Its ^1H NMR spectrum showed characteristic singlets at δ 7.86 (H-14), 7.93 (H-8) and 9.45 ppm (H-6), in addition to an exchangeable signals at δ 7.37 and 8.15 ppm attributed to $2NH_2$ protons. While, the IR spectrum of compound **21** showed specific absorption bands at 3297, 3155 (NH_2, NH) and 1651 cm^{-1} ($C{=}O_{\gamma\text{-pyrone}}$). Its ^1H NMR spectrum showed characteristic singlet signals at δ 7.25 (H-4), 7.93 (H-10), 9.09 ppm (H-12), as well as D_2O-exchangeable signals at δ 8.15, 8.39 ppm (2NH) and 9.96 ppm ($NH_{imidazole}$). Compounds **20** and **21** showed their molecular ion peaks at *m/z* 381 and 406 which agree with their formula weights and confirm their structures.



Scheme 7. Formation of heteroannulated chromones **20**-**22**

Finally, treatment of compound **2** with dimedone (5,5-dimethylcyclohexane-1,3-dione) in sodium ethoxide solution gave 3,3,10,14-tetramethyl-2,4-dihydrochromeno[2,3-*b*]benzo[*g*]quinoline-1,12-(2*H*,12*H*)-dione (**22**) (Scheme 7). Three specific singlet signals appeared in the ^{1}H NMR spectrum of compound **22** at δ 7.92 (H-5), 7.96 (H-11) and 8.92 ppm (H-13). The ^{13}C NMR spectrum of compound **22** exhibited distinctive signals at δ 20.7, 22.6, 25.3 and 25.5 ppm (attributed to four CH_3 groups), in addition the two CH_2 groups appeared at δ 29.9 and 44.1 ppm. The two signals attributed to the 2C=O groups appeared at δ 172.8 and 176.7 ppm. Structure of compound **22** was further deduced from its mass spectrum which revealed the molecular ion peak at *m/z* 371 corresponding to the molecular ion peak and confirms the structure.

ANTIMICROBIAL EVALUATION

The standardized disc agar diffusion method[15] was followed to determine the antimicrobial activity of the synthesized compounds against the sensitive organisms *Staphylococcus aureus* (ATCC 25923) and *Bacillus subtilis* (ATCC 6635) as examples of Gram-positive bacteria, *Escherichia coli* (ATCC 25922) and *Salmonella typhimurium* (ATCC 14028) as examples of Gram-negative bacteria, *Candida albicans* (ATCC 10231) as the yeast and *Asperigillus fumigatus* as the fungal strain. The antimicrobial activities were determined by measuring the inhibition zones, including the diameter of the disc (6 mm) as shown in Table 1. The results depicted in Table 1 revealed that:

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

[2] Remarkable increase in the inhibitory effect towards *A. fumigatus* was observed in compounds **5** and **14** and this may attribute to the presence of indole and/or quinoline moieties with chromeno[2,3-*b*]pyridine in the same molecule.

[3] The existence of triazine and chromeno[2,3-*b*]pyridine moieties in the same molecular frame as present in compounds **10** and **15** enhanced the antimicrobial activity towards the both types of Gram-negative bacteria and the fungus; *A. fumigatus*.

[4] The presence of *bis*-chromeno[2,3-*b*]pyridine moieties in the same molecule as exist in compounds **16** and **17** appeared remarkable inhibitory effects towards *S. aureus*, *B. subtilis* and *S. typhimurium*. In addition, compound **17** recorded high activity against *E. coli* and *A. fumigatus* strains.

[5] The novel chromone fused quinolines **20** and **21** recorded high activity towards all types of the selected microorganisms and this may attribute to the presence of additional nitrogen heterocyclic rings (pyridine in compound **20** and benzimidazole in compound **21**). While, other chromeno[2,3-*b*]quinolines **18**, **19** and **22** recorded high inhibitory effects towards *E. coli* and *C. albicans*.

[6] The above observations appeared that, some the prepared compounds showed high antimicrobial activity as comparable with the reference drugs and may serve as antimicrobial agents.

In conclusion, 3-acetyl-2,7-dimethyl-5*H*-chromeno[2,3-*b*]pyridin-5-one (**2**) was efficiently synthesized from ring-opening/ring-closure reactions of 6-methylchromone-3-carbonitrile (**1**) with acetylacetone under basic conditions. Compound **2** was used as a key intermediate for building of some novel heterocyclic systems bearing chromeno[2,3-*b*]pyridine moieties and some annulated compounds. Some chromeno[2,3-*b*]pyridines linked variable heterocyclic systems were synthesized from direct condensation of compound **2** with a variety of amines and hydrazines. The chemical reactivity of compound **2** was tested towards some carbon nucleophilic reagents leading to heteroannulated chromeno[2,3-*b*]quinolines **18-22**. The synthesized compounds revealed notable antimicrobial inhibitory effects against the selected microorganisms.

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	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
2	12 I	8 L	16 I	10 I	13 I	9 L	14 I	10 I	16 I	11 I	13 I	9 I
3	15 I	9 I	13 I	8 L	12 I	7 L	14 I	10 I	11 L	7 L	12 L	8 L
4	16 I	11 I	14 I	10 I	13 I	9 L	17 I	11 I	18 I	14 I	15 I	10 I
5	14 I	9 I	13 I	9 I	16 I	11 I	15 I	10 I	16 I	11 I	**27 H**	**19 H**
6	17 I	11 I	14 I	9 I	13 I	8 L	14 I	10 I	13 I	7 L	16 I	10 I
9	19 I	12 I	21 I	15 I	15 I	10 I	14 I	9 I	16 I	10 I	14 I	9 I
10	21 I	13 I	17 I	12 I	**26 H**	**19 H**	**27 H**	**19 H**	19 I	14 I	**28 H**	**21 H**
11	13 I	10 I	15 I	11 I	14 I	8 L	13 I	9 I	12 I	7 L	15 I	10 I
14	18 I	12 I	20 I	14 I	14 I	10 I	16 I	13 I	18 I	13 I	**26 H**	**18 H**
15	20 I	13 I	21 I	16 I	**28 H**	**19 H**	**27 H**	**19 H**	22 I	15 I	**28 H**	**22 H**
16	**26 H**	**19 H**	**28 H**	**20 H**	**30 H**	**20 H**	23 I	16 I	15 I	10 I	17 I	13 I
17	**29 H**	**22 H**	**32 H**	**20 H**	**28 H**	**19 H**	**26 H**	**19 H**	18 I	11 I	**29 H**	**20 H**
18	18 I	13 I	12 I	9 I	19 I	13 I	**30 H**	**21 H**	**28 H**	**22 H**	22 I	16 I
19	19 I	13 I	14 I	10 I	21 I	14 I	**28 H**	**20 H**	**25 H**	**20 H**	20 I	15 I
20	**29 H**	**22 H**	**27 H**	**20 H**	**30 H**	**23 H**	**26 H**	**19 H**	**26 H**	**20 H**	**27 H**	**19 H**
21	**28 H**	**20 H**	**25 H**	**18 H**	**28 H**	**20 H**	**28 H**	**19 H**	**25 H**	**19 H**	**32 H**	**21 H**
22	15 I	8 I	18 I	13 I	17 I	11 I	**27 H**	**21 H**	**27 H**	**21 H**	18 I	14 I
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 Chloramphenicol in the case of Gram-positive bacteria, Cephalothin in 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 spectra were measured on Mercury-300BB (300 MHz), using DMSO-d_6 as a solvent and TMS (δ) as the internal standard. ^{13}C NMR spectra were measured on Mercury-300BB (75 MHz), 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. 6-Methylchromone-3-carbonitrile (**1**)[16] was prepared according to literature.

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.[15]

3-Acetyl-2,7-dimethyl-5*H*-chromeno[2,3-*b*]pyridin-5-one (2)

A mixture of 6-methylchromone-3-carbonitrile (**1**) (1.87 g, 10 mmol) and acetylacetone (1.0 g, 1 mL, 10 mmol) in absolute EtOH (40 mL) containing piperidine (0.5 mL) was heated under reflux for 30 min. The pale yellow crystals obtained after cooling were filtered and crystallized from EtOH, mp 197-198 ^{o}C (lit.[10] mp 194-198 ^{o}C), yield 2.11 g (79%). IR (KBr, cm^{-1}): 3055 ($CH_{arom.}$), 2996, 2926 ($CH_{aliph.}$), 1685 ($C{=}O_{acetyl}$), 1668 ($C{=}O_{\gamma\text{-pyrone}}$), 1615 (C=N), 1580 (C=C). ^{1}H NMR (DMSO-d_6, δ, 300 MHz): 2.45 (s, 3H, $CH_{3\ benzo}$), 2.65 (s, 3H, $CH_{3\ pyridine}$), 2.73 (s, 3H, $CH_{3\ acetyl}$), 7.63 (d, 1H, J = 8.8 Hz, H-9), 7.73 (d, 1H, J = 8.8 Hz, H-8), 7.97 (s, 1H, H-6), 8.92 (s, 1H, H-4). Anal. Calcd for $C_{16}H_{13}NO_3$ (267.29): C, 71.90; H, 4.90; N, 5.24. Found: C, 71.84; H, 4.77; N, 5.13.

3-[1-Hydrazinylideneethyl]-2,7-dimethyl-5*H*-chromeno[2,3-*b*]pyridin-5-one (3)

A mixture of compound **2** (1.07 g, 4 mmol) and hydrazine hydrate (0.20 g, 0.2 mL, 4 mmol) in absolute EtOH (30 mL) was heated under reflux for 2 h. The pale yellow crystals so formed after cooling was filtered and crystallized from MeOH to, mp 236-237 ^{o}C, yield 0.67 g (60%). IR (KBr, cm^{-1}): 3378, 3250 (NH_2), 3076 ($CH_{arom.}$), 2926, 2875 ($CH_{aliph.}$), 1662 ($C{=}O_{\gamma\text{-pyrone}}$), 1621 (C=N), 1602 (C=C). ^{1}H NMR (DMSO-d_6, δ, 300 MHz): 2.44 (s, 3H, CH_3), 2.68 (s, 3H, CH_3), 2.74 (s, 3H, CH_3), 4.85 (bs, 2H, NH_2 exchangeable with D_2O). 7.62 (d, 1H, J = 8.0 Hz, H-9), 7.73 (d, 1H, J = 8.0 Hz, H-8), 7.96 (s, 1H, H-6), 8.86 (s, 1H, H-4). Mass spectrum (*m/z*, *I*%): 281 (21), 265 (46), 237 (11), 223 (20), 134 (100), 119 (13), 107 (9), 77 (54), 64 (82). Anal. Calcd for $C_{16}H_{15}N_3O_2$ (281.31): C, 68.31; H, 5.37; N, 14.94%. C, 68.10; H, 5.10; N, 14.70%.

3-{1-[(2-Hydroxybenzylidene)hydrazinylidene]ethyl}-2,7-dimethyl-5*H*-chromeno[2,3-*b*]-pyridin-5-one (4)

A mixture of hydrazone **3** (0.56 g, 2 mmol) and salicylaldehyde (0.24 g, 0.21 mL, 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 2-propanol, mp 267-268 °C, yield 0.58 g (75%). IR (KBr, cm^{-1}): 3288 (OH), 2922, 2860 ($CH_{aliph.}$), 1667 ($C=O_{\gamma\text{-pyrone}}$), 1607 (C=N), 1558 (C=C). ^1H NMR (DMSO-d_6, δ, 300 MHz): 2.39 (s, 3H, CH_3), 2.47 (s, 6H, $2CH_3$), 6.79- 6.83 (m, 1H, Ar-H), 6.92- 7.15 (m, 2H, Ar-H), 7.31-7.39 (m, 2H, Ar-H), 7.67 (d, 1H, *J* = 7.6 Hz, H-8), 7.81 (s, 1H, H-6), 8.97 (s, 1H, H-4), 9.02 (s, 1H, CH=N), 11.06 (bs, 1H, OH exchangeable with D_2O). ^{13}C NMR (DMSO-d_6, δ, 75 MHz): 20.7 (CH_3), 25.5 (CH_3), 29.9 (CH_3), 99.0, 113.7, 117.1, 118.8, 121.1, 122.2, 125.7, 130.6, 135.2, 137.6, 138.7, 151.7, 153.6, 159.8, 164.5, 165.9, 175.6, 176.6, 188.4, 199.1. Mass spectrum (*m/z*, *I*%): 385 (5), 321 (6), 251 (7), 201 (100), 185 (11), 175 (9), 135 (79), 106 (24), 91 (22), 77 (44), 64 (18). Anal. Calcd for $C_{23}H_{19}N_3O_3$ (385.43): C, 71.68; H, 4.97; N, 10.90%. Found: C, 71.39; H, 4.72; N, 10.78%.

2,7-Dimethyl-3-{1-[(2-oxo-1,2-dihydro-3*H*-indol-3-ylidene)hydrazinylidene] ethyl}-5*H*-chromeno-[2,3-*b*]pyridin-5-one (5)

A mixture of hydrazone **3** (0.56 g, 2 mmol) and 1*H*-indole-2,3-dione (0.29 g, 2 mmol) in absolute EtOH (20 mL) was heated under reflux for 2 h. The orange crystals so formed during heating were filtered and crystallized from 2-butanol, mp 276-277 °C, yield 0.56 g (68%). IR (KBr, cm^{-1}): 3352 (NH), 2931, 2855 ($CH_{aliph.}$), 1683 ($C=O_{indole}$), 1652 ($C=O_{\gamma\text{-pyrone}}$), 1608 (C=N), 1564 (C=C). ^1H NMR (DMSO-d_6, δ, 300 MHz): 2.39 (s, 3H, CH_3), 2.68 (s, 3H, CH_3), 2.79 (s, 3H, CH_3), 6.84-7.10 (m, 2H, Ar-H), 7.14 (t, 1H, *J* = 8.4 Hz, Ar-H), 7.32-7.93 (m, 2H, Ar-H), 7.62 (d, 1H, *J* = 8.4 Hz, Ar-H), 7.97 (s, 1H, H-6), 8.93 (s, 1H, H-4), 10.48 (bs, 1H, NH exchangeable with D_2O). Mass spectrum (*m/z*, *I*%): 410 (6), 265 (13), 251 (25), 237 (17), 201 (100), 145 (64), 135 (54), 119 (18), 107 (9), 91 (31), 77 (29), 65 (11). Anal. Calcd for $C_{24}H_{18}N_4O_3$ (410.44): C, 70.23; H, 4.42; N, 13.65%. Found: C, 70.04; H, 4.17; N, 13.50%.

3-[*N*-Benzylethanimidoyl]-2,7-dimethyl-5*H*-chromeno[2,3-*b*]pyridin-5-one (6)

A mixture of compound **2** (0.53 g, 2 mmol) and benzylamine (0.22 g, 0.22 mL, 2 mmol) in absolute EtOH (20 mL) was heated under reflux for 30 min. The white crystals obtained after cooling were filtered and crystallized from EtOH, mp 243-244 °C, yield 0.55 g (77%). IR (KBr, cm^{-1}): 2985, 2924, 2840 ($CH_{aliph.}$), 1671 ($C=O_{\gamma\text{-pyrone}}$), 1613 (C=N), 1582 (C=C). ^1H NMR (DMSO-d_6, δ, 300 MHz): 2.35 (s, 3H, CH_3), 2.67 (s, 3H, CH_3), 2.71 (s, 3H, CH_3), 4.70 (s, 2H, CH_2), 7.23-7.45 (m, 4H, Ar-H), 7.58 (d, 1H, *J* = 8.0 Hz, Ar-H), 7.70 (d, 1H, *J* = 8.0 Hz, Ar-H), 7.77 (d, 1H, 7.2 Hz, Ar-H), 7.92 (s, 1H, H-6), 8.79 (s, 1H, H-4). Mass spectrum (*m/z*, *I*%): 355 (M^+-1; 2%), 342 (3), 313 (7), 302 (4), 294 (7), 264 (14), 249 (11), 200 (46), 185 (10), 172 (11), 163 (17), 134 (100), 121 (6), 118 (7), 105 (25), 78 (34), 64 (10%). Anal. Calcd for $C_{23}H_{20}N_2O_2$ (356.43): C, 77.51; H, 5.66; N, 7.86%. Found: C, 77.22; H, 5.50; N, 7.64%.

2,7-Dimethyl-3-[*N*-(3-cyano-4,6-dimethyl-2-oxo-1,2-dihydropyridin-3-yl)ethanimidoyl]-5*H*-

chromeno[2,3-*b*]pyridin-5-one (9)

A mixture of compound **2** (0.53 g, 2 mmol) and 1-amino-4,6-dimethyl-2-oxo-1,2-dihydropyridine-3-carbonitrile (**7**) (0.33 g, 2 mmol) in absolute EtOH (20 mL) was heated under reflux for 30 min. The white crystals obtained during heating were filtered and crystallized from DMF/EtOH, mp 268-269 °C, yield 0.65 g (79%). IR (KBr, cm^{-1}): 3040 ($CH_{arom.}$), 2965, 2935, 2885 ($CH_{aliph.}$), 2219 (C≡N), 1684 ($C=O_{pyridone}$), 1653 ($C=O_{\gamma\text{-pyrone}}$), 1613 (C=N), 1576 (C=C). ^{1}H NMR (DMSO-d_6, δ, 300 MHz): 2.28 (s, 3H, CH_3), 2.37 (s, 3H, CH_3), 2.43 (s, 3H, CH_3), 2.68 (s, 3H, CH_3), 2.72 (s, 3H, CH_3), 6.92 (s, 1H, H-$5_{pyridone}$), 7.32 (d, 1H, *J* = 8.4 Hz, H-9), 7.51 (d, 1H, *J* = 8.4 Hz, H-8), 7.94 (s, 1H, H-6), 8.90 (s, 1H, H-4). Mass spectrum (*m/z*, *I*%): 412 (10), 372 (6), 329 (7), 265 (28), 251 (25), 237 (19), 201 (82), 134 (100), 119 (7), 106 (16), 77 (16), 64 (27). Anal. Calcd for $C_{24}H_{20}N_4O_3$ (412.45): C, 69.89; H, 4.89; N, 13.58%. Found: C, 69.56; H, 4.60; N, 13.51%.

2,7-Dimethyl-3-[*N*-(6-methyl-5-oxo-3-thioxo-2,5-dihydro-1,2,4-triazin-4(3*H*)-yl)ethanimidoyl]-5*H*-chromeno[2,3-*b*]pyridin-5-one (10)

A mixture of compound **2** (0.53 g, 2 mmol) and 4-amino-6-methyl-3-thioxo-3,4-dihydro-1,2,4-triazin-5(2*H*)-one (**8**) (0.32 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 *n*-butanol, mp 230-231 °C, yield 0.60 g (74%). IR (KBr, cm^{-1}): 3216 (NH), 3011 ($CH_{arom.}$), 2915, 2903 ($CH_{aliph.}$), 1684 ($C=O_{triazinone}$), 1633 ($C=O_{\gamma\text{-pyrone}}$), 1617 (C=N), 1605 (C=C), 1306 (C=S). ^{1}H NMR (DMSO-d_6, δ, 300 MHz): 2.15 (s, 3H, $CH_{3\ triazine}$), 2.38 (s, 3H, CH_3), 2.68 (s, 3H, CH_3), 2.73 (s, 3H, CH_3), 7.63 (d, 1H, *J* = 8.4 Hz, H-9), 7.73 (d, 1H, *J* = 8.8 Hz, H-8), 7.96 (s, 1H, H-6), 8.92 (s, 1H, H-4), 13.74 (bs, NH exchangeable with D_2O). ^{13}C NMR (DMSO-d_6, δ, 75 MHz): 17.0 ($CH_{3\ triazine}$), 20.7 (CH_3), 25.5 (CH_3), 29.9 (CH_3), 113.7, 118.8, 121.1, 125.7, 130.6, 135.3, 137.6, 138.7, 145.7, 149.3, 153.6, 159.6, 164.5, 168.9, 176.6, 199.2. Mass spectrum (*m/z*, *I*%): 407 (18), 265 (43), 251 (36), 134 (100), 119 (5), 106 (25), 77 (12), 64 (19). Anal. Calcd for $C_{20}H_{17}N_5O_3S$ (407.44): C, 58.96; H, 4.21; N, 17.19; S, 7.87%. Found: C, 58.71; H, 3.94; N, 17.02; S, 7.56%.

2,7-Dimethyl-3-[1-(2-phenylhydrazinylidene)ethyl]-5*H*-chromeno[2,3-*b*]pyridin-5-one (11)

A mixture of compound **2** (0.53 g, 2 mmol) and phenylhydrazine (0.22 g, 0.2 mL, 2 mmol) in absolute EtOH (20 mL) was heated under reflux for 2 h. The yellow crystals obtained after cooling were filtered and crystallized from AcOH/H_2O, mp 281-282 °C, yield 0.54 g (76%). IR (KBr, cm^{-1}): 3248 (NH), 3029 ($CH_{arom.}$) 2930, 2885 ($CH_{aliph.}$), 1641 ($C=O_{\gamma\text{-pyrone}}$), 1606 (C=N), 1551 (C=C). ^{1}H NMR (DMSO-d_6, δ, 300 MHz): 2.37 (s, 3H, CH_3), 2.48 (s, 6H, $2CH_3$), 6.68 (t, 1H, *J* = 7.2 Hz, Ar-H), 6.68-6.86 (m, 2H, Ar-H), 7.16-7.21 (m, 2H, Ar-H), 7.30 (d, 1H, *J* = 8.8 Hz, Ar-H), 7.46 (d, 1H, *J* = 8.4 Hz, Ar-H), 7.79 (s, 1H,

H-6), 8.43 (s, 1H, H-4), 10.04 (bs, NH exchangeable with D_2O). Mass spectrum (*m/z*, *I*%): 357 (13), 265 (18), 251 (39), 223 (8), 201 (42), 134 (65), 119 (18), 106 (28), 92 (100), 77 (59), 64 (14). Anal. Calcd for $C_{22}H_{19}N_3O_2$ (357.42): C, 73.93; H, 5.36; N, 11.76%. Found: C, 73.66; H, 5.25; N, 11.51%.

2,7-Dimethyl-3-{1-[2-(7-chloroquinolin-4-ylhydrazinylidene)-ethyl]}-5*H*-chromeno[2,3-*b*]pyridin-5-one (14)

A mixture of compound **2** (0.53 g, 2 mmol) and 7-chloro-4-hydrazinylquinoline (**12**) (0.39 g, 2 mmol) in absolute EtOH (20 mL) was heated under reflux for 15 min. The yellow crystals obtained during heating were filtered and crystallized from DMF/EtOH, mp 303-304 °C, yield 0.61 g (69%). IR (KBr, cm^{-1}): 3232 (NH), 3020 ($CH_{arom.}$), 2961 ($CH_{aliph.}$), 1655 (C=O $_{\gamma\text{-pyrone}}$), 1617 (C=N), 1560 (C=C). ^{1}H NMR (DMSO-d_6, δ, 300 MHz): 2.38 (s, 3H, CH_3), 2.47 (s, 6H, $2CH_3$), 7.25 (d, 1H, *J* = 6.4 Hz, Ar-H), 7.33 (d, 1H, *J* = 8.4 Hz, Ar-H), 7.50 (d, 1H, *J* = 6.4 Hz, Ar-H), 7.71 (d, 1H, *J* = 8.8 Hz, Ar-H), 7.81 (s, 1H, H-$8_{quinoline}$), 7.85 (s, 1H, H-6), 8.45 (d, 1H, *J* = 6.4 Hz, H-$3_{quinoline}$), 8.55 (d, 1H, *J* = 8.8 Hz, H-$2_{quinoline}$), 9.13 (s, 1H, H-$4_{pyridine}$), 9.43 (bs, 1H, NH exchangeable with D_2O. Mass spectrum (*m/z*, *I*%): 442 (3), 380 (9), 356 (7), 328 (9), 277 (19), 245 (26), 201 (20), 185 (31), 163 (13), 135 (100), 106 (16), 91 (12), 78 (8), 63 (7). Anal. Calcd for $C_{25}H_{19}ClN_4O_2$ (442.91): C, 67.80; H, 4.32; N, 12.65%. Found: C, 67.62; H, 4.18; N, 12.40%.

2,7-Dimethyl-3-{1-[2-(5,6-diphenyl[1,2,4]triazin-3-ylhydrazinylidene)ethyl]}-5*H*-chromeno[2,3-*b*]-pyridin-5-one (15)

A mixture of compound **2** (0.53 g, 2 mmol) and 3-hydrazinyl-5,6-diphenyl-1,2,4-triazine (**13**) (0.58 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 2-propanol, mp 251-252 °C, yield 0.67 g (65%). IR (KBr, cm^{-1}): 3228 (NH), 3056 ($CH_{arom.}$), 2945, 2890 ($CH_{aliph.}$), 1655 (C=O $_{\gamma\text{-pyrone}}$), 1608 (C=N), 1587 (C=C). ^{1}H NMR (DMSO-d_6, δ, 300 MHz): 2.32 (s, 3H, CH_3), 2.41 (s, 6H, $2CH_3$), 7.33-7.49 (m, 10H, Ar-H), 7.61 (d, 1H, *J* = 8.8 Hz, H-9), 7.71 (d, 1H, *J* = 8.4 Hz, H-8), 7.95 (s, 1H, H-6), 8.51 (s, 1H, H-4), 11.06 (bs, 1H, NH exchangeable with D_2O). Mass spectrum (*m/z*, *I*%): 512 (16), 409 (11), 318 (19), 237 (100), 196 (8), 178 (69), 134 (82), 119 (9), 106 (13), 77 (20), 64 (10). Anal. Calcd for $C_{31}H_{24}N_6O_2$ (512.58): C, 72.64; H, 4.72; N, 16.40%. Found: C, 72.35; H, 4.49; N, 16.11%.

***N*,*N*'-*Bis*[1-(2,7-dimethyl-5-oxo-5*H*-chromeno[2,3-*b*]pyridin-3-yl) ethylidene]ethane-1,2-diamine (16)**

A mixture of compound **2** (1.07 g, 4 mmol) and ethylenediamine (0.12 g, 0.14 mL, 2 mmol) in absolute EtOH (20 mL) was heated under reflux for 2 h. The pale yellow crystals obtained during heating were

filtered and crystallized from dioxane, mp 273-274 °C, yield 0.61 g (54%). IR (KBr, cm^{-1}): 3165 (NH), 3045 ($CH_{arom.}$), 2980, 2965, 2905, 2880 ($CH_{aliph.}$), 1667 (C=O $_{\gamma\text{-pyrone}}$), 1618 (C=N), 1586 (C=C). ^{1}H NMR (DMSO-d_6, δ, 300 MHz): 2.37 (s, 6H, $2CH_3$), 2.69 (s, 6H, $2CH_3$), 2.74 (s, 6H, $2CH_3$), 3.65 (s, 4H, CH_2), 7.57-7.74 (m, 4H, Ar-H), 7.98 (s, 2H, H-6), 8.93 (s, 2H, H-4). Mass spectrum (*m/z*, *I*%): 558 (5%), 292 (14), 279 (100), 267 (20), 252 (36), 238 (18), 224 (9), 127 (3), 77 (4). Anal. Calcd for $C_{34}H_{30}N_4O_4$ (558.64): C, 73.10; H, 5.41; N, 10.03%. Found: C, 72.87; H, 5.15; N, 9.79%.

_N''_,_N'''_-_Bis_[1-(2,7-dimethyl-5-oxo-5_H_-chromeno[2,3-_b_]pyridin-3-yl)ethylidene]thiocarbohydrazide (17)

A mixture of compound **2** (1.07 g, 4 mmol) and thiocarbohydrazide (0.21 g, 2 mmol) in absolute EtOH (20 mL) was heated under reflux for 2 h. The canary yellow crystals obtained during heating were filtered and crystallized from AcOH/H_2O, mp 298-299 °C, yield 0.71 g (60%). IR (KBr, cm^{-1}): 2917, 2840 ($CH_{aliph.}$), 1640 (C=O $_{\gamma\text{-pyrone}}$), 1621 (C=N), 1581 (C=C), 1309 (C=S) ^{1}H NMR (DMSO-d_6, δ, 300 MHz): 2.44 (s, 6H, $2CH_3$), 2.68 (s, 6H, $2CH_3$), 2.73 (s, 6H, $2CH_3$), 7.29 (d, 2H, *J* = 8.0 Hz, H-9), 7.48 (d, 2H, *J* = 8.8 Hz, H-8), 7.77 (s, 2H, H-6), 8.68 (s, 2H, H-4), 8.87 (bs, 2H, 2NH exchangeable with D_2O). Mass spectrum (*m/z*, *I*%): 604 (6%), 265 (61), 251 (40), 237 (32), 223 (13), 185 (17), 145 (18), 135 (100), 119 (28), 106 (3), 77 (4). Anal. Calcd for $C_{33}H_{28}N_6O_4S$ (604.69): C, 65.55; H, 4.67; N, 13.90; S, 5.30%. Found: C, 65.51; H, 4.46; N, 13.86; S, 5.13%.

3-Amino-1,9-dimethyl-11-oxo-11_H_-chromeno[2,3-_b_]quinoline-2-carbonitrile (18)

A mixture of compound **2** (0.53 g, 2 mmol) and malononitrile (0.13 g, 2 mmol) in absolute EtOH (20 mL) containing sodium ethoxide solution (prepared by dissolving 0.5 g sodium in 10 mL absolute EtOH) was heated under reflux for 2 h. After cooling, the reaction mixture was neutralized by conc. HCl. The solid so formed was filtered and crystallized from DMF/H_2O to give compound **18** as yellow crystals, mp > 300 °C, yield 0.47 g (75%). IR (KBr, cm^{-1}): 3381, 3335, 3242 (NH_2), 2222 (C≡N), 1652 ($C=O_{\gamma\text{-pyrone}}$), 1615 (C=N), 1581 (C=C). ^{1}H NMR (DMSO-d_6, δ, 300 MHz): 2.39 (s, 3H, CH_3), 2.45 (s, 3H, CH_3), 7.29 (s, 1H, H-4), 7.45 (d, 1H, *J* = 8.8 Hz, H-7), 7.62 (d, 1H, *J* = 8.4 Hz, H-8), 7.85 (s, 1H, H-10), 8.11 (bs, 2H, NH_2 exchangeable with D_2O), 8.59 (s, 1H, H-12). Mass spectrum (*m/z*, *I*%): 315 (3), 300 (2), 267 (2), 251 (100), 225 (3), 223 (11), 198 (35), 180 (4), 171 (4), 144 (9), 135 (13), 33 (16), 112 (11), 105 (17), 97 (11), 91 (13), 77 (55), 63 (32). Anal. Calcd for $C_{19}H_{13}N_3O_2$ (315.33): C, 72.37; H, 4.16; N, 13.33%. Found: C, 72.22; H, 4.00; N, 13.26%.

Ethyl 3-amino-1,9-dimethyl-11-oxo-11_H_-chromeno[2,3-_b_]quinoline-2-carboxylate (19)

A mixture of compound **2** (0.53 g, 2 mmol) and ethyl cyanoacetate (0.27 g, 0.25 mL, 2 mmol) in absolute

EtOH (20 mL) containing sodium ethoxide solution (prepared by dissolving 0.5 g sodium in 10 mL absolute EtOH) was heated under reflux for 2 h. After cooling, the reaction mixture was neutralized by conc. HCl. The solid so formed was filtered and crystallized from DMF/EtOH to give compound **19** as yellow crystals, mp 247-248 °C, yield 0.51 g (70%). IR (KBr, cm^{-1}): 3275, 3165 (NH_2), 3056 ($CH_{arom.}$), 2969, 2923, 2858 ($CH_{aliph.}$), 1698 ($C=O_{ester}$), 1669 ($C=O_{\gamma\text{-pyrone}}$), 1617 (C=N), 1586 (C=C). ^{1}H NMR (DMSO-d_6, δ, 300 MHz): 1.34 (t, 3H, J = 6.8 Hz, $CH_2\mathit{CH_3}$), 2.40 (s, 3H, CH_3), 2.44 (s, 3H, CH_3), 4.32 (q, 2H, J = 7.2 Hz, $\mathit{CH_2}CH_3$), 7.45 (d, 1H, J = 8.4 Hz, H-7), 7.60 (d, 1H, J = 8.8 Hz, H-8), 7.85 (s, 1H, H-4), 7.95 (s, 1H, H-10), 8.04 (bs, 1H, NH exchangeable with D_2O), 8.28 (bs, 1H, NH exchangeable with D_2O), 8.76 (s, 1H, H-12). Mass spectrum (*m/z*, *I*%): 362 (M^+; 3%), 361 (M^+-1; 6%), 328 (5), 295 (3), 264 (4), 243 (25), 218 (3), 201 (100), 178 (18), 162 (6), 150 (9), 135 (65), 123 (6), 107 (5), 91 (9), 67 (6). Anal. Calcd for $C_{21}H_{18}N_2O_4$ (362.39): C, 69.60; H, 5.01; N, 7.73%. Found: C, 69.39; H, 4.85; N, 7.50%.

2,4-Diamino-5,9-dimethyl-7-oxo-7*H*-chromeno[2,3-6`,5`]pyrido[2,3-*g*]quinoline-3-carbonitrile (20)

A mixture of compound **2** (0.53 g, 2 mmol) and malononitrile dimer (2-aminoprop-1-ene-1,1,3-tricarbonitrile) (0.26 g, 2 mmol), in absolute EtOH (20 mL) containing sodium ethoxide solution (prepared by dissolving 0.5 g sodium in 10 mL absolute EtOH), was heated under reflux for 2 h. After cooling, the reaction mixture was neutralized by conc. HCl. The solid obtained was filtered and crystallized from DMF/MeOH to give compound **20** as pale yellow crystals, mp > 300 °C, yield 0.49 g (64%). IR (KBr, cm^{-1}): 3354, 3325, 3219, 3176 ($2NH_2$), 2970, 2895 ($CH_{aliph.}$), 2224 (C≡N), 1635 ($C=O_{\gamma\text{-pyrone}}$), 1610,1601 (C=N), 1585 (C=C). ^{1}H NMR (DMSO-d_6, δ, 300 MHz): 2.40 (s, 3H, CH_3), 2.43 (s, 3H, CH_3), 7.37 (bs, 2H, NH_2 exchangeable with D_2O), 7.56 (d, 1H, J = 8.8 Hz, H-11), 7.67 (d, 1H, J = 8.8 Hz, H-10), 7.86 (s, 1H, H-14), 7.93 (s, 1H, H-8), 8.15 (bs, 2H, NH_2 exchangeable with D_2O), 9.45 (s,1H, H-6). Mass spectrum (*m/z*, *I*%): 381 (2), 343 (3), 292 (38), 279 (100), 267 (11), 251 (6), 238 (93), 222 (17) 210 (10), 195 (12), 180 (8), 167 (13), 152 (13), 135 (18), 111 (15), 107 (13), 91 (29), 77 (56), 64 (12). Anal. Calcd for $C_{22}H_{15}N_5O_2$ (381.40): C, 69.28; H, 3.96; N, 18.36%. Found: C, 69.05; H, 3.76; N, 18.17%.

3-Amino-2-(1*H*-benzimidazol-2-yl)-1,9-dimethylchromeno[2,3-*b*]quinolin-11(11*H*)-one (21)

A mixture of compound **2** (0.53 g, 2 mmol) and 1*H*-benzimidazol-2-ylacetonitrile (0.31 g, 2 mmol), in absolute EtOH (20 mL) containing sodium ethoxide solution (prepared by dissolving 0.5 g sodium in 10 mL absolute EtOH), was heated under reflux for 2 h. After cooling, the reaction mixture was neutralized by conc. HCl. The solid obtained was filtered and crystallized from DMF/H_2O to give compound **21** as pale brown crystals, mp > 300 °C, yield 0.55 g (68%). IR (KBr, cm^{-1}): 3297, 3155 (NH_2, NH), 3020 ($CH_{arom.}$), 1651 ($C=O_{\gamma\text{-pyrone}}$), 1612 (C=N), 1586 (C=C). ^{1}H NMR (DMSO-d_6, δ, 300 MHz): 2.36 (s, 3H,

CH_3), 2.42 (s, 3H, CH_3), 7.25 (s, 1H, H-4), 7.45-7.67 (m, 6H, Ar-H), 7.93 (s, 1H, H-10), 8.15 (bs, 1H, NH exchangeable with D_2O), 8.39 (bs, 1H, NH exchangeable with D_2O), 9.09 (s, 1H, H-12), 9.96 (bs, 1H, $NH_{imidazole}$ exchangeable with D_2O). Mass spectrum (*m/z*, *I* %): 406 (7), 365 (16), 339 (28), 323 (22), 284 (38), 251 (35), 228 (22), 201 (28), 185 (80), 145 (34), 130 (32), 113 (40), 77 (100). Anal. Calcd for $C_{25}H_{18}N_4O_2$ (406.45): C, 73.88; H, 4.46; N, 13.78%. Found: C, 73.65; H, 4.30; N, 13.52%.

3,3,10,14-Tetramethyl-2,4-dihydrochromeno[2,3-*b*]benzo[*g*]quinoline-1,12-(2*H*,12*H*)-dione (22)

A mixture of compound **2** (0.53 g, 2 mmol) and dimedone (5,5-dimethylcyclohexane-1,3-dione) (0.28 g, 2 mmol), in absolute EtOH (20 mL) containing sodium ethoxide solution (prepared by dissolving 0.5 g sodium in 10 mL absolute EtOH), was heated under reflux for 2 h. After cooling, the reaction mixture was neutralized by conc. HCl. The solid obtained was filtered and crystallized from DMF/H_2O to give compound **22** as yellow crystals, mp > 300 ^oC, yield 0.44 g (59%). IR (KBr, cm^{-1}): 2951, 2924, 2854 ($CH_{aliph.}$), 1682 ($C=O_{ketone}$), 1668 ($C=O_{\gamma\text{-pyrone}}$), 1617 (C=N), 1590 (C=N). ^1H NMR (DMSO-d_6, δ, 300 MHz): 1.37 (s, 3H, CH_3), 1.39 (s, 3H, CH_3), 1.89 (s, 3H, CH_3), 2.31 (s, 3H, CH_3), 2.67 (s, 2H, CH_2), 2.73 (s, 2H, CH_2), 7.62 (d, 1H, *J* = 8.4 Hz, H-8), 7.73 (d, 1H, *J* = 8.0 Hz, H-9), 7.92 (s, 1H, H-5), 7.96 (s, 1H, H-11), 8.92 (s,1H, H-13). ^{13}C NMR (DMSO-d_6, δ, 75 MHz): 20.7, 22.6, 25.3, 25.5, 26.6, 29.9, 44.1, 97.4, 101.6, 101.9, 102.7, 112.5, 113.8, 118.8, 121.7, 125.7, 130.7, 135.3, 137.7, 138.7, 153.7, 164.4, 172.8, 176.7. Mass spectrum (*m/z*, *I*%): 371 (4), 356 (4), 335 (3), 298 (3), 292 (6), 268 (5), 267 (11), 252 (13), 235 (8), 224 (14), 197 (15), 163 (26), 142 (8), 133 (9), 118 (39), 103 (31), 91 (26), 77 (100), 64 (19). Anal. Calcd for $C_{24}H_{21}NO_3$ (371.44): C, 77.61; H, 5.70; N, 3.77%. Found: C, 77.58; H, 5.45; N, 3.50%.

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