CYCLIZATION OF 3-ETHOXYCARBONYLIMINOCOUMARIN INTO BENZOPYRANO[2,3-c]PYRAZOLES

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ABSTRACT: New rearrangements of 3-ethoxycarbonyl iminocoumarin into benzopyrano[2,3-c]pyrazole under the action of various hydrazines and hydrazides as *N*-nucleophiles, were described. The structures of all the synthesized products were characterized by IR, ^{1}H NMR, ^{13}C NMR and elemental analysis.

Keywords: Iminocoumarin; benzopyrano[2,3-c]pyrazole; hydrazide, hydrazine.

RESUME: De nouveaux réarrangements de la 3-éthoxycarbonyliminocoumarine sous l'action de *N*-nucléophiles tels que les hydrazines et les hydrazides ont été décrits. Toutes les structures obtenues ont été clairement établies par les techniques spectroscopiques RMN ^{1}H, RMN ^{13}C, IRTF et analyse élémentaire.

Mots clés: Iminocoumarine ; benzopyrano[2,3-c]pyrazole; hydrazide; hydrazine.

INTRODUCTION

Compounds containing pyrazole scaffold have been shown to exhibit a wide spectrum of biological activity, such as antihyperglycemic [1], antibacterial [2], anti-inflammatory [3-4], antipyretic [5-6] and analgesic [7] activity. In addition, several studies dealing with the varied biological activities of benzopyran derivatives have been reported. They described their antiallergic, anticoagulant, antidiabetic, antitumor, antibacterial, anti-inflammatory, anti-HIV therapy and analgesic activities [8-10].

A combination of a benzopyran with a pyrazole moiety may increase their biological activities or create new medicinal properties. For example, some benzopyrano[4,3-c] pyrazoles have been proposed as inhibitors of Eg5 kinesin. We have previously shown that these derivatives are potent and highly efficacious inhibitors of cellular hyperproliferation and/or cell-cycle specific inducers of apoptosis in cancer cells [11-12]. Therefore, these compounds can particularly be useful for treating (hyper) proliferative diseases and/or disorders responsive to the induction of apoptosis, notably cancer [13].

Since the first synthesis of the benzopyrano-pyrazole scaffold by Ghosh, [14] there are so far few studies about the synthesis of heterocyclic compounds containing both benzopyran and pyrazole moieties using condensation of chromenone-3-carboxylic acid with arylhydrazine or with hydrazine hydrate, followed by an alkylation reaction. [15] All these routes led to similar structures in which benzopyran and pyrazole groups are fused at the 3,4 positions. It was confirmed that the biological properties of these organic materials would depend not only on the presence of benzopyran and pyrazole moieties but also on their association mode.

In the context of our ongoing studies concerning the preparation of potential biologically active heterocycles, and in diversifying our work on the synthesis of new benzopyrano compounds,

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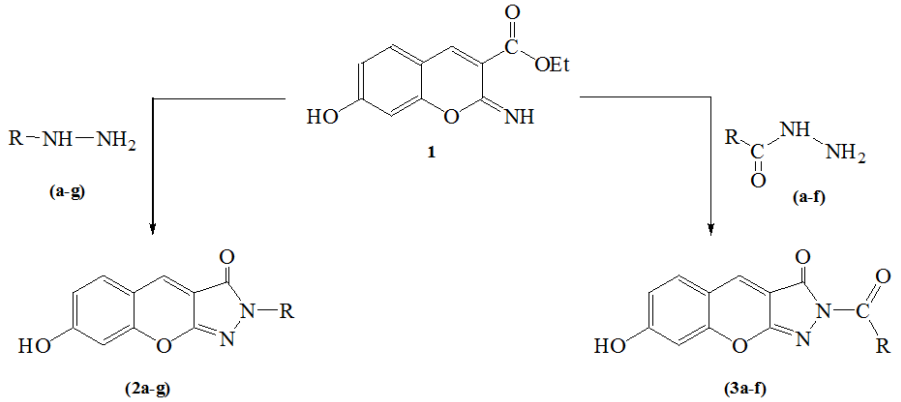
we wish to report herein a simple and efficient protocol for the synthesis of structurally novel benzopyrano-fused pyrazoles, namely 7-hydroxy 3-oxo-3H-benzopyrano[2,3-c]pyrazoles. The reaction is based on the condensation of hydrazines or hydrazides with 3-ethoxycarbonyl iminocoumarins under acidic conditions.

RESULTS AND DISCUSSION

In our first attempt, the treatment of compound **1** [16] with 4-methoxy phenylhydrazine **a** at room temperature in a mixture of chloroform/acetic acid (3:1 v/v) gave, after 6 hours, the corresponding benzopyranopyrazole **2a** in 85 % yield with high selectivity (Scheme 1).



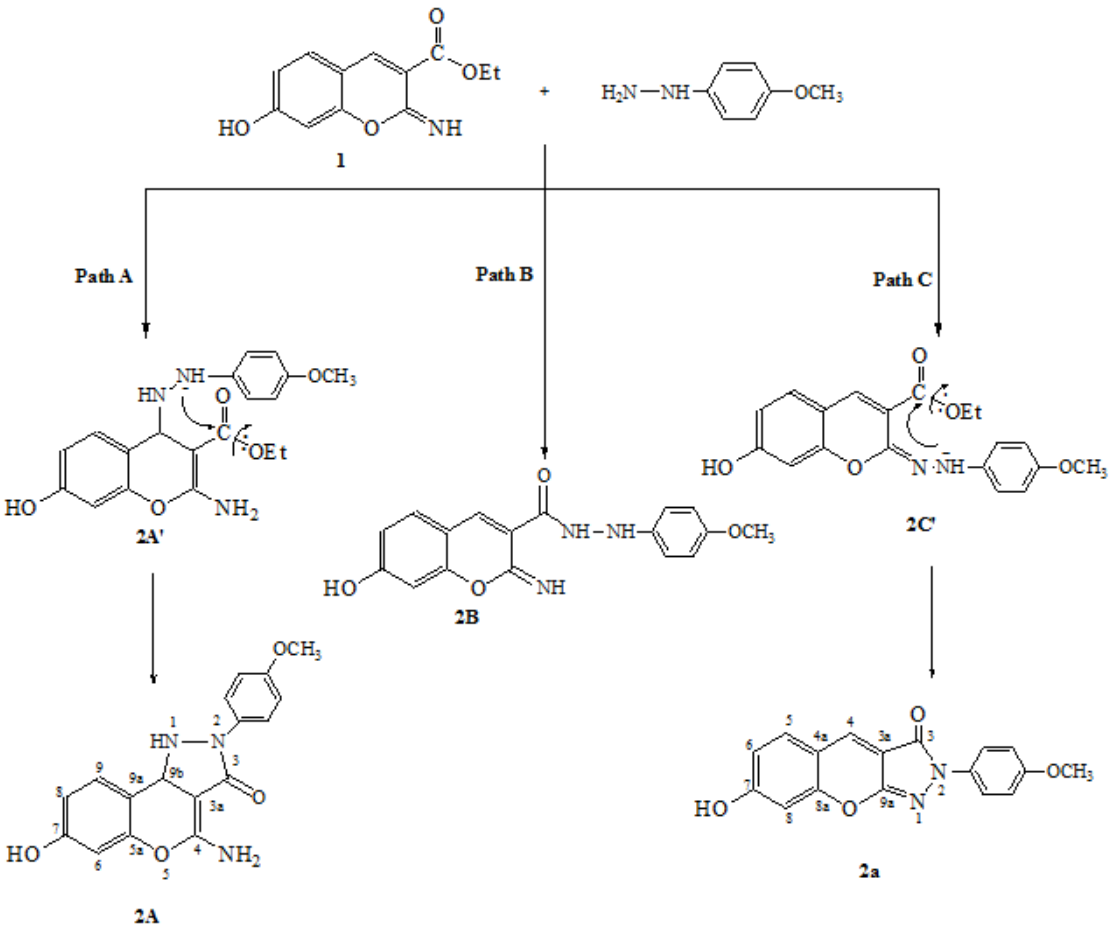
Scheme 1. Synthesis of benzopyranopyrazoles **2a-g and 3a-f**

It is notable that the compound **1** which is soluble in chloroform/acetic acid (3:1 v/v) is however insoluble in usual organic solvents, i.e., ethanol, methanol, acetonitrile, chloroform, dichloromethane or in some other chloroform/acetic acid mixtures (5:1 (v/v), 4:1 (v/v)). We believe that acetic acid behaves, on one side, as a solvent which may increase the solubility of iminocoumarin in chloroform and on the other side as a protonating catalyst of the carbonyl moiety. Moreover, the use of other acids, e.g., sulfuric acid, hydrochloric acid, formic acid in chloroform decreased both the reaction selectivity and yields. We noted that the increase in the reaction temperature from 25°C to 60°C had no effect on the yields and the selectivity of such reaction.

Three possible distinct pathways can be envisaged for this condensation: (**A**): Michael addition of 4-methoxy phenylhydrazine onto activated olefins, (**B**): attack of NH_2 group on the carbonyl moiety, (**C**): Schmidt reaction which involves aminolysis of **1** in the first step, then an intramolecular cyclisation in the second step (Scheme 2).

In this case, the IR, NMR data and the elemental analysis are in agreement with the suggested structure **2a** obtained through the pathway (**C**). In contrast, path (**A**) can be eliminated because ^{1}H NMR spectrum of the obtained product indicated the absence of the signal arising from hydrogen H_{9b} present in compound **2A**. Spectrum of obtained product **2a** showed, on the other hand, the presence of resonance of hydrogen H_4 at 8.38 ppm. Path (**B**) can also be excluded because the ^{1}H NMR spectrum indicated no signal related to the hydrazine fragment. Indeed, we observed in the IR spectrum of the obtained product the totally absence of the absorption at 3300 cm^{-1} corresponding to the imidic vibrator NH.

To explore the scope and the limitation of this protocol, the iminocoumarin **1** was reacted with other hydrazines **b-g**, giving the *N*-aryl-7-hydroxy-3-oxo-3H-benzopyrano[2,3-c]pyrazoles **2b-g** (Scheme1, table I). The structures of all the synthesized derivatives were established on the basis of their spectroscopic and elemental analysis.

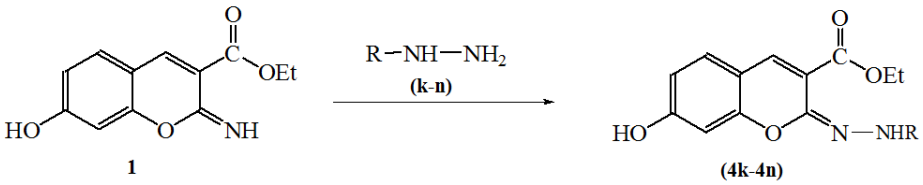


Scheme 2. Different possibilities of hydrazine reactivity

Table I. Benzopyranopyrazoles **(2a-g)** and **(3a-3f)** obtained by condensation of iminocoumarin **1** with hydrazines or hydrazides

Compound	R	Time (h or day)	Yield (%)	Mp (°C)
2a	4-MeO-Ph	6	85	230
2b	4-Br-Ph	24	40	228
2c	4-Me-Ph	6	45	200
2d	3-Cl-4-Me-Ph	5	45	240
2e	4-Cl-Ph	24	40	231
2f	Ph	20	35	256
2g	2,4,6-triCl-Ph	4	65	295
3a	3-MeO-Ph	3	55	266
3b	3-F-Ph	3	40	>280
3c	Ph	6	92	>280
3d	Me	1	60	>280
3e	Th	1	75	260
3f	Fu	3	45	>280
4k	2,5-diCl-PhPh	4 h	69	262
4l	CH_3-CO	1 day	45	260
4m	Th-CO	3 day	70	254
4n	Fu-CO	6 days	60	252

In contrast, it should be noted that in the case of the condensation of 2,5-dichloro phenylhydrazine with **1**, the final step, including the intramolecular cyclization, did not take place and we obtained the *N*-arylamino-3-ethoxycarbonyl-7-hydroxyiminocoumarin **4k** in 69% yield (Scheme 3, table 1). The ^{1}H NMR spectrum showed the presence of resonance at 1.38 and 4.31 ppm, suggesting the presence of the ethoxycarbonyl fragment. This result confirmed the mechanism of the reaction carried out in the pathway (iii). Unfortunately, our attempts to obtain the corresponding benzopyranopyrazole were unsuccessful albeit longer reaction times, higher reaction temperatures (25-60°C) or concentrations of acetic acid in chloroform.



1 **(4k-4n)**

R = 2,5-diCl-Ph-Cl-Ph, CH_3-CO, Th-CO, Fu-CO

Scheme 3. Synthesis of coumpounds 4k-4n

As part of our continuing studies on the reactivity of 3-ethoxy-carbonyl iminocoumarin **1** under the action of *N*-nucleophiles, we studied the behaviour of **1** towards hydrazides (Scheme 1) and we disclosed that it was similar to hydrazines, affording the corresponding compounds **3a-f**. In the case of hydrazides suh as the 4-methoxy phenyl hydrazide, 3-fluorobenzoic hydrazide and benzoic hydrazide, the reaction afforded the corresponding 2-acyl-7-hydroxy-3-oxo-3H-benzopyrano[2,3-c]pyrazoles **3a-f**. Under the previous conditions (25°C, chloroform/acetic acid 3:1 (v/v)), the expected condensation, for the other hydrazides, stopped at the first step, leading to the corresponding 2-*N*-acylamino-3-ethoxycarbonyl iminocoumarin **4l-n** (Scheme 3). This behaviour is similar to that of 2,5-dichloro phenylhydrazine; however, in refluxing chloroform/acetic acid (3:1,v/v), the reaction of these hydrazides with compound **1** afforded the corresponding benzopyranopyrazoles **3d-f**. Subsequently, the intramolecular cyclisation between NH and ethoxycarbonyl group tooke place. It should be noted that the reaction kinetic in the case of hydrazides was slower and the reaction times were longer. The RMN spectrum of theses derivatives and the elemental analyses were in agreement with the proposed structures.

CONCLUSION

We have described a *one-pot* protocol for the preparation of 7-hydroxy-benzopyrano[2,3-c]pyrazol-3(2*H*)-one through the condensation of 3-ethoxycarbonyl iminocoumarin with various hydrazines and hydrazides as *N*-nucleophiles. The mechanism of the reaction involved the aminolysis of the imidic nitrogen through a Schmidt reaction, followed by an intramolecular cyclization. In four cases, the reaction stops at the first step, affording the *N*-substituted iminocoumarines. Structures of all the obtained products have been identified on the basis of FT-IR, ^{1}H NMR, ^{13}C NMR and elemental analysis.

EXPERIMENTAL

2,4-Dihydroxybenzaldehyde, ethyl cyanoacetate, hydrazines and hydrazides were commercially available from Aldrich. 3-Ethoxycarbonyl-7-hydroxyiminocoumarin **1** was prepared as previously described in reference [16]. All melting points were determined on an Electrothermal 9100 apparatus. Infrared spectra were registered on a Perkin Elmer 100. ^{1}H and ^{13}C NMR spectra were recorded on a Bruker WP 200 spectrometer at 300 MHz in DMSO-d_6 with TMS as internal standard (chemical shifts in ppm). Elemental microanalyses were performed on an EA1112 analyzer from CE Instruments.

General procedure for the synthesis of benzopyranopyrazoles (2a-g), (3a-f) and iminocoumarins (4k-n): A solution of 3-ethoxycarbonyl-7-hydroxyiminocoumarin **1** (0,3 g, 1,28 mmol) and (1.28 mmol) of hydrazine or hydrazide dissolved in 18 mL of chloroform and 6 mL of acetic acid at room temperature or in refluxing solvent. After complete reaction, the benzopyranopyrazole obtained was separated by filtration and was washed with ethanol.

7-Hydroxy-2-(4-methoxyphenyl)chromeno[2, 3-c]pyrazol-3(2*H*)-one (2a)
Mp: 230°C. IR: O-H 3393, C=O 1715, C=N 1644, C=C 1607 cm^{-1}; ^1H NMR: δ = 3.70 (s, 3H, OCH_3), 6.88 (s, 1H, 8-H), 6.91 (d, 1H, 6-H, *J* = 13.0 Hz), 6.94 (d, 2H, CHAr, *J* = 3.5 Hz), 6.99 (d, 2H, CHAr, *J* = 3.5 Hz), 7.75 (d, 1H, 5-H, *J* = 13.0 Hz), 8.38 (s, 1H, 4-H), 8.68 (s, 1H, OH). ^{13}C NMR: δ = 55.4 (CH_3-O-), 102.3 (C8), 107.4 (C6), 108.8 (C4a), 114.8 (CHAr), 114.9 (CHAr) 115.5 (C3a), 129.1 (C5), 132.8 (C-N), 139.3 (C4), 154.4 (C8a), 156.4 (C7), 157.5 (C-OCH_3), 158.8 (C9a), 165.8 (C3). Anal.Calcd.for $C_{17}H_{12}N_2O_4$: C, 66.23; H, 3.92; N, 9.09. Found: C, 66.34; H, 4.02; N, 9.11.

2-(4-Bromophenyl)-7-hydroxychromeno[2, 3-c]pyrazol-3(2*H*)-one (2b)
Mp: 228°C. IR: O-H 3335, C=O 1707, C=N 1645, C=C 1601 cm^{-1}; ^1H NMR: δ= 6.93 (d, 2H, CHAr, *J* = 13.2 Hz), 6.95 (d, 1H, 8-H, *J* = 3.4 Hz), 7.01 (dd, 1H, 6-H, *J* = 12.8, 3.3 Hz), 7.45 (d, 2H, CHAr, *J* = 13.2 Hz), 7.75 (d, 1H, 5-H, *J* = 12.8 Hz), 8.77 (s, 1H, 4-H), 9.01 (s, 1H, OH). Anal.Calcd.for $C_{16}H_9BrN_2O_3$: C, 53.81; H, 2.54; N, 7.84. Found: C, 53.94; H, 2.51; N, 7.79.

7-Hydroxy-2-*p*-tolylchromeno[2, 3-c]pyrazol-3(2*H*)-one (2c)
Mp: 200 °C. IR: O-H 3415, C=O 1709, C=N 1648, C=C 1622 cm^{-1}; ^1H NMR: δ= 2.24 (s, 3H, CH_3), 6.88 (d, 2H, CHAr, *J* = 6.2 Hz), 6.97 (d, 1H, 8-H, *J* = 1.8 Hz), 7.02 (dd, 1H, 6-H, *J* = 6.6, 1.8, Hz), 7.10 (d, 2H, CHAr, *J* = 6.3 Hz), 7.75 (d, 1H, 5-H, *J* = 6.6 Hz), 8.66 (s, 1H, 4-H), 8.75 (s, 1H, OH). ^{13}C NMR: δ = 20.2 (CH_3), 102.2 (C8), 108.9 (C6), 109.7 (C4a), 113.8 (C3a), 114.7 (CHAr), 129.4 (C5), 129.6 (CHAr), 131.8 (C-CH_3), 143.5 (C-N), 148.1 (C4), 156.3 (C8a), 157.6 (C7), 160.7 (C9a), 164.7 (C3). Anal.Calcd. for $C_{17}H_{12}N_2O_3$: C, 69.86; H, 4.14; N, 9.58. Found: C, 69.81; H, 4.25; N, 9.62.

2-(3-Chloro-4-methylphenyl)-7-hydroxychromeno[2,3-c]pyrazol-3(2*H*)-one (2d)
Mp: 240°C. IR: O-H 3340, C=O 1704, C=N 1620, C=C 1659 cm^{-1}; ^1H NMR: δ= 2.25 (s, 3H, CH_3), 6.85 (dd, 1H, 6-H, *J* = 12.6, 3.6 Hz), 6.95 (d, 1H, 8-H, *J* = 3.9 Hz), 7.01 (dd, 1H, CHAr, *J* = 12.4, 3.0 Hz), 7.02 (d, 1H,CHAr, *J* = 3.0 Hz), 7.25 (d, 1H, CHAr, *J* = 12.4 Hz), 7.75 (d, 1H, 5-H, *J* = 13.0 Hz), 8.76 (s, 1H, 4-H), 8.94 (s, 1H, OH). Anal.Calcd. for $C_{17}H_{11}ClN_2O_3$: C, 62.48; H, 3.39; N, 8.57. Found: C, 62.04; H, 3.43; N, 8.49.

2-(4-Chlorophenyl)-7-hydroxychromeno[2, 3-c]pyrazol-3(2*H*)-one (2e)
Mp: 231 °C. IR: O-H 3325, C=O 1721, C=N 1665, C=C 1595 cm^{-1}; ^1H NMR: δ= 6.92 (d, 1H, 8-H, *J* = 3.7 Hz), 6.97 (dd, 1H, 6-H, *J* = 9, 3.6 Hz), 6.98 (d, 2H, CHAr, *J* = 13.0 Hz), 7.34 (t, 2H, CHAr, *J* = 13.2 Hz), 7.75 (d, 1H, 5-H, *J* = 13 Hz), 8.74 (s, 1H, 4-H), 8.92 (s, 1H, OH). Anal.Calcd. for $C_{16}H_9ClN_2O_3$: C, 61.45; H, 2.90; N, 8.96. Found: C, 61.52; H, 2.95; N, 9.05.

7-Hydroxy-2-phenylchromeno[2, 3-*c*]pyrazol-3(2*H*)-one (2f)
Mp: 256 °C. IR: O-H 3359, C=O 1706, C=N 1658, C=C 1595 cm^{-1}; ^1H NMR: δ = 6.90-7.01 (m, 5H, 5CHAr, 6-H, 8-H), 7.28 (t, 2H, CHAr, *J* = 11.7 Hz), 7.76 (d, 1H, 5-H, *J* = 13 Hz), 8.73 (s, 2H, 4-H and OH). Anal.Calcd. for $C_{16}H_{10}N_2O_3$: C, 69.06; H, 3.62; N, 10.07. Found: C, 69.11; H, 3.71; N, 10.13.

7-Hydroxy-2-(2,4,6-trichlorophenyl)chromeno[2,3-c]pyrazol-3(*2H*)-one (2g)
Mp: >280 °C. IR: O-H 3417, C=O 1692, C=N 1637, C=C 1575 cm^{-1}; ^1H NMR: δ = 6.75 (d, 1H, 8-H, *J* = 1.8 Hz), 6.81 (dd, 1H, 6-H, *J* = 6.2, 1.8Hz), 6.84 (s, 1H, OH), 7.56 (s, 1H, CHAr), 7.66 (d, 1H, 5-H, *J* = 6.4 Hz), 8.33 (s, 1H, 4-H). ^{13}C NMR: δ = 101.9 (C6), 111.3 (C8), 114.1 (C4a), 115.5 (C3a), 125.9 (CHAr), 128.6 (C5), 128.8/131.0 (3C-Cl), 141.1 (C-N), 142.6 (C4), 147.4 (8a), 155.6 (C7), 160.2 (C9a), 172.1 (C3). Anal.Calcd.for $C_{16}H_7Cl_3N_2O_3$: C, 50.36; H, 1.85; N, 7.34. Found: C, 50.48; H, 1.79; N, 7.52.

7-Hydroxy-2-(3-methoxybenzoyl)chromeno[2, 3-c]pyrazol-3(2*H*)-one (3a)
Mp: 266°C. IR: C=O 1743, C=N 1620, C=C 1606 cm^{-1}; ^1H NMR: δ = 3.75 (s, 3H, CH_3O), 6.81 (d, 1H, 8-H, *J* = 3.8 Hz), 6.90 (dd, 1H, 6-H, *J* = 12.8, 3.3 Hz), 7.23 (ddd, 1H, CHAr, *J* = 12.2, 4.2, 1.6 Hz), 7.56 (t, 1H, CHAr, *J* = 11.5 Hz), 7.59 (d, 1H, CHAr, *J* = 1.8 Hz), 7.67 (dt, 1H, CHAr, *J* = 11.9, 1.8 Hz), 7.80 (d, 1H, 5-H, *J* = 13.0 Hz), 8.91 (s, 1H, 4-H). Anal.Calcd.for $C_{18}H_{12}N_2O_5$: C, 64.29; H, 3.60; N, 8.33. Found: C, 64.15; H, 3.75; N, 8.21.

2-(3-Fluorobenzoyl)-7-hydroxychromeno[2,3-c]pyrazol-3(*2H*)-one (3b)
Mp: >280 °C. IR: C=O 1726, C=O 1700, C=N 1613, C=C 1557 cm^{-1}; ^1H NMR: δ = 6.77 (d, 1H, 8-H, *J* = 1.8 Hz), 6.88 (dd, 1H, 6-H, *J* = 6.4, 1.6 Hz), 7.52 (td, 1H, CHAr, *J* = 7.5, 1.8 Hz), 7.69-7.72 (m, 1H, CHAr), 7.77 (d, 1H, 5-H, *J* = 6.6 Hz), 7.91 (dt, 1H, CHAr, *J* = 7.5, 1.8 Hz), 7.93 (dd, 1H, CHAr, *J* = 7.5, 1.8 Hz), 8.92 (s, 1H, 4-H). ^{13}C NMR: δ = 102.3 (C8), 105.9 (C6), 110.6 (C4a), 113.4 (CHAr), 114.8 (CHAr), 119.1 (CHAr), 119.3 (C3a), 123.0 (C5), 125.3 (CAr), 131.8 (CHAr), 146.3 (C4), 156.2 (C8a), 156.8 (C7), 161.5 (C9a), 162.9 (C-F), 163.6(C3), 164.8 (C=O). Anal.Calcd.for $C_{17}H_9FN_2O_4$: C, 62.97; H, 2.80; N, 8.64. Found: C, 63.50; H, 2.94; N, 8.51.

2-Benzoyl-7-hydroxychromeno[2, 3-c]pyrazol-3(*2H*)-one (3c)
Mp: >280 °C. IR: C=O 1742, C=O 1711, C=N 1618, C=C 1597 cm^{-1}; ^1H NMR: δ = 6.81 (d, 1H, 8-H, *J* = 2.1 Hz), 6.90 (dd, 1H, 6-H, *J* = 8.7, 2.1Hz), 7.60-7.67 (m, 3H, 3CHAr), 7.78 (d, 1H, 5-H, *J* = 8.7 Hz), 8.07-8.11 (m, 2H, 2CHAr), 8.86 (s, 1H, 4-H). ^{13}C NMR: δ = 102.1 (C8), 106.6 (C6), 110.7 (C4a), 114.2 (C3a), 123.2 (CHAr), 126.6 (CHAr), 129.3 (C5), 131.5 (CHAr), 132.0 (CAr), 145.9 (C4), 156.1 (C8a), 156.5 (C7), 160.9 (C9a), 163.8 (C3), 163.8 (C=O). Anal.Calcd.for $C_{17}H_{10}N_2O_4$: C, 66.67; H, 3.29; N, 9.15. Found: C, 67.09; H, 3.37; N, 8.98.

2-Acetyl-7-hydroxychromeno[2, 3-c]pyrazol-3(*2H*)-one (3d)
Mp: >280 °C. IR: C=O 1738, C=N 1614, C=C 1579 cm^{-1}; ^1H NMR: δ = 2.58 (s, 3H, CH_3), 6.78 (s, 1H, 8-H), 6.86 (d, 1H, 6-H, *J* = 12.1 Hz), 7.78 (d, 1H, 5-H, *J* = 12.5 Hz), 8.72 (s, 1H, 4-H). Anal.Calcd.for $C_{12}H_8N_2O_4$: C, 59.02; H, 3.30; N, 11.47. Found: C, 60.09; H, 3.47; N, 12.50.

7-Hydroxy-2-(thiophene-5-carbonyl)chromeno[2,3-c]pyrazol-3(*2H*)-one (3e)
Mp: 260 °C. IR: C=O 1740, C=O 1724, C=N 1622, C=C 1584 cm^{-1}; ^1H NMR: δ = 6.58 (d, 1H, 8-H, *J* = 1.8 Hz), 6.73 (dd, 1H, 6-H, *J* = 6.4, 1.8Hz), 7.32 (dd, 1H, CHAr, *J* = 3.8, 2.7 Hz), 7.65 (d, 1H, 5-H, *J* = 6.4 Hz), 7.87 (dd, 1H, CHAr, *J* = 2.7, 0.9 Hz), 7.96 (dd, 1H, CHAr, *J* = 3.8, 0.9Hz), 8.68 (s, 1H, 4-H). ^{13}C NMR: δ = 102.4 (C8), 102.6 (C6), 108.8 (C4a), 116.7 (C3a), 124.5 (CHAr), 128.9 (C5), 130.3 (CHAr), 131.6 (CH-S), 145.7 (C4), 156.8 (CAr), 157.7 (C8a), 159.9 (C7), 161.2 (C9a), 169.9 (C3), 172.8 (C=O). Anal.Calcd.for $C_{15}H_8N_2O_4S$: C, 57.69; H, 2.58; N, 8.97. Found: C, 58.01; H, 2.35; N, 9.15.

2-(Furan-2-carbonyl)-7-hydroxychromeno[2, 3-c]pyrazol-3(*2H*)-one (3f)
Mp: >280 °C. IR: C=O 1740, C=N 1619, C=C 1601 cm^{-1}; ^1H NMR: δ = 6.77 (d, 1H, 8-H, *J* = 1.5 Hz), 6.82-6.84 (m, 1H, CHAr), 6.86 (dd, 1H, 6-H, *J* = 6.3, 1.5 Hz), 7.40 (d, 1H, CHAr, *J* = 2.7 Hz), 7.78 (d, 1H, 5-H, *J* = 6.3 Hz), 8.09-8.11 (m, 1H, CHAr), 8.80 (s, 1H, 4-H). ^{13}C NMR: δ = 102.6 (C8), 106.1 (C6), 110.9 (C4a), 113.2 (C3a), 115.0/115.2 (CHAr, C5), 132.1 (CHAr), 139.0 (C4), 146.4 (CH-O(Ar)), 147.5 (CAr), 156.6 (C8a), 157.1 (C7), 157.2 (C9a), 160.8 (C3), 165.2 (C=O). Anal.Calcd.for $C_{15}H_8N_2O_5$: C, 60.82; H, 2.72; N, 9.46. Found: C, 61.15; H, 2.68; N, 9.53.

Ethyl 2-(2-(2,4-dichlorophenyl)hydrazono)-7-hydroxy-2H-chromene-3-carboxylate (4k)
Mp: 262°C. IR: NH 3379, C=O 1681, C=N 1634 cm^{-1}, C=C 1593. ^1H NMR: δ = 1.38 (t, 3H, CH_3, *J* = 7.1 Hz), 4.31 (q, 2H, CH2O, *J* = 7.2 Hz), 6.66 (dd, 1H, 6-H, *J* = 8.4, 2.4 Hz), 6.71 (d, 1H, 8-H, *J* = 2.1 Hz), 6.82 (dd, 1H, CHAr, *J* = 8.4, 2.4 Hz), 7.36 (d, 1H, 5-H, *J* = 8.4 Hz), 7.42 (d, 1H, CHAr, *J* = 8.4 Hz), 7.44 (d, 1H, CHAr, *J* = 2.4 Hz), 7.72 (s, 1H, 4-H), 8.40 (s, 1H, NH). ^{13}C NMR: δ = 14,0 (CH_3), 60.8 (CH_2O), 102.0 (C3), 112.4 (C8), 113.2 (C6), 115.3 (C4a), 116.2, 118.9, 130.3, 130.6 (2CCl, C5, CHAr), 132.7 (CHAr), 135.8 (C4), 139.6 (CAr), 142.0 (C2), 154.1 (C8a), 161.9 (C7), 163.1 (C=O). Anal.Calcd.for $C_{18}H_{14}O_4N_2Cl_2$: C, 54.98; H, 3.59; N, 7.12. Found: C, 55.09; H, 3.64; N, 6.98.

Ethyl 2-(2-acetylhydrazono)-7-hydroxy-2H-chromene-3-carboxylate (4l)
Mp: 260°C. IR: NH 3251, C=O 1733, C=N 1633, C=C 1574 cm^{-1}; ^1H NMR: δ = 1.31 (t, 3H, CH_3, *J* = 10.8 Hz), 2.15 (s, 3H, $COCH_3$), 4.26 (q, 2H, OCH_2, *J* = 10.6 Hz), 6.65 (dd, 1H, 6-H, *J* = 12.5, 3.4 Hz), 6.85 (d, 1H, 8-H, *J* = 3.4 Hz), 7.43 (d, 1H, 5-H, *J* = 12.8 Hz), 7.80 (s, 1H, 4-H), 10.60 (s, 1H, NH). Anal.Calcd.for $C_{14}H_{14}N_2O_5$: C, 57.93; H, 4.86; N, 9.65. Found: C, 58.11; H, 4.74; N, 9.77.

Ethyl 7-hydroxy-2-(2-(thiophene-5-carbonyl)hydrazono)-2H-chromene-3-carboxylate (4m)
Mp: 254°C. IR: NH 3322, C=O 1722, C=N 1594, C=C 1509 cm^{-1}; ^1H NMR: δ = 1.31 (t, 3H, CH_3, *J* = 6.9 Hz), 4.32 (q, 2H, OCH_2, *J* = 6.9 Hz), 6.67 (dd, 1H, 6-H, *J* = 8.4, 2.4 Hz), 6.91 (s, 1H, 8-H), 7.20 (t, 1H, CHAr, *J* = 8.7 Hz), 7.45 (d, 1H, 5-H, *J* = 8.4 Hz), 7.85-7.87 (m, 2H, 2CHAr), 7.42 (s, 1H, 4-H), 11.02 (s, 1H, NH). ^{13}C NMR: δ = 14,0 (CH_3), 61.0 (CH_2O), 102.4 (C3), 110.1 (C8), 112.5 (C6), 115.5 (C4a), 127.4 (CHAr), 130.6,

130.6, 131.7 (2CHAr, CAr), 133.2 (C5), 134.4 (C4), 137.6 (C8a), 154.3 (C7), 161.1 (C2), 162.3, 163.0 (2C=O). Anal.Calcd.for $C_{17}H_{14}N_2O_5S$: C, 56.98; H, 3.94; N, 7.82. Found: C, 56.77; H, 3.86; N, 7.91.

Ethyl 2-(2-(furan-5-carbonyl)hydrazono)-7-hydroxy-2H-chromene-3-carboxylate (4n)

Mp: 252°C. IR: NH 3206, C=O 1712, C=N 1629, C=C 1606 cm^{-1}; ^1H NMR: δ = 1.32 (t, 3H, CH_3, *J* = 5.3 Hz), 4.30 (q, 2H, OCH_2, *J* = 5.3 Hz), 6.67-6.71 (m, 2H, 8-H, 6-H), 6.92 (br s, 1H, CHAr), 7.47 (d, 1H, 5-H, *J* = 6.4 Hz), 7.94 (br s, 2H, 2CHAr), 8.13 (s, 1H, 4-H), 10.68 (s, 1H, NH). ^{13}C NMR: δ = 14,2 (CH_3), 61.1 (CH_2O), 102.6 (C3), 110.3, 112.0 (C6, C8), 112.7 (C4a), 120.1 (CHAr), 131.0 (2CHAr, CAr, C5), 138.9 (C4), 140.3 (C8a), 146.1 (C7), 156.8 (C2), 162.4 (2C=O). Anal.Calcd. for $C_{17}H_{14}N_2O_6$: C, 59.65; H, 4.12; N, 8.18. Found: C, 60.11; H, 4.09; N, 8.38.

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