ISSN: 0975-8585

Research Journal of Pharmaceutical, Biological and Chemical Sciences

Synthesis and Characterization of Some Fluorinated Chromenes, Chromeno[3,4-*c*]pyridines, Chromeno[3,4-c][1,8]naphthyridine Derivatives.

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ABSTRACT

The reaction of cyanoacetamide derivatives **1a,b** with salicylaldehyde, and 2-hydroxy-1-naphthaldehyde in ethanolic ammonium acetate afforded 2-iminochromene derivatives **3** and **4**. Chromeno[3,4-*c*]pyridine derivatives **5** and **6** were obtained by refluxing of chromene **3** and benzochromenes **4** with malononitrile. In a similar manner, condensation of compounds **3b,4b** with ethyl cyanoacetate in dioxane under reflux in the presence of piperidine furnished chromeno[3,4-*c*]pyridines **8** and benzochromeno[3,4-*c*]pyridine **9**. Refluxing of chromene derivative **3b** with malononitrile dimer in dioxane in the presence of catalytic amount of triethylamine produced chromeno[3,4-c][1,8]naphthyridine-2-carbonitrile derivative **13**. The structures of the titled compounds cited in this article were elucidated by spectroscopic data (IR, ^{1}HNMR, ^{13}CNMR spectra).

Keywords: Fluorinated Chromenes; Michael reaction, chromeno[3,4-c]pyridines, chromeno[3,4-c][1,8]naphthyridine.

https://doi.org/10.33887/rjpbcs/2021.12.1.7

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ISSN: 0975-8585

INTRODUCTION

The chromene moiety appears as an important structural component in both biologically active and natural compounds [1]. Functionalized chromones have been played increasing roles in synthetic approaches to promising compounds in the field of medicinal chemistry [2-4]. Recently, structures containing the chromene and pyridine skeleton are rapidly gaining importance in synthetic and natural product chemistry. Chromenopyridine derivatives have been found to possess wide spectrum pharmacological activities, including antibacterial [5], anti-inflammatory [6], antimicrobial [7,8], anti-proliferative [9], hypotensive [10], anti-histaminic [11], antirheumatic [12], anti-asthmatic [13] and anticancer [14] activities. Fused chromenes such as chromeno[3,4-c]pyridines are found in several natural products and pharmaceutically active molecules. For example, schumanniophytine (A) and isoschumanniophytine (B) exhibit central and autonomic system depressant properties and potential antiviral activity [15,16]; chromeno[3,4-c]pyridine (C) is a selective D4 receptor antagonist and Potential Antipsychotic agents [17] (Figure 1). In addition, chromeno[3,4-c]pyridines display anti-inflammatory, antibacterial, antifungal [18] and antitubercular [19] activities.

Further, incorporation of the lipophilic trifluoromethyl groups on chromene ring exerts a variety of dramatic effects on the pharmacological properties of the molecule making its partition into cell membranes much easier and hence increasing the selectivity, efficacy and bioavailability [20]. In view of the above mentioned benefits and in continuation of our previous work directed towards the synthesis of biologically active heterocycles cyanoacetamides [21-27], we report herein the synthesis of versatile hitherto unknown chromenes, chromeno[3,4-c]pyridine, benzo[f]chromeno[3,4-c]-pyridine, chromeno[3,4-c][1,8]naphthyridine, derivatives utilizing inexpensive cyanoacetamide intermediates **1a,b** [28,29] as starting material.

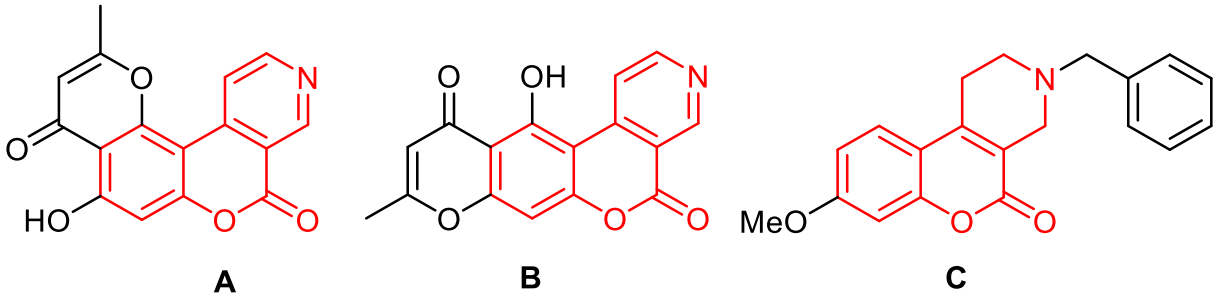
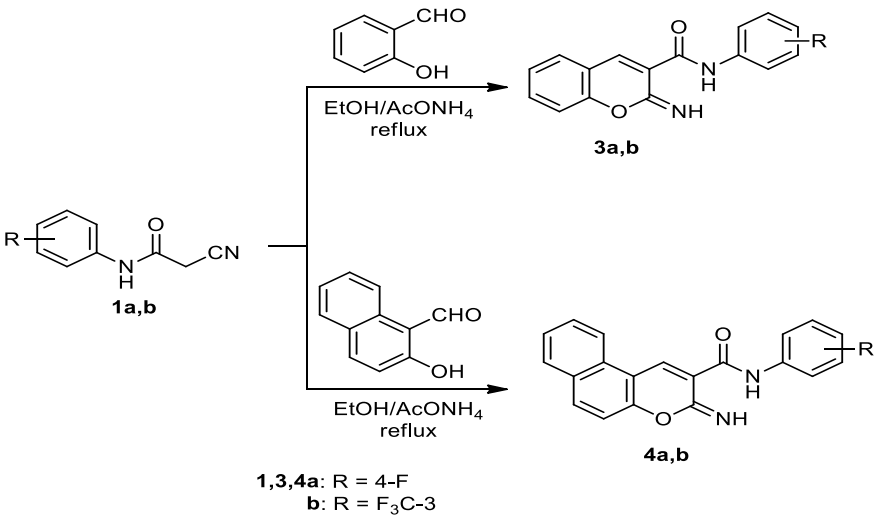


Figure 1: Natural products and bioactive molecules contain chromeno[3,4-c]pyridine core

RESULTS AND DISCUSSION

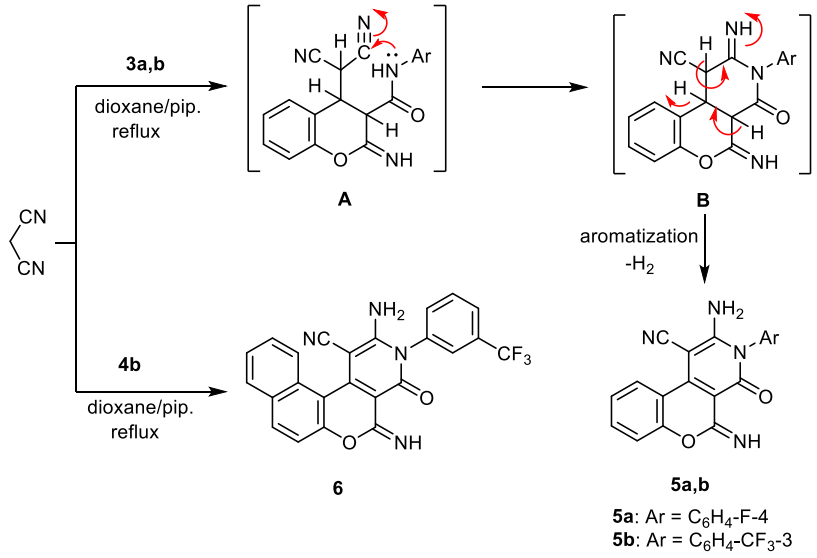
Refluxing of cyanoacetamide derivatives **1a,b** with salicylaldehyde in ethanol in the presence of a catalytic amount of ammonium acetate resulted in the formation of 2-iminochromenes **3a,b** [26]. In a similar manner, the cyclocondensation reaction of **1a,b** with 2-hydroxy-1-naphthaldehyde afforded 2-iminobenzo[f]-chromenes **4a,b**, Scheme 1. The molecular structure of **4a,b** was established through analytical and spectral data. The infrared spectrum of compounds **4a,b** showed the absence of absorption band of carbonitrile group. Evidence of the structure of compounds **4a,b** included the infrared spectrum which revealed a strong absorption bands at 3239, 3224 cm^{-1}, respectively for the NH group and the absence of the characteristic absorption band of the carbonitrile group. The ^{1}HNMR spectrum (DMSO-d_6) of **4a** revealed three singlet signals at δ 9.15, 9.24 and 12.85 ppm for chromene-H4, and two NH protons, respectively. The aromatic protons were found in the spectrum at δ 7.19-8.46 ppm, while its ^{13}CNMR (DMSO-d_6) showed signals at δ 159.65, 159.25, 157.33, 155.68, 153.26, 136.56, 134.54, 134.324, 129.58, 129.10, 128.74, 128.56, 125.67, 121.57, 121.32, 119.06, 115.50, 115.32, 111.81 ppm. Furthermore, ^{1}HNMR spectrum (DMSO-d_6) of **4b** exhibited signals at δ 9.16 ppm for chromene-H4, two singlets at 9.26, 13.10 for two NH, aromatic protons at 7.42-8.45 ppm.

ISSN: 0975-8585



Scheme 1

The chromene derivatives **3a,b** and benzochromene derivatives **4a,b** have encouraged us to study their reactivities as a synthons for construction of a novel chromeno[3,4-c]pyridine derivatives by treatment with different nucleophiles. Thus, treatment of chromene derivative **3a,b** with malononitrile in dioxane in the presence of a catalytic amount of piperidine gave the corresponding 2-amino-*4H*-chromeno[3,4-c]pyridine-1-carbonitrile derivatives **5a,b,** Scheme 2. In a similar manner, the reaction of benzo[f]chromene derivative **4b** with malononitrile under the same conditions gave 2-amino-5-imino-4-oxo-3-(3-(trifluoromethyl)phenyl)-3,5-dihydro-4H-benzo[5,6]chromeno[3,4-c]pyridine-1-carbonitrile **6,** Scheme 2. The reaction pathway turned to proceed via Michael addition of the active methylene group in malononitrile to the activated double bond of compounds **3** to give Michael adduct **A** followed by intramolecular cyclization through nucleophilic addition of the amino group to the cyano group and tautomerization to afford the 2-amino-4H-chromeno[3,4-c]pyridine-1-carbonitrile derivatives **5a,b**. The infrared spectrum of compound **5a** showed strong absorption bands for amino groups at 3442, 3336, 3235 cm^{-1}, carbonitrile at 2209 cm^{-1}, carbonyl group at 1687 cm^{-1} (C=O). The infrared spectrum of compound **6** exhibited absorption bands at 3440, 3349, 3238 cm^{-1} for amino groups, 2207 cm^{-1} for C≡N, 1682 cm^{-1} for C=O. The ^{1}HNMR spectrum (DMSO-d_6) of **5a** showed the presence of singlet at 6.67 ppm assigned to amino group, singlet at 9.10 ppm attributed to NH group and aromatic protons at 6.97-7.77 ppm. ^{1}HNMR spectrum (DMSO-d_6) of compound **5b** revealed signals at 7.32 ppm for amino group, singlet at 9.36 ppm for NH and aromatic protons at 7.66-9.20 ppm. ^{13}CNMR of compounds **5a,b** showed signals that are consistent with their structures (cf. Experimental part). The ^{1}HNMR spectrum (DMSO-d_6) of **6** indicates the presence of singlet at 6.98 ppm assigned to amino protons, singlet at 8.94 ppm assigned to NH proton and aromatic protons at 7.08-7.97 ppm.



Scheme 2

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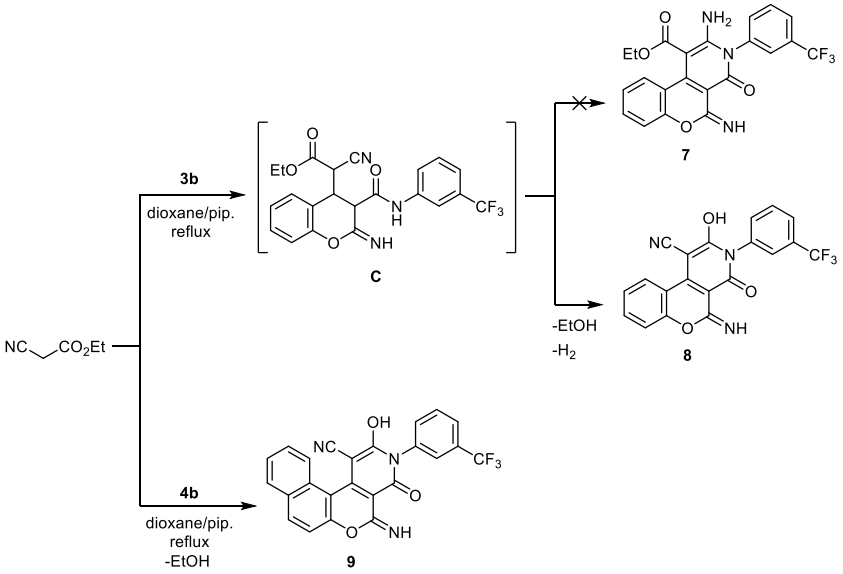
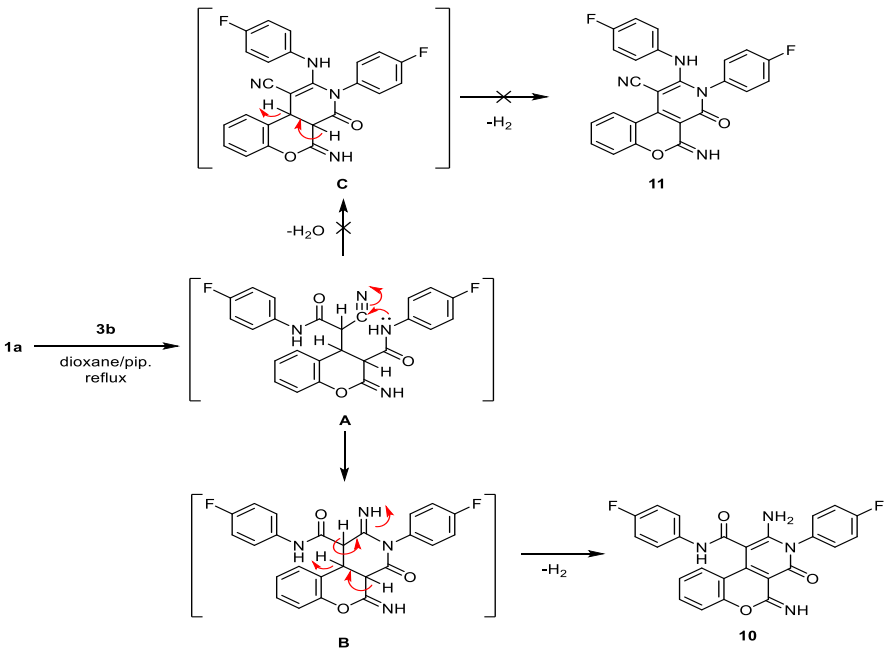
The reaction of compound **3b** with ethyl cyanoacetate in refluxing dioxane in the presence of piperidine as a catalyst afforded chromeno[3,4-c]pyridine derivative **8**, and the other possible structure **7** was eliminated on the basis of analytical and spectral data. Similarly, reaction of compound **4b** with ethyl cyanoacetate under the same conditions, gave 4H-benzo[5,6]chromeno[3,4-c]pyridine **9**, Scheme 3. The infrared spectrum of compounds **8** exhibited bands at 3321, 3308 (OH/NH), 2212 (C≡N) and 1718 cm^{-1} (C=O). Also, infrared spectrum of compound **9** showed absorption bands at 3373, 3324 (OH/NH), 2216 (C≡N), 1733 cm^{-1} (C=O). The ^{1}H NMR spectrum (DMSO-d_6) of **8** showed two singlet signals at δ 9.12, 12.34 ppm for imino and hydroxy groups, respectively together with aromatic protons at 7.36-8.32 ppm. ^{13}CNMR of compound **8** revealed signals at 164.25, 162.18, 156.35, 154.81, 152.49, 140.22, 134.63, 130.41, 129.58, 129.12, 128.71, 126.26, 121.55, 115.89, 112.87, 70.45 ppm. The ^{1}H NMR and ^{13}CNMR spectra of compound **9** were in complete agreement with its proposed structure (cf. Experimental part). The formation of compound **8** was assumed to proceed *via* Michael addition of the active methylene group in ethyl cyanoacetate to the activated double bond of compound **3b** to give Michael adduct **C** followed by intramolecular cyclization through nucleophilic addition of the amino group to the ethyl ester group followed by loss of ethanol molecule then tautomerization and oxidation, Scheme 3.



Scheme 3

Also, thre reaction of cyanoacetamide derivative **1a** with 2-iminochromene derivative **3b** in boiling ethanol containing piperidine as a catalyst afforded chromeno[3,4-c]pyridine derivative of type **10,** and the other possible structure **11** was excluded according to the elemental and spectra data, Scheme 4. The infrared spectrum of the reaction product revealed the absence of absorption band of carbonitrile functional group and showed absorption bands at 3410, 3235, 3185 cm^{-1} for amino/imino functional groups and 1686 cm^{-1} for carbonyl group. ^{1}HNMR spectrum of compound **10** showed three singlet signals at δ 7.19, 9.45, 10.85 ppm corresponding to amino and two NH groups, respectively. The aromatic protons were found in the spectrum at δ 7.62-8.62 ppm. The reaction pathway turned to proceed *via* Michael addition of the active methylene group in compound **1a** to the activated double bond of compound **3b** to give Michael adduct **A** followed by intramolecular cyclization through nucleophilic addition of the amino group to the cyano group to give the cyclic adduct **B** followed by tautomerization and oxidation to afford **10**. The second route of the mechanism that involves the elimination of water molecule from Michael adduct **A** was not formed, since the absorption band of carbonitrile group was not observed infrared spectrum of compound **11**.

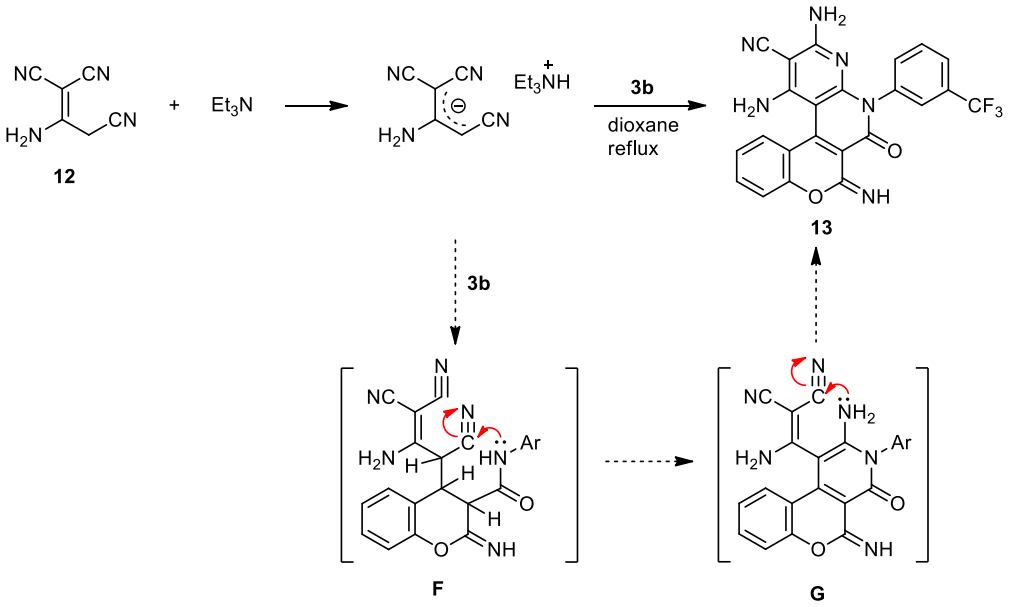
ISSN: 0975-8585



Scheme 4

Treatment of compound **3b** with malononitrile dimer (2-aminoprop-1-ene-1,1,3-tricarbonitrile) **12** in refluxing dioxane in the presence of triethylamine as a catalyst resulted in the formation of chromeno[3,4-c][1,8]naphthyridine-2-carbonitrile derivative **13**, Scheme 5. The infrared spectrum showed absorption bands for amino groups at 3438, 3318, 3251, 3182 cm^{-1}, carbonitrile at 2206 cm^{-1}, carbonyl group at 1681 cm^{-1}. Its ^1H NMR (DMSO-d_6) revealed two singlet signals at δ 6.52 ppm and 7.23 ppm assigned to two amino groups, singlet at 8.95 ppm assigned to NH, the aromatic protons in the spectrum were found at 7.49-8.99 ppm.

The first step of the reaction is thought to involve the formation of the Michael adduct **F**, which undergoes intramolecular heterocyclization to give non-isolable chromenopyridine derivative **G** followed by intramolecular cyclization via intramolecular nucleophilic addition of the amino group to the cyano group to afford **13.**



Scheme 5

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EXPERIMENTAL

General methods

Melting points were determined on a Stuart melting point apparatus and are uncorrected; IR spectra were recorded in KBr on a Shimadzu 440 spectrometer (ν, cm^{-1}). NMR spectra were recorded at 25ºC on a JEOL ECA-500 spectrometer. The chemical shifts were recorded in ppm relative to tetramethylsilane (TMS) and with the solvent resonance as the internal standard. ^{1}H, ^{13}C NMR data are reported as follows: chemical shift, multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, quint = quintet, m = multiplet, br = broad). The elemental analyses were performed at the Microanalytical Center, Cairo University, Cairo (Egypt). The compounds **1a,b** and **3a,b** were prepared according to the previous literature [26].

Preparation of 2-Iminochromene derivatives (3a,b and 4a,b): General procedure: A mixture of cyanoacetamide derivative **1a,b** (0.01 mol) and the requisite salicyaldehyde derivative (0.01 mol), ammonium acetate (2 g) was refluxed in ethanol (30 ml) for 3h. The resulting solid that obtained on hot was filtered off and recrystallized from dioxane to give **3a,b** and **4a,b**.

N-(4-Fluorophenyl)-3-imino-3H-benzo[f]chromene-2-carboxamide (**4a**).

Yellow crystals: Yield 75%, mp 283-285°C; IR (KBr, cm^{-1}): 3239 (NH), 1675 (C=O); ^{1}H NMR (500 MHz, DMSO-d_6, δ/ppm): 7.19-7.23 (t, 2H, Ar-H), 7.43-7.45 (d, 1H, Ar-H), 7.57-7.60 (d, 1H, Ar-H), 7.70-7.74 (d, 3H, Ar-H), 8.01-8.02 (d, 1H, Ar-H), 8.17-8.18 (d, 1H, Ar-H), 8.44-8.46 (d, 1H, Ar-H), 9.15 (s, 1H, chromene-H4), 9.24, 12.85 (2s, 2H, 2NH); ^{13}C NMR (125 MHz, DMSO-d_6): δ 159.65, 159.25, 157.33, 155.68, 153.26, 136.56, 134.54, 134.324, 129.58, 129.10, 128.74, 128.56, 125.67, 121.57, 121.32, 119.06, 115.50, 115.32, 111.81. Anal. calcd for $C_{20}H_{13}FN_2O_2$: C, 72.28; H, 3.94; N, 8.43; found: C, 72.10; H, 3.77; N, 8.36.

3-Imino-N-(3-(trifluoromethyl)phenyl)-3H-benzo[f]chromene-2-carboxamide (**4b**).

Yellow crystals: Yield 81%, mp 256-58°C; IR (KBr, cm^{-1}): 3224 (NH), 1683 (C=O); ^{1}H NMR (500 MHz, DMSO-d_6, δ/ppm): 7.42-7.47 (t, 2H, Ar-H), 7.58-7.66 (d, 1H, Ar-H), 7.73-7.79 (d, 3H, Ar-H), 7.99-8.01 (t, 1H, Ar-H), 8.16-8.18 (d, 1H, Ar-H), 8.26 (s, 1H, Ar-H), 8.43-8.45 (d, 1H, Ar-H), 9.16 (s, 1H, chromene-H4), 9.26, 13.10 (2s, 2H, 2NH); ^{13}C NMR (125 MHz, DMSO-d_6): δ 159.67, 159.35, 157.45, 155.73, 153.51, 141.61, 134.63, 133.29, 130.14, 124.22, 121.45, 121.39, 120.03, 118.47, 115.76, 115.58, 115.22, 114.97. Anal. Calcd. for $C_{21}H_{13}F_3N_2O_2$: C, 65.97; H, 3.43; N, 7.33; Found: C, 65.88; H, 3.32; N, 7.25.

Synthesis of chromeno[3,4-c]pyridine derivatives 5a,b and 6a:

General procedure: A mixture of chromene derivatives **3a,b** or **4a,b** (0.01 mol), and malononitrile (0.01 mol), piperidine (0.5 ml) in dioxane (30 mL) was heated under reflux for 4-8 hours, The resulting solid that obtained on hot was filtered off and recrystallized from dioxane/DMF to give **5a,b** and **6a**, respectively.

2-Amino-3-(4-fluorophenyl)-5-imino-4-oxo-3,5-dihydro-4H-chromeno[3,4-c]pyridine-1-carbonitrile **5a**.

Yellow crystals: Yield 56%, mp 262-64°C; IR (KBr, cm^{-1}): 3442, 3336, 3235 (NH_2/NH), 2209 (C≡N), 1676 (C=O); ^{1}H NMR (500 MHz, DMSO-d_6, δ/ppm): 6.67 (s, 2H, NH_2), 6.97-7.08 (d, 1H, Ar-H), 7.12-7.15 (t, 2H, Ar-H), 7.26-7.29 (d, 1H, Ar-H), 7.35-7.38 (d, 1H, Ar-H), 7.44-7.50 (d, 1H, Ar-H), 7.70-7.73 (dd, 2H, Ar-H), 9.10 (s, 1H, NH); ^{13}C NMR (125 MHz, DMSO-d_6): δ 162.41, 162.28, 157.88, 157.53, 143.00, 135.68, 130.83, 128.55, 127.67, 126.59, 117.19, 116.47, 110.38, 99.58, 82.18, 75.13. Anal. calcd. for $C_{19}H_{11}FN_4O_2$: C, 65.90; H, 3.20; N, 16.18; found: C, 65.82; H, 3.12; N, 16.13.

2-Amino-5-imino-4-oxo-3-(3-(trifluoromethyl)phenyl)-3,5-dihydro-4H-chromeno[3,4-c]pyridine-1-carbonitrile **5b**.

Yellow crystals: Yield 70%, mp 275-77°C; IR (KBr, cm^{-1}): 3411, 3334, 3218 (NH_2/NH), 2216 (C≡N), 1711 (C=O); ^{1}H NMR (500 MHz, DMSO-d_6, δ/ppm): 7.32 (s, 2H, NH_2), 7.66-7.69 (t, 2H, Ar-H), 7.80-7.82 (t, 1H, Ar-H), 8.10-8.11 (d, 1H, Ar-H), 8.33-8.35 (d, 1H, Ar-H), 8.64-8.65 (d, 1H, Ar-H), 9.00-9.02 (s, 1H, Ar-H), 9.18-9.20 (d, 1H, Ar-H), 9.36 (s, 1H, NH); ^{13}C NMR (125 MHz, DMSO-d_6): δ 166.48, 161.54, 158.87, 158.18, 156.92, 154.12, 142.05,

135.67, 130.05, 129.08, 128.96, 126.72, 122.49, 119.73, 116.57, 116.44, 114.92, 112.00. Anal. calcd for $C_{20}H_{11}F_3N_4O_2$: C, 60.61; H, 2.80; N, 14.14; found: C, 60.52; H, 2.69; N, 14.05.

2-Amino-5-imino-4-oxo-3-(3-(trifluoromethyl)phenyl)-3,5-dihydro-4H-benzo[5,6]chromeno[3,4-c]pyridine-1-carbonitrile **6a**.

Yellow crystals: Yield 69%, mp 293-95°C; IR (KBr, cm^{-1}): 3440, 3349, 3238 (NH_2/NH), 2207 (C≡N), 1682 (C=O); ^{1}H NMR (500 MHz, DMSO-*d*$_6$, δ/ppm): 6.98 (s, 2H, NH_2), 7.08 (s, 1H, Ar-H), 7.14-7.18 (t, 2H, Ar-H), 7.27-7.30 (t, 1H, Ar-H), 7.38-7.40 (t, 1H, Ar-H), 7.42-7.44 (d, 1H, Ar-H), 7.49-7.51 (d, 1H, Ar-H), 7.72-7.74 (dd, 2H, Ar-H), 7.95-7.97 (d, 1H, Ar-H), 8.94 (s, 1H, NH). Anal. calcd for $C_{24}H_{13}F_3N_4O_2$: C, 64.58; H, 2.94; N, 12.55; found: C, 64.48; H, 2.86; N, 12.42.

2-Hydroxy-5-imino-4-oxo-3-(3-(trifluoromethyl)phenyl)-3,5-dihydro-4H-chromeno[3,4-c]pyridine-1-carbonitrile **8.**

A mixture of 2-iminochromene derivative **3b** (0.01 mol), ethyl cyanoacetate (0.01 mol), piperidine (0.5 ml) in dioxane (30 mL) was heated under reflux for 3hours, the resulting solid that obtained on hot was filtered off and recrystallized from dioxane to give **8**.

Brown crystals: Yield 72%, mp 253-55°C; IR (KBr, cm^{-1}): 3321, 3308 (OH/NH), 2212 (C≡N), 1718 (C=O); ^{1}H NMR (500 MHz, DMSO-*d*$_6$, δ/ppm): 7.36-7.38 (d, 1H, Ar-H), 7.42-7.44 (d, 1H, Ar-H), 7.63-7.66 (t, 1H, Ar-H), 7.77-7.79 (d, 1H, Ar-H), 7.85-7.88 (t, 2H, Ar-H), 8.06-8.08 (d, 1H, Ar-H), 8.32 (s, 1H, Ar-H), 9.12 (s, 1H, NH), 12.34 (s, 1H, OH); ^{13}C NMR (125 MHz, DMSO-*d*$_6$): δ 164.25, 162.18, 156.35, 154.81, 152.49, 140.22, 134.63, 130.41, 129.58, 129.12, 128.71, 126.26, 121.55, 115.89, 112.87, 70.45. Anal. Calcd. for $C_{20}H_{10}F_3N_3O_3$: C, 60.46; H, 2.54; N, 10.58. Found: C, 60.30; H, 2.35; N, 10.41.

2-Hydroxy-5-imino-4-oxo-3-(3-(trifluoromethyl)phenyl)-3,5-dihydro-4H-benzo-[5,6]chromeno[3,4-c]pyridine-1-carbonitrile **9.**

A mixture of benzo[f]chromene derivative **4b** (0.01 mol), ethyl cyanoacetate (0.01 mol), piperidine (0.5 ml) in dioxane (30 mL) was heated under reflux for 4hours, the resulting solid that obtained on hot was filtered off and recrystallized from dioxane to give **9**.

Brown crystals: Yield 68%, mp >300°C; IR (KBr, cm^{-1}): 3373, 3324 (OH/NH), 2216 (C≡N), 1733 (C=O); ^{1}H NMR (500 MHz, DMSO-*d*$_6$, δ/ppm): 7.54-7.49 (dd, 1H, Ar-H), 7.66-7.68 (t, 1H, Ar-H), 8.02-8.04 (d, 1H, Ar-H), 8.10-8.11 (d, 1H, Ar-H), 8.19-8.21 (d, 1H, Ar-H), 8.29 (s, 1H, Ar-H), 8.47-8.49 (d, 1H, Ar-H), 8.64-8.66 (d, 1H, Ar-H), 9.19 (s, 1H, NH), 9.26-9.29 (t, 2H, Ar-H), 13.13 (s, 1H, OH); ^{13}C NMR (125 MHz, DMSO-*d*$_6$): δ 166.63, 164.53, 157.28, 155.73, 153.81, 140.94, 135.12, 130.30, 130.04, 129.25, 129.05, 128.93, 126.61, 122.52, 121.68, 116.55, 112.18, 71.66. Anal. Calcd. for $C_{24}H_{12}F_3N_3O_3$: C, 64.43; H, 2.70; N, 9.39. Found: C, 64.31; H, 2.55; N, 9.26.

2-Amino-N,3-bis(4-fluorophenyl)-5-imino-4-oxo-3,5-dihydro-4H-chromeno-[3,4-c]pyridine-1-carboxamide (10). Yellow crystals: Yield 75%, mp 275-77°C; IR (KBr, cm^{-1}): 3410, 3235, 3185 (NH_2/NH), 1686 (C=O); ^{1}HNMR (500 MHz, DMSO-*d*$_6$, δ/ppm): 7.19-21 (s, 2H, NH_2), 7.62-7.63 (d, 2H, Ar-H), 7.65-7.68 (t, 2H, Ar-H), 7.78-7.80 (d, 2H, Ar-H), 8.08-8.10 (d, 2H, Ar-H), 8.35-8.37 (d, 2H, Ar-H), 8.60-8.62 (d, 2H, Ar-H), 9.45, 10.85 (2s, 2H, 2NH); ^{13}C NMR (125 MHz, DMSO-*d*$_6$): δ 164.75, 160.29, 159.72, 157.15, 154.95, 149.48, 137.12, 129.92, 129.35, 129.03, 128.71, 126.85, 122.49, 116.70, 115.00, 112.23, 100.70. Anal. Calcd. For $C_{25}H_{16}F_2N_4O_3$: C, 65.50; H, 3.52; N, 12.22. Found: C, 65.37; H, 3.41; N, 12.10.

1,3-Diamino-7-imino-6-oxo-5-(3-(trifluoromethyl)phenyl)-5,7-dihydro-6H-chromeno[3,4-c][1,8]naphthyridine-2-carbonitrile (13).

A mixture of chromene derivative **3b** (0.01 mol), 2-aminoprop-1-ene-1,1,3-tricarbonitrile, triethylamine (0.5 ml) in dioxane (30 mL) was heated under reflux for 4hours, the resulting solid that obtained on hot was filtered off and recrystallized from dioxane/DMF.

Brown crystals: Yield 66%, mp >300°C; IR (KBr, cm^{-1}): 3438, 3318, 3251, 3182 (NH_2/NH), 2206 (C≡N), 1681 (C=O); ^{1}H NMR (500 MHz, DMSO-*d*$_6$, δ/ppm): 6.52 (s, 2H, NH_2), 7.23 (s, 2H, NH_2), 7.49 (d, 1H, Ar-H), 7.51 (t, 1H,

Ar-H), 7.52 (d, 1H, Ar-H), 7.53 (d, 1H, Ar-H), 7.55 (d, 1H, Ar-H), 7.76 (t, 1H, Ar-H), 7.78 (d, 1H, Ar-H), 8.99 (s, 1H, Ar-H), 8.95 (s, 1H, NH). Anal. Calcd. for $C_{23}H_{13}F_3N_6O_2$: C, 59.74; H, 2.83; N, 18.18. Found: C, 59.55; H, 2.69; N, 18.07.

ACKNOWLEDGEMENT

The authors would like to express their deep gratitude's to the Northern Border University, Kingdom of Saudi Arabia for providing financial support of this research (project 2017-1-8-F-7413).

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