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Manipulating a Multicomponent Reaction: A Straightforward Approach to Chromenopyrazole Hybrid Scaffolds

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Dedicated to Prof. C. A. Tsoleridis on the occasion of his 67th birthday

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Abstract An easy access to hybrid bioactive molecules, such as the chromenopyrazoles, is described based on the three-component reactions of 3-formylchromones, arylhydrazines, and acetylenedicarboxylates. By manipulating the reaction, four different scaffolds can be derived in an easy, versatile, and robust fashion. To underscore the potential, generality, and diversity that can be generated, representative libraries of each scaffold were synthesized. Moreover, a comprehensive NMR analysis with full assignment of all ^1H and ^{13}C NMR chemical shifts has been performed.

Key words 3-formylchromones, multicomponent reactions, chromenopyrazoles, microwave irradiation, hybrid molecules, zwitterions

The use of combinatorial chemistry techniques and robotized screening, the so-called high throughput synthesis and high throughput screening (HTS), has greatly influenced both the design of new chemical libraries for bioassays and the level of research conducted in industrial laboratories. However during recent years, more scientists have applied HTS to the identification of chemical probes and drug leads for an expanding number of biological targets and because of this the limitations and pitfalls of HTS technologies are becoming obvious. Inflation-adjusted industrial R&D costs per novel drug have increased nearly 100-fold between 1950 and 2010 and drugs are more likely to fail in clinical development today than in the 1970s.^{1–6} The quality of the libraries in terms of diversity and complexity seems to be a major issue, thus alternative, complementary techniques have been applied, for example advanced *in silico* approaches,^{7–9} fragment-based ligand dis-

covery with various biophysical screening systems,^{10–16} or other types of synthetic approaches e.g. multicomponent reaction (MCR) chemistry.^{17–23} In the same direction, we currently know that a few structural subunits of a certain bioactive molecule may be more relevant to a specific pharmacologic activity, governing the main interactions with a receptor. Therefore, some molecular scaffolds may have pharmacophoric characteristics for a certain type of receptor and not for others. These types of scaffolds are called privileged and the privileged scaffold concept is commonly used in medicinal chemistry, either alone or as a combined strategy, mixing other molecular design techniques such as bioisosterism.^{24,25} Combining two privileged structures in one chemical entity leading to hybrid molecules, also known as designed multiple ligands, for a specific biological target is an emerging approach in drug discovery that could generate a lead compound being more effective than its individual components. Furthermore, a hybrid molecule can independently act at two distinct pharmacological target structures in an overall synergistic manner and consequently is designed in order to maintain its individual components at these two targets. Due to the complexity of certain diseases, such as neurodegenerative disorders that are not effectively targeted by one highly selective ligand, the hybrid approach would have inherent advantages.^{26–29}

Chromenopyrazoles, as a characteristic example of a hybrid molecule combining both a chromone³⁰ and a pyrazole ring,^{25,31} exhibit a wide range of biological and pharmacological activities. Recently, they gained attention as Δ^9 -tetrahydrocannabinoid analogues (Figure 1, compounds **1** and **2**) with non-psychoactive CB1 and CB2 receptor selectivity, exhibiting *in vivo* activity in a model of multiple sclerosis³²

Figure 1 Recent examples of chromenopyrazole scaffolds with enhanced biological activity

and having peripheral antinociceptive properties in a rat model.³³ The chromenopyrazole-based conjugates **3**, which bear the bioactive phenyl-4*H*-pyrazol-3-one moiety (Edaravone, brand name: Radicut)³⁴ were identified as anti-inflammatory molecules (inhibition of COX-2, COX-1, and 5-LOX),³⁵ anticancer agents on 60 different cell lines³⁶ and multi-ion detectors.³⁷ Finally, compounds **4** demonstrated *in vitro* antibacterial and antifungal activities.³⁸ There are few synthetic approaches towards chromenopyrazole scaffolds, but they are limited in scope, availability of starting materials, and difficulty in parallel producing libraries for screening. Some syntheses are based on chromone phenylhydrazones in a three-step sequence³⁹ or a four-component reaction involving nitroketene *N,S*-acetals.⁴⁰ Chromenopyrazolines were synthesized from chromonyl chalcones either by 1,3-dipolar cycloaddition with diazomethane^{41,42} or by refluxing with hydrazines.^{43–46}

In addition, direct condensation of 3-formylchromones with 1-phenyl-1*H*-pyrazol-5(4*H*)-ones towards the desired Knoevenagel adduct was also employed for the synthesis of chromenopyrazolinones.^{47,48} Recently, a three-component reaction catalyzed by Lewis acid was described involving differently substituted aromatic aldehydes, ethyl acetoacetate, and phenylhydrazine yielded pyrazolone derivatives.⁴⁹ Overall we could comment that the diversification opportunities in the above-mentioned synthetic approaches are relatively low, since most of the structural modifications of the scaffolds occurred at the chromene ring. We believe that a cheap, scalable, and one-pot, diverse parallel approach to chromenopyrazoles could be of high interest and a valuable tool for constructing vast libraries as screening decks.

Due to our long experience and extensive studies of employing amphiphilic species on the 3-formyl-^{50–55} (Scheme 1, compounds **5–8**) or 3-cyanochromone^{56,57} and taking into account the general concepts existing in literature of

constructing the chromenopyrazole and chromenopyrazolinone scaffolds, we envisioned providing an easy access to these hybrid molecules. A versatile and robust procedure with as many as possible diversity in order to build decks for screening would be our goal.

For this reason, we designed a multicomponent reaction that is based on the zwitterionic intermediates of a hydrazine derivative and an acetylenedicarboxylate molecule reacting with an aldehyde,^{58–61} in our case the 3-formylchromone. This reaction could serve our purpose; cheap and

Scheme 1 Studies on the 3-formylchromone derivatives of our group based on the generation of amphiphilic species

Scheme 2 Strategy and optimization of the 3-component reaction of 3-formylchromones, arylhydrazines, and acetylenedicarboxylates leading to the scaffolds **12**, **13**, **15**, and **16**

easily available starting materials that give adducts with at least four points of diversification incorporating both the chromene and pyrazole core.

We started our investigation on the multicomponent reaction of the 6-chloro-3-formylchromone (**9a**) with *p*-chlorophenylhydrazine (**10a**) and dimethyl acetylenedicarboxylate (DMAD, **11a**) in 1:1:1 ratio (Scheme 2). After quite

some optimization, we performed this reaction in acetic acid^{60,62} under microwave irradiation (130 °C, 10 min) affording, to our delight, the chromenopyrazole hybrid (**Z**)-**12a** in 61% yield. As it was expected, compound **12a** was derived from the intermediate zwitterion of the hydrazine and DMAD (mechanism on Scheme 5, intermediate A). It is worth mentioning, when a different ratio of the reagents

Scheme 3 Three-component reaction of 3-formylchromones, arylhydrazines, and acetylenedicarboxylates leading to the scaffolds **12** and **13**

Figure 2 Library synthesis of the scaffolds **12** and **13** demonstrating the diversity of the reaction

was used, **9a/10a/11a** in 1:2:1 ratio with similar experimental conditions (120 °C, 5 min), then an additional molecule of hydrazine was added to the initial chromenopyrazole derivative **12a** on the chromene ring (4-oxo), yielding the compound (Z)-**13a** in 59% yield (Scheme 2 and Scheme 3). These kinds of reactions on the carbonyl group of the chromone are not commonly reported in literature, since the 3-formylchromone ring is quite prone to ring opening.⁶⁰ These hybrid molecules, **12** and **13**, offer many possibilities for building libraries since they can be highly diversified and easily obtained (pathway A). Next, we investigated the potential outcome of the reaction if a different pathway is followed (pathway B) rather than through a zwitterionic intermediate. To ensure this, we firstly obtained hydrazone **14b** from the reaction of 6-methyl-3-formylchromone (**9b**) with *p*-methylphenylhydrazine (**10b**).³⁶ This time, we wanted to build the targeted hybrid compound by forming the pyrazole core utilizing the C=N bond.^{39,64–66} Thus, compound **14b** was reacted with DMAD in order to isolate the corresponding cycloadduct. Indeed, the reaction proceeded smoothly and after microwave irradiation at 120 °C for only 5 minutes, we were able to isolate the [3+2] cycloadduct **15b** in 49% yield along with compound **17b**. In the latter, DMAD is not being incorporated whereas the chromone ring adopts an open form.^{63,67–69} In addition, we were also interested in obtaining directly the aromatic pyrazoles; Therefore we treated, according to literature,⁷⁰ the hydrazone **14b** with DMAD in refluxing toluene in the presence of Yb(OTf)₃ (50 mol%) affording the desired derivative **16b** in 53% yield along again with compound **17b**.

To underscore the potential and generality of our three-component reaction, we built easily a representative library with various substituted 3-formylchromones, phenylhydrazines, and acetylenedicarboxylates based on the pathway A (Figure 2). We synthesized both the two scaffolds **12** and **13** in moderate to good yields, using both electron-donating as well as -withdrawing substituents. The preferred stereochemistry of both compounds **12a–g** and **13a–l** is (Z)-con-

figuration (see structure assignments section). In addition it seems that the substituents on the chromene ring or on the hydrazine do not play a significant role in the yield of the reaction.

Next, starting from the hydrazones **14a–d** (obtained in 60–75% yield)^{39,71} following the pathway B depending on the optimized conditions, we built a representative library of the chromenopyrazolines **15a–d** (relatively stereochemistry depicted, the *cis* other isomer formed by approximately 10%, see structure assignments section) and chromenopyrazoles **16a–d** in moderate to good yields (Scheme 4 and Figure 3).

It is worth mentioning that treatment of **15a–d** with Yb(OTf)₃ in refluxing toluene for 5 hours or in MW (90 °C, 20 min) did not afford the corresponding aromatic compounds **16a–d**.

The plausible mechanism of the derivatives **12** is depicted in Scheme 5. It includes the formation of the zwitterion A which through the formation of the intermediate C, attacks the 3-formylchromone leading to the chromenopyrazoles **12**. Further reaction with an additional arylhydrazine molecule, afforded the imine derivative **13**. Compounds **15** and **16** are formed after a [3+2] cycloaddition,⁶⁴ whereas the mechanism of compounds **17** includes the addition of one molecule of hydrazine and subsequent opening of the chromone ring.

The assigned molecular structures of the new compounds **12**, **13** and **15** were based on rigorous spectroscopic analysis including NMR (¹H, ¹³C, COSY, NOESY, HETCOR, and COLOC), MS, and elemental analysis data. In Figure 4 the COLOC correlations of protons with carbons via ²J and ³J coupling for compounds **12g**, **13k**, and **15a** are depicted.

Concerning the identification of compound **12g**, in ¹H NMR the aromatic hydrogens of the chromone ring appeared at δ = 8.23 (s, 1 H) and 7.43 (s, 1 H) whereas the corresponding carbons resonate at δ = 126.4 and 120.5. The two quaternary carbons at positions 6' and 7' of the chromone ring absorb at δ = 133.4 and 144.3 respectively, while

Scheme 4 Reaction of arylhydrazones and acetylenedicarboxylates leading to the scaffolds **15** and **16**

Figure 3 Library synthesis of the scaffolds **15** and **16** along with the ‘open-form’ chromones **17**

Figure 4 HMBC correlations between hydrogens and carbons via $^2J_{C-H}$ and $^3J_{C-H}$ couplings for the compounds **12g**, **13k**, and **15a**, respectively

the C-3' and C-4a' give signals at $\delta = 118.9$ and 123.0 . The H-2' absorbs at $\delta = 10.6$, giving a single peak and the corresponding carbon at $\delta = 164.2$. The C-8a' (next to oxygen) resonates at $\delta = 154.3$ and the hydrogen of the double bond at position 6 shows signal at $\delta = 9.12$ with its carbon at $\delta = 142.6$. In the five-membered ring, the carbonyl carbon at position 5 absorbs at $\delta = 162.6$ and the C-4 and C-3 at $\delta = 124.0$ and 141.1 , respectively. The H-2'', H-3'', and H-4'' give signals at $\delta = 7.92$, 7.44 , and 7.28 , respectively with their carbons resonating at $\delta = 120.54$, 129.0 , and 126.5 . The C-1'' absorbs at $\delta = 137.6$. From the 2D spectra is concluded that the hydrogen at $\delta = 10.6$ corresponds to position 2', as has HMBC correlations with the C-3', C-8a', C-6, and the carbonyl carbon of the chromone ring. The hydrogen at $\delta = 9.12$ belongs to the double bond at position 6 as it is correlated with the C-4, C-3, C-3', C-2', C-5, and C-4'.

The configuration of the double bond is concluded from the coupling of the hydrogen at $\delta = 9.12$ with the carbons at $\delta = 162.6$ ($^3J_{C-H} = 10.8$ Hz) and 141.1 ($^3J_{C-H} = 6.6$ Hz), i.e. large coupling is *trans* configuration, while the small coupling is *cis* configuration (see the Supporting Information for more details).

For compound **13k**, the aromatic hydrogens of the chromone ring absorb at $\delta = 6.90$ (s, 1 H), 7.14 (d, $J = 8.3$ Hz, 1 H), and 6.87 (d, $J = 8.3$ Hz, 1 H) whereas the corresponding carbons resonate at $\delta = 131.9$, 132.4 , and 116.5 . The C-6 absorbs at $\delta = 128.7$ and the methyl group as substituent at $\delta = 20.3$. The C-3 and C-4a absorb at $\delta = 119.3$ and 114.2 respectively. The H-2 absorbs at $\delta = 9.65$ giving a single peak with its carbon at $\delta = 145.0$. The C-4 resonates at $\delta = 147.7$ and the C-4', C-3' and C-5' absorb at $\delta = 118.3$, 139.9 and 162.5 , respectively. The H-9 absorbs at $\delta = 8.38$ and the corresponding carbon resonates at $\delta = 142.3$. The H-2'' and H-3'' give signals at $\delta = 7.29$ and 7.11 respectively, while their

Scheme 5 Plausible mechanism of the derivatives **12a–g**

carbons absorb at $\delta = 123.7$ and 129.32 . The C-1''' and C-4''' absorb at $\delta = 137.3$ and 137.7 . From the 2D spectra is concluded that the hydrogen at $\delta = 8.38$ corresponding to position 9, shows HMBC correlation with the C-2, C-4, C-3', C-4', and C-5'. The hydrogen at $\delta = 9.65$ has HMBC correlation with C-3 and C-4 (see the Supporting Information for more details). Finally, concerning compound **15a** the aromatic hydrogens of the chromone ring give signals at $\delta = 7.41$ (d, $J = 8.5$ Hz, 1 H), 7.51 (dd, $J = 8.5, 1.8$ Hz, 1 H), and 8.01 (d, $J = 1.8$ Hz, 1 H), and the corresponding carbons absorb at $\delta = 118.0, 135.3$, and 125.4 , respectively. The C-3, C-4a, and C-6 resonate at $116.6, 123.7$, and 135.9 , respectively. The H-2 absorbs at $\delta = 8.64$ giving a single peak and the corresponding carbon absorbs at $\delta = 154.4$.

The C-8a (adjacent to oxygen) resonates at $\delta = 154.4$. In the five-membered ring, the H-5' and H-4' absorb at $\delta = 5.06$ and 5.21 with the carbons at $\delta = 64.7$ and 56.7 , respectively. The C-3' and the carbonyls of the ester groups on C-5' and C-4' give signals at $\delta = 140.3, 169.7$, and 169.2 , respectively. The H-2'' and H-3'' absorb at $\delta = 7.01$ and 7.23 with their carbons to resonate at $\delta = 114.4$ and 129.1 . Carbons at positions 1'' and 4'' absorb at $\delta = 142.2$ and 125.3 . From the 2D spectra is concluded that the hydrogen at $\delta = 8.64$ corresponds to the hydrogen at C-2 as shows a large coupling ($J = 200$ Hz) which is characteristic for a hydrogen at this position. It is worth mentioning that the other isomer formed by approximately 10%, with the ester group in *cis* position, the hydrogens absorb at $\delta = 5.03$ and 5.39 with $J = 13$ Hz, while the corresponding methoxy groups absorb at $\delta = 3.68$ and 3.72 (see the Supporting Information for more details).

In conclusion, in the present work we described a thorough study of the 3-component reaction of 3-formylchromones with arylhydrazines and acetylenedicarboxylates. Following the different pathways (pathway A or B) of the reaction, we built a representative library of four scaffolds that possess two privileged structures. These chromenopyrazole derivatives could be used against various biological targets (e.g., CB1 and CB2 receptors, COX-1,2 and 5-LOX). Furthermore, we demonstrated the different routes that an

MCR can follow and how these in our case can be accessed by the formation of the zwitterion ion or not. Finally, a thorough NMR analysis with full assignment of all ^1H and ^{13}C NMR chemical shifts has been unambiguously achieved which will be useful for the interpretation of similar scaffolds.

Melting points were measured on a Kofler hot stage. Column chromatography was carried out using Merck silica gel. TLC was performed using precoated silica gel glass plates 0.25 mm containing fluorescent indicator UV254 purchased from Macherey-Nagel using petroleum ether (bp 60 – 80 °C)/EtOAc (3:1). NMR spectra were recorded at r.t. either on an Agilent 500 spectrometer (for ^1H at 500 MHz and for ^{13}C at 125 MHz) or a Bruker AM 300 spectrometer at 300 MHz for ^1H and 75 MHz for ^{13}C , respectively, using CDCl_3 as solvent relative to TMS as internal standard for ^1H and relative to TMS ($\delta = 0.00$) or to CDCl_3 ($\delta = 77.05$) for ^{13}C NMR spectra. Second order ^1H spectra in the aromatic region, where it was possible, were analyzed by simulation (simulation program SpinWorks version 2.5). LR-MS (EI+) were recorded on a 6890N LC/MS system (Agilent Technology). Structural assignments of the derived compounds were established by analysis of their MS and NMR spectra (^1H , ^{13}C , DEPT, H-H COSY, H-H NOESY, HETCOR, and COLOC). Microwave irradiation was completed using a Biotage Initiator 2.0 microwave oven.

Reaction of 3-Formylchromones/Arylhidrazines/Acetylenedicarboxylates (Ratio 1:1:1); General Procedure

In a microwave reaction vial (0.5 – 2.0 mL), the acetylenedicarboxylate **11a,b** (0.5 mmol), phenylhydrazine or its HCl salt **10a–c** (0.5 mmol), and AcOH (1.0 mL) were mixed and then stirred at r.t. for 1 min. Then, the 3-formylchromone **9a–d** (0.5 mmol) was added to the mixture and it was irradiated in a microwave oven at 130 °C for 10 min. The progress of the reaction was monitored by TLC. The solvent was removed under vacuum and the resulting residue was subjected to column chromatography (silica gel, petroleum ether/EtOAc, 5:1–3:1) to afford **12a–g**.

Methyl (Z)-4-[(6-Chloro-4-oxo-4H-chromen-3-yl)methylene]-1-(4-chlorophenyl)-5-oxo-4,5-dihydro-1H-pyrazole-3-carboxylate (**12a**)

Yellow solid; yield: 63 mg (61%); mp 225 – 227 °C.

FT-IR (KBr): $3453, 3069, 2360, 1740, 1686$ cm^{-1} .

¹H NMR (500 MHz, CDCl₃): δ = 4.04 (s, 3 H, OCH₃), 7.42 (d, J = 8.5 Hz, 2 H, 2''-H, 6''-H), 7.54 (d, J = 8.8 Hz, 1 H, 7'-H), 7.70 (d, J = 8.8 Hz, 1 H, 8'-H), 7.90 (d, J = 8.5 Hz, 2 H, 3''-H, 5''-H), 8.27 (s, 1 H, 5'-H), 9.14 (s, 1 H, 6-H), 10.62 (s, 1 H, 2'-H).

¹³C NMR (125 MHz, CDCl₃): δ = 52.9 (OCH₃), 118.8 (C-3'), 120.4 (C-8'), 121.4 (C-2'', C-6''), 123.7 (C-4a'), 124.8 (C-4), 126.2 (C-7'), 129.1 (C-3'', C-5''), 131.9 (C-4''), 132.8 (C-6'), 135.0 (C-5'), 136.0 (C-1''), 140.8 (C-3), 143.0 (C-6), 154.3 (C-8a'), 160.7 (3-C=O), 162.3 (C-5), 164.3 (C-2'), 173.9 (C=O).

LC-MS (ESI, 1.65 eV): m/z (%) = 444/446 [4, (M + H)⁺], 484/486 [85, (M + CH₃CN)⁺].

Anal. Calcd for C₂₁H₁₂Cl₂N₂O₅: C, 56.91; H, 2.73; N, 6.32; Cl, 16.00. Found: C, 56.90; H, 2.67; N, 6.31; Cl, 15.54.

Methyl (Z)-4-[(6-Chloro-4-oxo-4H-chromen-3-yl)methylene]-5-oxo-1-phenyl-4,5-dihydro-1H-pyrazole-3-carboxylate (12b)

Yellow solid; yield: 62 mg (60%); mp 225–227 °C.

FT-IR (KBr): 3446, 3078, 2362, 1722, 1697 cm⁻¹.

¹H NMR (500 MHz, CDCl₃): δ = 4.03 (s, 3 H, OCH₃), 7.29 (d, J = 7.4 Hz, 1 H, 6'-H), 7.45 (t, J = 7.5 Hz, 2 H, 3''-H, 5''-H), 7.52 (d, J = 7.4 Hz, 1 H, 7'-H), 7.69 (dd, J = 7.5 Hz, 1 H, 4''-H), 7.89 (d, J = 7.5 Hz, 2 H, 2''-H, 6''-H), 8.25 (s, 1 H, 5'-H), 9.11 (s, 1 H, 6-H), 10.64 (s, 1 H, 2'-H).

¹³C NMR (125 MHz, CDCl₃): δ = 52.8 (OCH₃), 118.8 (C-3'), 120.4 (C-8'), 120.5 (C-2'', C-6''), 123.8 (C-4a'), 124.7 (C-4), 126.1 (C-7'), 126.6 (C-4''), 129.0 (C-3'', C-5''), 132.7 (C-6'), 134.9 (C-5'), 137.3 (C-1''), 140.4 (C-3), 142.4 (C-6), 154.2 (C-8a'), 160.7 (3-C=O), 162.4 (C-5), 164.3 (C-2'), 173.9 (C=O).

LC-MS (ESI, 1.65 eV): m/z (%) = 409/411 [4, (M + H)⁺], 504/506 [100, (M + Na + MeOH + CH₃CN)⁺].

Anal. Calcd for C₂₁H₁₃ClN₂O₅: C, 61.70; H, 3.21; N, 6.85; Cl, 8.67. Found: C, 61.60; H, 3.19; N, 6.79; Cl, 8.50.

Ethyl (Z)-5-Oxo-4-[(4-oxo-4H-chromen-3-yl)methylene]-1-phenyl-4,5-dihydro-1H-pyrazole-3-carboxylate (12c)

Yellow solid; yield: 55 mg (64%); mp 196–198 °C.

FT-IR (KBr): 3440, 3071, 2361, 1731, 1690 cm⁻¹.

¹H NMR (500 MHz, CDCl₃): δ = 1.49 (t, J = 7.2 Hz, 3 H, CH₃), 4.51 (q, J = 7.2 Hz, 2 H, CH₂), 7.30 (d, J = 7.2 Hz, 1 H, 4'-H), 7.43 (ddd, J = 8.1, 6.8, 0.9 Hz, 1 H, 6'-H), 7.46 (t, J = 8.7 Hz, 2 H, 3''-H, 5''-H), 7.52 (d, J = 6.8 Hz, 1 H, 8'-H), 7.74 (ddd, J = 8.1, 6.8, 0.9 Hz, 1 H, 7'-H), 7.93 (d, J = 7.5 Hz, 2 H, 2''-H, 6''-H), 8.31 (dd, J = 8.1, 0.9 Hz, 1 H, 5'-H), 9.17 (s, 1 H, 6-H), 10.66 (s, 1 H, 2'-H).

¹³C NMR (125 MHz, CDCl₃): δ = 13.9 (CH₃), 61.7 (CH₂), 118.7 (C-8'), 119.0 (C-3'), 120.5 (C-2'', C-6''), 123.8 (C-4a'), 124.0 (C-1), 126.5 (C-5'), 126.6 (C-6'), 126.8 (C-4''), 129.0 (C-3'', C-5''), 134.7 (C-7'), 137.6 (C-1''), 141.3 (C-2), 143.0 (C-6), 156.1 (C-8a'), 160.5 (3-C=O), 162.7 (C-5), 164.4 (C-2'), 175.1 (C=O).

LC-MS (ESI, 1.65 eV): m/z (%) = 389 [6, (M + H)⁺], 484 [85, (M + Na + MeOH + CH₃CN)⁺].

Anal. Calcd for C₂₂H₁₆N₂O₅: C, 68.04; H, 4.15; N, 7.21. Found: C, 68.02; H, 4.12; N, 7.18.

Ethyl (Z)-4-[(6-Chloro-4-oxo-4H-chromen-3-yl)methylene]-5-oxo-1-phenyl-4,5-dihydro-1H-pyrazole-3-carboxylate (12d)

Yellow solid; yield: 78 mg (75%); mp 195–197 °C.

FT-IR (KBr): 3448, 3062, 1716, 1686 cm⁻¹.

¹H NMR (500 MHz, CDCl₃): δ = 1.49 (t, J = 7.2 Hz, 3 H, CH₃), 4.51 (q, J = 7.2 Hz, 2 H, CH₂), 7.26 (d, J = 7.4 Hz, 1 H, 7'-H), 7.44 (t, J = 7.5 Hz, 2 H, 3''-H, 5''-H), 7.51 (d, J = 7.4 Hz, 1 H, 8'-H), 7.69 (dd, J = 7.5, 2.4 Hz, 1 H, 4''-H), 7.91 (d, J = 7.5 Hz, 2 H, 2''-H, 6''-H), 8.25 (d, J = 2.4 Hz, 1 H, 5'-H), 9.10 (s, 1 H, 6-H), 10.63 (s, 1 H, 2'-H).

¹³C NMR (125 MHz, CDCl₃): δ = 14.3 (CH₃), 62.1 (CH₂), 118.9 (C-3'), 120.4 (C-8'), 120.5 (C-2'', C-6''), 124.2 (C-4a'), 124.9 (C-4), 126.2 (C-7'), 126.6 (C-4''), 129.0 (C-3'', C-5''), 132.7 (C-6'), 134.9 (C-5'), 137.6 (C-1''), 141.0 (C-3), 142.2 (C-6), 154.4 (C-8a'), 160.4 (3-C=O), 162.5 (C-5), 164.1 (C-2'), 174.0 (C=O).

LC-MS (ESI, 1.65 eV): m/z (%) = 423/425 [4, (M + H)⁺], 520/522 [100, (M + Na + MeOH + CH₃CN)⁺].

Anal. Calcd for C₂₂H₁₅ClN₂O₅: C, 62.49; H, 3.58; N, 6.36; Cl, 8.38. Found: C, 62.42; H, 3.12; N, 6.18; Cl, 8.37.

Ethyl (Z)-4-[(6-Methyl-4-oxo-4H-chromen-3-yl)methylene]-5-oxo-1-phenyl-4,5-dihydro-1H-pyrazole-3-carboxylate (12e)

Yellow solid; yield: 61 mg (65%); mp 198–200 °C.

FT-IR (KBr): 3442, 3060, 2359, 1714, 1652 cm⁻¹.

¹H NMR (500 MHz, CDCl₃): δ = 1.50 (t, J = 7.2 Hz, 3 H, CH₃), 2.48 (s, 3 H, 7-CH₃), 4.52 (q, J = 7.2 Hz, 2 H, CH₂), 7.27 (d, J = 8.2 Hz, 1 H, 8'-H), 7.44 (d, J = 7.5 Hz, 2 H, 3''-H, 5''-H), 7.45 (d, J = 7.5 Hz, 1 H, 4''-H), 7.54 (d, J = 8.2 Hz, 1 H, 7'-H), 7.92 (d, J = 7.5 Hz, 2 H, 2''-H, 6''-H), 8.08 (s, 1 H, 5'-H), 9.18 (s, 1 H, 6-H), 10.67 (s, 1 H, 2'-H).

¹³C NMR (125 MHz, CDCl₃): δ = 14.3 (CH₃), 21.1 (7-CH₃), 62.1 (CH₂), 118.5 (C-8'), 118.8 (C-3'), 120.5 (C-2'', C-6''), 123.3 (C-4a'), 123.5 (C-4), 126.1 (C-4''), 126.4 (C-7'), 128.9 (C-3'', C-5''), 135.9 (C-5'), 136.8 (C-6'), 137.5 (C-1''), 141.0 (C-3), 143.3 (C-6), 154.2 (C-8a'), 160.4 (3-C=O), 162.6 (C-5), 164.5 (C-2'), 175.1 (C=O).

LC-MS (ESI, 1.65 eV): m/z (%) = 403 [3, (M + H)⁺], 498 [100, (M + Na + MeOH + MeCN)⁺].

Anal. Calcd for C₂₃H₁₈N₂O₅: C, 68.65; H, 4.51; N, 6.96. Found: C, 68.42; H, 4.42; N, 6.78.

Ethyl (Z)-4-[(6-Chloro-4-oxo-4H-chromen-3-yl)methylene]-5-oxo-1-(p-tolyl)-4,5-dihydro-1H-pyrazole-3-carboxylate (12f)

Yellow solid; yield: 55 mg (53%); mp 197–199 °C.

FT-IR (KBr): 3453, 3069, 2360, 1740, 1686 cm⁻¹.

¹H NMR (500 MHz, CDCl₃): δ = 1.49 (t, J = 7.2 Hz, 3 H, CH₃), 2.37 (s, 3 H, 4''-CH₃), 4.51 (q, J = 7.2 Hz, 2 H, CH₂), 7.24 (d, J = 8.2 Hz, 2 H, 2''-H, 6''-H), 7.52 (d, J = 8.9 Hz, 1 H, 7'-H), 7.68 (d, J = 8.9 Hz, 1 H, 8'-H), 7.76 (d, J = 8.2 Hz, 2 H, 3''-H, 5''-H), 8.25 (s, 1 H, 5'-H), 9.11 (s, 1 H, 6-H), 10.67 (s, 1 H, 2'-H).

¹³C NMR (125 MHz, CDCl₃): δ = 14.3 (CH₃), 21.1 (4''-CH₃), 62.1 (CH₂), 118.8 (C-3'), 120.4 (C-8'), 120.5 (C-2'', C-6''), 124.1 (C-4a'), 124.8 (C-1'), 126.1 (C-7'), 129.5 (C-3'', C-5''), 132.6 (C-6'), 134.8 (C-5'), 134.9 (C-4''), 136.5 (C-1''), 140.6 (C-3), 142.2 (C-6), 154.3 (C-8a'), 160.4 (3-C=O), 162.4 (C-5), 164.2 (C-2'), 174.0 (C=O).

LC-MS (ESI, 1.65 eV): m/z (%) = 437/439 [5, (M + H)⁺], 532/534 [100, (M + Na + MeOH + CH₃CN)⁺].

Anal. Calcd for C₂₃H₁₇ClN₂O₅: C, 63.24; H, 3.92; N, 6.41; Cl, 8.12. Found: C, 63.12; H, 3.42; N, 6.28; Cl, 7.89.

Ethyl (Z)-4-[(6-Chloro-7-methyl-4-oxo-4H-chromen-3-yl)methylene]-5-oxo-1-phenyl-4,5-dihydro-1H-pyrazole-3-carboxylate (12g)

Yellow solid; yield: 84 mg (76%); mp 196–198 °C.

FT-IR (KBr): 3447, 3059, 2361, 1716, 1693 cm^{-1} .

^1H NMR (500 MHz, CDCl_3): δ = 1.49 (t, J = 7.2 Hz, 3 H, CH_3), 2.53 (s, 3 H, 7'- CH_3), 4.51 (q, J = 7.2 Hz, 2 H, CH_2), 7.28 (t, J = 7.5 Hz, 1 H, 4''-H), 7.43 (s, 1 H, 8''-H), 7.44 (t, J = 7.5 Hz, 2 H, 3''-H, 5''-H), 7.92 (d, J = 7.5 Hz, 2 H, 2''-H, 6''-H), 8.23 (s, 1 H, 5'-H), 9.12 (s, 1 H, H-6), 10.6 (s, 1 H, 2'-H).

^{13}C NMR (125 MHz, CDCl_3): δ = 14.3 (CH_3), 20.9 (7'- CH_3), 62.1 (CH_2), 118.9 (C-3'), 120.51 (C-8'), 120.54 (C-2'', C-6''), 123.0 (C-4a'), 124.0 (C-4), 126.4 (C-5'), 126.5 (C-4''), 129.0 (C-3'', C-5''), 133.4 (C-6'), 137.6 (C-1''), 141.1 (C-3), 142.6 (C-6), 144.3 (C-7'), 154.3 (C-8a'), 160.4 (3-C=O), 162.6 (C-5), 164.2 (C-2'), 173.9 (C=O).

LC-MS (ESI, 1.65 eV): m/z (%) = 437/439 [4, (M + H)⁺], 532/534 [100, (M + Na + MeOH + CH_3CN)⁺].

Anal. Calcd for $\text{C}_{23}\text{H}_{17}\text{ClN}_2\text{O}_5$: C, 63.24; H, 3.92; N, 6.41; Cl, 8.12. Found: C, 63.12; H, 3.42; N, 6.28; Cl, 8.08.

Reaction of 3-Formylchromones/Arylhydrazines/Acetylenedicarboxylates (Ratio 1:2:1); General Procedure

In a microwave reaction vial (0.5–2.0 mL), the acetylenedicarboxylate **11a,b** (0.5 mmol), phenylhydrazine or its HCl salt **10a–c** (1.0 mmol), and AcOH (1.0 mL) were mixed and then stirred at r.t. for 1 min. Then, the 3-formylchromone **9a–d** (0.5 mmol) was added to the mixture and it was irradiated in a microwave oven at 120 °C for 5 min. The progress of the reaction was monitored by TLC. The solvent was removed under vacuum and the resulting residue was subjected to column chromatography (silica gel, petroleum ether/EtOAc, 5:1–3:1) to afford **13a–l**.

Methyl (Z)-4-((Z)-6-Chloro-4-[2-(4-chlorophenyl)hydrazono]-4H-chromen-3-yl)methylene)-1-(4-chlorophenyl)-5-oxo-4,5-dihydro-1H-pyrazole-3-carboxylate (**13a**)

Yellow solid; yield: 71 mg (59%); mp 250–252 °C.

FT-IR (KBr): 3368, 1716, 1701 cm^{-1} .

^1H NMR (500 MHz, CDCl_3): δ = 3.88 (s, 3 H, OCH_3), 6.95 (d, J = 8.5 Hz, 1 H, 8-H), 7.15 (d, J = 8.5 Hz, 1 H, 7-H), 7.30–7.37 (m, 6 H), 7.41 (s, 1 H, 5-H), 7.98 (d, J = 8.1 Hz, 2 H, 2''-H, 6''-H), 8.35 (s, 1 H, 9-H), 9.66 (s, 1 H, 2-H).

^{13}C NMR (125 MHz, CDCl_3): δ = 52.2 (OCH_3), 115.4 (C-4a'), 118.0 (C-8), 119.0 (C-4), 119.3 (C-3'), 121.1 (C-2'', C-6''), 124.1 (C-6), 124.8 (C-2''', C-6'''), 128.7 (C-3'', C-5''), 129.0 (C-3''', C-5'''), 130.8 (C-5), 131.0 (C-4''), 132.0 (C-7'), 133.5 (C-1''), 136.3 (C-4'''), 137.9 (C-1'''), 140.5 (C-3), 141.6 (C-9), 145.2 (C-2), 146.0 (C-4'), 154.3 (C-8a), 160.8 (2-C=O), 162.1 (5-C=O).

LC-MS (ESI, 1.65 eV): m/z (%) = 568/570 [5, (M + H)⁺], 622/624 [90, (M + Na + MeOH)⁺].

Anal. Calcd for $\text{C}_{27}\text{H}_{17}\text{Cl}_3\text{N}_4\text{O}_4$: C, 57.11; H, 3.02; N, 9.87; Cl, 18.73. Found: C, 57.04; H, 2.92; N, 9.67; Cl, 18.43.

Methyl (Z)-5-Oxo-1-phenyl-4-((Z)-4-[2-(phenylhydrazono)-4H-chromen-3-yl)methylene]-4,5-dihydro-1H-pyrazole-3-carboxylate (**13b**)

Yellow solid; yield: 71 mg (82%); mp 215–217 °C.

FT-IR (KBr): 3417, 1720, 1691 cm^{-1} .

^1H NMR (500 MHz, CDCl_3): δ = 3.80 (s, 3 H, OCH_3), 6.94 (d, J = 8.2 Hz, 1 H, 8-H), 7.02 (t, J = 7.5 Hz, 1 H, 7'-H), 7.12 (d, J = 8.2 Hz, 1 H), 7.21–7.24 (m, 5 H), 7.38 (d, J = 8.2 Hz, 1 H), 7.43 (t, J = 7.5 Hz, 3 H), 7.93 (d, J = 7.5 Hz, 2 H, 2''-H, 6''-H), 8.34 (s, 1 H, 9-H), 9.63 (s, 1 H, 2-H).

^{13}C NMR (125 MHz, CDCl_3): δ = 52.3 (OCH_3), 114.6 (C-4a), 117.0 (C-8), 119.4 (C-4), 119.5 (C-3'), 120.5 (C-2'', C-6''), 121.2 (C-7), 124.1 (C-2''', C-6'''), 126.2 (C-5), 128.3 (C-6), 128.92 (C-3'', C-5''), 128.98 (C-3''', C-5'''), 132.0 (C-4''), 132.3 (C-4'''), 137.8 (C-1''), 138.9 (C-1'''), 139.9 (C-3), 141.2 (C-9), 145.3 (C-2), 146.0 (C-4'), 154.0 (C-8a), 161.3 (3-C=O), 162.5 (5-C=O).

LC-MS (ESI, 1.65 eV): m/z (%) = 465 [100, (M + H)⁺].

Anal. Calcd for $\text{C}_{27}\text{H}_{20}\text{N}_4\text{O}_4$: C, 69.82; H, 4.34; N, 12.07. Found: C, 67.04; H, 3.92; N, 11.67.

Methyl (Z)-4-((Z)-6-Methyl-4-(2-phenylhydrazono)-4H-chromen-3-yl)methylene)-5-oxo-1-phenyl-4,5-dihydro-1H-pyrazole-3-carboxylate (**13c**)

Yellow solid; yield: 88 mg (81%); mp 235–237 °C.

FT-IR (KBr): 3422, 1719, 1629 cm^{-1} .

^1H NMR (500 MHz, CDCl_3): δ = 2.28 (s, 3 H, CH_3), 3.74 (s, 3 H, OCH_3), 6.83 (d, J = 8.3 Hz, 1 H, 8-H), 6.88 (d, J = 8.3 Hz, 1 H, 5-H), 7.18 (d, J = 8.3 Hz, 1 H, 7-H), 7.25 (m, 1 H, 4''-H), 7.28 (m, 1 H, 4'''-H), 7.29 (m, 2 H, 3''-H, 5''-H), 7.34 (m, 2 H, 2''-H, 6''-H), 7.42 (m, 2 H, 3'''-H, 5'''-H), 7.97 (d, J = 9.6 Hz, 2 H, 2''-H, 6''-H), 8.25 (s, 1 H, 9-H), 9.45 (s, 1 H, 2-H).

^{13}C NMR (125 MHz, CDCl_3): δ = 20.3 (6- CH_3), 52.2 (OCH_3), 114.3 (C-4a), 117.0 (C-8), 119.2 (C-4), 119.5 (C-3'), 120.6 (C-2'', C-6''), 124.1 (C-2''', C-6'''), 126.1 (C-4''), 128.2 (C-4'''), 128.93 (C-3'', C-5''), 129.01 (C-3''', C-5'''), 130.3 (C-6), 132.0 (C-5), 132.9 (C-7), 137.8 (C-1''), 138.1 (C-1'''), 139.6 (C-3), 141.5 (C-9), 145.5 (C-2), 146.5 (C-4'), 152.0 (C-8a), 161.3 (3-C=O), 162.5 (5-C=O).

LC-MS (ESI, 1.65 eV): m/z (%) = 479 [100, (M + H)⁺], 517 [4, (M + K)⁺].

Anal. Calcd for $\text{C}_{28}\text{H}_{22}\text{N}_4\text{O}_4$: C, 70.28; H, 4.63; N, 11.71. Found: C, 69.04; H, 4.52; N, 11.67.

Methyl (Z)-1-(4-Chlorophenyl)-4-((Z)-4-[2-(4-chlorophenyl)hydrazono]-6-methyl-4H-chromen-3-yl)methylene)-5-oxo-4,5-dihydro-1H-pyrazole-3-carboxylate (**13d**)

Yellow solid; yield: 62 mg (44%); mp 235–238 °C.

FT-IR (KBr): 3358, 1693, 1604 cm^{-1} .

^1H NMR (500 MHz, CDCl_3): δ = 2.29 (s, 3 H, 6- CH_3), 3.74 (s, 3 H, OCH_3), 6.84 (d, J = 8.2 Hz, 1 H, 8-H), 6.88 (s, 1 H, 5-H), 7.16 (d, J = 8.1 Hz, 2 H), 7.17 (d, J = 8.2 Hz, 1 H, 7-H), 7.24 (d, J = 8.1 Hz, 2 H), 7.33 (d, J = 8.1 Hz, 2 H), 7.86 (d, J = 8.1 Hz, 2 H), 8.25 (s, 1 H, 9-H), 9.45 (s, 1 H, 2-H).

^{13}C NMR (125 MHz, CDCl_3): δ = 20.4 (6- CH_3), 52.3 (OCH_3), 113.9 (C-4a), 117.3 (C-8), 119.1 (C-4), 119.7 (C-3'), 121.1 (C-2'', C-6''), 124.9 (C-2''', C-6'''), 128.9 (C-3'', C-5''), 129.1 (C-3''', C-5'''), 130.6 (C-6), 131.2 (C-4''), 131.8 (C-5), 133.2 (C-7), 134.0 (C-1''), 136.3 (C-4'''), 137.3 (C-1'''), 140.1 (C-3), 141.8 (C-9), 145.1 (C-2), 146.5 (C-4'), 152.0 (C-8a), 161.1 (3-C=O), 162.1 (5-C=O).

LC-MS (ESI, 1.65 eV): m/z (%) = 548/550 [100, (M + H)⁺], 560/562 [5, (M + Na)⁺].

Anal. Calcd for $\text{C}_{28}\text{H}_{20}\text{Cl}_2\text{N}_4\text{O}_4$: C, 61.44; H, 3.68; N, 10.24; Cl, 12.95. Found: C, 61.04; H, 3.52; N, 10.47; Cl, 12.76.

Methyl (Z)-5-Oxo-1-(p-tolyl)-4-((Z)-4-[2-(p-tolyl)hydrazono]-4H-chromen-3-yl)methylene)-4,5-dihydro-1H-pyrazole-3-carboxylate (**13e**)

Yellow solid; yield: 72 mg (58%); mp 254–256 °C.

FT-IR (KBr): 3408, 1701, 1690 cm^{-1} .

¹H NMR (500 MHz, CDCl₃): δ = 2.29 (s, 3 H, CH₃), 2.37 (s, 3 H, CH₃), 3.77 (s, 3 H, OCH₃), 6.95 (d, *J* = 8.2 Hz, 1 H, 5-H), 7.00 (t, *J* = 7.5 Hz, 1 H, 8-H), 7.06 (d, *J* = 8.3 Hz, 2 H, 2''-H, 6'''-H), 7.14 (d, *J* = 8.2 Hz, 1 H, 6-H), 7.2 (d, 8.3 Hz, 2 H, 3'''-H, 5'''-H), 7.26 (d, *J* = 8.3 Hz, 2 H, 3''-H, 5''-H), 7.40 (t, *J* = 8.2 Hz, 1 H, 7-H), 7.80 (d, *J* = 8.3 Hz, 2 H, 2''-H, 6'''-H), 8.29 (s, 1 H, 9-H), 9.59 (s, 1 H, 2-H).

¹³C NMR (125 MHz, CDCl₃): δ = 21.07 (CH₃), 21.1 (CH₃), 52.2 (OCH₃), 114.8 (C-4a), 117.1 (C-8), 119.4 (C-4), 119.5 (C-3'), 120.3 (C-2'', C-6''), 121.0 (C-7), 123.8 (C-2''', C-6'''), 129.4 (C-3'', C-5''), 129.5 (C-3''', C-5'''), 131.7 (C-6), 132.1 (C-5), 135.3 (C-4'), 135.8 (C-1''), 136.6 (C-4'''), 138.2 (C-1'''), 139.5 (C-3), 141.0 (C-9), 145.0 (C-2), 145.2 (C-4'), 154.2 (C-8a), 161.3 (3-C=O), 162.4 (5-C=O).

LC-MS (ESI, 1.65 eV): *m/z* (%) = 493 [100, (M + H)⁺], 531 [5, (M + K)⁺].

Anal. Calcd for C₂₉H₂₄N₄O₄: C, 70.72; H, 4.91; N, 11.38. Found: C, 70.04; H, 4.52; N, 11.17.

Methyl (Z)-1-(4-Chlorophenyl)-4-(((Z)-4-[2-(4-chlorophenyl)hydrazono]-4H-chromen-3-yl)methylene)-5-oxo-4,5-dihydro-1H-pyrazole-3-carboxylate (13f)

Yellow solid; yield: 57 mg (40%); mp 242–244 °C.

FT-IR (KBr): 3411, 1719, 1694 cm⁻¹.

¹H NMR (500 MHz, CDCl₃): δ = 3.84 (s, 3 H, OCH₃), 6.95 (d, *J* = 8.1 Hz, 1 H, 5-H), 7.08 (t, *J* = 7.4 Hz, 1 H), 7.15 (d, *J* = 7.4 Hz, 1 H), 7.25–7.28 (m, 4 H), 7.40 (d, *J* = 8.3 Hz, 2 H), 7.44 (t, *J* = 7.4 Hz, 1 H), 7.94 (d, *J* = 8.3 Hz, 2 H, 2''-H, 6''-H), 8.36 (s, 1 H, 9-H), 9.63 (s, 1 H, 2-H).

¹³C NMR (125 MHz, CDCl₃): δ = 51.7 (OCH₃), 113.5 (C-4a), 116.2 (C-8), 117.8 (C-7), 118.9 (C-4), 119.2 (C-3'), 120.6 (C-2'', C-6''), 124.5 (C-3'', C-5''), 128.3 (C-2''', C-6'''), 128.37 (C-3''', C-5'''), 130.3 (C-6), 131.4 (C-4''), 131.7 (C-5), 132.6 (C-1''), 136.5 (C-4'''), 137.7 (C-1'''), 139.7 (C-3), 141.3 (C-9), 144.8 (C-2), 147.3 (C-4'), 155.1 (C-8a), 160.5 (3-C=O), 161.8 (5-C=O).

LC-MS (ESI, 1.65 eV): *m/z* (%) = 534/536 [100, (M + H)⁺], 556/558 [4, (M + Na)⁺].

Anal. Calcd for C₂₇H₁₈Cl₂N₄O₄: C, 60.80; H, 3.41; N, 10.50; Cl, 13.29. Found: C, 60.04; H, 3.22; N, 10.17; Cl, 12.79.

Methyl (Z)-4-(((Z)-6-Chloro-7-methyl-4-(2-phenylhydrazono)-4H-chromen-3-yl)methylene)-5-oxo-1-phenyl-4,5-dihydro-1H-pyrazole-3-carboxylate (13g)

Yellow solid; yield: 85 mg (77%); mp 268–270 °C.

FT-IR (KBr): 3430, 1720, 1690 cm⁻¹.

¹H NMR (500 MHz, CDCl₃): δ = 2.37 (s, 3 H, 7-CH₃), 3.89 (s, 3 H, OCH₃), 6.81 (s, 1 H, 5-H), 7.05 (s, 1 H), 7.24 (t, 1 H), 7.37 (m, 4 H), 7.47 (m, 3 H), 7.93 (d, *J* = 7.7 Hz, 2 H), 8.41 (s, 1 H, 9-H), 9.67 (s, 1 H, 2-H).

¹³C NMR (125 MHz, CDCl₃): δ = 19.9 (7-CH₃), 52.1 (OCH₃), 118.4 (C-4a), 118.7 (C-4), 119.0 (C-3'), 120.5 (C-2'', C-6''), 122.9 (C-1''), 124.0 (C-2''', C-6'''), 124.5 (C-4'''), 126.1 (C-8), 128.15 (C-1'''), 128.68 (C-3'', C-5''), 128.72 (C-3''', C-5'''), 131.2 (C-7), 137.5 (C-6), 138.9 (C-5), 139.95 (C-4''), 140.0 (C-3), 141.8 (C-9), 145.0 (C-2), 146.2 (C-4'), 153.9 (C-8a), 161.3 (3-C=O), 162.4 (5-C=O).

LC-MS (ESI, 1.65 eV): *m/z* (%) = 513/515 [100, (M + H)⁺], 551/553 [4, (M + K)⁺].

Anal. Calcd for C₂₈H₂₁ClN₄O₄: C, 65.56; H, 4.13; N, 10.92; Cl, 6.91. Found: C, 65.04; H, 4.02; N, 10.17; Cl, 5.79.

Ethyl (Z)-5-Oxo-1-phenyl-4-(((Z)-4-(2-phenylhydrazono)-4H-chromen-3-yl)methylene)-4,5-dihydro-1H-pyrazole-3-carboxylate (13h)

Yellow solid; yield: 65 mg (60%); mp 218–220 °C.

FT-IR (KBr): 3425, 1720, 1697 cm⁻¹.

¹H NMR (500 MHz, CDCl₃): δ = 1.17 (t, *J* = 7.5 Hz, 3 H, CH₃), 4.24 (q, *J* = 7.5 Hz, 2 H, OCH₂), 6.92 (d, *J* = 8.1 Hz, 1 H, 5'-H), 6.97 (t, *J* = 7.5 Hz, 1 H), 7.09 (d, *J* = 7.5 Hz, 1 H), 7.26–7.32 (m, 6 H), 7.34 (t, *J* = 7.7 Hz, 1 H), 7.41 (t, *J* = 7.8 Hz, 2 H), 7.93 (d, *J* = 8.0 Hz, 2 H), 8.28 (s, 1 H, 9-H), 9.65 (s, 1 H, 2'-H).

¹³C NMR (125 MHz, CDCl₃): δ = 13.9 (CH₃), 61.8 (OCH₂), 114.6 (C-4a), 116.9 (C-8), 119.4 (C-3'), 120.5 (C-2'', C-6''), 120.8 (C-4), 124.2 (C-2''', C-6'''), 126.1 (C-4''), 128.2 (C-4'''), 128.8 (C-3'', C-5''), 128.9 (C-3''', C-5'''), 128.91 (C-1''), 131.8 (C-7), 131.9 (C-6), 132.1 (C-5), 137.7 (C-1'''), 138.9 (C-3), 141.3 (C-9), 145.1 (C-2), 146.1 (C-4'), 154.3 (C-8a), 161.1 (3-C=O), 162.4 (5-C=O).

LC-MS (ESI, 1.65 eV): *m/z* (%) = 479 [100, (M + H)⁺], 501 [5, (M + Na)⁺].

Anal. Calcd for C₂₈H₂₂N₄O₄: C, 70.28; H, 4.63; N, 11.71. Found: C, 69.04; H, 4.02; N, 10.97.

Ethyl (Z)-4-(((Z)-6-Methyl-4-[2-(*p*-tolyl)hydrazono]-4H-chromen-3-yl)methylene)-5-oxo-1-(*p*-tolyl)-4,5-dihydro-1H-pyrazole-3-carboxylate (13i)

Yellow solid; yield: 55 mg (45%); mp 238–240 °C.

FT-IR (KBr): 3429, 1736, 1688 cm⁻¹.

¹H NMR (500 MHz, CDCl₃): δ = 1.20 (t, *J* = 7.5 Hz, 3 H, CH₃), 2.27 (s, 3 H, CH₃), 2.31 (s, 3 H, CH₃), 2.36 (s, 3 H, CH₃), 4.28 (q, *J* = 7.5 Hz, 2 H, CH₂), 6.84 (d, *J* = 8.1 Hz, 1 H, 5-H), 6.90 (s, 1 H), 7.10 (d, *J* = 8.1 Hz, 1 H), 7.55–7.19 (m, 3 H), 7.21 (d, 2 H), 7.23 (s, 1 H), 7.80 (d, *J* = 8.3 Hz, 2 H), 8.26 (s, 1 H, 9-H), 9.64 (s, 1 H, 2-H).

¹³C NMR (125 MHz, CDCl₃): δ = 13.9 (CH₃), 20.4 (CH₃), 21.09 (CH₃), 21.1 (CH₃), 61.5 (CH₂), 114.4 (C-4a), 116.5 (C-8), 116.8 (C-4), 119.5 (C-3'), 120.5 (C-2'', C-6''), 123.7 (C-6), 129.4 (C-3'', C-5''), 129.5 (C-3''', C-5'''), 130.5 (C-9), 132.1 (C-7), 132.8 (C-2''', C-6'''), 135.4 (C-4''), 135.8 (C-1''), 136.6 (C-4'''), 138.2 (C-1'''), 140.1 (C-3), 140.9 (C-9), 145.2 (C-2), 145.6 (C-4'), 151.7 (C-8a), 160.9 (3-C=O), 162.5 (5-C=O).

LC-MS (ESI, 1.65 eV): *m/z* (%) = 521 [100, (M + H)⁺], 559 [5, (M + K)⁺].

Anal. Calcd for C₃₁H₂₈N₄O₄: C, 71.52; H, 5.43; N, 10.71. Found: C, 70.14; H, 4.92; N, 10.37.

Ethyl (Z)-4-(((Z)-6-Methyl-4-(2-phenylhydrazono)-4H-chromen-3-yl)methylene)-5-oxo-1-phenyl-4,5-dihydro-1H-pyrazole-3-carboxylate (13j)

Yellow solid; yield: 57 mg (53%); mp 238–240 °C.

FT-IR (KBr): 3428, 1723, 1692 cm⁻¹.

¹H NMR (500 MHz, CDCl₃): δ = 1.22 (t, 3 H, CH₃), 2.27 (s, 3 H, CH₃), 4.28 (q, *J* = 10 Hz, 2 H, OCH₂), 6.83 (d, *J* = 10 Hz, 1 H), 6.90 (s, 1 H), 7.30 (m, 5 H), 7.33 (d, *J* = 10 Hz, 1 H), 7.44–7.45 (m, 2 H), 7.95 (d, *J* = 7.7 Hz, 2 H), 8.31 (s, 1 H, 9-H), 9.68 (s, 1 H, 2-H).

¹³C NMR (125 MHz, CDCl₃): δ = 14.0 (CH₃), 20.4 (6-CH₃), 61.5 (OCH₂), 114.4 (C-4a), 116.7 (C-8), 118.3 (C-4), 119.8 (C-3'), 120.5 (C-2'', C-6''), 124.0 (C-2''', C-6'''), 125.9 (C-4'''), 126.1 (C-1''), 128.1 (C-4''), 128.8 (C-3'', C-5''), 128.9 (C-3''', C-5'''), 130.5 (C-5), 132.1 (C-7), 132.8 (C-6), 137.9 (C-1'''), 138.9 (C-3), 140.4 (C-4'), 141.1 (C-9), 145.3 (C-2), 151.8 (C-8a), 160.1 (3-C=O), 162.3 (5-C=O).

LC-MS (ESI, 1.65 eV): *m/z* (%) = 493 [100, (M + H)⁺], 531 [3, (M + K)⁺].

Anal. Calcd for $C_{29}H_{24}N_4O_4$: C, 70.72; H, 4.91; N, 11.38. Found: C, 70.24; H, 4.52; N, 11.07.

Methyl (Z)-4-((Z)-6-Methyl-4-[2-(p-tolyl)hydrazono]-4H-chromen-3-yl)methylene-5-oxo-1-(p-tolyl)-4,5-dihydro-1H-pyrazole-3-carboxylate (13k)

Yellow solid; yield: 74 mg (69%); mp 248–250 °C.

FT-IR (KBr): 3385, 1747, 1717, 1687 cm^{-1} .

1H NMR (500 MHz, $CDCl_3$): δ = 2.27 (s, 3 H, 6- CH_3), 2.32 (s, 3 H, 4'''- CH_3), 2.37 (s, 3 H, 4''- CH_3), 3.82 (s, 3 H, OCH₃), 6.87 (d, J = 8.3 Hz, 1 H, H-8), 6.90 (s, 1 H, H-5), 7.11 (d, J = 8.2 Hz, 2 H, 3'''-H, 5'''-H), 7.14 (d, J = 8.3 Hz, 1 H, H-7), 7.24 (d, J = 8.3 Hz, 2 H, 3''-H, 5''-H), 7.29 (d, J = 8.2 Hz, 2 H, 2'''-H, 6'''-H), 7.82 (d, J = 8.3 Hz, 2 H, 2''-H, 6''-H), 8.38 (s, 1 H, H-9), 9.65 (s, 1 H, H-2).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 20.3 (6- CH_3), 21.01 (4'''- CH_3), 21.04 (4''- CH_3), 52.0 (OCH₃), 114.2 (C-4a), 116.5 (C-8), 118.3 (C-4'), 119.3 (C-3), 120.5 (C-2'', C-6''), 123.7 (C-2''', C-6'''), 128.7 (C-6), 129.3 (C-3'', C-5''), 129.32 (C-3''', C-5'''), 131.9 (C-5), 132.4 (C-7), 135.4 (C-4''), 135.7 (C-1''), 137.3 (C-1'''), 137.7 (C-4'''), 139.9 (C-3'), 142.3 (C-9), 145.0 (C-2), 147.7 (C-4), 153.3 (C-8a), 160.9 (3-C=O), 162.3 (5-C=O).

LC-MS (ESI, 1.65 eV): m/z (%) = 507 [100, (M + H)⁺], 529 [80, (M + Na)⁺], 561 [10, (M + Na + MeOH)⁺].

Anal. Calcd for $C_{30}H_{26}N_4O_4$: C, 71.12; H, 5.17; N, 11.08. Found: C, 70.84; H, 5.02; N, 11.07.

Methyl (Z)-4-((Z)-6-Chloro-4-[2-(p-tolyl)hydrazono]-4H-chromen-3-yl)methylene-5-oxo-1-(p-tolyl)-4,5-dihydro-1H-pyrazole-3-carboxylate (13l)

Yellow solid; yield: 64 mg (62%); mp 258–260 °C.

FT-IR (KBr): 3371, 1716, 1697 cm^{-1} .

1H NMR (500 MHz, $CDCl_3$): δ = 2.37 (s, 3 H, 4''- CH_3), 2.40 (s, 3 H, 4'''- CH_3), 3.86 (s, 3 H, OCH₃), 6.98 (d, J = 8.2 Hz, 1 H, 8-H), 7.12 (d, J = 8.2 Hz, 1 H, 7-H), 7.16 (d, J = 8.3 Hz, 2 H, 3'''-H, 5'''-H), 7.25–7.34 (m, 4 H), 7.43 (s, 1 H, 5-H), 7.84 (d, J = 8.3 Hz, 2 H, 2''-H, 6''-H), 8.35 (s, 1 H, 9-H), 9.68 (s, 1 H, 2-H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 20.73 (4''- CH_3), 20.78 (4'''- CH_3), 52.0 (OCH₃), 115.7 (C-4a), 117.6 (C-8), 118.5 (C-4), 118.9 (C-3'), 120.1 (C-2'', C-6''), 123.5 (C-2''', C-6'''), 123.6 (C-6), 129.0 (C-3'', C-5''), 129.1 (C-3''', C-5'''), 130.7 (C-5), 131.3 (C-7), 135.0 (C-4''), 135.3 (C-1''), 136.6 (C-4'''), 137.7 (C-1'''), 139.9 (C-3), 141.0 (C-9), 144.7 (C-2), 145.6 (C-4'), 154.3 (C-8a), 160.9 (3-C=O), 162.1 (5-C=O).

LC-MS (ESI, 1.65 eV): m/z (%) = 527 [100, (M + H)⁺], 581 [5, (M + Na + MeOH)⁺].

Anal. Calcd for $C_{29}H_{23}ClN_4O_4$: C, 66.10; H, 4.40; N, 10.63; Cl, 6.73. Found: C, 65.84; H, 4.02; N, 10.07; Cl, 6.70.

Reaction of Arylhydrazones with Acetylenedicarboxylates in Acetic Acid; General Procedure

In a microwave reaction vial (0.5–2.0 mL), the acetylenedicarboxylate **11a,b** (1.5 mmol), arylhydrazones **14a–d** (0.3 mmol), and AcOH (1.0 mL) were mixed and then the mixture was irradiated in a microwave oven at 120 °C for 5 min. The progress of the reaction was monitored by TLC. The solvent was removed under vacuum and the resulting residue was subjected to column chromatography (silica gel, petroleum ether/EtOAc, 5:1–3:1) to afford **15**.

Dimethyl (4R,5S)-1-(4-Chlorophenyl)-3-(6-methyl-4-oxo-4H-chromen-3-yl)-4,5-dihydro-1H-pyrazole-4,5-dicarboxylate (15a)

Yellow solid; yield: 57 mg (42%); mp 180–182 °C.

FT-IR (KBr): 1742, 1651 cm^{-1} .

1H NMR (500 MHz, $CDCl_3$): δ = 2.47 (s, 3 H, 6- CH_3), 3.73 (s, 3 H, OCH₃), 3.78 (s, 3 H, OCH₃), 5.06 (d, J = 5.2 Hz, 1 H, 5'-H), 5.21 (d, J = 5.2 Hz, 1 H, 4'-H), 7.01 (d, J = 8.5 Hz, 2 H, 2''-H, 6''-H), 7.23 (d, J = 8.5 Hz, 2 H, 3''-H, 5''-H), 7.41 (d, J = 8.5 Hz, 1 H, 8-H), 7.51 (dd, J = 8.5, 1.8 Hz, 1 H, 7-H), 8.01 (d, J = 1.8 Hz, 1 H, 5-H), 8.64 (s, 1 H, 2-H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 21.0 (6- CH_3), 53.07 (OCH₃), 53.11 (OCH₃), 56.7 (C-4'), 64.7 (C-5'), 114.4 (C-2'', C-6''), 116.6 (C-3'), 118.0 (C-8), 123.7 (C-4a), 125.3 (C-4''), 125.4 (C-5'), 129.1 (C-3'', C-5''), 135.3 (C-7), 135.9 (C-6), 140.3 (C-3), 142.2 (C-1''), 154.4 (C-8a), 154.4 (C-2), 169.2 (CO₂Me), 169.7 (CO₂Me), 175.7 (C=O).

LC-MS (ESI, 1.65 eV): m/z (%) = 455/457 [100, (M + H)⁺].

Anal. Calcd for $C_{23}H_{19}ClN_2O_6$: C, 60.73; H, 4.21; N, 6.16; Cl, 7.79. Found: C, 65.84; H, 4.02; N, 10.07; Cl, 6.71.

Dimethyl (4R,5S)-3-(6-Methyl-4-oxo-4H-chromen-3-yl)-1-(p-tolyl)-4,5-dihydro-1H-pyrazole-4,5-dicarboxylate (15b)

Yellow solid; yield: 64 mg (49%); mp 185–187 °C.

FT-IR (KBr): 1731, 1645 cm^{-1} .

1H NMR (500 MHz, $CDCl_3$): δ = 2.29 (s, 3 H, 4''- CH_3), 2.46 (s, 3 H, 6- CH_3), 3.72 (s, 3 H, OCH₃), 3.77 (s, 3 H, OCH₃), 5.05 (d, J = 5.3 Hz, 1 H, 5-H), 5.17 (d, J = 5.3 Hz, 1 H, 4-H), 6.99 (d, J = 8.3 Hz, 2 H, 2''-H, 6''-H), 7.09 (d, J = 8.3 Hz, 2 H, 3''-H, 5''-H), 7.41 (d, J = 8.6 Hz, 1 H, 8-H), 7.50 (dd, J = 8.6, 2.0 Hz, 1 H, 7-H), 8.01 (s, 1 H, 5-H), 8.65 (s, 1 H, 2-H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 20.6 (4''- CH_3), 21.05 (6- CH_3), 53.0 (OCH₃), 53.03 (OCH₃), 56.6 (C-4'), 65.2 (C-5'), 113.3 (C-2'', C-6''), 116.9 (C-3'), 118.0 (C-8), 123.7 (C-4a), 124.3 (C-4''), 125.4 (C-5), 129.8 (C-3'', C-5''), 135.2 (C-7), 135.7 (C-6), 139.1 (C-3), 141.5 (C-1''), 154.2 (C-8a), 154.4 (C-2), 169.5 (CO₂Me), 170.1 (CO₂Me), 175.7 (C=O).

LC-MS (ESI, 1.65 eV): m/z (%) = 435 [100, (M + H)⁺].

Anal. Calcd for $C_{24}H_{22}N_2O_6$: C, 66.35; H, 5.10; N, 6.45. Found: C, 66.24; H, 5.02; N, 6.37.

Dimethyl (4R,5S)-3-(6-Chloro-4-oxo-4H-chromen-3-yl)-1-(p-tolyl)-4,5-dihydro-1H-pyrazole-4,5-dicarboxylate (15c)

Yellow solid; yield: 59 mg (43%); mp 179–181 °C.

FT-IR (KBr): 1735, 1654 cm^{-1} .

1H NMR (500 MHz, $CDCl_3$): δ = 2.28 (s, 3 H, 4''- CH_3), 3.72 (s, 3 H, OCH₃), 3.77 (s, 3 H, OCH₃), 5.05 (d, J = 5.3 Hz, 1 H, 5'-H), 5.17 (d, J = 5.3 Hz, 1 H, 4'-H), 7.00 (d, J = 8.5 Hz, 2 H, 2''-H, 6''-H), 7.09 (d, J = 8.5 Hz, 2 H, 3''-H, 5''-H), 7.42 (dd, J = 7.9, 7.2 Hz, 1 H, 7-H), 7.50 (d, J = 8.4 Hz, 1 H, 8-H), 7.69 (ddd, J = 8.4, 7.2, 1.7 Hz, 1 H, 6-H), 8.24 (dd, J = 7.9, 1.7 Hz, 1 H, 5-H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 20.5 (4''- CH_3), 52.9 (OCH₃), 53.07 (OCH₃), 56.7 (C-4'), 65.5 (C-5'), 113.6 (C-2'', C-6''), 117.4 (C-3'), 118.1 (C-4a), 118.3 (C-8), 124.4 (C-4''), 125.6 (C-5), 126.3 (C-6), 129.8 (C-3'', C-5''), 133.8 (C-7), 139.3 (C-3), 141.7 (C-1''), 154.5 (C-2), 156.2 (C-8a), 169.4 (CO₂Me), 170.1 (CO₂Me), 175.7 (C=O).

LC-MS (ESI, 1.65 eV): m/z (%) = 455 [100, (M + H)⁺].

Anal. Calcd for $C_{23}H_{19}ClN_2O_6$: C, 60.73; H, 4.21; N, 6.16; Cl, 7.79. Found: C, 60.85; H, 4.30; N, 6.17; Cl, 6.99.

Dimethyl (4*R*,5*S*)-3-(6-Chloro-7-methyl-4-oxo-4*H*-chromen-3-yl)-1-phenyl-4,5-dihydro-1*H*-pyrazole-4,5-dicarboxylate (15d)

Yellow solid; yield: 54 mg (40%); mp 181–183 °C.

FT-IR (KBr): 1746, 1650 cm⁻¹.¹H NMR (500 MHz, CDCl₃): δ = 2.51 (s, 3 H, 7-CH₃), 3.73 (s, 3 H, OCH₃), 3.78 (s, 3 H, OCH₃), 5.08 (d, *J* = 5.3 Hz, 1 H, 5'-H), 5.16 (d, *J* = 5.3 Hz, 1 H, 4'-H), 6.91 (t, *J* = 7.3 Hz, 1 H, 4''-H), 7.08 (d, *J* = 7.9 Hz, 2 H, 2''-H, 6''-H), 7.28 (t, *J* = 7.9 Hz, 2 H, 3''-H, 5''-H), 7.40 (s, 1 H, 8-H), 8.16 (s, 1 H, 5-H), 8.61 (s, 1 H, 2-H).¹³C NMR (125 MHz, CDCl₃): δ = 21.0 (7-CH₃), 53.0 (OCH₃), 53.03 (OCH₃), 56.3 (C-4'), 64.9 (C-5'), 113.1 (C-2'', C-6''), 117.0 (C-3'), 120.1 (C-8), 120.6 (C-4''), 123.1 (C-4a), 125.7 (C-5), 129.2 (C-3'', C-5''), 132.5 (C-6), 139.01 (C-1''), 143.2 (C-3), 143.5 (C-7), 154.2 (C-2), 154.3 (C-8a), 169.3 (CO₂Me), 169.8 (CO₂Me), 174.5 (C=O).LC-MS (ESI, 1.65 eV): *m/z* (%) = 455/457 [(M + H)⁺], 477/479 [(M + Na)⁺].Anal. Calcd for C₂₃H₁₉ClN₂O₆: C, 60.73; H, 4.21; N, 6.16; Cl, 7.79. Found: C, 60.64; H, 4.02; N, 6.07; Cl, 7.55.**Reaction of Arylhydrazones with Acetylenedicarboxylates in Toluene; General Procedure**To a stirred solution of the arylhydrazone **14a–d** (0.2 mmol) in toluene (10 mL), acetylenedicarboxylate **11a,b** (0.2 mmol) and catalytic amount of Yb(OTf)₃ (0.1 mmol) were added. The mixture was refluxed for 5 h monitoring by TLC. The solvent was removed under vacuum and the solid was subjected to column chromatography (silica gel, petroleum ether/EtOAc 5:1–3:1).**Diethyl 3-(6-Methyl-4-oxo-4*H*-chromen-3-yl)-1-(*p*-tolyl)-1*H*-pyrazole-4,5-dicarboxylate (16a)**

Yellow solid; yield: 47 mg (58%); mp 169–172 °C.

FT-IR (KBr): 1649, 1716, 1736 cm⁻¹.¹H NMR (500 MHz, CDCl₃): δ = 1.20 (t, *J* = 7.1 Hz, 3 H, CH₃), 1.24 (t, *J* = 7.1 Hz, 3 H, CH₃), 2.44 (s, 3 H, OCH₃), 2.49 (s, 3 H, OCH₃), 4.26 (q, *J* = 7.1 Hz, 2 H, CH₂), 4.32 (q, *J* = 7.1 Hz, 2 H, CH₂), 7.28 (d, *J* = 8.1 Hz, 2 H, 2''-H, 6''-H), 7.40 (d, *J* = 8.5 Hz, 2 H, 3''-H, 5''-H), 7.51 (dd, *J* = 8.5, 2.0 Hz, 1 H, 8-H), 7.70 (t, 1 H, 7-H), 8.07 (s, 1 H, 5-H), 8.20 (s, 1 H, 2-H).¹³C NMR (125 MHz, CDCl₃): δ = 13.8 (CH₃), 13.9 (CH₃), 20.9 (CH₃), 21.2 (CH₃), 60.8 (OCH₂), 62.4 (OCH₂), 116.1 (C-3'), 117.8 (C-8), 117.9 (C-4'), 123.9 (C-4a), 124.3 (C-2'', C-6''), 125.6 (C-5'), 129.7 (C-3'', C-5''), 135.0 (C-7), 135.4 (C-6), 136.6 (C-5), 137.1 (C-4''), 139.2 (C-3), 144.4 (C-1''), 154.3 (C-8a), 154.6 (C-2), 160.2 (CO₂Et), 162.1 (CO₂Et), 175.3 (C=O).LC-MS (ESI, 1.65 eV): *m/z* (%) = 461 [100, (M + H)⁺].Anal. Calcd for C₂₆H₂₄N₂O₆: C, 67.82; H, 5.25; N, 6.08. Found: C, 67.61; H, 5.18; N, 6.04.**Dimethyl 3-(6-Methyl-4-oxo-4*H*-chromen-3-yl)-1-(*p*-tolyl)-1*H*-pyrazole-4,5-dicarboxylate (16b)**

Yellow solid; yield: 34 mg (53%); mp 174–176 °C.

FT-IR (KBr): 1620, 1715, 1732 cm⁻¹.¹H NMR (500 MHz, CDCl₃): δ = 2.41 (s, 3 H, CH₃), 2.46 (s, 3 H, CH₃), 3.75 (s, 3 H, OCH₃), 3.84 (s, 3 H, OCH₃), 7.26 (d, *J* = 7.5 Hz, 2 H, 2''-H, 6''-H), 7.38 (d, *J* = 7.5 Hz, 2 H, 3''-H, 5''-H), 7.39 (d, *J* = 8.6 Hz, 1 H, 7-H), 7.49 (d, *J* = 8.6 Hz, 1 H, 8-H), 8.08 (d, *J* = 2.1 Hz, 1 H, 5-H), 8.22 (s, 1 H, 2-H).¹³C NMR (125 MHz, CDCl₃): δ = 20.98 (CH₃), 21.2 (CH₃), 50.8 (OCH₃), 52.4 (OCH₃), 116.2 (C-3'), 117.6 (C-8), 117.9 (C-4'), 123.8 (C-4a), 124.3 (C-2'', C-6''), 124.6 (C-5'), 125.7 (C-4''), 129.8 (C-3'', C-5''), 135.1 (C-7), 135.5 (C-6), 136.5 (C-5), 139.3 (C-3), 144.3 (C-1''), 154.4 (C-2), 154.6 (C-8a), 160.6 (CO₂Me), 162.7 (CO₂Me), 175.3 (C=O).LC-MS (ESI, 1.65 eV): *m/z* (%) = 433 [100, (M + H)⁺].Anal. Calcd for C₂₄H₂₀N₂O₆: C, 66.66; H, 4.66; N, 6.48. Found: C, 66.61; H, 4.58; N, 6.37.**Dimethyl 3-(4-Oxo-4*H*-chromen-3-yl)-1-(*p*-tolyl)-1*H*-pyrazole-4,5-dicarboxylate (16c)**

Yellow solid; yield: 42 mg (66%); mp 177–179 °C.

FT-IR (KBr): 1654, 1714, 1735 cm⁻¹.¹H NMR (500 MHz, CDCl₃): δ = 2.41 (s, 3 H, CH₃), 3.78 (s, 3 H, OCH₃), 3.85 (s, 3 H, OCH₃), 7.26 (m, 2 H, 2''-H, 6''-H), 7.38 (d, *J* = 8.4 Hz, 2 H, 3''-H, 5''-H), 7.43 (dd, *J* = 7.95–7.14 Hz, 1 H), 7.49 (d, 8.43 Hz, 1 H), 7.69 (ddd, *J* = 8.43, 7.14, 1.7 Hz, 1 H), 8.24 (s, 1 H, 2-H), 8.29 (dd, *J* = 7.95, 1.7 Hz, 1 H, 5-H).¹³C NMR (125 MHz, CDCl₃): δ = 21.2 (CH₃), 50.7 (OCH₃), 52.3 (OCH₃), 116.4 (C-3'), 118.0 (C-8), 118.2 (C-4'), 124.4 (C-4a), 124.5 (C-2'', C-6''), 125.5 (C-5'), 126.4 (C-4''), 129.8 (C-3'', C-5''), 133.8 (C-7), 136.5 (C-5), 136.7 (C-6), 139.3 (C-3), 144.3 (C-1''), 154.5 (C-2), 156.4 (C-8a), 160.6 (CO₂Me), 162.7 (CO₂Me), 175.2 (C=O).LC-MS (ESI, 1.65 eV): *m/z* (%) = 419 [100, (M + H)⁺].Anal. Calcd for C₂₃H₁₈N₂O₆: C, 66.02; H, 4.34; N, 6.70. Found: C, 66.01; H, 4.28; N, 6.47.**Diethyl 3-(4-Oxo-4*H*-chromen-3-yl)-1-(*p*-tolyl)-1*H*-pyrazole-4,5-dicarboxylate (16d)**

Yellow solid; yield: 37 mg (57%); mp 165–167 °C.

FT-IR (KBr): 1651, 1717, 1732 cm⁻¹.¹H NMR (500 MHz, CDCl₃): δ = 1.18 (t, *J* = 7.1 Hz, 3 H, CH₃), 1.23 (t, *J* = 7.1 Hz, 3 H, CH₃), 2.41 (s, 3 H, CH₃), 4.25 (q, *J* = 7.1 Hz, 2 H, CH₂), 4.30 (q, *J* = 7.1 Hz, 2 H, CH₂), 7.28 (d, *J* = 7.1 Hz, 2 H, 2''-H, 6''-H), 7.39 (d, *J* = 7.1 Hz, 2 H, 3''-H, 5''-H), 7.43 (d, *J* = 8.5 Hz, 1 H, 7-H), 7.50 (d, *J* = 8.5 Hz, 1 H, 8-H), 7.70 (ddd, *J* = 8.5, 7.1, 2.0 Hz, 1 H, 6-H), 8.23 (s, 1 H, 2-H), 8.30 (dd, *J* = 8.5, 2.0 Hz, 1 H, 5-H).¹³C NMR (125 MHz, CDCl₃): δ = 13.8 (CH₃), 13.9 (CH₃), 21.2 (CH₃), 60.9 (OCH₂), 62.4 (OCH₂), 116.1 (C-3'), 118.0 (C-8), 118.1 (C-4'), 124.2 (C-4a), 124.3 (C-2'', C-6''), 125.4 (C-5'), 126.3 (C-7), 129.7 (C-3'', C-5''), 133.7 (C-6), 136.5 (C-5), 137.1 (C-4''), 139.2 (C-3), 144.2 (C-1''), 154.4 (C-8a), 156.3 (C-2), 160.2 (CO₂Et), 162.1 (CO₂Et), 175.2 (C=O).LC-MS (ESI, 1.65 eV): *m/z* (%) = 447 [100, (M + H)⁺].Anal. Calcd for C₂₅H₂₂N₂O₆: C, 67.26; H, 4.97; N, 6.27. Found: C, 67.11; H, 4.88; N, 6.07.**[1-(4-Chlorophenyl)-1*H*-pyrazol-4-yl](2-hydroxy-5-methylphenyl)methanone (17a)**

Yellow solid; yield: 46 mg (49%); mp 115–117 °C.

FT-IR (KBr): 1629, 3436 cm⁻¹.¹H NMR (500 MHz, CDCl₃): δ = 2.33 (s, 3 H), 6.96 (d, *J* = 5.6 Hz, 1 H), 7.33 (d, 6.2 Hz, 1 H), 7.47 (d, *J* = 5.6 Hz, 2 H), 7.68 (d, *J* = 8.0 Hz, 2 H), 8.15 (s, 1 H), 8.43 (s, 1 H), 11.74 (s, 1 H).¹³C NMR (125 MHz, CDCl₃): δ = 21.0 (CH₃), 114.4, 118.4, 119.8, 123.8, 125.3, 128.2, 129.8, 130.9, 133.6, 137.2, 137.8, 142.5, 158.1, 191.9 (C=O).LC-MS (ESI, 1.65 eV): *m/z* (%) = 313 [100, (M + H)⁺].

Anal. Calcd for $C_{17}H_{13}ClN_2O_6$: C, 65.29; H, 4.19; N, 8.96; Cl, 11.34. Found: C, 65.11; H, 4.18; N, 8.04; Cl, 10.32.

(2-Hydroxy-5-methylphenyl)[1-(*p*-tolyl)-1*H*-pyrazol-4-yl]methanone (17b)

Yellow solid; yield: 40 mg (43%); mp 117–119 °C.

FT-IR (KBr): 1621, 3425 cm^{-1} .

1H NMR (500 MHz, $CDCl_3$): δ = 2.34 (s, 3 H), 2.41 (s, 3 H), 5.35 (s, 1 H), 5.42 (s, 1 H), 7.02 (s, 1 H), 7.36 (d, J = 8.5 Hz, 2 H), 7.40 (d, J = 8.5 Hz, 2 H), 7.43 (d, J = 8.5 Hz, 1 H), 7.50 (dd, J = 8.5, 1.8 Hz, 1 H), 8.15 (s, 1 H), 11.43 (s, 1 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 21.3, 21.4, 114.2, 114.6, 117.1, 119.2, 126.8, 129.4, 129.8, 129.9, 131.3, 134.7, 135.9, 142.1, 158.7, 191.2.

LC-MS (ESI, 1.65 eV): m/z (%) = 293 [100, (M + H) $^+$].

Anal. Calcd for $C_{18}H_{16}N_2O_6$: C, 73.95; H, 5.52; N, 9.58. Found: C, 73.81; H, 5.46; N, 9.04.

(2-Hydroxyphenyl)[1-(*p*-tolyl)-1*H*-pyrazol-4-yl]methanone (17c)

Yellow solid; yield: 32 mg (37%); mp 122–124 °C.

FT-IR (KBr): 1632, 3438 cm^{-1} .

1H NMR (500 MHz, $CDCl_3$): δ = 2.33 (s, 3 H), 5.82 (s, 1 H), 6.97 (s, 1 H), 7.20 (t, J = 7.5 Hz, 2 H), 7.42 (d, J = 7.5 Hz, 2 H), 7.5 (d, J = 8.5 Hz, 1 H), 7.72 (d, J = 7.5 Hz, 2 H), 8.15 (d, J = 8.5 Hz, 1 H), 11.76 (s, 1 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 21.3 (CH_3), 114.2, 116.1, 119.2, 124.5, 124.6, 129.3, 129.7, 132.4, 134.2, 135.9, 136.5, 142.1, 162.1, 192.3.

LC-MS (ESI, 1.65 eV): m/z (%) = 279 [100, (M + H) $^+$].

Anal. Calcd for $C_{17}H_{14}N_2O_6$: C, 73.37; H, 5.07; N, 10.07. Found: C, 73.11; H, 5.06; N, 10.04.

(5-Chloro-2-hydroxy-4-methylphenyl)(1-phenyl-1*H*-pyrazol-4-yl)methanone (17d)

Yellow solid; yield: 58 mg (53%); mp 121–123 °C.

FT-IR (KBr): 1625, 3434 cm^{-1} .

1H NMR (500 MHz, $CDCl_3$): δ = 2.41 (s, 3 H), 6.96 (s, 1 H), 7.26 (t, J = 7.5 Hz, 1 H), 7.42 (s, 1 H), 7.45 (d, J = 7.5 Hz, 2 H), 7.93 (d, J = 7.5 Hz, 2 H), 8.16 (s, 1 H), 8.43 (s, 1 H), 11.84 (s, 1 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 21.3 (CH_3), 113.5, 114.6, 119.4, 119.6, 124.5, 126.2, 129.4, 129.6, 133.7, 139.4, 141.6, 145.8, 161.2, 190.6 (C=O).

LC-MS (ESI, 1.65 eV): m/z (%) = 313 [(M + H) $^+$].

Anal. Calcd for $C_{17}H_{13}ClN_2O_6$: C, 65.29; H, 4.19; N, 8.96; Cl, 11.34. Found: C, 65.11; H, 4.18; N, 8.84; Cl, 11.29.

Supporting Information

Supporting information for this article is available online at <https://doi.org/10.1055/s-0036-1589013>.

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