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Synthesis and characterization of new chromeno[2,3-*b*]pyridines via the Friedländer reactions of 8-allyl-2-amino-4-oxo-4*H*-chromene-3-carboxaldehyde

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ABSTRACT

New series of chromeno[2,3-*b*]pyridines, **2**-**8**, have been obtained from 1,8-diazabicyclo [5.4.0]undec-7-ene catalyzed Friedländer reaction of 8-allyl-2-aminochromone-3-carboxaldehyde (**1**) with some carbonyl compounds containing a reactive α-methyl or methylene group namely 2-acetylthiophene, 3-acetylpyridine, 4-chloroacetophenone, 4,6-diacetylresorcinol, acetylacetone, dibenzoyl methane and acetoacetanilide. Heteroannulated chromones, **13**-**16**, were prepared from Friedländer reaction of **1** with some cyclic α-methylene ketones namely 2-phenyliminothiazolidin-4-one, pyrazoline-3,5-dione, 5,5-dimethylcyclohexane-1,3-dione and thiobarbituric acid. Structures of the newly synthesized compounds have been established from elemental analysis and spectroscopic data.

1. Introduction

4-Oxo-4*H*-chromenes (chromones) are well known natural and synthetic products that possess diverse biological activities, namely anticancer [1-3], neuroprotective [4], HIV-inhibitory [5,6], antimicrobial [7,8], antioxidant [9], anti-inflammatory [10], and antibiotic [11]. Due to their abundance in plants and low mammalian toxicity, chromone derivatives are present in large amounts in the diets of humans [12]. Chromones bearing an allyl group at position 8 have special medicinal importance; 8-allyl-2-styrylchromones were used as inhibitors for the growth of tumors [13]. Also, the 8-allyl derivatives were used as precursors for the synthesis of the 8-acetic acid derivatives which exhibit anticancer properties [14-16]. Heteroannulated chromones showed significant biological activity including pharmacological [17], anti-inflammatory and antiplatelet activities [18]. In continuation with our interest in the chemistry of linear annulation of chromone rings [19,20], the present work describes the synthesis of some new heteroannulated chromones bearing an allyl group starting from 8-allyl-2-amino-4-oxo-4*H*-chromene-3-carboxaldehyde (**1**) [19] with some active methyl and methylene compounds in the presence of 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU) as a basic catalyst.

2. Experimental

2.1. Instrumentation

Melting points are uncorrected and were recorded in open capillary tubes on Stuart SMP3 melting point apparatus. Infrared spectra were recorded on FT-IR Bruker Vector 22 spectrophotometer using KBr wafer technique. ^{1}H-NMR and ^{13}C-NMR spectra (chemical shift in δ) were measured on Gemini spectrometer 200 MHz using DMSO-d_6 as solvent and TMS as an internal standard. Mass spectra were obtained using GCMS Qp 1000 ex Shimadzu instrument mass spectrometer (70 eV). Elemental microanalyses were performed on a Perkin–Elmer CHN-2400 analyzer.

2.2. 9-Allyl-2-(thien-2-yl)-5-oxo-5H-chromeno[2,3-b]pyridine (2)

A mixture of 8-allyl-2-amino-4-oxo-4*H*-chromene-3-carboxaldehyde (**1**) (0.458 g, 2 mmol) and 2-acetylthiophene (0.18 mL, 2 mmol), in absolute ethanol (20 mL) and DBU (0.1 mL) was refluxed for 30 min (Scheme 1). The solid obtained after cooling was filtered and recrystallized from ethanol to give **2** as yellow crystals, mp 231 °C, yield 0.35 g (55%). IR (KBr, cm^{-1}): 3071 ($CH_{arom.}$), 1663 ($C{=}O_{\gamma\text{-pyrone}}$), 1608 (C=N). ^{1}H NMR (DMSO, δ): 3.64 (d, 2H, *J* = 5.6 Hz, H-1'), 5.18-5.21 (m, 2H, H-3'), 6.05-6.10 (m, 1H, H-2'), 6.65-7.68 (5H, m, Ar-H), 8.14 (d, 1H, *J* = 7.6 Hz, H-6), 8.32 (d, 1H, *J* = 7.2 Hz, H-3), 8.64 (d, 1H, *J* = 7.2 Hz, H-4). Anal. Calcd for $C_{19}H_{13}NO_2S$ (319.38): C, 71.45; H, 4.10; N, 4.39; S, 10.04. Found C, 71.31; H, 3.94; N, 4.28; S, 10.01.

2.3. 9-Allyl-2-(pyridin-3-yl)-5-oxo-5H-chromeno[2,3-b] pyridine (3)

A mixture of **1** (0.458 g, 2 mmol) and 3-acetylpyridine (0.22 mL, 2 mmol), in absolute ethanol (20 mL) and DBU (0.1 mL), was refluxed for 30 min. The solid obtained during heating was filtered and recrystallized from DMF/EtOH to give **3** as yellow crystals, mp > 310 °C, yield 0.34 g (54%). IR (KBr, cm^{-1}): 3067 ($CH_{arom.}$), 1670 ($C{=}O_{\gamma\text{-pyrone}}$), 1600 (C=N). ^{1}H NMR (DMSO, δ): 3.56 (d, 2H, *J* = 6.6 Hz, H-1'), 5.28-5.34 (m, 2H, H-3'), 5.98-6.14

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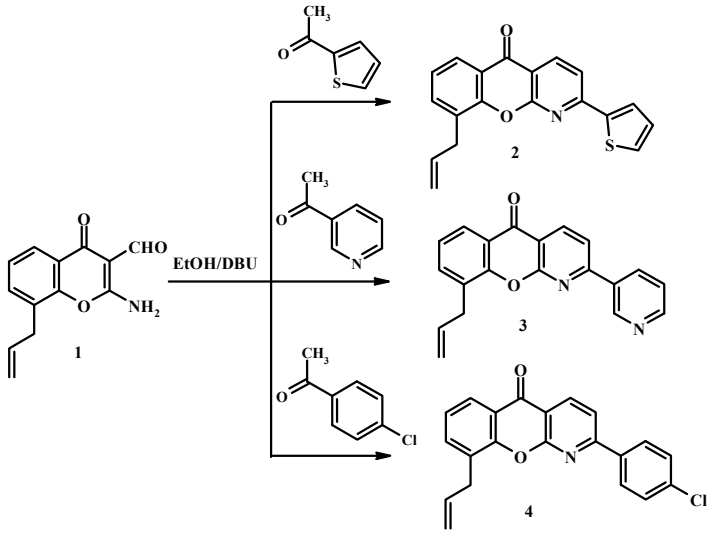


Scheme 1

(m, 1H, H-2'), 7.32-7.88 (m, 8H, Ar-H), 8.56 (d, 1H, *J* = 6.8 Hz, H-4). M/z (*I* %): 314 (100), 183 (25), 155 (48), 143 (7), 133 (18), 116 (9), 105 (13), 89 (8), 78 (81), 65 (35). Anal. Calcd for $C_{20}H_{14}N_2O_2$ (314.35): C, 76.42; H, 4.49; N, 8.91. Found C, 76.22; H, 4.31; N, 8.75.

2.4. 9-Allyl-2-(4-chlorophenyl)-5-oxo-5H-chromeno[2,3-b] pyridine (4)

A mixture of **1** (0.458 g, 2 mmol) and 4-chloroacetophenone (0.31 g, 2 mmol), in absolute ethanol (20 mL) and DBU (0.1 mL) was refluxed for 30 min. The solid obtained after cooling was filtered and recrystallized from DMF/H_2O to give **4** as yellow crystals, mp 280 °C, yield 0.39 g (56%). IR (KBr, cm^{-1}): 3053 ($CH_{arom.}$), 1666 ($C=O_{\gamma\text{-pyrone}}$), 1603 (C=N). ^{1}H NMR (DMSO, δ): 3.62 (d, 2H, *J* = 6.4 Hz, H-1'), 5.17-5.22 (m, 2H, H-3'), 6.10-6.21 (m, 1H, H-2'), 7.44 (d, 2H, *J* = 7.4, Ar-H), 7.52 (2H, d, *J* = 7.4, Ar-H), 7.61-7.82 (m, 2H, H-7 and H-8), 8.34 (d, 1H, *J* = 7.6 Hz, H-6), 8.54-8.69 (m, 2H, H-3 and H-4). Anal. Calcd for $C_{21}H_{14}ClNO_2$ (347.80): C, 72.52; H, 4.06; N, 4.03. Found C, 72.46; H, 4.02; N, 4.00.

2.5. 2-(5-Acetyl-2,4-dihydroxyphenyl)-9-allyl-5-oxo-5H-chromeno[2,3-b]pyridine (5)

A mixture of **1** (0.458 g, 2 mmol) and 4,6-diacetylresorcinol (0.388 g, 2 mmol), in absolute ethanol (20 mL) and DBU (0.1 mL), was refluxed for 1 h (Scheme 2). The solid obtained after cooling was filtered and recrystallized from DMF/H_2O to give **5**, mp 287 °C, yield 0.37 g (48%). IR (KBr, cm^{-1}): 3415 (2OH), 3071 ($CH_{arom.}$), 2941, 2874 (CH_3), 1682 ($C=O_{acetyl}$), 1660 ($C=O_{\gamma\text{-pyrone}}$), 1603 (C=N). ^{1}H NMR (DMSO, δ): 2.72 (s, 3H, CH_3), 3.58 (d, 2H, *J* = 6.4 Hz, H-1'), 5.04-5.08 (m, 2H, H-3'), 6.14-6.21 (m, 1H, H-2'), 6.41 (s, 1H, $H\text{-}2_{resorcinol}$), 7.28 (s, 1H, $H\text{-}5_{resorcinol}$), 7.46 (t, 1H, *J* = 6.8 Hz, H-7), 7.61 (d, 1H, *J* = 6.6, H-8), 8.32 (d, 1H, *J* = 7.4, H-6), 8.50 (d, 1H, *J* = 7.2, H-3), 8.87 (d, 1H, *J* = 7.2, H-4), 12.15 (bs, 2H, 2 OH exchangeable with D_2O). Anal. Calcd for $C_{23}H_{17}NO_5$ (387.40): C, 71.31; H, 4.42; N, 3.62. Found C, 71.18; H, 4.26; N, 3.55.

2.6. 4,6-Bis(9-allyl-5-oxo-5H-chromeno[2,3-b]pyridin-2-yl)resorcinol (6)

***Method A*:** A mixture of **1** (0.916 g, 4 mmol) and 4,6-diacetylresorcinol (0.388 g, 2 mmol), in absolute ethanol (30 mL) and DBU (0.2 mL) was refluxed for 1 h. The solid obtained during heating was filtered and crystallized from DMF to give **6** as yellow crystals, mp > 310 ºC, yield 0.48 g (41%).

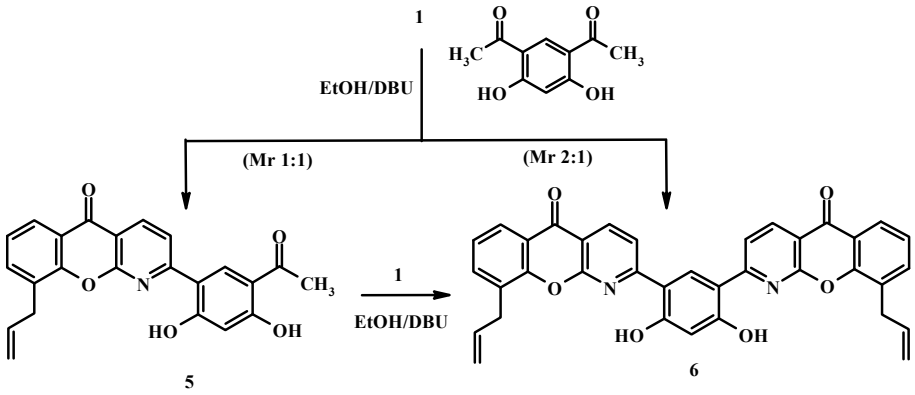
***Method B*:** A mixture of compound **5** (0.387 g, 1 mmol) and carboxaldehyde **1** (0.229 g, 1 mmol), in absolute ethanol (20 mL) and DBU (0.1 mL), was refluxed for 1 h. The solid obtained during heating was filtered and crystallized from DMF to give **6**, mp > 310 °C, yield 0.25 g (43%). IR (KBr, cm^{-1}): 3420 (2 OH), 3038 ($CH_{arom.}$), 1666 ($C=O_{\gamma\text{-pyrone}}$), 1609 (C=N). ^{1}H NMR (DMSO, δ): 3.58-3.67 (m, 4H, H-1'), 5.11-5.28 (4H, m, H-3'), 6.04-6.23 (2H, m, H-2'), 6.26 (s, 1H, $H\text{-}2_{resorcinol}$), 7.38 (s, 1H, $H\text{-}5_{resorcinol}$), 7.62-7.85 (m, 4H, Ar-H), 8.31-8.74 (6H, m, Ar-H), 10.25 (bs, 2H, 2 OH exchangeable with D_2O). M/z (*I* %): 580 (43), 237 (20), 208 (35), 133 (17), 116 (15), 109 (62), 93 (23), 77 (100), 64 (32). Anal. Calcd for $C_{36}H_{24}N_2O_6$ (580.60): C, 74.47; H, 4.17; N, 4.82. Found C, 74.24; H, 4.05; N, 4.68.

2.7. 3-Acetyl-9-allyl-2-methyl-5-oxo-5H-chromeno[2,3-b]pyridines (7a)

A mixture of **1** (0.458 g, 2 mmol) and acetylacetone (0.2 mL, 2 mmol), in absolute ethanol (20 mL) and DBU (0.1 mL), was refluxed for 30 min. The solid obtained after cooling was filtered and crystallized from ethanol to give **7a** as yellow crystals, mp 192 °C, yield 0.41 g (70%). IR (KBr, cm^{-1}): 3045 ($CH_{arom.}$), 1710 ($C=O_{acetyl}$), 1663 ($C=O_{\gamma\text{-pyrone}}$), 1602 (C=N). ^{1}H NMR (DMSO, δ): 2.38 (s, 3H, CH_3) 3.2 (s, 3H, CH_3) 3.60 (d, 2H, *J* = 6.0 Hz, H-1'), 5.07-5.10 (m, 2H, H-3'), 6.06-6.13 (m, 1H, H-2'), 7.32 (t, 1H, *J* = 6.8 Hz, H-7), 7.54 (d, 1H, *J* = 6.8 Hz, H-8), 8.23 (d, 1H, *J* = 7.4 Hz, H-6), 8.59 (s, 1H, H-4). ^{13}C NMR (DMSO, δ): 23.1 (CH_3), 29.5 (CH_3 as acetyl), 31.5 (C`$_1$), 114.6 (C`$_3$), 115.4 (C_{4a}), 118.3 (C_7), 125.1 (C_6), 125.6 (C_{5a}), 127.3 (C_9), 131.6 (C_3) 132.9 (C_8), 135.4 (C`$_2$), 139.2 (C_4), 151.2 (C_{9a}), 152.8 (C_{10a}), 167.7 (C_2), 185.0 (C=O as γ-pyrone), 194.2 (C=O as acetyl). Anal. Calcd for $C_{18}H_{15}NO_3$ (293.33): C, 73.71; H, 5.15; N, 4.78. Found C, 73.60; H, 4.96; N, 4.56.

2.8. 9-Allyl-3-benzoyl-2-methyl-5-oxo-5H-chromeno[2,3-b]pyridines (7b)

A mixture of **1** (0.458 g, 2 mmol) and dibenzoylmethane (0.45 g, 2 mmol), in absolute ethanol (20 mL) and DBU (0.1 mL), was refluxed for 30 min. The solid obtained after cooling was filtered and crystallized from ethanol to give **7a** as yellow crystals, mp 206 °C, yield 0.53 g (63%). IR (KBr, cm^{-1}): 3074 ($CH_{arom.}$), 1716 ($C=O_{acetyl}$), 1658 ($C=O_{\gamma\text{-pyrone}}$), 1600 (C=N).



Scheme 2

^{1}H NMR (DMSO, δ): 3.64 (d, 2H, *J* = 5.6 Hz, H-1'), 5.06-5.14 (m, 2H, H-3'), 6.11-6.17 (m, 1H, H-2'), 7.20-7.91 (m, 12H, Ar-H), 8.22 (d, 1H, *J* = 7.6 Hz, H-6), 8.51 (s, 1H, H-4). Anal. Calcd for $C_{28}H_{19}NO_3$ (417.47): C, 80.56; H, 4.59; N, 3.36. Found C, 80.36; H, 4.37; N, 3.25.

2.9. 9-Allyl-2-methyl-5-oxo-N-phenyl-5H-chromeno[2,3-b]pyridine-3-carboxamide (8)

A mixture of **1** (0.458 g, 2 mmol) and acetoacetanilide (0.354 g, 2 mmol), in absolute ethanol (20 mL) and DBU (0.1 mL), was refluxed for 30 min. The yellow crystals obtained after cooling was filtered and recrystallized from ethanol to give **8** as pale yellow crystals, mp 252 °C, yield 0.36 g (48%). IR (KBr, cm^{-1}): 3270 (NH), 3036 ($CH_{arom.}$), 2942, 2855 (CH_3), 1675 ($C=O_{amide}$), 1652 ($C=O_{\gamma\text{-pyrone}}$), 1599 (C=N). ^{1}H NMR (DMSO, δ): 2.25 (s, 3H, CH_3), 3.61 (d, 2H, *J* = 5.8 Hz, H-1'), 5.11-5.18 (m, 2H, H-3'), 6.01-6.07 (m, 1H, H-2'), 7.25-7.84 (m, 7H, Ar-H), 8.18 (d, 1H, *J* = 7.4 Hz, H-6), 8.70 (s, 1H, H-4), 11.32 (bs, 1H, NH exchangeable with D_2O). M/z (*I* %): 370 (11), 278 (50), 250 (21), 222 (26), 143 (7), 133 (9), 116 (15), 92 (72), 77 (100), 65 (46). Anal. Calcd for $C_{23}H_{18}N_2O_3$ (370.41): C, 74.58; H, 4.90; N, 7.56. Found C, 74.52; H, 4.85; N, 7.49.

2.10. 9-Allyl-2-anilino-chromeno[2,3-b][1,3]thiazolo[5,4-e]pyridin-10-one (13)

A mixture of **1** (0.458 g, 3 mmol) and 2-phenylimino-1,3-thiazolidin-4-one (**9**) (0.384 g, 2 mmol), in absolute ethanol (20 mL) and DBU (0.1 mL), was refluxed for 30 min. The solid obtained during heating was filtered and recrystallized from DMF/EtOH to give **13** as pale brown crystals, mp > 310 °C, yield 0.38 g (49 %). IR (KBr, cm^{-1}): 3380 (NH), 3055 ($CH_{arom.}$), 1657 $C=O_{\gamma\text{-pyrone}}$), 1612 (C=N). ^{1}H NMR (DMSO, δ): 3.67 (2H, d, *J* = 6.3 Hz, H-1'), 5.10-5.15 (m, 2H, H-3'), 6.04-6.12 (m, 1H, H-2'), 7.39-8.14 (m, 8H, Ar-H), 8.38 (s, 1H, H-4), 9.54 (bs, 1H, NH exchangeable with D_2O). Anal. Calcd for $C_{22}H_{15}N_3O_2S$ (385.45): C, 68.56; H, 3.92; N, 10.90; S, 8.32. Found C, 68.42; H, 3.81; N, 10.79; S, 8.28.

2.11. 9-Allyl-3-hydroxy-chromeno[2,3-b]pyrazolo[4,3-e]pyridin-5(1H)-one (14)

A mixture of **1** (0.458 g, 2 mmol) and pyrazolidine-3,5-dione (**10**) (0.2 g, 2 mmol), in absolute ethanol (20 mL) and DBU (0.1 mL), was refluxed for 15 min. The yellow crystals obtained during heating was filtered and recrystallized from DMF/H_2O to give **14**, mp > 310 °C, yield 0.35 g (60%). IR (KBr, cm^{-1}): 3347 (OH), 3215 (NH), 3047 ($CH_{arom.}$), 1663 ($C=O_{\gamma\text{-pyrone}}$), 1604 (C=N). ^{1}H NMR (DMSO, δ): 3.62 (d, 2H, *J* = 6.0 Hz, H-1'), 5.07-5.10 (m, 2H, H-3'), 6.02-6.14 (m, 1H, H-2'), 7.53 (t, 1H, *J* = 7.2 Hz, H-7), 7.60 (d, 1H, *J* = 7.2 Hz, H-8), 8.21 (d, 1H, *J* = 7.4 Hz, H-6), 8.74 (s, 1H, H-4), 9.64 (s, 1H, NH exchangeable with D_2O), 12.42 (s, 1H, OH exchangeable with D_2O). Anal. Calcd for $C_{16}H_{11}N_3O_3$ (293.28): C, 65.53; H, 3.78; N, 14.33. Found C, 65.38; H, 3.74; N, 14.27.

2.12. 10-Allyl-2,2-dimethyl-1,3-dihydro-chromeno[2,3-b]quinoline-4,6(4H,6H)-dione (15)

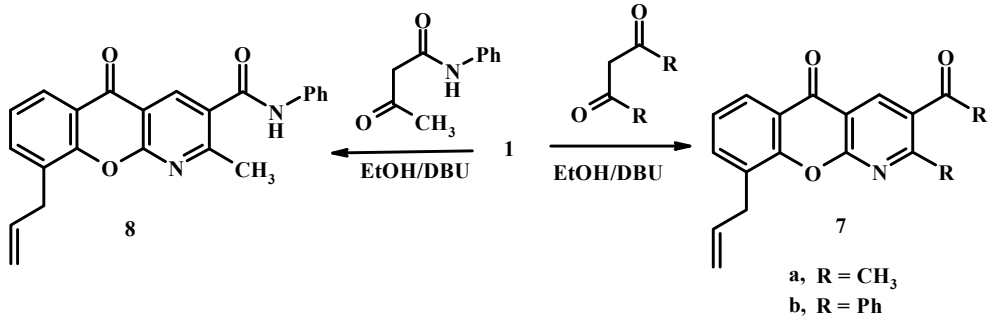
A mixture of **1** (0.458 g, 2 mmol) and 5,5-dimethyl-cyclohexane-1,3-dione (**11**) (0.28 g, 2 mmol), in absolute ethanol (20 mL) and DBU (0.1 mL), was refluxed for 15 min. The white crystals obtained after cooling was filtered and recrystallized from dioxane to give **15**, mp 216 °C, yield 0.41g (61%). IR (KBr, cm^{-1}): 3065 ($CH_{arom.}$), 2947, 2915 2885 (CH_2, CH_3), 1680 (C=O), 1660 ($C=O_{\gamma\text{-pyrone}}$), 1600 (C=N). ^{1}H NMR (DMSO, δ): 1.13 (s, 6H, 2 CH_3), 2.68 (s, 2H, CH_2), 3.12 (s, 2H, CH_2), 3.54 (d, 2H, *J* = 6.4 Hz, H-1'), 5.18-5.26 (m, 2H, H-3'), 6.08-6.19 (m, 1H, H-2'), 7.44-8.16 (m, 4H, Ar-H), 8.87 (s, 1H, H-5). M/z (*I* %): 333 (100), 305 (68), 264 (26), 209 (45), 132 (23), 116 (12), 77 (53), 65 (24). Anal. Calcd for $C_{21}H_{19}NO_3$ (333.39): C, 75.66; H, 5.74; N, 4.20. Found C, 75.42; H, 5.64; N, 4.04.

2.13. 10-Allyl-2-thioxo-chromeno[3`,2`:5,6]pyrido[2,3-d]pyrimidine-4,6(1H,3H)-dione (16)

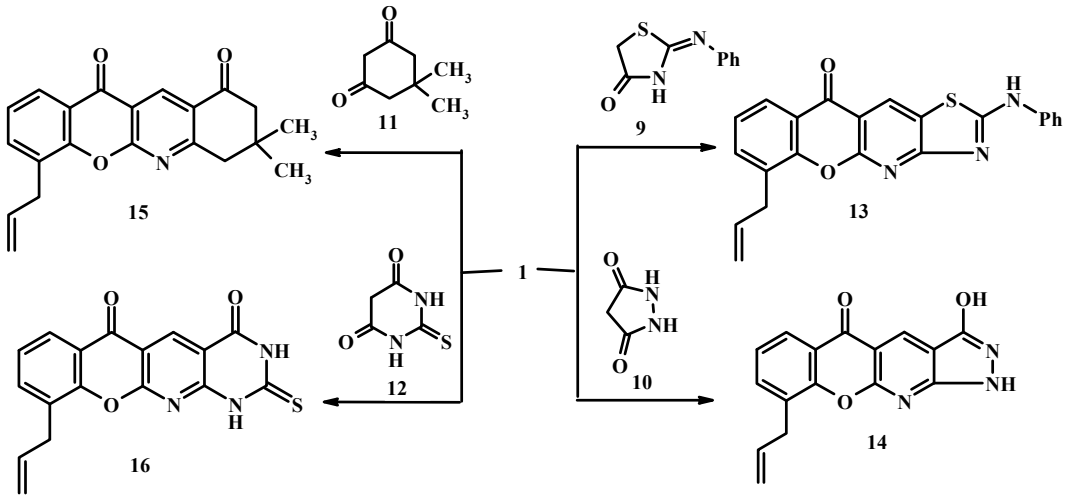
A mixture of **1** (0.458 g, 2 mmol) and thiobarbituric acid (**12**) (2 mmol), in absolute ethanol (20 mL) and DBU (0.1 mL), was refluxed for 15 min. The orange crystals obtained during heating was filtered and recrystallized from DMF to give **16** as orange crystals, mp > 310 °C, yield 0.44 g (65%). IR (KBr, cm^{-1}): 3310 (2 NH), 3081 ($CH_{arom.}$), 1682 (C=O), 1667 ($C=O_{\gamma\text{-pyrone}}$), 1613 (C=N). ^{1}H NMR (DMSO, δ): 3.61 (d, 2H, *J* = 5.6 Hz, H-1'), 5.16-5.21 (m, 2H, H-3'), 6.17-6.28 (m, 1H, H-2'), 7.46 (m, 1H, *J* = 7.2 Hz, H-8), 7.63 (d, 1H, *J* = 7.2 Hz, H-9), 8.18 (d, 1H, *J* = 7.2 Hz, H-7), 8.86 (s, 1H, H-5), 11.83 (bs, 2H, 2NH exchangeable with D_2O). ^{13}C NMR (DMSO, δ): 31.8 ($C`_1$), 105.9 ($C_{4a}$), 114.3 ($C`_3$), 109.8 (C_{5a}), 118.4 (C_8), 125.8 (C_{6a}), 126.8 (C_7), 127.1 (C_{10}), 132.4 (C_9), 136.1 ($C`_2$), 140.2 (C_5), 151.4 (C_{10a}), 162.5 (C=O as cyclic amide), 166.3 (C_{12a}), 167.6 (C_{11a}), 174.5 (C=O as thioxo), 185.3 (C=O as γ-pyrone). Anal. Calcd for $C_{17}H_{11}N_3O_3S$ (337.36): C, 60.53; H, 3.29; N, 12.46; S, 9.50. Found C, 60.51; H, 3.25; N, 12.38; S, 9.47.

3. Results and Discussion

Friedländer synthesis involves a condensation followed by cyclodehydration between an aromatic *ortho*-aminoaldehyde or ketone and an aldehyde or ketone bearing α-methylene functionality. Friedländer reaction is a well-known method for



Scheme 3



Scheme 4

the preparation of heteroannulated compounds [21-23], and we considered it to be the most useful method for the preparation of chromeno[2,3-*b*]pyridine derivatives. Thus, reaction of 8-allyl-2-aminochromone-3-carboxaldehyde (**1**) with 2-acetylthiophene, 3-acetylpyridine and 4-chloro acetophenone, in absolute ethanol containing few drops of 1,8-diazabicyclo [5.4.0]undec-7-ene (DBU) as a basic catalyst, afforded chromeno[2,3-*b*]pyridines **2-4**, respectively (Scheme 1). Formation of compounds **2-4** was accomplished *via* a tandem base catalyzed condensation reaction of the active methyl group with the carboxaldehyde group giving rise to 3-vinyl-2-aminochromone intermediates (non-isolable) which undergo cyclo-dehydration to furnish chromeno[2,3-*b*]pyridi nes, **2-4**.

Also, Friedländer condensation of *ortho*-amino carboxaldehyde **1** with 4,6-diacetylresorcinol [24] was studied in different molar ratio. Thus, treatment of **1** with 4,6-diacetyl resorcinol in 1:1 and 2:1 molar ratio gave chromeno[2,3-*b*]pyridines **5** and **6**, respectively. *Bis*(chromenopyridin-2-yl)resorcinol **6** was also obtained authentically from the interaction of **5** with compound **1** under the same Friedländer condition (Scheme 2). The IR spectrum of compound **5** showed characteristic absorption bands at 1682 ($C=O_{acetyl}$) and 1660 ($C=O_{\gamma\text{-pyrone}}$), while its ^{1}H NMR spectrum showed characteristic singlet signals for H-$2_{resorcinol}$, H-$5_{resorcinol}$ at δ 6.41 and 7.28 ppm, respectively. The mass spectrum of compound **6** revealed the molecular ion peak at m/z 580, which is coincident with the formula weight (580.60) and supports the identity of the structure.

On the other hand, Friedländer condensation of **1** with active methylene compounds containing (–CH_2CO–) moiety was studied. Thus, Treatment of **1** with acetylacetone and/or dibenzoylmethane in boiling ethanol containing DBU gave 5-oxo-5*H*-chromeno[2,3-*b*]pyridines **7a** and **7b**, respectively (Scheme 3). The ^{1}H NMR spectra of compounds **7a** and **7b** showed characteristic singlet signals for the H-4 protons at δ 8.59 and 8.51 ppm, respectively. In addition, the ^{13}C NMR spectrum of compound **7a** revealed the presence of two characteristic signals at δ 185.0 (C=O as γ-pyrone) and 194.2 ppm (C=O as acetyl).

In Friedländer reactions with unsymmetrical ketones such as acetoacetanilide, two modes of cyclization should be theoretically possible, depending on whether α-methyl or α-methylene group undergoes condensation with the aldehyde group of compound **1** [25]. Herein, DBU catalyzed condensation of acetoacetanilide with compound **1** yielded only 9-allyl-2-methyl-5-oxo-*N*-phenyl-5*H*-chromeno[2,3-*b*]pyridine-3-carbox amide (**8**) (Scheme 3). This conclusion was based upon the ^{1}H NMR spectrum of compound **8** and in particular the two singlet signals at δ 2.25 and 8.70 ppm assigned to CH_3 and H-4 protons, respectively.

Cyclic α-methylene ketones and cyclic 1,3-diketones also undergo smooth and efficient Friedländer reaction for compound **1** yielding heteroannulated chromenes. Thus, reaction of **1** with 2-phenyliminothiazolidin-4-one (**9**), pyrazoline-3,5-dione (**10**), 5,5-dimethylcyclohexane-1,3-dione (**11**) and thiobarbituric acid (**12**) afforded a new series of tetracyclic systems **13-16**, respectively (Scheme 4). The novel polyfused systems **13-16** showed the pyridine ring protons as characteristic singlets in the region δ 8.38-8.87 ppm in their ^{1}H-NMR spectra. Also, ^{13}C NMR spectrum of compound **16** showed characteristic signals at δ 162.5, 174.5 and 185.3 ppm attributed to C=O as cyclic amide, C=O as thioxo and C=O as γ-pyrone, respectively. The mass spectrum of compound **15**

revealed the molecular ion peak at m/z 333, as the base peak, which is coincident with the formula weight (333.39) and supports the identity of the structure.

4. Conclusions

In conclusion, we have described a mild and efficient protocol for the synthesis of chromeno[2,3-*b*]pyridines and heteroannulated chromones *via* DBU catalyzed Friedländer condensation reactions of 8-allyl-2-aminochromone-3-carboxaldehyde with some α-methyl or α-methylene ketones.

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