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Multicomponent Reactions

An Efficient Synthetic Access to Substituted Thiazolyl-pyrazolyl-chromene-2-ones from Dehydroacetic Acid and Coumarin Derivatives by a Multicomponent Approach

Soumaya Ben Mohamed,[a] Yahia Rachedi*[a] Maamar Hamdi,[a] Franck Le Bideau,[b] Camille Dejean,[c] and Françoise Dumas*[b]

Abstract: Two new series of pyran- or coumarin-substituted thiazolyl-pyrazole-chromen-2-one derivatives **10a**–**10d** and **11a**–**11d** were efficiently synthesized under environmentally friendly reaction conditions through a convenient one-pot multicomponent reaction of a heterocyclic bromoacetyl derivative **3** or **4** with thiosemicarbazide and a substituted 3-(acetoacetyl)coumarin derivative **5a**–**5d** in anhydrous ethanol. The reaction proceeds through Hantzsch thiazole and Knorr pyrazole syntheses in refluxing ethanol. The key features of this approach are its operational simplicity, the quick access to the desired products, and the good to excellent yields. The structures of the newly synthesized compounds were established by IR spectroscopy, ^{1}H, ^{13}C, and 2D NMR spectroscopy, and mass spectrometry.

Introduction

Heterocyclic chemistry has constituted one of the largest areas of research in organic chemistry, starting with Perkin's mauve dye. Heterocycles have become key compounds in society's development through their contributions to the understanding of life processes, and their use in the improvement of health conditions in particular. Indeed, more than 80 % of drugs are based on heterocyclic molecules. They have also contributed to industrial development and to the improvement of the quality of life through their applications as agrochemicals, dyes, fluorescent agents, plastics, food additives, cosmetics, and so on.[1]

Genetic information carriers such as DNA and RNA, or oxygen carriers in living organisms, are made of aromatic heterocycles, which therefore play an essential role in biochemical processes. Heterocycles are present in a wide variety of drugs, many natural products, biomolecules, and biologically active compounds, and they are often key structural units in pharmaceuticals and agrochemicals.[1–5]

[a] *Laboratory of Applied Organic Chemistry, Faculty of Chemistry, University of Science and Technology Houari Boumediene, BP 32, El-Alia, 16111 Bab-Ezzouar, Algiers, Algeria*
E-mail: yrachedi@usthb.dz
http://www.lcoa.usthb.dz/
[b] *Laboratoire BioCIS, UMR CNRS 8076, Chimie des Substances Naturelles, IPSIT and LabEx LERMIT, CNRS, Université Paris-Saclay, Université Paris-Sud, Faculté de Pharmacie, 5, rue Jean-Baptiste Clément, 92296 Châtenay-Malabry CEDEX, France*
E-mail: francoise.dumas@u-psud.fr
http://www.biocis.u-psud.fr/
[c] *Département de RMN, BioCIS UMR CNRS 8076, Université Paris-Saclay, Université Paris-Sud, 5, rue Jean-Baptiste Clément, 92296 Châtenay-Malabry CEDEX, France*
Supporting information and ORCID(s) from the author(s) for this article are available on the WWW under http://dx.doi.org/10.1002/ejoc.201600173.

Sulfur–nitrogen-containing heterocyclic compounds, and specifically thiazoles and their derivatives, represent a medicinally and pharmaceutically important class of heterocycles that are found in a variety of drug molecules, such as sulfathiazole, ritonavir, and abafungin (Figure 1). They also have a wide range of biological and pharmacological activities, including antituberculosis,[6] anticancer,[7,8] and anti-HIV[9] activities; more recently, they have also been found to be of interest for materials science.[10] When nitrogen and sulfur heteroatoms take the place of ring carbon atoms, or of a complete ethylene group, in aromatic carbocycles, this formally results in the corresponding aromatic heterocycles. The presence of these heteroatoms induces significant changes in the stereoelectronic properties of such heterocycles relative to their carbon analogues, in part because of their unshared electron pairs and different electronegativities.[4]

On the other hand, pyrazole and its derivatives, which make up a class of well-known nitrogen heterocycles, have been reported in the literature to show various therapeutic activities[11,12] such as anti-inflammatory,[13] antihypertensive,[14] antimicrobial,[15] antidiabetic,[16] and anticancer[17] activities. Blockbuster drugs such as celecoxib and pyrazofurin, among others, incorporate such a pyrazole ring in their core structure (Figure 1). In addition, compounds of this class have played a crucial role in the development of heterocyclic chemistry, and they are also used extensively in organic synthesis.[18,19]

Pyran-2-one and coumarin derivatives form an exceptional class of oxygen-containing heterocyclic compounds. They are useful intermediates for the synthesis of various compounds, and they play a key role in the medicinal area due to their structural diversity and their pharmaceutical properties.[20,21] Consequently, the synthesis of compounds containing such pyran or coumarin heterocycles has attracted considerable at-

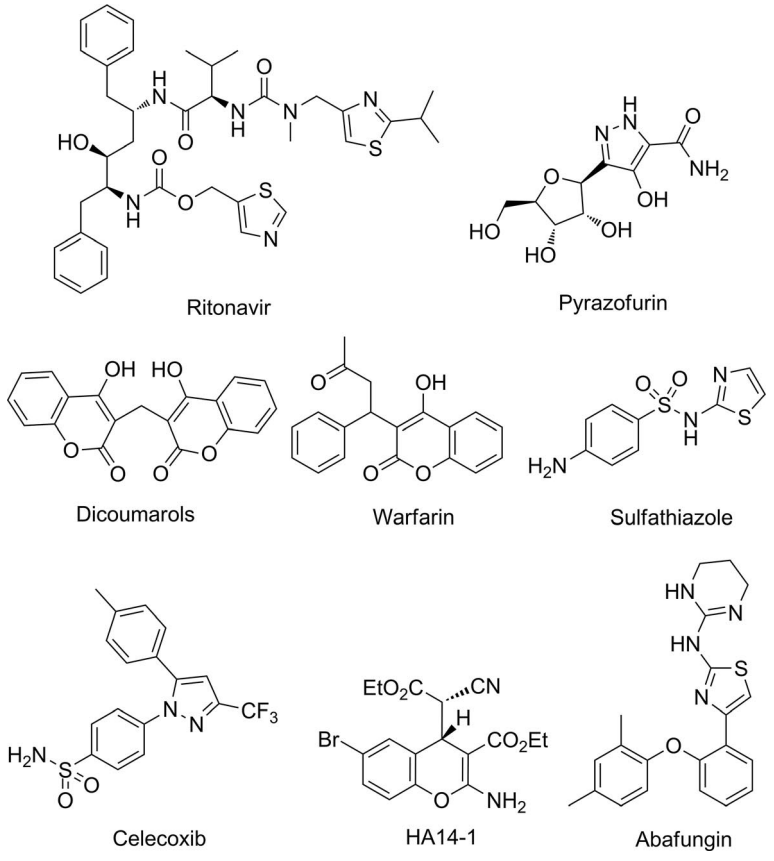
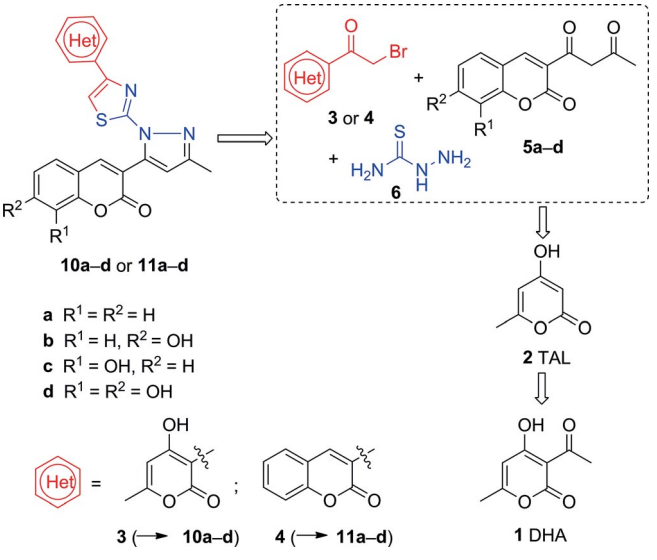


Figure 1. Some biologically active drugs containing thiazole, pyrazole, or coumarin moieties.

tention for years, and several syntheses of these derivatives have been reported. The great interest in these compounds stems from their physiological and biological activities, as exemplified by their roles as anticoagulants (dicoumarols and their derivatives, warfarin), spasmolytics, anti-inflammatories, and antioxidants (Figure 1).[22–26] They have been extensively investigated for decades, and have been found to exert other valuable biological effects such as antiapoptotic (HA14-1),[27] anticancer[28,29] and antiviral activities;[30] interesting optical,[31] photophysical, photochemical, and fluorescent properties have also been found.[32–34]

Multicomponent reactions (MCRs) have emerged as useful tools for exploring chemical space. They involve domino processes in which at least three different reactants are directly converted into products in a one-pot fashion.[35] Compared to classical multistep synthesis, MCRs offer higher atom economy and selectivity, and give easy access to molecular complexity and diversity while generating fewer by-products. As a result, the importance of MCRs in modern organic chemistry is growing,[36] and MCRs are being developed for the efficient production of medicinally relevant scaffolds.

In view of the various activities of pyrans, coumarins, thiazoles, and pyrazolones, we have developed a research program focussed on the synthesis of new heterocyclic systems related to chemical transformations of 3-acetyl-4-hydroxy-6-methyl-2*H*-pyran-2-one [**1**; also named dehydroacetic acid (DHA)],[37–39] 4-hydroxy-6-methyl-2*H*-pyran-2-one [**2**; or triacetic lactone (TAL)],[40–43] as found in bromoacetyl derivative **3**, and coumarin,[33] as found in bromoacetyl derivative **4**. Our current study is aimed towards the development of new routes for the synthesis of two new series of thiazolyl-pyrazolyl-chromen-2-one-containing pyran-2-ones (**10a**–**10d**) and coumarins (**11a**–**11d**) through Hantzsch thiazole[44] and Knorr pyrazole[45] MCRs,



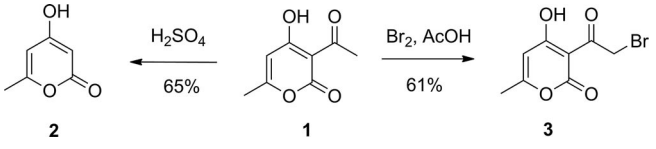
Scheme 1. Strategy for the synthesis of substituted thiazolyl-pyrazolyl-chromene-2-ones **10a**–**10d** and **11a**–**11d**.

respectively, involving bromoacetyl heterocycles **3** or **4** combined with coumarins **5a**–**5d** and thiosemicarbazide **6** as a double dinucleophilic coupling partner (Scheme 1).

Results and Discussion

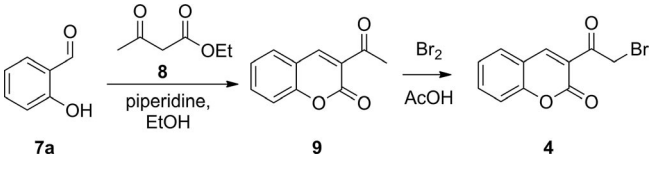
One reason behind the continuous research into the design of synthetic approaches to new heterocyclic systems lies in the wide use of heterocycles in modern pharmaceuticals. The first task in this study was to prepare the starting materials, i.e., α-bromo ketones **3** and **4**, and coumarins **5a**–**5d**.

The procedure started from DHA (**1**), which was converted into TAL (**2**) in 65 % yield through deacetylation under acidic conditions[46,47] (Scheme 2). Compound **2** would then be used for the synthesis of coumarins **5a**–**5d** (see Scheme 4). Studies dealing with the bromination of DHA (**1**) and coumarins are significant, because the resulting α-bromo ketones are potential precursors for the synthesis of various heterocyclic compounds. In this context, 3-(bromoacetyl)-4-hydroxy-6-methyl-2*H*-pyran-2-one (**3**) and 3-(bromoacetyl)-2*H*-chromene-2-one (**4**) were synthesized as key starting materials for the preparation of target compounds **10** and **11**. Thus, bromination of DHA (**1**) in glacial acetic acid gave the desired bromoacetyl derivative (i.e., **3**) in 61 % yield (Scheme 2).[38]



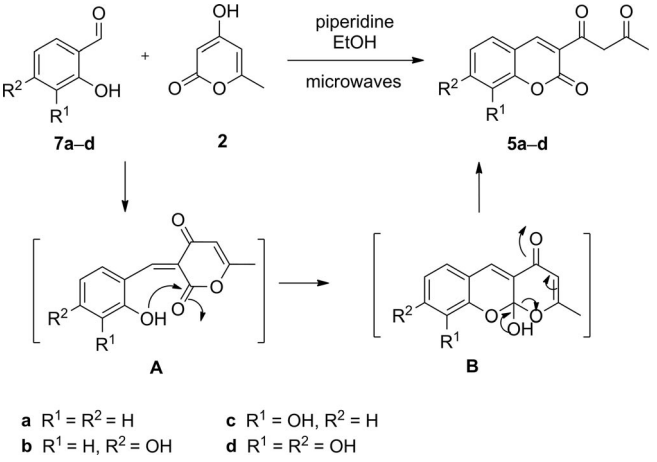
Scheme 2. Synthesis of 4-hydroxy-6-methyl-2*H*-pyran-2-one (**2**) and 3-(bromoacetyl)-4-hydroxy-6-methyl-2*H*-pyran-2-one (**3**) from DHA (**1**).

3-(Bromoacetyl)coumarin **4** was synthesized by a two-stage process, viz., Knoevenagel condensation then bromination. The first stage was carried out by treating salicylaldehyde (**7a**) with ethyl acetoacetate (**8**) in the presence of piperidine to give 3-acetylcoumarin **9**[48] in 77 % yield. This compound was then brominated using bromine in acetic acid to give the corresponding bromoacetyl compound (i.e., **4**)[49] in 60 % yield (Scheme 3).



Scheme 3. Synthesis of 3-acetylcoumarin (**6**) and 3-(bromoacetyl)coumarin (**7**).

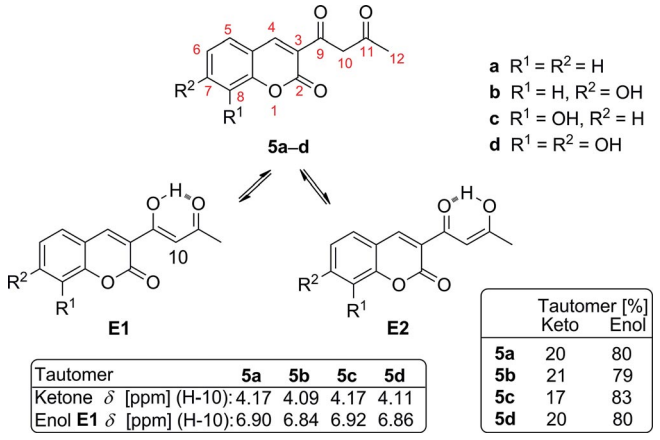
The second part of the synthesis of the target compounds involved the preparation of 3-(acetoacetyl)coumarin derivatives **5a**–**5d** by the reaction of TAL (**2**) with 2-hydroxybenzaldehydes **7a**–**7d** using piperidine in ethanol under microwave irradiation (Scheme 4). The reaction gave excellent yields after only short reaction times; this means that less energy was wasted in heating, which makes the process environmentally friendly.



Scheme 4. Synthesis of 3-(acetoacetyl)coumarin derivatives **5a**–**5d** and a plausible mechanism for their formation.

The following mechanism supports the formation of compounds **5a**–**5d**. First, a Knoevenagel condensation of pyranone **2** with salicylaldehydes **7a**–**7d** could give the intermediate 3-salicylidenepyrane-2,4-dione (**A**). This could then undergo an intramolecular translactonisation through nucleophilic attack of the phenol group onto the lactone carbonyl group to give intermediate **B**. In turn, this could lead to a ring-opening reaction of the pyranone unit in **B**, resulting in the formation of 3-(acetoacetyl)coumarin β-diketones **5a**–**5d** (Scheme 4). The β-diketone moiety in structures **5a**–**5d** undergoes keto/enol tautomerism in DMSO solution, as shown by ^{1}H NMR spectroscopy (Scheme 5). The relative proportions of the keto and enol tautomers of **5a**–**5d** were easily determined by ^{1}H NMR spectroscopy by integration of the ketone α-methylene signals (between δ = 4.09 and 4.17 ppm in [D_6]DMSO) and the enol ethylene signals (from δ = 6.84 to 6.92 ppm in [D_6]DMSO). The proportion of the enol form was in the range 79–83 %. The relative contributions of the keto and enol tautomers depend on several factors, such as the solvent characteristics, temperature, and ring structure. In general, most β-diketones exist in solution at room temperature predominantly in the enol form. The enol form can exist in different *cis*- and *trans*-isomeric forms depending on the temperature and on the polarity and hydrogen-bonding nature of the solvents.[50] The presence of a *trans*-enol form is controversial in the case of β-diketones.[11,41,50] In contrast, the *cis*-enol form is generally stable, due to the presence of intramolecular hydrogen bonding.[41] In the case of unsymmetrical β-dicarbonyl compounds, two possible enol isomers **E1** and **E2** can be formed by the transfer of an enol proton from one oxygen atom to the other.[50,51] MNDO-PM3 calculations for such enol forms **E1** and **E2** of compound **5a** recently reported by Makhloufi-Chebli et al. showed that enol form **E1** is favored over its isomer **E2**. The bonds are highly polarized, and the atoms bear higher charges in enol form **E1** than in enol form **E2**.[32]

The structures of coumarins **5a**–**5d** were deduced from spectroscopic data and high-resolution mass spectra (HRMS), as discussed here for the new derivative **5d**. The infrared spectrum of **5d** showed prominent peaks at $\tilde{\nu}$ = 3331 (OH) and 1692 (C=

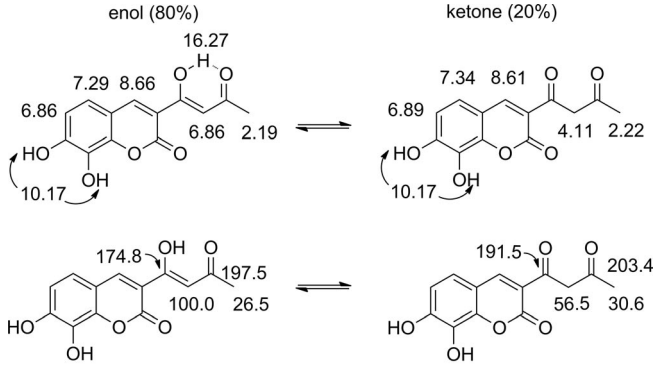


Tautomer	5a	5b	5c	5d
Ketone δ [ppm] (H-10):	4.17	4.09	4.17	4.11
Enol **E1** δ [ppm] (H-10):	6.90	6.84	6.92	6.86

	Tautomer [%] Keto	Enol
5a	20	80
5b	21	79
5c	17	83
5d	20	80

Scheme 5. Keto/enol tautomerism and atom numbering of 3-(acetoacetyl)coumarins **5a**–**5d**, their ^{1}H characteristic chemical shifts (10-H), and their ratios from ^{1}H NMR spectroscopy in DMSO.

O) cm^{-1}. The ^{1}H NMR spectrum of compound **5d** was consistent with a mixture of two compounds, which suggests that both keto and enol forms of the acetoacetyl moiety are present in DMSO solution. Characteristic singlets at δ = 2.22 and 4.11 ppm assigned to the protons of the methyl group and to the 10-H methylene protons, respectively, correspond to the minor diketone tautomer (Scheme 5 and Figure 2). Singlet signals at δ = 2.19 and 6.86 ppm were assigned to the methyl group and the 10-H enol proton of major enol form **E1**. Doublet signals centred at δ = 6.86/7.29 and 6.89/7.34 ppm (J = 8.6 Hz) correspond to the adjacent aromatic protons 5-H and 6-H, respectively. Further characteristic singlets appeared for 4-H at δ = 8.66/8.61 ppm and a broad singlet at δ = 10.17 ppm accounting for two phenolic hydroxy groups. Finally, the appearance of a hydroxy proton signal at δ = 16.27 ppm provides evidence for the predominance of the enol form in the acetoacetyl moiety with a ratio of 80:20. This high value is a result of stabilization of the enol by a strong intramolecular hydrogen bond with the oxygen atom of the β-carbonyl group.



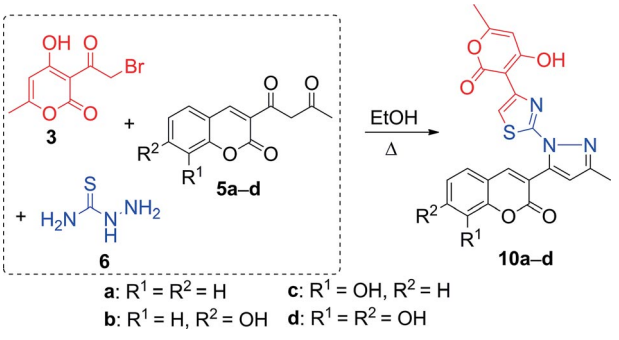
Tautomer	C2	C3	C4	C4a	C5	C6	C7	C8	C8a
Enol	157.8	114.1	147.2	111.8	121.8	113.5	152.7	131.7	144.2
Ketone	159.4	118.0	149.1	111.6	122.7	113.6	153.2	131.8	144.9

Figure 2. Selected ^{1}H (top) and ^{13}C (middle) chemical shifts of **5d** tautomers, and table of the remaining signals in the ^{13}C NMR spectra.

The ^{13}C NMR spectrum of **5d** showed the characteristic peaks at δ = 26.5 ppm for the methyl group, and at δ = 157.8 ppm for the C=O group of the coumarin nucleus, and two signals at δ = 174.8 and 197.5 ppm that are assigned to the carbonyl groups at C-9 and C-11, respectively, of the enol form of the acetoacetyl moiety. The mass spectrum of **5d** showed peaks at m/z (%) = 263.0552 (20) [M + H]$^+$ and 285.0375 (100) [M + Na]$^+$, confirming its molecular formula as $C_{13}H_{10}O_6$.

With compounds **5a**–**5d** in hand, we went on to develop a facile, one-pot method for the synthesis of two new series of pyran or coumarin-thiazole-pyrazole-coumarin derivatives, **10a**–**10d** and **11a**–**11d**, which incorporate three or four important pharmacophores: pyran, coumarin ring, thiazole, and pyrazolone heterocycles. According to the strategy shown in Scheme 1, these series were synthesized by multicomponent reactions of 3-(bromoacetyl) heterocycles **3** or **4**, 3-(acetoacetyl)coumarin derivatives **5a**–**5d**, and thiosemicarbazide **6**. Isolation of the products was easily achieved by filtration, followed by washing with hot ethanol, then DMSO, and finally by drying. This process is fairly general, quick, and efficient, and is does not give any side-products.

The condensation of an equimolar mixture of 3-(bromoacetyl)-4-hydroxy-6-methyl-2*H*-pyran-2-one (**3**) with thiosemicarbazide **6** and 3-(acetoacetyl)coumarin derivatives **5a**–**5d** in refluxing anhydrous ethanol delivered the first series of substituted coumarin derivatives 3-{1-[4-(4-hydroxy-6-methyl-2-oxo-2*H*-pyran-3-yl)thiazol-2-yl]-3-methyl-1*H*-pyrazol-5-yl}-2*H*-chromen-2-ones **10a**–**10d** in good yields (73–84 %; Scheme 6). No regioisomers or intermediates were isolated (see Scheme 8).



Scheme 6. One-pot synthesis of substituted thiazolyl-pyrazolyl-coumarin derivatives **10a**–**10d**.

The structures of the products were confirmed by spectroscopic analysis, including IR, ^{1}H and ^{13}C NMR, 2D-NMR, and mass spectral analysis, as described here in detail for a representative compound **10b**. The molecular formula $C_{22}H_{15}N_3O_6S$ for this compound was deduced on the basis of ESI-HRMS data, which showed a peak at m/z = 472.0579 attributed to [M + Na]$^+$. This confirmed the success of the multicomponent synthesis. The IR spectrum of **10b** showed prominent peaks due to lactone (C=O) and imine (C=N) functional groups at $\tilde{\nu}$ = 1715 and 1687 cm^{-1}, and a broad band centered at $\tilde{\nu}$ = 3410 cm^{-1} due to the hydroxy groups of the pyran and coumarin rings. The ^{1}H NMR spectrum of compound **10b** in DMSO showed six characteristic singlets: of a CH_3 group at δ = 2.31 ppm and of a CH group at δ = 6.56 ppm assigned to the pyrazolone ring; of a CH_3 group at δ = 2.16 ppm and of a CH group at δ = 5.87 ppm assigned to the pyrone; the signals of the thiazole

proton and of the proton at C-4 of the coumarin nucleus appeared at δ = 7.96 and 8.17 ppm, respectively. This last signal at δ = 8.17 ppm showed 2D-NOESY correlations with the signals at δ = 7.96 (H-14) and 6.56 (H-10) ppm, indicating that the thiazole and coumarin heterocycles are not coplanar with the pyrazole ring.

The ^{13}C NMR spectrum of **10b** showed peaks at δ = 13.0 and 19.1 ppm due to the pyrazolone and pyran methyl carbon atoms, respectively, and at δ = 144.5 and 158.9 ppm due to C-4 and C-2, respectively, of the coumarin. From the HSQC correlation chart, protons with resonances at δ = 5.87, 6.56, 7.96, and 8.17 ppm are linked to the carbon atoms with signals appearing at δ = 100.5, 112.7, 112.1, and 144.5 ppm, which is typical of pyran-2-one, pyrazolone, thiazole, and coumarin heterocycles, respectively (Figure 3a). The long-range connectivities seen in the HMBC spectrum (e.g., δ_H = 6.56 ppm → δ_C = 13.0, 138.5, 152.4, and 160.2 ppm; δ_H = 7.96 ppm → δ_C = 144.5 and 160.2 ppm; δ_H = 8.17 ppm → δ_C = 102.2, 111.3, 130.5, 138.5, 156.2, and 158.9 ppm) supported the structure of **10b** (Figure 3b). Further support for the presence of a thiazole ring is provided by the signals at δ = 112.1 (C-14), 144.1 (C-13), and 160.2 (C-15) ppm. The spectroscopic data described above are consistent with those expected for 3-methyl-1,5-diarylpyrazole structures,[52,53] and thus the structure of compound **10b** is confirmed.

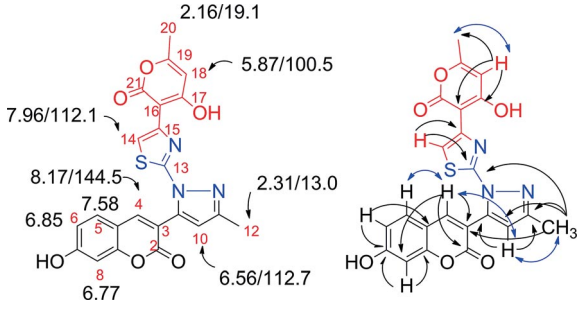
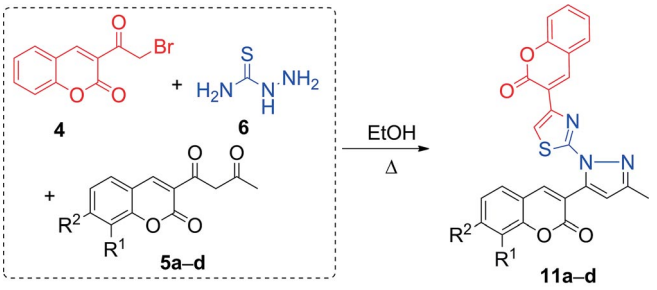


Figure 3. Selected ^{1}H/^{13}C NMR chemical shifts (δ [ppm]) (left); HMBC correlations of compound **10b** (black arrows), and significant nOe correlations (double-ended blue arrows) (right).

Following this successful strategy, a second series of coumarin derivatives **11a**–**11d** was prepared by a related route. Hantzsch cyclocondensation of 3-(bromoacetyl)coumarin **4** and thiosemicarbazide **6** with a range of differentially substituted 3-(acetoacetyl)coumarins **5a**–**5d** in ethanol under reflux gave coumarin derivatives **11a**–**11d** in very good yields (75–82 %), without isolation of any intermediates (Scheme 7).

The structures of these bis(coumarin) derivatives were established on the basis of spectroscopic data, as exemplified for derivative **11c**. Infrared spectroscopic analysis of compound **11c** showed absorption bands at $\tilde{\nu}$ = 1719, 1687, and 1347 cm^{-1} due to lactone (C=O), imine (C=N), and (C–S) functional groups, respectively. The ^{1}H NMR spectrum of **11c** showed singlet signals corresponding to the methine protons of two coumarins (δ = 8.13 and 7.82 ppm, assigned through their strong NOESY correlation with signals at δ = 7.22 and 7.06 ppm, respectively), a thiazole (δ = 8.07 ppm, without NOESY correlation) and a pyrazolone (δ = 6.61 ppm, showing a NOESY correlation with



a $R^1 = R^2 = H$; **b** $R^1 = H$, $R^2 = OH$; **c** $R^1 = OH$, $R^2 = H$; **d** $R^1 = R^2 = OH$

Scheme 7. One-pot synthesis of coumarin derivatives **11a**–**11d**.

the methyl group singlet at δ = 2.34 ppm), thus confirming the presence of the four heterocycles. Moreover, the ^{1}H NMR spectrum of this compound showed two doublets at δ = 7.06 and 7.33 ppm, which were not related by an H,H-COSY correlation, and which were readily assignable to the two coumarin protons H-5′ and H-8′. These two protons were found to be linked to carbon atoms that resonated at δ = 128.3 and 116.0 ppm, respectively.

^{13}C NMR spectroscopic analysis also confirmed the structural identity, with resonances observed at δ = 111.9 ppm due to the pyrazolone, δ = 116.9 ppm due to the thiazole, δ = 152.1 ppm due to the C=N group, and δ = 158.8 and 158.6 ppm due to the C=O groups. Analysis of the HSQC spectrum allowed the assignment of all the protonated carbon resonances (Figure 4a); the connectivities encountered in the HMBC spectrum (e.g., δ_H = 7.82 ppm → δ_C = 120.3, 144.4, and 158.6 ppm; δ_H = 8.07 ppm → δ_C = 160.1 ppm; and δ_H = 8.13 ppm → δ_C = 138.1, 142.3, 144.8, and 158.8 ppm) allowed the assignment of all the quaternary carbon atoms, and confirmed the structure of compound **11c** as 3-{2-[5-(7-hydroxy-2-oxo-2*H*-chromen-3-yl)-3-methyl-1*H*-pyrazol-1-yl]thiazol-4-yl}-2*H*-chromen-2-one (Figure 4b). The molecular ion peaks of compound **11c** were found in the mass spectrum at *m/z* (%) = 469.0732 (19) $[M + H]^+$ and 492.0630 (100) $[M + Na]^+$, corresponding to the molecular formula $C_{25}H_{15}N_3O_5S$. All the above spectroscopic data clearly indicate the formation of the target product.

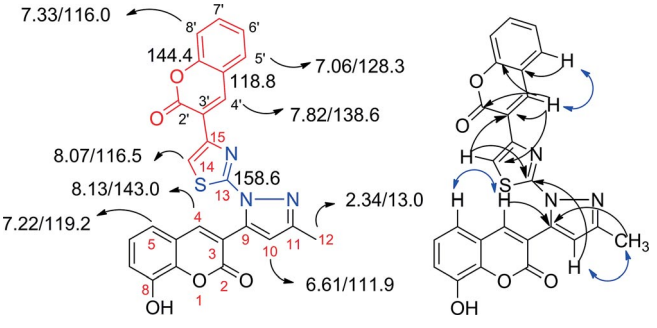
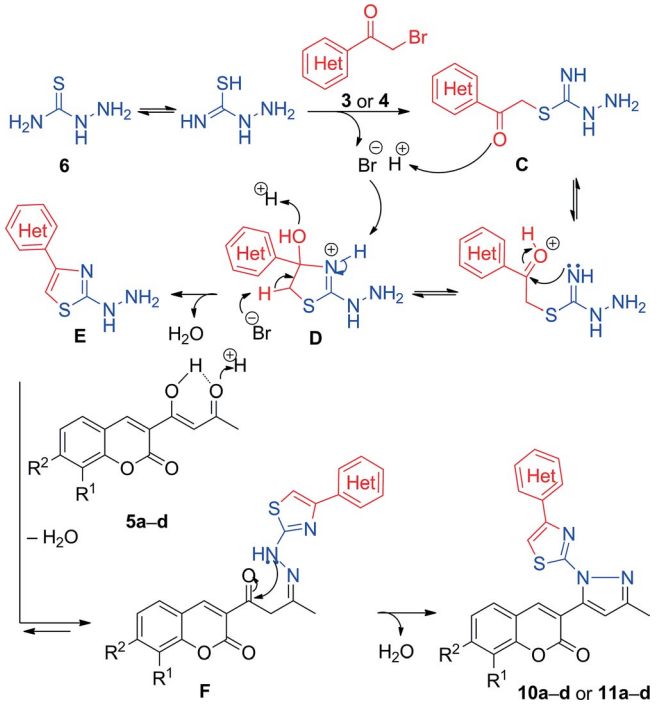


Figure 4. Selected ^{1}H/^{13}C NMR chemical shifts (δ [ppm]) (left); HMBC correlations (black arrows), and NOESY correlations (red arrows) for compound **11c** (right).

A plausible mechanism for the formation of derivatives **10a**–**10d** and **11a**–**11d** is shown in Scheme 8. First, the thiosemicarbazide could react with 3-(bromoacetyl) heterocycle **3** or **4**

with successive loss of HBr and water to give a Hantzsch thiazole product.[44,52] Nucleophilic displacement of the bromine atom of the bromoacetyl group by the sulfur atom of the thiosemicarbazide could give an open-chain α-thioketone, which, after protonation and nucleophilic attack onto the carbonyl group gives 4-hydroxythiazoline intermediate **D**. Dehydration then gives α-hydrazino-thiazole **E**. A product of type **E** has been obtained in high yield from the reaction of bromide **3** with thiosemicarbazide **6** in ethanol.[57] Subsequently, condensation reaction of 2-hydrazino-thiazole derivative **E** with (acetoacetyl)coumarins **5a**–**5d** could result in formation of the Knorr-pyrazole skeleton,[45,53,54] and give the final products via thiazolyl-hydrazono-butanoyl-coumarin derivative **F**. The reaction is initiated by protonation of one of the carbonyl groups of the 1,3-diketone to form an imine. Although such a Knorr pyrazole cyclocondensation is generally known to occur with poor regioselectivity, we observed only the 3-methyl-1,5-diarylpyrazoles (i.e., **10** and **11**) through this MCR protocol. Similar highly regioselective access to analogous 3-alkyl-1,5-diarylpyrazoles has previously been described starting from arylhydrazines and β-diketones in water under supported acid catalysis,[52] at 50–60 °C for 4–5 h in neutral or basic ethanol,[45] or under acidic conditions.[53] This further supports the proposed mechanism starting with formation of the thiazole, because production of HBr in the first step will favor the high regioselectivity of the MCR, leading to the exclusive formation of the 1,5-diarylpyrazoles **10** and **11**. Overall, this three-component domino transformation leads to the generation of one C–S, one C=N, and two C–N bonds. In this reaction, two heterocyclic ring systems, thiazole and pyrazole, were developed successively.



Scheme 8. A plausible mechanism for the formation of **10a**–**10d** and **11a**–**11d**.

Conclusions

A new, facile, one-pot, multicomponent reaction for the synthesis of substituted 3-{1-[4-(4-hydroxy-6-methyl-2-oxo-2*H*-pyran-3-yl)thiazol-2-yl]-3-methyl-1*H*-pyrazol-5-yl}coumarins **10a**–**10d** and 3-{2-[5-(substituted-2-oxo-2*H*-chromen-3-yl)-3-methyl-1*H*-pyrazol-1-yl]thiazol-4-yl}coumarins **11a**–**11d** is presented. This approach provides various advantages, such as short reaction times, good yields, no catalyst requirements, high regioselectivity, and easy workup. It does not involve the use of volatile organic solvents, which makes it an environmentally friendly process. These highly functionalized derivatives containing up to four different types of heterocyclic rings may be beneficially used in drug research; their biological evaluation is in progress. Moreover, intermediate α-hydrazonothiazoles or related α-hydrazono heterocycles are useful building blocks in MCRs;[57–60] these compounds deserve further study as they could provide access to greater skeletal diversity.

Experimental Section

General Remarks: Anhydrous ethanol, ethyl acetoacetate, 2-hydroxybenzaldehydes, dehydroacetic acid, and thiosemicarbazide were purchased from Sigma–Aldrich, and were used without further purification unless otherwise stated. Melting points were determined with a Stuart scientific SPM3 apparatus fitted with a microscope. FTIR spectra were recorded as neat solids with a Fourier Transform Bruker Vector 22 spectrometer. NMR spectra were recorded with a Bruker Avance 1 spectrometer [400 MHz (^{1}H) and 100 MHz (^{13}C)] or a Bruker AH 300 FT spectrometer [300 MHz (^{1}H) and 75 MHz (^{13}C)]. Chemical shifts are expressed in parts per million (ppm) downfield from the TMS signal. Data are reported as follows: chemical shift [multiplicity (s: singlet, d: doublet, dd: doublet of doublets, ddd: doublet of doublet of doublets, dt: doublet of triplets, t: triplet, m: multiplet), integration, coupling constants (*J*) in Hertz (Hz)]. The numbers of attached proton(s) in the ^{13}C NMR spectra were elucidated using JMOD experiments, and are described as: (CH_3) methyl, (CH_2) methylene, (CH) methine, (C) quaternary carbon atom. Shifts of ^{1}H and ^{13}C NMR spectra were calibrated using the solvent residual isotopic peak as internal reference. Reference peaks for the NMR spectra in $(CD_3S)_2O$: δ = 2.50 (^{1}H) and 39.52 (^{13}C) ppm. ^{13}C NMR assignments were checked using the free CSEARCH Robot Referee online service.[61] Deviations less than 5 ppm were observed for new compounds. The enol and keto forms are described as they appear in the spectra as a mixture of Major (M) and/or minor (m) tautomers. Mass spectra were determined with a Waters Micromass LCT Premier Q-TOF mass spectrometer coupled with a Waters Alliance HPLC system. Syntheses under microwave irradiation were carried out with a CEM Discover monomode microwave apparatus.

Synthesis of 3-Acetyl-2*H*-chromen-2-one (9) and 3-(Bromoacetyl)-2*H*-chromen-2-one (4): 3-Acetylcoumarin (**9**) and 3-(bromoacetyl)coumarin (**4**) were prepared as follows: A mixture of salicylaldehyde (12.212 g, 10.6 mL, 0.1 mol) and ethyl acetoacetate (13.014 g, 12.8 mL, 0.1 mol) was stirred in ethanol (20 mL) in the presence of a catalytic amount of piperidine (5 drops) at room temperature for 30 min. The yellowish solid was collected by filtration, then washed and recrystallized from ethanol to give 3-acetylcoumarin (**9**; 14.49 g, 77 %) as fine yellow needles; m.p. 120 °C (ref.[48] m.p. 119–121 °C). ^{1}H NMR (300 MHz, [D$_6$]DMSO): δ = 2.58 (s, 3 H), 7.37–7.45 (m, 2 H), 7.73 (ddd, *J* = 8.3, 7.3, 1.6 Hz, 1 H), 7.93 (dd, *J* = 7.7,

1.6 Hz, 1 H), 8.63 (s, 1 H) ppm. ^{13}C NMR (75 MHz, [D$_6$]DMSO): 30.5 (CH$_3$), 116.5 (CH), 118.6 (C), 124.9 (C), 125.3 (CH), 131.2 (CH), 134.9 (CH), 147.5 (CH), 155.0 (C), 158.8 (C), 195.5 (C) ppm. Coumarin **9** (3.764 g, 20 mmol) was dissolved in acetic acid (20 mL), and a solution of bromine (3.196 g, 1.03 mL, 20 mmol) in acetic acid (10 mL) was added dropwise with stirring. The mixture was heated at reflux for 1 h, then it was cooled, and the crude solid was collected by filtration. The solid was purified by recrystallization from glacial acetic acid to give 3-(bromoacetyl)coumarin (**4**; 3.205 g, 60 %) as a dark yellow solid; m.p. 160–163 °C (ref.[49] m.p. 160–163 °C). ^{1}H NMR (300 MHz, [D$_6$]DMSO): δ = 4.70 (s, 2 H$_m$), 4.90 (s, 2 H$_M$), 7.46 (dd, J = 17.2, 8.0 Hz, 2 H), 7.72–7.81 (m, 1 H), 7.96–8.00 (m, 1 H), 8.74 (s, 1 H$_m$), 8.83 (s, 1 H$_M$) ppm. HRMS (ESI): calcd. for $C_{11}H_8O_3{}^{79}Br$ [M + H]$^+$ 266.9657; found 266.9661 (21 %); calcd. for $C_{11}H_8O_3{}^{81}Br$ [M + H]$^+$ 268.9636; found 268.9639 (20 %); calcd. for $C_{11}H_7O_3{}^{79}BrNa$ [M + Na]$^+$ 288.9476; found 288.9471 (100 %); calcd. for $C_{11}H_7O_3{}^{81}BrNa$ [M + Na]$^+$ 290.9456; found 290.9451 (99 %).

General Procedure for the Synthesis of 3-Acetoacetylcoumarin Derivatives 5a–5d: Substituted 2-hydroxybenzaldehydes **7a**–**7d** (5 mmol), TAL (**2**; 0.630 g, 5 mmol), and piperidine (2 mL) were placed into a dry microwave glass flask (80 mL). The mixture was submitted to microwave irradiation at 300 W for 5–10 min. Then, the mixture was cooled to room temperature, and the solid material was collected by filtration and washed with water. The crude product was purified by recrystallization from ethanol to give pure products **5a**–**5d**.

3-(1-Hydroxy-3-oxobut-1-enyl)-2*H*-chromen-2-one (5a): Yellow solid (0.806 g, 70 %); m.p. 149 °C (ref.[42,55] m.p. 148–150 °C). M: 80 % enol form, m: 20 % ketone form. IR (neat): $\tilde{\nu}$ = 3063, 1729, 1608, 1584, 1262, 1187, 1010, 818 cm^{-1}. ^{1}H NMR (300 MHz, [D$_6$]DMSO): δ = 2.23 (s, 3 H$_m$), 2.24 (s, 3 H$_M$), 4.17 (s, 2 H$_m$), 6.90 (s, 1 H$_M$), 7.39–7.48 (m, 2 H), 7.74 (ddd, J = 8.7, 7.3, 1.6 Hz, 1 H), 7.96 (dd, J = 7.8, 1.6 Hz, 1 H), 8.81 (s, 1 H), 16.04 (s, 1 H$_M$) ppm. ^{13}C NMR (75 MHz, [D$_6$]DMSO): δ = 27.0 (CH$_{3M}$), 30.4 (CH$_{3m}$), 56.4 (CH$_{2m}$), 101.0 (CH), 116.0 (CH$_M$), 116.0 (CH$_m$), 118.1 (C$_m$), 118.3 (C$_M$), 119.7 (C$_M$), 120.5 (C$_m$), 124.9 (CH$_M$), 125.1 (CH$_m$), 130.3 (CH$_M$), 131.1 (CH$_m$), 134.4 (CH$_M$), 134.9 (CH$_m$), 146.1 (CH$_M$), 147.9 (CH$_m$), 153.9 (C), 157.3 (C), 172.9 (C), 199.0 (C) ppm. HRMS (ESI): calcd. for $C_{13}H_{11}O_4$ [M + H]$^+$ 231.0657; found 231.0652 (40 %); calcd. for $C_{13}H_{10}NaO_4$ [M + Na]$^+$ 253.0477; found 253.0471 (100 %).

7-Hydroxy-3-(1-hydroxy-3-oxobut-1-enyl)-2*H*-chromen-2-one (5b): Yellow solid (0.887 g, 72 %); m.p. 214 °C (ref.[42] m.p. 215 °C). M: enol form, 79 %; m: keto form, 21 %. IR (neat): $\tilde{\nu}$ = 3362, 1688, 1623, 1560, 1284, 1134, 1023, 822 cm^{-1}. ^{1}H NMR (300 MHz, [D$_6$]DMSO): δ = 2.19 (s, 3 H$_M$, CH$_3$), 2.21 (s, 3 H$_m$, CH$_3$), 4.09 (s, 2 H, CH$_{2m}$), 6.72 (d, J = 2.1 Hz, 1 H$_M$), 6.82 (d, 1 H$_M$, J = 2.2 Hz), 6.84 (s, 1 H$_M$), 6.85 (s, 1 H$_m$), 7.76 (d, J = 8.6 Hz, 1 H$_M$), 8.65 (s, 1 H$_m$), 8.70 (s, 1 H$_M$), 9.91 (s, 1 H, OH), 16.24 (s, 1 H, OH) ppm. ^{13}C NMR (75 MHz, [D$_6$]DMSO): δ = 26.5 (CH$_{3M}$), 30.4 (CH$_{3m}$), 56.5 (CH$_{2m}$), 100 (CH$_M$), 101.7 (CH$_M$), 101.8 (CH$_m$), 110.7 (C$_m$), 110.8 (C$_M$), 114.3 (C$_m$), 114.4 (CH$_M$), 114.6 (CH$_m$), 117.6 (C$_M$), 132.2 (CH$_M$), 133 (C$_m$), 146.6 (CH$_M$), 148.4 (CH$_M$), 156.6 (C$_M$), 157.4 (C$_m$), 157.8 (C$_M$), 164.5 (C$_M$), 165 (C$_m$), 174.9 (C$_M$), 191.3 (C$_m$), 197.4 (C$_M$), 203.3 (C$_m$) ppm. HRMS (ESI): calcd. for $C_{13}H_{11}O_5$ [M + H]$^+$ 247.0606; found 247.0609 (22 %); calcd. for $C_{13}H_{10}NaO_5$ [M + Na]$^+$ 269.0426; found 269.0426 (100 %).

8-Hydroxy-3-(1-hydroxy-3-oxobut-1-enyl)-2*H*-chromen-2-one (5c): Yellow solid (0.911 g, 74 %); m.p. 230 °C (ref.[56] m.p. 235 °C). M: enol form 83 %, m: keto form 17 %. IR (neat): $\tilde{\nu}$ = 3189, 1719, 1612, 1470, 1290, 1113, 1077, 816 cm^{-1}. ^{1}H NMR (300 MHz, [D$_6$]DMSO): δ = 2.23 (s, 3 H$_m$, CH$_3$), 2.24 (s, 3 H$_M$, CH$_3$), 4.17 (s, 2 H, CH$_{2m}$), 6.92 (s, 1 H$_M$), 7.19–7.25 (m, 2 H$_{M+m}$), 7.33–7.42 (m, 1 H$_{M+m}$), 8.69 (s, 1 H$_m$), 8.76 (s, 1 H$_M$), 10.42 (s, 1 H, OH), 16.04 (s, 1 H) ppm. ^{13}C NMR (75 MHz, [D$_6$]DMSO): δ = 27 (CH$_{3M}$), 30.39 (CH$_{3m}$), 56.4 (CH$_{2m}$), 100.9 (CH$_M$), 119.0 (C$_m$), 119.2 (C$_M$), 119.5 (C$_M$), 120.2 (CH$_M$), 120.5 (CH$_M$), 120.9 (CH$_m$), 124.9 (CH$_M$), 125.1 (CH$_m$), 142.6 (C$_M$), 144.3 (C$_M$), 146.5 (CH$_M$), 148.3 (C$_m$), 157.3 (C$_M$), 173.1 (C$_M$), 191.8 (C$_m$), 199.0 (C$_M$), 203.3 (C$_m$) ppm. HRMS (ESI): calcd. for $C_{13}H_{11}O_5$ [M + H]$^+$ 247.0606; found 247.0607 (20 %); calcd. for $C_{13}H_{10}NaO_5$ [M + Na]$^+$ 269.0426; found 269.0426 (100 %).

7,8-Dihydroxy-3-(1-hydroxy-3-oxobut-1-enyl)-2*H*-chromen-2-one (5d): Yellow solid (0.905 g, 69 %); m.p. 252 °C. M: enol form 80 %, m: keto form 20 %. IR (neat): $\tilde{\nu}$ = 3331, 1692, 1612, 1464, 1253, 1159, 1078, 813 cm^{-1}. ^{1}H NMR (300 MHz, [D$_6$]DMSO): δ = 2.19 (s, 3 H$_M$, CH$_3$), 2.22 (s, 3 H$_m$, CH$_3$), 4.11 (s, 2 H$_m$, CH$_2$), 6.86 (d, J = 8.6 Hz, 1 H$_M$), 6.89 (s, 1 H$_M$), 6.89 (d, J = 8.6 Hz, 1 H$_m$), 7.29 (d, J = 8.6 Hz, 1 H$_M$), 7.34 (d, J = 8.6 Hz, 1 H$_m$), 8.61 (s, 1 H$_m$), 8.66 (s, 1 H$_M$), 10.17 (br. s, 2 H, OH), 16.27 (s, 1 H$_M$, OH) ppm. ^{13}C NMR (75 MHz, [D$_6$]DMSO): δ = 26.5 (CH$_{3M}$), 30.6 (CH$_{3m}$), 56.5 (CH$_{2m}$), 100.0 (CH$_M$), 111.6 (C$_m$), 111.8 (C$_M$), 113.5 (CH$_M$), 113.6 (CH$_m$), 114.1 (C$_M$), 118.0 (C$_m$), 121.8 (CH$_M$), 122.7 (CH$_m$), 131.7 (C$_M$), 131.8 (C$_m$), 144.2 (C$_M$), 144.9 (C$_m$), 147.2 (CH$_M$), 149.1 (CH$_m$), 152.7 (C$_M$), 153.2 (C$_m$), 157.8 (C$_M$), 159.4 (C$_m$), 174.8 (C$_M$), 191.5 (C$_m$), 197.5 (C$_M$), 203.4 (C$_m$) ppm. HRMS (ESI): calcd. for $C_{13}H_{11}O_6$ [M + H]$^+$ 263.0566; found 263.0552 (20 %); calcd. for $C_{13}H_{10}NaO_6$ [M + Na]$^+$ 285.0375; found 285.0368 (100 %).

General Procedure for the Synthesis of Compounds 10a–10d: A mixture of 3-(bromoacetyl)-4-hydroxy-6-methyl-2*H*-pyran-2-one (**3**; 0.247 g, 1 mmol), thiosemicarbazide (0.091 g, 1 mmol), and 3-(acetoacetyl)coumarin derivative (**5a**–**5d**; 1 mmol), in anhydrous ethanol (10 mL) was heated at reflux for 4 h. The products obtained were collected by filtration, washed with hot ethanol, dried, then washed again with DMSO in order to remove all traces of the starting materials.

3-{1-[4-(4-Hydroxy-6-methyl-2-oxo-2*H*-pyran-3-yl)thiazol-2-yl]-3-methyl-1*H*-pyrazol-5-yl}-2*H*-chromen-2-one (10a): Yellow solid (0.347 g, 80 %); m.p. 262–264 °C. IR (neat): $\tilde{\nu}$ = 3410, 1715, 1687, 1346 cm^{-1}. ^{1}H NMR (300 MHz, [D$_6$]DMSO): δ = 2.16 (s, 3 H, pyrone), 2.36 (s, 3 H, pyrazole), 5.90 (s, 1 H, pyrone), 6.71 (s, 1 H, pyrazole), 7.41–7.57 (m, 2 H), 7.73 (t, J = 7.4 Hz, 1 H), 7.83 (d, J = 7.7 Hz, 1 H), 7.98 (s, 1 H, thiazole), 8.45 (s, 1 H, coumarin), 12.47 (s, 1 H, OH) ppm. ^{13}C NMR (75 MHz, [D$_6$]DMSO): δ = 13.2 (CH$_3$-12), 19.2 (CH$_3$-20), 94.1 (C-16), 100.4 (CH), 112.3 (CH), 113.1 (CH), 116.2 (CH), 117.7 (C), 118.4 (C), 125.0 (CH), 129.1 (CH), 133.1 (CH), 137.5 (C), 143.7 (C), 144.3 (CH), 152.3 (C), 153.7 (C), 158.3 (C), 159.9 (C), 161.1 (C), 162.8 (C), 167.5 (C) ppm. HRMS (ESI): calcd. for $C_{22}H_{16}N_3O_5S$ [M + H]$^+$ 434.0811; found 434.0814 (43 %); calcd. for $C_{22}H_{15}N_3NaO_5S$ [M + Na]$^+$ 456.063; found 456.0638 (100 %).

7-Hydroxy-3-{1-[4-(4-hydroxy-6-methyl-2-oxo-2*H*-pyran-3-yl)thiazol-2-yl]-3-methyl-1*H*-pyrazol-5-yl}2*H*-chromen-2-one (10b): Yellow solid (0.328 g, 73 %); m.p. >300 °C. IR (neat): $\tilde{\nu}$ = 3410, 1715, 1687, 1346 cm^{-1}. ^{1}H NMR (400 MHz, [D$_6$]DMSO): δ = 2.16 (s, 3 H, pyrone), 2.31 (s, 3 H, pyrazole), 5.87 (s, 1 H, pyrone), 6.56 (s, 1 H, pyrazole), 6.77 (d, J = 1.6 Hz, 1 H, 8-H), 6.85 (dd, J = 8.4, 1.6 Hz, 1 H, 6-H), 7.58 (d, J = 8.4 Hz, 1 H, 5-H), 7.96 (s, 1 H, thiazole), 8.17 (s, 1 H, 4-H), 10.60 (s, 1 H, OH), 12.45 (s, 1 H, OH) ppm. ^{13}C NMR (100 MHz, [D$_6$]DMSO): δ = 13.0 (CH$_3$-12), 19.1 (CH$_3$-20), 94.4 (C-16), 100.5 (CH-18), 102.2 (CH-8), 111.3 (C-4a), 112.1 (CH-14), 112.7 (CH-10), 113.1 (C-3), 113.8 (CH-6), 130.5 (CH-5), 138.5 (C-9), 144.1 (C-15), 144.5 (CH-4), 152.4 (C-11), 156.2 (C-8a), 158.9 (CO-2), 160.2 (C-13), 161.4 (CO-21), 162.4 (C-7), 162.8 (C-17 and C-19) ppm. HRMS (ESI): calcd. for $C_{22}H_{16}N_3O_6S$ [M + H]$^+$ 450.0760; found 450.0760 (19 %); calcd. for $C_{22}H_{15}N_3NaO_6S$ [M + Na]$^+$ 472.0579; found 472.0579 (100 %).

8-Hydroxy-3-{1-[4-(4-hydroxy-6-methyl-2-oxo-2*H*-pyran-3-yl)thiazol-2-yl]-3-methyl-1*H*-pyrazol-5-yl}-2*H*-chromen-2-one (10c): Yellow solid (0.342 g, 76 %); m.p. >300 °C. IR (neat): $\tilde{\nu}$ = 3201, 1730, 1672, 1360 cm^{-1}. ^1H NMR (300 MHz, [D_6]DMSO): δ = 2.17 (s, 3 H, pyrone), 2.34 (s, 3 H, pyrazole), 5.94 (s, 1 H, pyrone), 6.70 (s, 1 H, pyrazole), 7.00–7.35 (m, 3 H), 7.99 (s, 1 H, thiazole), 8.39 (s, 1 H, coumarin), 10.30 (s, 1 H, OH), 12.45 (s, 1 H, OH) ppm. ^{13}C NMR (75 MHz, [D_6]DMSO): δ = 13.2 (CH_3-12), 19.2 (CH_3-20), 94.1 (C-16), 100.5 (CH), 112.2 (CH), 113.1 (CH), 117.5 (C), 119.0 (CH), 119.3 (CH), 119.4 (C), 124.9 (CH), 137.6 (C), 142.4 (C), 143.7 (C), 144.5 (C), 144.7 (CH), 152.3 (C), 158.2 (C), 159.9 (C), 161.1 (C), 162.7 (C), 167.6 (C) ppm. HRMS (ESI): calcd. for $C_{22}H_{16}N_3O_6S$ [M + H]$^+$ 450.0760; found 450.0763 (33 %); calcd. for $C_{22}H_{15}N_3NaO_6S$ [M + Na]$^+$ 472.0579; found 472.0573 (100 %).

7,8-Dihydroxy-3-{1-[4-(4-hydroxy-6-methyl-2-oxo-2*H*-pyran-3-yl)thiazol-2-yl]-3-methyl-1*H*-pyrazol-5-yl}-2*H*-chromen-2-one (10d): Yellow solid (0.391 g, 84 %); m.p. >300 °C. IR (neat): $\tilde{\nu}$ = 3419, 1719, 1668, 1342 cm^{-1}. ^1H NMR (300 MHz, [D_6]DMSO): δ = 2.14 (s, 3 H, pyrone), 2.29 (s, 3 H, pyrazole), 5.93 (s, 1 H, pyrone), 6.60 (s, 1 H, pyrazole), 6.88 (d, *J* = 8.5 Hz, 1 H), 7.14 (d, *J* = 8.5 Hz, 1 H), 7.93 (s, 1 H, thiazole), 8.22 (s, 1 H, coumarin), 9.54 (s, 1 H, OH), 10.41 (s, 1 H, OH), 12.51 (s, 1 H, OH) ppm. ^{13}C NMR (75 MHz, [D_6]DMSO): δ = 13.7 (CH_3-12), 19.2 (CH_3-20), 94.1 (C-16), 100.6 (CH), 111.8 (CH), 112.0 (C), 112.4 (C), 112.8 (CH), 113.1 (CH), 119.8 (CH), 132.0 (C), 138.3 (C), 143.7 (C), 143.9 (C), 145.1 (CH), 150.7 (C), 152.2 (C), 158.6 (C), 160.0 (C), 161.1 (C), 162.7 (C), 167.7 (C) ppm. HRMS (ESI): calcd. for $C_{22}H_{16}N_3O_7S$ [M + H]$^+$ 466.0709; found 466.0715 (20 %); calcd. for $C_{22}H_{15}N_3NaO_7S$ [M + Na]$^+$ 488.0528; found 488.0541 (100 %).

General Procedure for the Synthesis of Compounds 11a–11d: A mixture of 3-(bromoacetyl)-2*H*-chromen-2-one (**7**; 0.267 g, 1 mmol), thiosemicarbazide (0.091 g, 1 mmol), and 3-(acetoacetyl)coumarin derivatives (**5a**–**5d**; 1 mmol) in anhydrous ethanol (10 mL) was heated at reflux for 4 h. The products obtained were collected by filtration, washed with hot ethanol, dried, then washed again with DMSO in order to remove all traces of the starting materials.

3-{2-[3-Methyl-5-(2-oxo-2*H*-chromen-3-yl)-1*H*-pyrazol-1-yl]thiazol-4-yl}-2*H*-chromen-2-one (11a): Yellow solid (0.372 g, 82 %); m.p. >300 °C. ^1H NMR (300 MHz, [D_6]DMSO): δ = 2.36 (s, 3 H), 6.71 (s, 1 H, pyrazole), 6.79 (dd, *J* = 7.8, 1.3 Hz, 1 H), 7.30 (td, *J* = 7.6, 0.9 Hz, 1 H), 7.41 (d, *J* = 8.3 Hz, 1 H), 7.51 (td, *J* = 7.6, 1.0 Hz, 1 H), 7.58–7.63 (m, 1 H), 7.68 (d, *J* = 8.1 Hz, 1 H), 7.74 (s, 1 H, thiazole), 7.78–7.84 (m, 1 H), 7.87 (dd, *J* = 7.7, 1.4 Hz, 1 H), 8.13 (s, 1 H, coumarin), 8.34 (s, 1 H, coumarin) ppm. ^{13}C NMR (75 MHz, [D_6]DMSO): δ = 13.8 (CH_3), 112.5 (CH), 116.6 (CH), 116.8 (CH), 117.3 (CH), 118.9 (C), 119.2 (C), 120.4 (C), 120.6 (C), 125.3 (CH), 125.9 (CH), 128.2 (CH), 129.7 (CH), 132.7 (CH), 133.3 (CH), 138.6 (CH), 139.6 (C), 143.1 (CH), 143.3 (C), 152.4 (C), 152.8 (C), 153.8 (C), 155.7 (CS), 157.4 (C), 160.2 (C) ppm. HRMS (ESI): calcd. for $C_{25}H_{16}N_3O_4S$ [M + H]$^+$ 454.0862; found 454.0857 (28 %); calcd. for $C_{25}H_{15}N_3NaO_4S$ [M + Na]$^+$ 476.0681; found 476.0677 (100 %).

3-{2-[5-(7-Hydroxy-2-oxo-2*H*-chromen-3-yl)-3-methyl-1*H*-pyrazol-1-yl]thiazol-4-yl}-2*H*-chromen-2-one (11b): Yellow solid (0.352 g, 75 %); m.p. >300 °C. IR (neat): $\tilde{\nu}$ = 3380, 1723, 1603, 1354 cm^{-1}. ^1H NMR (300 MHz, [D_6]DMSO): δ = 2.34 (s, 3 H), 6.65 (s, 1 H, pyrazole), 6.91–6.95 (m, 3 H), 7.30 (t, *J* = 7.5 Hz, 1 H), 7.43 (d, *J* = 8.3 Hz, 1 H), 7.60–7.69 (m, 2 H), 7.78 (s, 1 H, thiazole), 8.11 (s, 1 H, coumarin), 8.18 (s, 1 H, coumarin), 10.92 (s, 1 H, OH) ppm. ^{13}C NMR (75 MHz, [D_6]DMSO): δ = 13.3 (CH_3), 102.1 (CH), 111.0 (C), 111.7 (CH), 113.7 (CH), 114.9 (C), 116.2 (CH), 116.7 (CH), 118.5 (C), 120.1 (C), 124.7 (CH), 127.7 (CH), 130.6 (CH), 132.2 (CH), 135 (C), 138.1 (CH), 143.1 (CH), 143.9 (C), 151.7 (C), 152.4 (C), 155.4 (C), 158.3 (C), 159.1 (C), 159.8 (C), 162.2 (C) ppm. HRMS (ESI): calcd. for $C_{25}H_{16}N_3O_5S$ [M + H]$^+$ 470.0811; found 470.0818 (18 %); calcd. for $C_{25}H_{15}N_3NaO_5S$ [M + Na]$^+$ 492.0630; found 492.0642 (100 %).

3-{2-[5-(8-Hydroxy-2-oxo-2*H*-chromen-3-yl)-3-methyl-1*H*-pyrazol-1-yl]-thiazol-4-yl}-2*H*-chromen-2-one (11c): Yellow solid (0.357 g, 76 %); m.p. >300 °C. IR (neat): $\tilde{\nu}$ = 3140, 1719, 1687, 1347 cm^{-1}. ^1H NMR (400 MHz, [D_6]DMSO): δ = 2.34 (s, 3 H, CH_3), 6.61 (s, 1 H, pyrazole), 7.06 (d, *J* = 7.4 Hz, 1 H, 5′-H), 7.21–7.25 (m, 4 H, 5-H, 6-H, 7-H, 6′-H), 7.33 (d, *J* = 8.1 Hz, 1 H, 8′-H), 7.56 (t, *J* = 7.5 Hz, 1 H, 7′-H), 7.82 (s, 1 H, 4′-H), 8.07 (s, 1 H, thiazole), 8.13 (s, 1 H, 4-H) ppm. ^{13}C NMR (100 MHz, [D_6]DMSO): δ = 13.0 (CH_3-12), 111.9 (CH-10), 116.0 (CH-8′), 116.5 (CH-14), 118.9 (C-4′a), 119.1 (CH-7), 119.2 (CH-5), 119.9 (C-4a), 120.1 (C-3), 120.3 (C-3′), 124.7 (CH-6′), 125.1 (CH-6), 128.3 (CH-5′), 132.1 (CH-7′), 138.1 (C-9), 138.6 (CH-4′), 142.3 (C-8), 143.0 (CH-4), 144.4 (C-15), 144.8 (C-8a), 152.1 (C-11), 152.7 (C-8′a), 158.6 (C-2′), 158.8 (C-2), 160.1 (C-13) ppm. HRMS (ESI): calcd. for $C_{25}H_{16}N_3O_5S$ [M + H]$^+$ 470.0811; found 470.0813 (19 %); calcd. for $C_{25}H_{15}N_3NaO_5S$ [M + Na]$^+$ 492.063; found 492.0630 (100 %).

3-{2-[5-(7,8-Dihydroxy-2-oxo-2*H*-chromen-3-yl)-3-methyl-1*H*-pyrazol-1-yl]thiazol-4-yl}-2*H*-chromen-2-one (11d): Yellow solid (0.388 g, 79 %); m.p. >300 °C. IR (neat): $\tilde{\nu}$ = 3348, 1703, 1625, 1345 cm^{-1}. ^1H NMR (400 MHz, [D_6]DMSO): δ = 2.35 (s, 3 H, CH_3), 6.62 (s, 1 H, pyrazole), 6.92 (d, *J* = 8.4 Hz, 1 H), 7.07–7.18 (m, 2 H), 7.29 (td, *J* = 7.7, 0.9 Hz, 1 H), 7.39 (d, *J* = 8.3 Hz, 1 H), 7.58–7.64 (m, 1 H), 7.86 (s, 1 H, coumarin), 8.09 (s, 1 H, thiazole), 8.10 (s, 1 H, coumarin), 9.49 (s, 1 H, OH), 10.19 (s, 1 H, OH) ppm. ^{13}C NMR (100 MHz, [D_6]DMSO): δ = 13.3 (CH_3), 111.8 (CH), 111.9 (C), 113.0 (CH), 114.8 (C), 116.0 (CH), 116.6 (CH), 118.6 (C), 119.6 (CH), 120.1 (C), 124.9 (CH), 128.2 (CH), 132.2 (CH), 132.3 (COH), 138.3 (C), 138.4 (CH), 143.4 (C), 143.7 (CH), 144.0 (C), 150.4 (C), 151.7 (C), 152.4 (C), 158.4 (C), 159.2 (C), 159.8 (C) ppm. HRMS (ESI): calcd. for $C_{25}H_{16}N_3O_6S$ [M + H]$^+$ 486.0754; found 486.0756 (17 %); calcd. for $C_{25}H_{15}N_3NaO_6S$ [M + Na]$^+$ 508.0574; found 508.0579 (100 %).

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