 DOI: 10.17344/acsi.2017.3453 *Acta Chim. Slov.* **2018,** *65,* 34–49

Scientific paper

Synthesis and Anti-proliferative Activity of 4*H*-Chromone Based Phenylhydrazones, Pyrazolecarboxylates and Pyrazolylmethanones

Nageswara Rao Rayala,[1] Rajkumar Kommera,[1] Dayakar Cherupally,[1] Ramalinga Murthy Thampunuri,[2] V. Kalivendi Shasi[2] and China Raju Bhimapaka[1,*]

[1] *Natural Products Chemistry Division,*

[2] *Chemical Biology Division,*
CSIR-Indian Institute of Chemical Technology, Hyderabad-500 007, India.

** Corresponding author: E-mail: chinaraju@iict.res.in*
Tel: +91-40-27191725; Fax: +91-40-27160512

Received: 18-04-2017

Abstract

Series of 4*H*-chromone-based hydrazones **3a**–**z**, pyrazolecarboxylates **5a**–**x** and pyrazolylmethanones **6a**–**u** were prepared and screened for their anti-proliferative activity on A549, HeLa, DU145 and MDAMB 231 cell lines. The hydrazone compound **3s** with a chloro substituent on the chromanone moiety and a methoxy group on the phenyl ring displayed promising activity on A549, HeLa and DU145 cell lines. The compound **5p** with a bromo substituent on the chromanone moiety and a methyl group on the phenyl ring displayed potent activity on DU145. Furopyrazolecarboxylate **5w** having a methyl substituent on the phenyl ring displayed potent activity on HeLa cell line. The pyrazolylmethanone **6e** with a fluoro substituent on the phenyl ring and compound **6j** having a methyl substituent on the chromanone moiety and a methoxy group on the phenyl ring have shown promising anti-proliferative activity on HeLa cell line.

Keywords: 3-Formylchromones, pyrazolecarboxylates, pyrazolylmethanones, cycloaddition, anti-proliferative activity.

1. Introduction

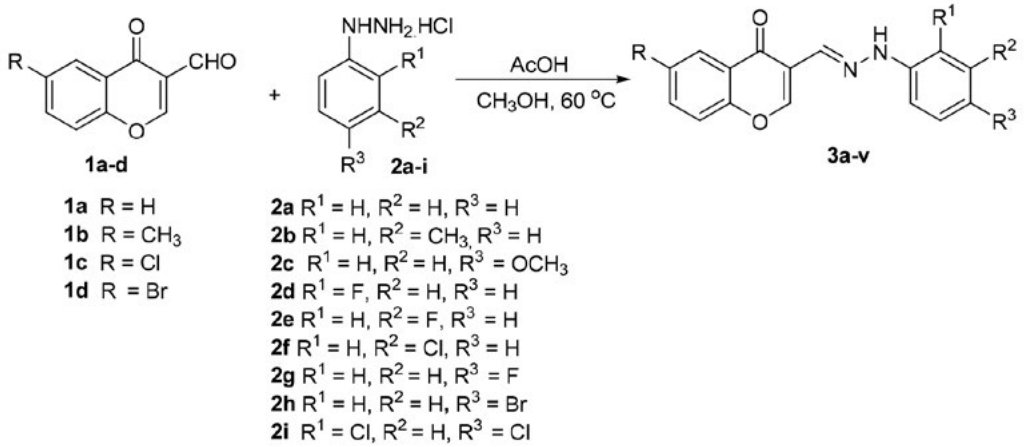
Hydrazones, pyrazoles and pyrazolylmethanones are important heterocyclic compounds.[1] The hydrazone-containing compounds obtained from carboxaldehydes with hydrazines have been shown to exhibit a variety of biological and pharmacological activities,[2–5] namely antimicrobial, anti-inflammatory, anti-tumor and anti-tubercular. Celebrex and Sildenafil are the pyrazole-based potent drug molecules. Celebrex is a COX-2 selective non-steroidal anti-inflammatory drug used to treat the pain and inflammation.[6] Sildenafil is a pharmaceutical drug used to treat erectile dysfunction.[7] Pyrazolylmethanones prepared by the reduction of carboxaldehydes were found to be anti-microbial and anti-inflammatory agents.[8]

In the course of our efforts in discovery and identification of biologically active compounds,[9–12] we focused research on 3-formylchromones and prepared series of 4*H*-chromen-1,2,3,4-tetrahydropyrimidine-5-carboxylates.[13] Further, pyridine, pyridone and benzopyridocarboxylates were reported by three-component, one-pot reaction of 3-formylchromones, benzylamines, 2-aminophenols with 3-oxobutanoates.[14] The present manuscript describes the preparation of 3-formylchromone-based hydrazones, pyrazolecarboxylates, pyrazolylmethanones and their anti-proliferative activity.

2. Results and Discussion

2. 1. Preparation of (*E*)-3-((2-Phenylhydrazono)methyl)-4*H*-chromen-4-ones 3a–z

Schemes 1–3 describe the preparation of target compounds **3a**–**z** starting from 3-formylchromones **1**. The required 3-formylchromones **1a**–**f** were prepared as per our earlier reported method.[13] Condensation of 3-formylchromones **1a**–**d** with phenylhydrazine hydrochlorides **2a**–**i** in the presence of acetic acid in methanol at 60 °C provided



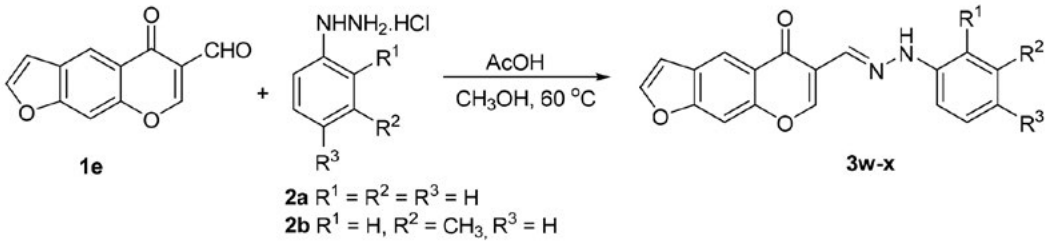
Scheme 1. Preparation of hydrazones **3a**–**v**

the corresponding hydrazones **3a**–**v** as yellow color solids (Scheme 1, Table 1). The compounds **3a**, **3j** and **3t** are known and were compared with the literature data.[15–18] The compounds **3b**–**i**, **3k**–**s** and **3u**–**z** are unknown and were well characterized by spectral data.

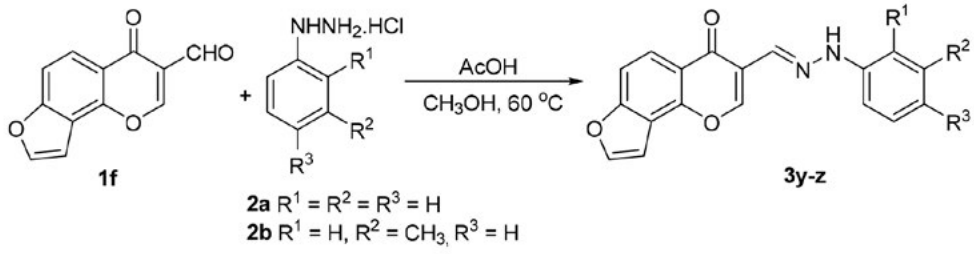
Schemes 2 and 3 describe the preparation of linear and angular furo hydrazones **3w**–**z**. The carboxaldehydes **1e**,**f** was prepared as per our previous reported method.[13] Condensation of carbaldehydes **1e**,**f** with phenylhydrazine hydrochlorides **2a,b** provided the hydrazones **3w**–**z** (Table 1).

2. 2. Preparation of Pyrazolecarboxylates 5a–x

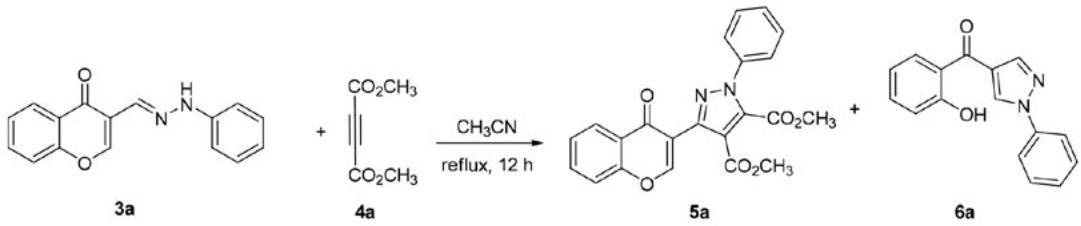
Schemes 4–7 describe the preparation of pyrazolecarboxylates **5a**–**x** by cycloaddition reaction of hydrazones



Scheme 2. Preparation of hydrazones **3w**–**x**



Scheme 3. Preparation of hydrazones **3y**–**z**

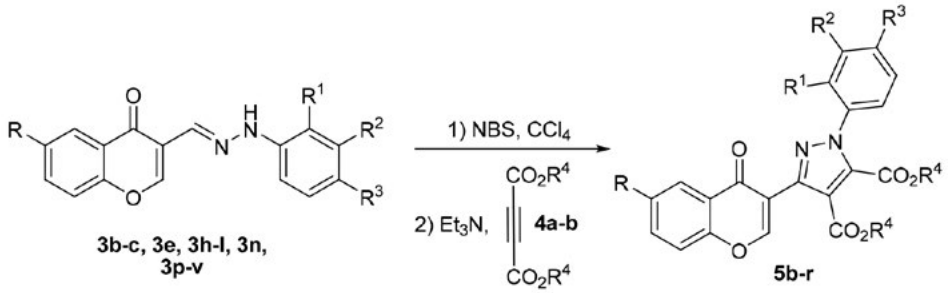


Scheme 4. Preparation of pyrazolecarboxylate **5a**

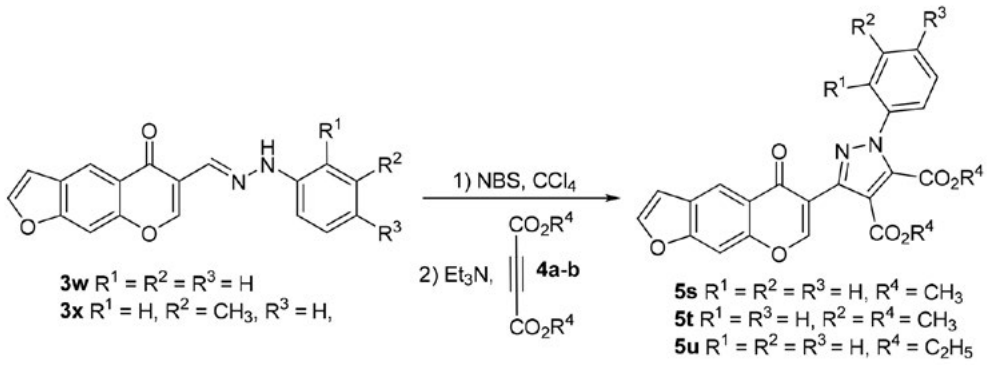
and activated alkynes. Initially, the cycloaddition reaction has been conducted with hydrazone **3a** and acetylenedicarboxylate **4a** in acetonitrile as the solvent under reflux conditions. This reaction provided two compounds, pyrazolecarboxylate **5a** and pyrazolylmethanone **6a** (Scheme 4). These two compounds were separated by column chromatography and characterized by spectral data.

In order to prepare the compound **5a** in an exclusive manner, bromination reaction has been carried out on **3a** with *N*-bromosuccinimide (NBS) in carbon tetrachloride at 55–60 °C. The reaction was monitored by TLC (3–4 h) and the usual workup afforded the corresponding **α**-bromophenylhydrazonochromone.[19] Next, the [3+2] cycloaddition reaction have been conducted between **α-bromophenylhydrazonochromone** and acetylenedicarboxylates **4a**–**b** in the presence of triethylamine. This provided the corresponding pyrazolecarboxylates **5a** and **5r**. In order to prepare series of pyrazolecarboxylates **5**, the bromination and cycloaddition reactions have been carried out on hydrazones **3b**–**c**, **3e**, **3h**–**l**, **3n** and **3p**–**v** with **4a** to provide a set of pyrazolecarboxylates **5b**–**q** (Scheme 5, Table 2). The compound **5a** is known and was compared with the literature data.[19] Compounds **5b**–**r** are new and were well characterized by spectral data.

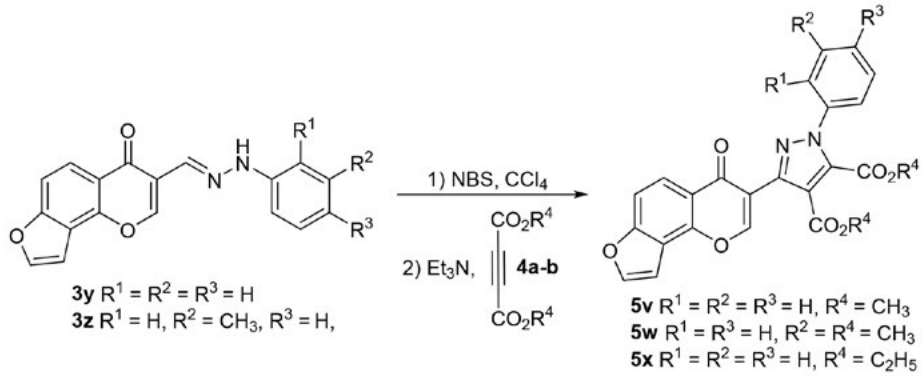
Having achieved the pyrazolecarboxylates, further the preparation of linear and angular pyrazolecarboxylates **5s**–**x** has been planned. Accordingly, the bromination followed by cycloaddition reaction have been carried out with hydrazones **3w**–**z** and activated alkynes **4a**–**b** to provide corresponding pyrazolecarboxylates **5s**–**x** (Schemes 6 and 7, Table 2). The compounds **5s**–**x** are unknown and were well characterized by spectral data.



Scheme 5. Preparation of pyrazolecarboxylates **5b**–**r**



Scheme 6. Preparation of linear furochromenyl pyrazolecarboxylates **5s**–**u**



Scheme 7. Preparation of angular furochromenyl pyrazolecarboxylates **5v**–**x**

2. 3. Preparation of pyrazolylmethanones 6a–u

The cycloaddition reaction of hydrazone **3a** with acetylenedicarboxylate **4a** provided two compounds, pyrazolecarboxylate **5a** and pyrazolylmethanone **6a** Scheme 4. The pyrazolylmethanone compound **6a** is known in the literature, however, the development of synthetic procedures for these molecules and their biological properties are not well established, yet. Therefore, a series of pyrazolylmethanones **6b**–**u** have been prepared by the reaction of hydrazones **3a**–**h**, **3k**–**s**, **3u**–**x** with K_2CO_3 in acetonitrile at room temperature (Schemes 8 and 9, Table 3). The known compound **6a** was compared with the literature data[20] and the unknown compounds **6b**–**u** are were well characterized by spectral data.

3. Biology

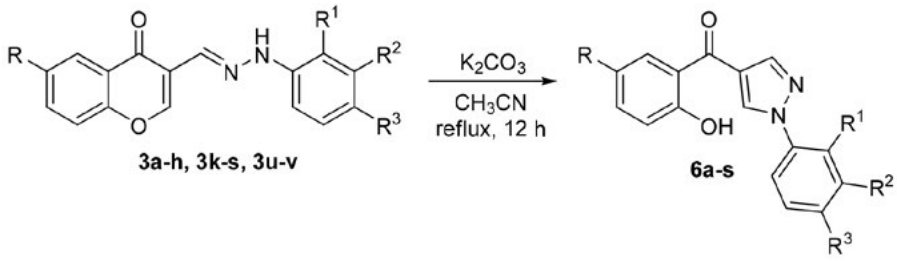
Thus synthesized hydrazones **3a**–**z**, pyrazolecarboxylates **5a**–**x** and pyrazolylmethanones **6a**–**u** were screened for their anti-proliferative activity against four cancer cell lines, *viz.* A549 (lung), HeLa (cervical), DU145 (prostate), MDA MB 231 (breast) by MTT assay.[13]

3. 1. Anti-proliferative Activity of Hydrazones 3a–z

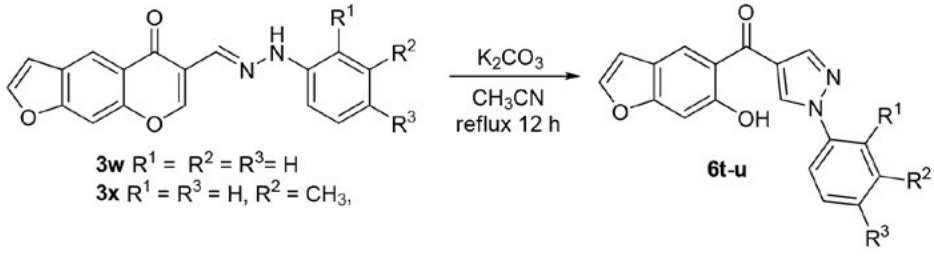
The anti-proliferative activity of hydrazones and their IC_{50} values along with standard drug doxorubicin are presented in Table 1. The compounds **3a**–**i** displayed activity in the range of IC_{50} 46.0–170.1 μM in all the tested cell lines. The presence of a methyl group on the chromanone moiety and a halogen, methyl and methoxy substituents on the phenyl ring in **3j**–**p** displayed activity in the range of IC_{50} 41.2–494.7 μM in all the tested cell lines. The presence of halogens on chromanones and a methyl or a methoxy group on the phenyl ring in **3q**–**v** displayed activity in the range of IC_{50} 14.0–355.5 μM in all the tested cell lines. However, compound **3s** (IC_{50} 19.7, 14.0, 17.8 μM) has shown promising activity on A549, HeLa and DU145, respectively. The linear **3w**–**x** and angular **3y**–**z** furo chromanones showed activity in the range of IC_{50} 42.1–183.7 μM in all the tested cell lines.

3. 2. Anti-proliferative Activity of Pyrazolecarboxylates 5a–x

The anti-proliferative activity of pyrazolecarboxylates **5a**–**x** and their IC_{50} values along with the data for the standard drug are presented in Table 2. The compound **5d** (IC_{50} 24.0 μM) having a fluoro substituent on the phenyl ring has shown better activity on A549 when compared to the methyl **5b**, methoxy **5c**, bromo **5e** and chloro **5f** derivatives. The methyl substituted chromanones **5g** (IC_{50} 13.0 μM) and **5h** (IC_{50} 19.0 μM) displayed promising activity on HeLa and DU145, respectively when compared to **5i**–**k**. The bromo substituted chromanone with a methyl group **5p** (IC_{50} 5.0 μM) or a methoxy group **5q** (IC_{50} 11.0 μM) on the phenyl ring displayed the potent activity. Chloro substituted chromanone **5m** (IC_{50} 24.0 μM) displayed better activity on DU145 when compared to the corresponding methoxy derivative **5n**. The angular furo derivative **5w** (IC_{50} 5.0 μM) has shown potent activity on HeLa and promising activity on DU145 (IC_{50} 15.0 μM) when compared to the corresponding linear furo derivative **5t**.



Scheme 8. Preparation of pyrazolylmethanones **6a**–**s**



Scheme 9. Preparation of linear pyrazolylmethanones **6t**–**u**

Table 1. Anti-proliferative activity of hydrazones*

Compounds	R	R^1	R^2	R^3	A549	HeLa	DU145	MDA MB 231
3a	H	H	H	H	170.1 ± 8.4	48.5 ± 2.9	91.1 ± 3.8	78.2 ± 3.1
3b	H	H	CH_3	H	70.6 ± 5.1	151.7 ± 7.8	57.4 ± 2.6	58.3 ± 4.5
3c	H	H	H	OCH_3	69.7 ± 3.9	63.5 ± 4.5	101.9 ± 5.8	85.4 ± 3.9
3d	H	F	H	H	77 ± 4.8	72.3 ± 6.4	82.8 ± 6.8	69.1 ± 3.9
3e	H	H	F	H	66.2 ± 2.8	77.4 ± 4.9	50.7 ± 2.4	85.6 ± 6.4
3f	H	H	Cl	H	46 ± 2.5	84.5 ± 6.7	59.2 ± 2.9	156.9 ± 11.5
3g	H	H	H	F	49.7 ± 2.1	67.9 ± 3.8	84 ± 3.1	87.3 ± 4.5
3h	H	H	H	Br	46.4 ± 4.6	104.7 ± 8.3	56.8 ± 2.7	154.2 ± 9.7
3i	H	Cl	H	Cl	80.5 ± 6.1	128.2 ± 8.5	80.4 ± 2.5	124.3 ± 9.4
3j	CH_3	H	H	H	63.3 ± 3.4	164.6 ± 9.8	102.3 ± 8.9	157.2 ± 9.5
3k	CH_3	H	CH_3	H	76.6 ± 3.4	77.7 ± 4.8	91.4 ± 3.4	112.5 ± 7.9
3l	CH_3	H	H	OCH_3	80.2 ± 3.9	494.7 ± 13.2	103.2 ± 4.9	345.6 ± 16.7
3m	CH_3	F	H	H	41.2 ± 1.3	101.6 ± 8.7	46.7 ± 3.8	68.3 ± 3.5
3n	CH_3	H	F	H	92.5 ± 5.4	48 ± 2.1	93.5 ± 2.7	91.5 ± 4.1
3o	CH_3	H	H	F	63.1 ± 3.4	68.5 ± 6.7	80 ± 3.4	76.5 ± 6.8
3p	CH_3	H	H	Br	73.7 ± 6.1	58.2 ± 4.4	152.1 ± 10.2	225.3 ± 9.8
3q	Cl	H	H	H	52.2 ± 2.8	75 ± 5.1	355.5 ± 12.1	312.2 ± 18.4
3r	Cl	H	CH_3	H	45.1 ± 4.8	53.9 ± 4.1	48.1 ± 3.5	78.5 ± 2.7
3s	Cl	H	H	OCH_3	19.7 ± 2.1	14 ± 1.7	17.8 ± 2.1	74.2 ± 2.8
3t	Br	H	H	H	191.2 ± 12	134.8 ± 9.7	72.1 ± 3.7	69.6 ± 4.1
3u	Br	H	CH_3	H	76.9 ± 3.7	65.9 ± 4.1	91.2 ± 7.1	227.1 ± 12.1
3v	Br	H	H	OCH_3	63.4 ± 5.4	66.6 ± 3.4	59.6 ± 3.9	75.4 ± 3.3
3w	–	H	H	H	54.9 ± 3.6	68.9 ± 3.1	92.7 ± 3.8	98.5 ± 6.7
3x	–	H	CH_3	H	81.2 ± 4.9	64.7 ± 2.4	47.6 ± 1.9	89.3 ± 5.8
3y	–	H	H	H	45.9 ± 2.7	183.7 ± 12.9	62.3 ± 2.5	128.3 ± 8.7
3z	–	H	CH_3	H	125.6 ± 8.9	95.7 ± 6.4	42.1 ± 2.8	74.2 ± 4.7
Doxorubicin					3.04 ± 1.1	2.51 ± 0.9	3.73 ± 1.3	5.05 ± 1.7

* IC_{50} (μM) Inhibitory concentration; **3w**, **3x** are linear and **3y**, **3z** are the angular compounds.

Table 2. Anti-proliferative activity of pyrazolecarboxylates

Compounds	R	R^1	R^2	R^3	R^4	A549	HeLa	DU-145	MDAMB 231
5a	H	H	H	H	CH_3	311 ± 6.7	296 ± 5.7	112 ± 5.2	130 ± 3.8
5b	H	H	CH_3	H	CH_3	070 ± 3.5	164 ± 4.9	087 ± 4.3	057 ± 4.5
5c	H	H	H	OCH_3	CH_3	200>	211 ± 3.9	061 ± 3.7	128 ± 2.5
5d	H	H	F	H	CH_3	024 ± 3.8	233 ± 4.1	054 ± 2.5	080 ± 3.2
5e	H	H	H	Br	CH_3	255 ± 5.4	194 ± 3.9	148 ± 3.6	200>
5f	H	Cl	H	Cl	CH_3	108 ± 4.5	139 ± 4.6	149 ± 3.5	200>
5g	CH_3	H	H	H	CH_3	045 ± 4.9	013 ± 2.6	200>	070 ± 4.6
5h	CH_3	H	CH_3	H	CH_3	051 ± 3.4	235 ± 6.9	019 ± 2.1	131 ± 4.9
5i	CH_3	H	H	OCH_3	CH_3	047 ± 3.2	081 ± 5.6	200>	098 ± 4.5
5j	CH_3	H	F	H	CH_3	165 ± 5.2	330 ± 6.8	088 ± 2.4	128 ± 4.9
5k	CH_3	H	H	Br	CH_3	083 ± 1.5	072 ± 2.9	200>	119 ± 4.6
5l	Cl	H	H	H	CH_3	056 ± 3.7	282 ± 5.8	123 ± 4.2	113 ± 3.8
5m	Cl	H	CH_3	H	CH_3	119 ± 5.7	200>	024 ± 1.4	078 ± 3.4
5n	Cl	H	H	OCH_3	CH_3	085 ± 6.4	228 ± 7.7	065 ± 4.2	094 ± 4.1
5o	Br	H	H	H	CH_3	055 ± 3.4	213 ± 7.6	100>	065 ± 6.1
5p	Br	H	CH_3	H	CH_3	111 ± 6.1	194 ± 5.1	005 ± 1.0	019 ± 2.1
5q	Br	H	H	OCH_3	CH_3	183 ± 8.7	073 ± .2	200>	011 ± 2.1
5r	H	H	H	H	C_2H_5	066 ± 4.0	161 ± 4.8	084 ± 2.4	200>
5s	–	H	H	H	CH_3	025 ± 2.5	200>	200>	094 ± 3.9
5t	–	H	CH_3	H	CH_3	068 ± 3.7	200>	200>	200>
5u	–	H	H	H	C_2H_5	90 ± 5.10	027 ± 2.2	067 ± 5.1	200>
5v	–	H	H	H	CH_3	200>	200>	200>	049 ± 2.8
5w	–	H	CH_3	H	CH_3	115 ± 4.1	005 ± 1.5	015 ± 2.1	075 ± 4.4
5x	–	H	H	H	C_2H_5	079 ± 4.8	033 ± 2.9	200>	076 ± 4.5
Doxorubicin						3.04 ± 1.1	3.73 ± 1.3	2.51 ± 0.9	5.05 ± 1.7

* IC_{50} (μM) Inhibitory concentration; **5s**–**u** are the linear and **5v**–**x** are the angular compounds.

3. 3. Anti-proliferative Activity of Pyrazolylmethanones 6a–u

The anti-proliferative activity of pyrazolylmethanones **6a**–**u** and their IC_{50} values along with the standard drug are presented in Table 3. The compounds **6a**–**h** displayed activity in the range of IC_{50} 10.8–164.9 μM in all the tested cell lines. The fluoro substituted pyrazole **6e** (IC_{50} 10.8 μM) has shown potent activity on HeLa cell line and promising activity on A549 (IC_{50} 15.6 μM) when compared to the corresponding methyl **6b**, methoxy **6c**, chloro **6f** and bromo **6h** derivatives. It is interesting to note that the fluoro substituent on the *meta* position **6e** displayed activity when compared to *ortho* **6d** and *para* **6g** analogues. The compound having a methyl substituent on the phenyl ring and a methoxy group on the pyrazole phenyl moiety **6j** (IC_{50} 7.9 μM) has shown potent activity on HeLa cell line and promising activity on DU145, A549 (IC_{50} 16.1, 19.9 μM), respectively when compared to methyl **6i** and halogen derivatives **6k**–**6n**.

Overall in the present series of compounds the hydrazone derivative **3s** displayed promising activity on three cell lines (A549, IC_{50} 19.7; HeLa, IC_{50} 14.0; DU145, IC_{50} 17.8 μM). Pyrazole carboxylates **5p** and **5w** (IC_{50} 5.0 μM) displayed potent activity on DU145, HeLa and promising activity on MDAMB 231(IC_{50} 19.0 μM) and DU145 (IC_{50} 15.0 μM). The compound **5q** (IC_{50} 11.0 μM) displayed potent activity selectively on MDAMB 231. Pyrazolylmethanone **6e** (IC_{50} 10.8, 15.6 μM) displayed potent activity on HeLa and promising activity on A549. Compound **6j** (IC_{50} 7.9, 16.1, 19.9 μM) displayed potent activity on HeLa, promising activity on DU145 and A549, respectively.

4. Experimental

4. 1. Chemistry

^{1}H NMR and ^{13}C NMR spectra were recorded on an Avance 300 MHz spectrometer in $CDCl_3$ using TMS as internal standard. FT-IR spectra were recorded on a Nicollet 740 FT-IR spectrometer. Mass spectra were obtained on Agilent ESI-MS instrument. Melting points were determined in open glass capillary tubes on a Mettler FP 51 melting point apparatus and are uncorrected. All the reactions were monitored by thin layer chromatography (TLC) on pre-coated silica gel (60 F_{254} mesh); spots were visualized under UV light. Merck silica gel (60–120; 100–200 mesh) was used for chromatography. All the reactions were carried out using reagent-grade solvents. The reagents were purchased from Sigma-Aldrich and local suppliers (Sd fine & AVRA chemicals Pvt. Ltd, Hyderabad, India).

4. 2. General Procedure for the Preparation of Hydrazones 3a–z

The warmed solution of phenylhydrazine hydrochloride **2a** (0.172 g, 1.2 mmol) and acetic acid (0.5 mL in 1 mL

Table 3. Anti-proliferative activity of pyrazolylmethanones

Compounds	R	R^1	R^2	R^3	A549	HeLa	DU-145	MDAMB 231
6a	H	H	H	H	44.4 ± 2.4	164.9 ± 9.5	45.1 ± 2.7	52.1 ± 3.4
6b	H	H	CH_3	H	126.7 ± 6.	86.8 ± 2.8	83.3 ± 3.5	93.5 ± 4.8
6c	H	H	H	OCH_3	143.2 ± 9	85.3 ± 3.1	46.7 ± 6.1	119.3 ± 7.7
6d	H	F	H	H	62.3 ± 2.5	51.1 ± 2.9	87.2 ± 5.8	98.7 ± 3.9
6e	H	H	F	H	15.6 ± 2.7	10.8 ± 1.6	26.1 ± 2.4	45.8 ± 3.1
6f	H	H	Cl	H	98.5 ± 8.1	83.8 ± 4.1	60 ± 3.8	86.6 ± 5.6
6g	H	H	H	F	82.1 ± 4.6	164.9 ± 5.8	51.2 ± 5.2	91.5 ± 4.9
6h	H	H	H	Br	42.5 ± 3.7	56.9 ± 2.7	63.7 ± 4.9	65.2 ± 3.5
6i	CH_3	H	CH_3	H	68.5 ± 3.1	45.5 ± 3.5	47.2 ± 2.9	78.6 ± 5.1
6j	CH_3	H	H	OCH_3	19.9 ± 1.9	7.9 ± 1.1	16.1 ± 2.5	35.2 ± 2.8
6k	CH_3	F	H	H	70.8 ± 4.3	73.7 ± 3.1	245.9 ± 9.7	215.1 ± 12.4
6l	CH_3	H	F	H	82.2 ± 3.5	58.2 ± 3.7	54.4 ± 4.1	119.4 ± 8.9
6m	CH_3	H	H	F	59.9 ± 2.9	49.3 ± 2.1	66.7 ± 1.9	185.4 ± 9.1
6n	CH_3	H	H	Br	164.9 ± 7.	67.7 ± 3.9	54.3 ± 2.3	85.2 ± 3.7
6o	Cl	H	H	H	82.7 ± 6.4	50.2 ± 3.1	119.5 ± 6.7	175.2 ± 9.4
6p	Cl	H	CH_3	H	52.9 ± 2.9	71.3 ± 2.4	55.5 ± 3.1	76.5 ± 1.8
6q	Cl	H	H	OCH_3	98.3 ± 8.1	51.4 ± 2.9	116.1 ± 5.8	83.5 ± 2.7
6r	Br	H	CH_3	H	220.2 ± 11	170.3 ± 9.8	64.5 ± 6.4	128.3 ± 6.7
6s	Br	H	H	OCH_3	61.3 ± 3.8	51.4 ± 1.9	66.1 ± 2.9	75.8 ± 4.1
6t	–	H	H	H	45.6 ± 5.4	164.9 ± 11.2	62.4 ± 4.5	86.5 ± 1.6
6u	–	H	CH_3	H	125.9 ± 9.	50.9 ± 3.7	82.7 ± 2.3	75.6 ± 2.4
Doxorubicin					3.04 ± 1.1	2.51 ± 0.9	3.73 ± 1.3	5.05 ± 1.7

* IC_{50} (μM) Inhibitory concentration; **6t**–**u** are the linear compounds.

H_2O) was added to a stirred solution of 3-formylchromone (0.174 g, 1 mmol) in methanol (2 mL) at room temperature. The reaction mixture was heated to 60 °C for 30 min and then cooled to room temperature. The solid separated was filtered, washed with ice-cold water (5 mL) and then recrystallized from hot methanol providing the corresponding hydrazone **3a**. Similarly, the other hydrazones **3b–z** were prepared from the corresponding 3-formylchromones **1a–f** and phenylhydrazine hydrochlorides **2a–i** under optimized reaction conditions.

(*E*)-3-((2-Phenylhydrazono)methyl)-4*H*-chromen-4-one (3a)

Yellow solid. Yield 88%. M.p. 212–213 °C. FT-IR (KBr): *ν* 3265, 1618, 1526, 1258, 1171 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$+DMSO-d_6): δ 8.66 (s, 1H, imine), 8.14 (dd, 1H, J_1 = 6.2 Hz, J_2 = 7.8 Hz), 7.97 (s, 1H, Ar-H), 7.77 (t, 1H, *J* = 6.2 Hz, Ar-H), 7.60 (d, 1H, *J* = 8.5 Hz, Ar-H), 7.47 (t, 1H, *J* = 8.8 Hz, Ar-H), 7.17 (t, 2H, *J* = 7.0 Hz, Ar-H), 7.04 (d, 2H, *J* = 7.0 Hz, Ar-H), 6.72 (t, 1H, *J* = 7.8 Hz, Ar-H). ^{13}C NMR (75 MHz, $CDCl_3$+DMSO-d_6): δ 173.6, 154.9, 152.1, 144.5, 142.0, 133.7, 132.1, 128.7, 128.4, 127.1, 123.7, 122.3, 118.9, 118.4, 111.7. ESI-MS: *m/z* $[M+H]^+$ 265.

(*E*)-3-((2-*m*-Tolylhydrazono)methyl)-4*H*-chromen-4-one (3b)

Yellow solid. Yield 76%. M.p. 231–233 °C. FT-IR (KBr): *ν* 2977, 1622, 1571, 1491, 1206, 1130, 1094, 872, 748 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$+DMSO-d_6): δ 8.46 (s, 1H, imine), 7.90 (s, 1H, Ar-H), 7.86 (s, 1H, Ar-H), 7.43 (d, 1H, *J* = 8.8 Hz, Ar-H), 7.34 (d, 1H, *J* = 8.8 Hz, Ar-H), 7.07 (t, 2H, *J* = 8.8, 6.8 Hz, Ar-H), 6.95 (d, 2H, *J* = 7.8 Hz, Ar-H), 6.63 (t, 1H, *J* = 7.8 Hz, Ar-H). ESI-MS: *m/z* $[M+H]^+$ 278.

(*E*)-3-((2-(4-Methoxyphenyl)hydrazono)methyl)-4*H*-chromen-4-one (3c)

Yellow solid. Yield 89%. M.p. 237–239 °C. FT-IR (KBr): *ν* 3271, 2901, 1621, 1570, 1464, 1228, 1042, 827, 791 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$+DMSO-d_6): δ 8.66 (s, 1H, imine), 8.13 (dd, 1H, J_1 = 6.8 Hz, J_2 = 8.8 Hz, Ar-H), 7.92 (s, 1H, *J* = 7.8 Hz, Ar-H), 7.82–7.76 (m, 1H, Ar-H), 7.66–7.60 (m, 1H, Ar-H), 7.52–7.46 (m, 1H, Ar-H), 7.02–6.98 (m, 2H, Ar-H), 6.82–6.76 (m, 2H, Ar-H), 3.72 (s, 3H, OCH_3). ^{13}C NMR (75 MHz, $CDCl_3$+DMSO-d_6): δ 163.5, 150.3, 145.4, 131.9, 131.1, 128.4, 123.9, 119.2, 119.1, 117.2, 115.3, 52.3. ESI-MS: *m/z* 295 $[M+H]^+$.

(*E*)-3-((2-(2-Fluorophenyl)hydrazono)methyl)-4*H*-chromen-4-one (3d)

Yellow solid. Yield 71%. M.p. 232–234 °C. ^1H NMR (300 MHz, $CDCl_3$+DMSO-d_6): δ 8.60 (s, 1H, imine), 8.23 (s, 1H, Ar-H), 8.16 (d, 1H, *J* = 7.9 Hz, Ar-H), 7.73 (t, 1H, *J* = 6.9 Hz, Ar-H), 7.50–7.42 (m, 2H, Ar-H), 7.04–6.94 (m, 2H, Ar-H), 6.70 (t, 1H, *J* = 6.9 Hz, Ar-H). ^{13}C NMR (75 MHz, $CDCl_3$+DMSO-d_6): δ 175.1, 155.9, 153.0, 150.8, 142.5, 134.5, 131.2, 130.6, 125.4, 123.5, 118.8, 114.3. ESI-MS: *m/z* $[M+H]^+$ 283.

(*E*)-3-((2-(3-Fluorophenyl)hydrazono)methyl)-4*H*-chromen-4-one (3e)

Yellow solid. Yield 73%. M.p. 249–251 °C. FT-IR (KBr): *ν* 3265, 2793, 1623, 1484, 1171, 816, 779 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$+DMSO-d_6): δ 8.78 (s, 1H, imine), 8.02 (s, 1H), 7.98 (s, 1H, Ar-H), 7.60 (d, 1H, *J* = 8.8 Hz, Ar-H), 7.54 (d, 1H, *J* = 8.8 Hz, Ar-H), 6.98 (s, 2H, Ar-H), 6.74 (s, 1H, Ar-H).

(*E*)-3-((2-(3-Chlorophenyl)hydrazono)methyl)-4*H*-chromen-4-one (3f)

Yellow solid. Yield 69%. M.p. 254–256 °C. ^1H NMR (300 MHz, $CDCl_3$+DMSO-d_6): δ 8.67 (s, 1H, imine), 8.21 (d, 1H, *J* = 7.9 Hz, Ar-H), 8.04 (s, 1H, Ar-H), 7.93 (d, 1H, *J* = 1.2 Hz, Ar-H), 7.76 (d, 1H, *J* = 7.9 Hz, Ar-H), 7.65–7.43 (m, 2H, Ar-H), 7.11 (s, 1H, Ar-H), 6.96 (d, 1H, *J* = 8.6 Hz, Ar-H), 7.70 (d, 1H, *J* = 7.2 Hz, Ar-H). ^{13}C NMR (75 MHz, $CDCl_3$+DMSO-d_6): δ 173.4, 161.0, 154.2, 150.3, 144.7, 132.5, 132.2, 128.5, 127.6, 123.6, 121.8, 117.9, 116.6, 109.9, 108.9.

(*E*)-3-((2-(4-Fluorophenyl)hydrazono)methyl)-4*H*-chromen-4-one (3g)

Yellow solid. Yield 73%. M.p. 241–243 °C. ^1H NMR (300 MHz, $CDCl_3$+DMSO-d_6): δ 8.80 (s, 1H, imine), 8.12 (dd, 1H, J_1 = 7.9 Hz, J_2 = 1.5 Hz, Ar-H), 7.96 (s, 1H, Ar-H), 7.82 (dt, 1H, J_1 = 8.6 Hz, J_2 = 7.6 Hz, J_3 = 1.8 Hz, Ar-H), 7.69 (d, 1H, *J* = 8.1 Hz, Ar-H), 7.52 (t, 2H, *J* = 7.1 Hz, Ar-H), 7.06 (d, 3H, *J* = 6.6 Hz, Ar-H). ^{13}C NMR (75 MHz, $CDCl_3$+DMSO-d_6): δ 190.3, 175.2, 158.7, 152.5, 142.7, 134.5, 132.1, 130.9, 128.1, 125.4, 123.4, 119.5, 118.8, 117.5, 115.9.

(*E*)-3-((2-(4-Bromophenyl)hydrazono)methyl)-4*H*-chromen-4-one (3h)

Pale yellow solid. Yield 77%. M.p. 226–228 °C. FT-IR (KBr): *ν* 3271, 2901, 1621, 1570, 1464, 1228, 1042, 827, 791 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$+DMSO-d_6): δ 8.81 (s, 1H, imine), 8.11 (d, 2H, *J* = 7.8 Hz, Ar-H), 7.97 (s, 1H, Ar-H), 7.81 (t, 1H, *J* = 8.4 Hz, Ar-H), 7.68 (d, 1H, *J* = 8.3 Hz, Ar-H), 7.35 (d, 2H, *J* = 8.6 Hz, Ar-H), 7.01 (d, 2H, *J* = 8.6 Hz, Ar-H). ^{13}C NMR (75 MHz, $CDCl_3$+DMSO-d_6): δ 173.2, 153.9, 150.2, 142.4, 132.2, 129.7, 127.0, 123.6, 123.4, 121.5, 117.7, 116.6, 112.1, 108.0.

(*E*)-3-((2-(2,4-Dichlorophenyl)hydrazono)methyl)-4*H*-chromen-4-one (3i)

Yellow solid. Yield 64%. M.p. 225–227 °C. FT-IR (KBr): *ν* 3265, 2793, 1623, 1484, 1171 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$ + DMSO-d_6): δ 8.76 (s, 1H, imine), 8.40 (s, 1H), 8.14 (t, 1H, J_1 = 6.8 Hz, J_2 = 8.8 Hz, Ar-H), 7.80 (dd, 2H, J_1 = 7.9 Hz, J_2 = 7.1 Hz, Ar-H), 7.66–7.46 (m, 3H, Ar-H), 6.20 (d, 1H, *J* = 7.8 Hz, Ar-H). ESI-MS: *m/z* $[M+H]^+$ 333.

(*E*)-6-Methyl-3-((2-phenylhydrazono)methyl)-4*H*-chromen-4-one (3j)

Yellow solid. Yield 72%. M.p. 203–205 °C. FT-IR (KBr): *v* 3265, 2977, 1622, 1571, 1491, 1206, 1130, 1094, 872, 748 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$ + DMSO-d_6): δ 8.55 (s, 1H, imine), 8.03 (d, 1H, *J* = 8.8 Hz), 7.98 (s, 1H, Ar-H), 7.35 (s, 1H, Ar-H), 7.26 (d, 1H, *J* = 8.8 Hz, Ar-H), 7.17 (t, 2H, *J* = 8.8 Hz, Ar-H), 7.04 (d, 2H, *J* = 7.8 Hz, Ar-H), 6.73 (t, 1H, *J* = 7.8 Hz, Ar-H). ^{13}C NMR (75 MHz, $CDCl_3$ + DMSO-d_6): δ 173.6, 161.6, 150.4, 146.6, 141.3, 138.2, 130.3, 129.7, 128.7, 126.8, 124.4, 122.4, 119.6, 118.7, 117.4, 111.4, 21.0. ESI-MS: *m/z* $[M+H]^+$ 279.

(*E*)-6-Methyl-3-((2-*m*-tolylhydrazono)methyl)-4*H*-chromen-4-one (3k)

Yellow solid. Yield 71%. M.p. 222–224 °C. FT-IR (KBr): *v* 3276, 1640, 1608 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$ + DMSO-d_6): δ 8.55 (s, 1H, imine), 7.96 (s, 1H, Ar-H), 7.92 (s, 1H, Ar-H), 7.52 (d, 1H, *J* = 7.0 Hz, Ar-H), 7.44 (d, 1H, *J* = 8.0 Hz, Ar-H), 7.02 (t, 1H, *J* = 8.0 Hz, Ar-H), 6.85 (s, 1H, Ar-H), 6.81 (d, 1H, *J* = 8.0 Hz, Ar-H), 6.52 (d, 1H, *J* = 7.0 Hz, Ar-H). ^{13}C NMR (75 MHz, $CDCl_3$ + DMSO-d_6): δ 174.6, 153.7, 151.7, 144.7, 137.9, 135.0, 134.9, 128.6, 127.5, 124.1, 122.6, 119.5, 119.1, 118.1, 112.2, 109.1, 21.0, 20.2. ESI-MS: *m/z* $[M+H]^+$ 293.

(*E*)-3-((2-(4-Methoxyphenyl)hydrazono)methyl)-6-methyl-4*H*-chromen-4-one (3l)

Yellow solid. Yield 79%. M.p. 246–248 °C. FT-IR (KBr): *v* 3271, 2901, 1621, 1570, 1464, 1228, 1042, 827, 791 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$ + DMSO-d_6): δ 8.57 (s, 1H, imine), 7.95 (d, 1H, *J* = 7.8 Hz, Ar-H), 7.54 (s, 1H, Ar-H), 7.37 (s, 1H, Ar-H), 7.20 (s, 1H, Ar-H), 7.01 (d, 2H, *J* = 8.6 Hz, Ar-H), 6.78 (d, 2H, *J* = 8.6 Hz, Ar-H), 3.74 (s, 3H, OCH_3), 2.48 (s, 3H, CH_3). ^{13}C NMR (75 MHz, $CDCl_3$ + DMSO-d_6): δ 173.0, 152.1, 150.8, 149.4, 137.2, 124.8, 122.5, 121.1, 117.8, 116.3, 112.5, 111.1, 53.3, 18.7. ESI-MS: *m/z* $[M+H]^+$ 309.

(*E*)-3-((2-(2-Fluorophenyl)hydrazono)methyl)-6-methyl-4*H*-chromen-4-one (3m)

Yellow solid. Yield 83%. M.p. 230–232 °C. FT-IR (KBr): *v* 3283, 1623, 1525, 1462, 1130, 753 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$ + DMSO-d_6): δ 8.75 (s, 1H, imine), 8.25 (s, 1H, Ar-H), 7.91 (s, 1H, Ar-H), 7.63 (dd, 1H, J_1 = 8.4 Hz, J_2 = 18 Hz, Ar-H), 7.57 (s, 1H, Ar-H), 7.55–7.49 (m, 1H, Ar-H), 7.06 (d, 2H, *J* = 7.7 Hz, Ar-H), 6.75 (t, 1H, *J* = 6.6 Hz, Ar-H), 2.46 (s, 3H, CH_3). ^{13}C NMR (75 MHz, $CDCl_3$ + DMSO-d_6): δ 184.1, 173.0, 169.6, 152.2, 150.4, 133.3, 129.2, 122.8, 122.5, 121.2, 117.5, 116.4, 113.0, 112.1, 18.7. ESI-MS: *m/z* $[M+H]^+$ 297.

(*E*)-3-((2-(3-Fluorophenyl)hydrazono)methyl)-6-methyl-4*H*-chromen-4-one (3n)

Yellow solid. Yield 67%. M.p. 261–263 °C. ^1H NMR (300 MHz, $CDCl_3$ + DMSO-d_6): δ 8.57 (s, 1H, imine), 8.18 (s, 1H, Ar-H), 7.87 (s, 1H, Ar-H), 7.52 (d, 1H, *J* = 8.0 Hz, Ar-H), 7.43 (d, 1H, *J* = 8.0 Hz, Ar-H), 7.00–6.93 (m, 2H, Ar-H), 6.67 (t, 2H, *J* = 6.0 Hz, Ar-H), 2.43 (s, 3H, CH_3). ^{13}C NMR (75 MHz, $CDCl_3$ + DMSO-d_6): δ 175.3, 154.5, 153.1, 147.6, 135.8, 131.1, 129.9, 124.8, 123.4, 119.5, 118.9, 108.6, 105.3, 98.9, 20.9. ESI-MS: *m/z* $[M+H]^+$ 297.

(*E*)-3-((2-(4-Fluorophenyl)hydrazono)methyl)-6-methyl-4*H*-chromen-4-one (3o)

Yellow solid. Yield 72%. M.p. 264–266 °C. ^1H NMR (300 MHz, $CDCl_3$ + DMSO-d_6): δ 8.64 (s, 1H, imine), 7.98 (s, 1H, Ar-H), 7.92 (s, 1H, Ar-H), 7.58 (dd, 1H, J_1 = 8.6 Hz, J_2 = 1.8 Hz, Ar-H), 7.50 (d, 1H, *J* = 8.4 Hz, Ar-H), 7.07–7.01 (m, 2H, Ar-H), 6.95 (t, 2H, *J* = 8.4 Hz, Ar-H), 2.47 (s, 3H, CH_3). ^{13}C NMR (75 MHz, $CDCl_3$ + DMSO-d_6): δ 189.4, 161.2, 157.9, 157.0, 140.6, 134.4, 133.8, 129.7, 129.2, 126.4, 121.7, 119.8, 115.9, 114.4, 114.7, 18.6. ESI-MS: *m/z* $[M+H]^+$ 297.

(*E*)-3-((2-(4-Bromophenyl)hydrazono)methyl)-6-methyl-4*H*-chromen-4-one (3p)

Yellow solid. Yield 78%. M.p. 246–248 °C. FT-IR (KBr): *v* 3265, 2977, 1622, 1571, 1491, 1206, 872, 748 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$ + DMSO-d_6): δ 8.56 (s, 1H, imine), 7.97 (s, 1H, Ar-H), 7.92 (s, 1H, Ar-H), 7.52 (d, 1H, *J* = 7.0 Hz, Ar-H), 7.44 (d, 1H, *J* = 8.0 Hz, Ar-H), 7.02 (t, 1H, *J* = 7.0 Hz, Ar-H), 6.85 (s, 1H, Ar-H), 6.81 (d, 1H, *J* = 8.0 Hz, Ar-H), 6.53 (d, 1H, *J* = 7.0 Hz, Ar-H). ^{13}C NMR (75 MHz, $CDCl_3$ + DMSO-d_6): δ 171.3, 154.6, 151.0, 148.5, 144.0, 137.7, 133.3, 106.9, 40.2. ESI-MS: *m/z* $[M+H]^+$ 357.

(*E*)-6-Chloro-3-((2-phenylhydrazono)methyl)-4*H*-chromen-4-one (3q)

Yellow solid. Yield 72%. M.p. 229–231 °C. ^1H NMR (300 MHz, $CDCl_3$ + DMSO-d_6): δ 8.68 (s, 1H, imine), 8.08 (d, 1H, *J* = 3.2 Hz, Ar-H), 7.97 (s, 1H, Ar-H), 7.74 (dd, 1H, J_1 = 8.8 Hz, J_2 = 2.6 Hz, Ar-H), 7.65 (d, 1H, *J* = 8.8 Hz, Ar-H), 7.19 (t, 2H, *J* = 8.4 Hz, Ar-H), 7.06 (d, 2H, *J* = 7.5 Hz, Ar-H), 6.75 (t, 1H, *J* = 7.1 Hz, Ar-H). ESI-MS: *m/z* $[M+H]^+$ 299.

(*E*)-6-Chloro-3-((2-*m*-tolylhydrazono)methyl)-4*H*-chromen-4-one (3r)

Yellow solid. Yield 57%. M.p. 215–217 °C. FT-IR (KBr): *v* 3276, 2920, 1640, 1608, 1460, 1297, 1160, 813, 772 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$ + DMSO-d_6): δ 8.56 (s, 1H, imine), 8.02 (s, 1H, Ar-H), 7.86 (s, 1H, Ar-H), 7.60 (dd, 2H, J_1 = 6.8 Hz, J_2 = 8.8 Hz, Ar-H), 6.96 (t, 1H, *J* = 7.8 Hz, Ar-H), 6.79 (s, 1H, Ar-H), 6.75 (d, 1H, *J* = 7.8 Hz, Ar-H), 6.48 (d, 1H, *J* = 7.8 Hz, Ar-H). ^{13}C NMR (75 MHz, $CDCl_3$ + DMSO-d_6): δ 179.6, 169.4, 161.6, 159.2, 154.7, 153.2, 150.3, 149.5, 148.9, 148.1, 144.4, 143.1, 142.3, 139.9, 139.3, 136.3, 40.8. ESI-MS: *m/z* $[M+H]^+$ 313.

(*E*)-6-Chloro-3-((2-(4-methoxyphenyl)hydrazono)methyl)-4*H*-chromen-4-one (3s)

Yellow solid. Yield 61%. M.p. 219–221 °C. FT-IR (KBr): *v* 3271, 2901, 1621, 1570, 1464, 1228, 1042 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$ + DMSO-d_6): δ 8.56 (s, 1H,

imine), 8.08 (s, 1H, Ar-H), 7.88 (s, 1H, Ar-H), 7.68 (d, 1H, *J* = 8.8 Hz, Ar-H), 7.56 (d, 1H, *J* = 8.8 Hz, Ar-H), 6.96 (d, 2H, *J* = 8.4 Hz, Ar-H), 6.74 (d, 2H, *J* = 8.4 Hz, Ar-H), 3.72 (s, 3H, OCH_3). ^{13}C NMR (75 MHz, $CDCl_3$ + DMSO-d_6): δ 173.2, 164.2, 150.4, 146.2, 134.4, 132.2, 129.7, 124.3, 115.9, 117.2, 119.8, 53.2. ESI-MS: *m/z* $[M+H]^+$ 329.

(*E*)-6-Bromo-3-((2-phenylhydrazono)methyl)-4*H*-chromen-4-one (3t)

Yellow solid. Yield 72%. M.p. 218–220 °C. FT-IR (KBr): *v* 3283, 1623, 1525, 1462, 1258, 1182, 1027, 753 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$ + DMSO-d_6): δ 8.61 (s, 1H, imine), 8.24 (d, 1H, *J* = 1.3 Hz, Ar-H), 7.94 (s, 1H, Ar-H), 7.82 (dd, 1H, J_1 = 6.4 Hz, J_2 = 8.8 Hz, Ar-H), 7.53 (d, 1H, *J* = 8.8 Hz, Ar-H), 7.16 (t, 2H, *J* = 7.5 Hz, Ar-H), 7.02 (d, 2H, *J* = 7.7 Hz, Ar-H), 6.72 (t, 1H, *J* = 7.1 Ar-H).

(*E*)-6-Bromo-3-((2-*m*-tolylhydrazono)methyl)-4*H*-chromen-4-one (3u)

Yellow solid. Yield 81%. M.p. 240–242 °C. FT-IR (KBr): *v* 3276, 2918, 1639, 1602, 1454, 1296, 1159, 813, 773 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$ + DMSO-d_6): δ 8.70 (s, 1H, imine), 8.23 (d, 1H, *J* = 2.5 Hz, Ar-H), 7.94 (s, 1H, Ar-H), 7.90 (dd, 1H, J_1 = 8.8 Hz, J_2 = 6.8 Hz, Ar-H), 7.63 (d, 1H, *J* = 8.2 Hz, Ar-H), 7.07 (t, 1H, *J* = 7.8 Hz, Ar-H), 6.89 (s, 1H, Ar-H), 6.84 (d, 1H, *J* = 8.3 Hz, Ar-H), 6.57 (d, 1H, *J* = 7.5 Hz, Ar-H). ESI-MS: *m/z* $[M+H]^+$ 357.

(*E*)-6-Bromo-3-((2-(4-methoxyphenyl)hydrazono)methyl)-4*H*-chromen-4-one (3v)

Yellow solid. Yield 66%. M.p. 245–247 °C. FT-IR (KBr): *v* 3271, 2901, 1621, 1570, 1464, 1228, 1042, 827, 791 cm^{-1}. ^1H NMR (75 MHz, $CDCl_3$ + DMSO-d_6): δ 8.58 (s, 1H, imine), 8.16 (d, 1H, *J* = 8.8 Hz, Ar-H), 8.02 (d, 1H, *J* = 7.8 Hz, Ar-H), 7.74 (s, 1H, Ar-H), 7.72–7.66 (m, 1H, Ar-H), 7.56–7.40 (m, 2H, Ar-H), 7.23 (d, 2H, *J* = 8.4 Hz, Ar-H), 6.96 (d, 2H, *J* = 8.4 Hz, Ar-H), 3.20 (s, 3H, OCH_3). ^{13}C NMR (75 MHz, $CDCl_3$ + DMSO-d_6): δ 172.8, 148.3, 141.1, 137.0, 132.2, 130.0, 124.8, 120.5, 119.7, 119.3, 113.8, 113.7, 54.7.

(*E*)-6-((2-Phenylhydrazono)methyl)-5*H*-furo[3,2-*g*]chromen-5-one (3w)

Yellow solid. Yield 72%. M.p. 235–236 °C. FT-IR (KBr): *v* 3270, 1631, 1592, 1275, 1173, 1044, 750 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$ + DMSO-d_6): δ 8.81 (s, 1H, imine), 8.42 (s, 1H, Ar-H), 8.20 (d, 1H, *J* = 8.0 Hz, Ar-H), 8.00 (s, 2H, Ar-H), 7.20 (t, 3H, *J* = 8.1 Hz, Ar-H), 7.06 (d, 2H, *J* = 7.7 Hz, Ar-H), 6.74 (t, 1H, *J* = 7.1 Hz, Ar-H). ^{13}C NMR (75 MHz, $CDCl_3$ + DMSO-d_6): δ 190.6, 159.2, 144.5, 141.1, 137.9, 129.7, 128.4, 127.8, 126.4, 123.8, 122.2, 119.1, 118.4, 116.4, 113.8, 105.9, 98.4. ESI-MS: *m/z* $[M+H]^+$ 305.

(*E*)-6-((2-*m*-Tolylhydrazono)methyl)-5*H*-furo[3,2-*g*]chromen-5-one (3x)

Yellow solid. Yield 81%. M.p. 238–240 °C. FT-IR (KBr): *v* 3265, 2793, 1623, 1484, 1171, 816, 779 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$ + DMSO-d_6): δ 9.00 (s, 1H, imine), 8.26 (s, 1H, Ar-H), 8.21 (s, 1H, Ar-H), 7.77 (d, 1H, *J* = 1.8 Hz, Ar-H), 7.22 (d, 1H, *J* = 8.0 Hz, Ar-H), 7.40 (d, 1H, *J* = 8.0 Hz, Ar-H), 7.19 (d, 2H, *J* = 7.3 Hz, Ar-H), 7.10 (s, 1H, Ar-H), 6.91 (s, 1H, Ar-H), 2.45 (s, 1H, CH_3). ^{13}C NMR (75 MHz, $CDCl_3$ + DMSO-d_6): δ 189.7, 158.0, 156.8, 144.0, 140.5, 137.6, 129.5, 127.5, 126.4, 123.3, 121.6, 118.3, 116.5, 114.9, 105.5, 97.6, 19.5. ESI-MS: *m/z* $[M+H]^+$ 319.

(*E*)-3-((2-Phenylhydrazono)methyl)-4*H*-furo[2,3-*h*]chromen-4-one (3y)

Yellow solid. Yield 85%. M.p. 236–238 °C. FT-IR (KBr): *v* 3270, 1631, 1592, 1275, 1173, 1044, 750 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$ + DMSO-d_6): δ 8.66 (s, 1H, imine), 8.08 (d, 1H, *J* = 8.3 Hz, Ar-H), 7.96–8.00 (m, 3H, Ar-H), 7.62 (d, 1H, *J* = 8.8 Hz, Ar-H), 7.05 (t, 1H, *J* = 7.8 Hz, Ar-H), 6.86 (s, 1H, Ar-H), 6.84 (d, 1H, *J* = 7.8 Hz, Ar-H), 6.54 (d, 1H, *J* = 7.8 Hz, Ar-H). ^{13}C NMR (75 MHz, $CDCl_3$ + DMSO-d_6): δ 190.4, 157.4, 143.6, 140.9, 129.5, 128.2, 127.7, 126.6, 126.2, 120.6, 119.8, 118.2, 113.6, 113.1, 103.6, 102.6: ESI-MS: *m/z* $[M+H]^+$ 305

(*E*)-3-((2-*m*-Tolylhydrazono)methyl)-4*H*-furo[2,3-*h*]chromen-4-one (3z)

Yellow solid. Yield 42%. M.p. 239–241 °C. FT-IR (KBr): *v* 3270, 1631, 1592, 1275, 1173, 1044, 750 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$ + DMSO-d_6): δ 8.89 (s, 1H, imine), 8.08 (d, 1H, *J* = 8.3 Hz, Ar-H), 7.95 (d, 1H, *J* = 8.8 Hz, Ar-H), 7.77 (s, 1H, Ar-H), 7.72 (s, 1H, Ar-H), 7.68 (d, 1H, *J* = 7.8 Hz, Ar-H), 7.38 (t, 1H, *J* = 7.7 Ar-H), 7.18 (t, 2H, *J* = 8.6 Hz, Ar-H), 7.03 (s, 1H, Ar-H), 2.43 (s, 3H, CH_3). ^{13}C NMR (75 MHz, $CDCl_3$ + DMSO-d_6): δ 189.4, 157.1, 155.8, 143.5, 140.3, 137.3, 137.0, 129.2, 127.4, 126.1, 121.1, 117.9, 114.6, 112.6, 102.8, 101.9, 19.0. ESI-MS: *m/z* $[M+H]^+$ 319.

4. 3. General Procedure for the Preparation of Pyrazolecarboxylates 5a–x

The *N*-bromosuccinimide (0.267 g, 1.5 mmol) was added to a stirred solution of (*E*)-3-((2-phenylhydrazono) methyl)-4*H*-chromen-4-one **3a** (0.264 g, 1 mmol) in benzene at room temperature. The reaction was monitored by TLC, after completion of the reaction, the solvent was removed under reduced pressure and the crude product was used for further reaction without purification. The dimethyl acetylenedicarboxylate (**4a**, 0.168 g, 1.2 mmol) was added to a stirred solution of bromohydrazone derivative in acetonitrile (3 mL) at room temperature under nitrogen atmosphere. The reaction mixture was refluxed for 12 h and after completion of the reaction (TLC), the solvent was removed under reduced pressure, and the resulting residue was purified by column chromatography using silica gel (60–120, hexane–ethylacetate, 9:1) affording **5a** as a colourless solid. Similarly, the compounds **5b–x** were prepared from the corresponding (*E*)-3-((2-phenylhydrazo-

no)methyl)-4*H*-chromen-4-ones **3b**–**c**, **3e**, **3h**–**l**, **3n**, **3p**–**v** with acetylenedicarboxylates **4a**–**b** under optimized conditions.

Dimethyl 3-(4-Oxo-4*H*-chromen-3-yl)-1-phenyl-1*H*-pyrazole-4,5-dicarboxylate (5a)

Colourless solid. Yield 78%, M.p. 144–145 °C. FT-IR (KBr): *ν* 2923, 1721, 1656, 1547, 1462, 1245, 1009, 755 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ 8.30 (dd, 1H, J_1 = 7.8 Hz, J_2 = 6.4 Hz, Ar-H), 8.25 (s, 1H, Ar-H), 7.70 (t, 1H, *J* = 1.8 Hz, Ar-H), 7.52–7.41 (m, 7H, Ar-H), 3.85 (s, 3H, OCH_3), 3.79 (s, 3H, OCH_3). ^{13}C NMR (75 MHz, $CDCl_3$): δ 174.5, 162.2, 160.1, 156.2, 154.1, 144.1, 139.0, 133.5, 129.0, 128.8, 126.5, 125.3, 124.3, 118.1, 52.9, 51.8. ESI-MS: *m/z* $[M+H]^+$ 405.

Dimethyl 3-(4-Oxo-4*H*-chromen-3-yl)-1-*m*-tolyl-1*H*-pyrazole-4,5-dicarboxylate (5b)

Pale yellow solid. Yield 67%. M.p. 156–158 °C. FT-IR (KBr): *ν* 2925, 1732, 1657, 1463, 1234, 1149, 762 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ 8.28 (dd, 1H, J_1 = 7.4 Hz, J_2 = 6.0 Hz, Ar-H), 8.23 (s, 1H, Ar-H), 7.68 (t, 1H, *J* = 1.5 Hz, Ar-H), 7.60 (d, 2H, *J* = 8.6 Hz, Ar-H), 7.50–7.40 (m, 2H, Ar-H), 7.34 (s, 2H, Ar-H), 7.28–7.21 (m, 3H, Ar-H), 3.86 (s, 3H, OCH_3), 3.78 (s, 3H, OCH_3), 2.45 (s, 3H, CH_3). ^{13}C NMR (75 MHz, $CDCl_3$): δ 173.0, 166.7, 160.4, 154.5, 154.2, 145.0, 143.3, 139.0, 136.5, 135.3, 134.9, 129.8, 128.9, 125.7, 125.1, 123.9, 121.3, 117.9, 117.6, 53.0, 52.0, 21.0. ESI-MS: *m/z* $[M+H]^+$ 419.

Dimethyl 1-(4-Methoxyphenyl)-3-(4-oxo-4*H*-chromen-3-yl)-1*H*-pyrazole-4,5-dicarboxylate (5c)

Colourless solid. Yield 57%. M.p. 149–151 °C. FT-IR (KBr): *ν* 2947, 1727, 1603, 1440, 1240, 1103 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ 8.28 (dd, 1H, J_1 = 7.8 Hz, J_2 = 6.8 Hz, Ar-H), 8.23 (s, 1H, Ar-H), 7.68 (t, 1H, *J* = 2.2 Hz, Ar-H), 7.50–7.38 (m, 4H, Ar-H), 6.94 (d, 2H, *J* = 8.8 Hz, Ar-H), 3.86 (s, 3H, OCH_3), 3.84 (s, 3H, OCH_3), 3.74 (s, 3H, OCH_3). ESI-MS: *m/z* $[M+H]^+$ 435.

Dimethyl 1-(2-Fluorophenyl)-3-(4-oxo-4*H*-chromen-3-yl)-1*H*-pyrazole-4,5-dicarboxylate (5d)

Pale yellow solid. Yield 72%. FT-IR (KBr): *ν* 2950, 2856, 1733, 1655, 1464, 1244, 1125 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ 8.30 (s, 1H, imine), 8.26 (d, 1H, *J* = 7.5 Hz, Ar-H), 7.68 (t, 1H, *J* = 2.4 Hz, Ar-H), 7.56 (t, 1H, *J* = 1.5 Hz, Ar-H), 7.50–7.40 (m, 3H, Ar-H), 7.32–7.16 (m, 2H, Ar-H), 3.82 (s, 3H, OCH_3), 3.80 (s, 3H, OCH_3). ^{13}C NMR (75 MHz, $CDCl_3$): δ 174.8, 162.9, 158.9, 157.6, 154.4, 144.2, 133.8, 130.9, 127.9, 126.1, 125.4, 124.6, 118.0, 116.3, 116.0, 52.7, 52.1. ESI-MS: *m/z* $[M+H]^+$ 423.

Dimethyl 1-(4-Bromophenyl)-3-(4-oxo-4*H*-chromen-3-yl)-1*H*-pyrazole-4,5-dicarboxylate (5e)

Colourless solid. Yield 57%. M.p. 136–138 °C. FT-IR (KBr): *ν* 2923, 1732, 1655, 1463, 1272, 1157, 769 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ 8.28 (dd, 1H, J_1 = 7.8 Hz, J_2 = 6.6 Hz, Ar-H), 8.23 (s, 1H, Ar-H), 7.68 (t, 1H, *J* = 2.6 Hz, Ar-H), 7.60 (d, 2H, *J* = 8.6 Hz, Ar-H), 7.50–7.42 (m, 2H, Ar-H), 7.38 (d, 2H, *J* = 8.6 Hz, Ar-H), 3.86 (s, 3H, OCH_3), 3.78 (s, 3H, OCH_3). ^{13}C NMR (75 MHz, $CDCl_3$): δ 174.4, 162.1, 159.9, 154.1, 144.4, 136.1, 133.6, 132.2, 126.6, 126.0, 125.4, 124.4, 118.1, 117.8, 117.4, 53.0, 52.0.

Dimethyl 1-(2,4-Dichlorophenyl)-3-(4-oxo-4*H*-chromen-3-yl)-1*H*-pyrazole-4,5-dicarboxylate (5f)

Brown solid. Yield 66%. M.p. 129–131 °C. FT-IR (KBr): *ν* 2793, 1622, 1484, 1301, 1171, 779 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ 8.28 (dd, 1H, J_1 = 7.8 Hz, J_2 = 6.8 Hz, Ar-H), 8.24 (s, 1H, imine), 7.69 (t, 1H, *J* = 1.6 Hz, Ar-H), 7.50 (d, 1H, *J* = 7.8 Hz, Ar-H), 7.46–7.42 (m, 4H, Ar-H), 3.92 (s, 3H, OCH_3), 3.80 (s, 3H, OCH_3). ESI-MS: *m/z* $[M+H]^+$ 473.

Diethyl 3-(6-Methyl-4-oxo-4*H*-chromen-3-yl)-1-phenyl -1*H*-pyrazole-4,5-dicarboxylate (5g)

Colourless solid. Yield 61%. M.p. 131–133 °C. FT-IR (KBr): *ν* 2923, 2852, 1721, 1656, 1547, 1462, 1245, 1009 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ 8.20 (s, 1H, Ar-H), 8.06 (s, 1H, Ar-H), 7.53–7.42 (m, 6H, Ar-H), 7.38 (d, 1H, *J* = 8.6 Hz, Ar-H), 4.29 (q, 2H, *J* = 6.8 Hz, OCH_2), 4.24 (q, 2H, *J* = 6.8 Hz, OCH_2), 1.25 (t, 3H, *J* = 6.8 Hz, CH_3), 1.21 (t, 3H, *J* = 6.8 Hz, CH_3), 2.50 (s, 3H, CH_3). ^{13}C NMR (75 MHz, $CDCl_3$): δ 175.1. 161.9, 160.0, 154.2, 144.5, 139.0, 137.0, 135.4, 129.1, 125.6, 124.5, 117.8, 62.3, 60.8, 20.9, 14.0, 13.7. ESI-MS: *m/z* $[M+H]^+$ 447.

Dimethyl 3-(6-Methyl-4-oxo-4*H*-chromen-3-yl)-1-*m*-tolyl-1*H*-pyrazole-4,5-dicarboxylate (5h)

Colourless solid. Yield 82%. M.p. 168–170 °C. FT-IR (KBr): *ν* 2925, 2534, 1735, 1655, 1485, 1233, 1156 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ 8.22 (s, 1H, Ar-H), 8.09 (d, 1H, *J* = 1.6 Hz, Ar-H), 7.46 (dd, 1H, J_1 = 8.3 Hz, J_2 = 6.0 Hz, Ar-H), 7.40–7.30 (m, 3H, Ar-H), 7.28–7.20 (m, 2H, Ar-H), 3.86 (s, 3H, OCH_3), 3.76 (s, 3H, OCH_3), 2.52 (s, 3H, CH_3), 2.46 (s, 3H, CH_3). ^{13}C NMR (75 MHz, $CDCl_3$): δ 174.3, 160.4, 154.2, 139.4, 135.3, 134.9, 129.8, 128.9, 125.7, 125.1, 123.9, 121.3, 117.9, 53.0, 52.0, 21.3, 21.0. ESI-MS: *m/z* $[M+H]^+$ 433.

Dimethyl 1-(4-Methoxyphenyl)-3-(6-methyl-4-oxo-4*H*-chromen-3-yl)-1*H*-pyrazole-4,5-dicarboxylate (5i)

Colourless solid. Yield 62%. M.p. 179–181 °C. FT-IR (KBr): *ν* 2923, 1732, 1656, 1222, 1148, 772 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ 8.22 (s, 1H, Ar-H), 8.06 (s, 1H, Ar-H), 7.46 (d, 1H, *J* = 8.4, 6.4 Hz, Ar-H), 7.42–7.36 (m, 3H, Ar-H), 6.94 (d, 2H, *J* = 8.6 Hz, Ar-H), 3.86 (s, 3H, OCH_3), 3.84 (s, 3H, OCH_3), 3.76 (s, 3H, OCH_3), 2.50 (s, 3H, CH_3). ESI-MS: *m/z* $[M+H]^+$ 449.

Dimethyl 1-(2-Fluorophenyl)-3-(6-methyl-4-oxo-4*H*-chromen-3-yl)-1*H*-pyrazole-4,5-dicarboxylate (5j)

Colourless solid. Yield 71%. M.p. 170–172 °C. FT-IR (KBr): *ν* 2924, 2856, 1740, 1648, 1467, 1240, 1190, 1088

cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.28 (s, 1H, Ar-H), 8.06 (s, 1H, Ar-H), 7.58 (t, 1H, *J* = 1.7 Hz, Ar-H), 7.50–7.17 (m, 5H, Ar-H), 3.84 (s, 3H, OCH_3), 3.82 (s, 3H, OCH_3), 2.50 (s, 3H, CH_3). ^{13}C NMR (75 MHz, $CDCl_3$): δ 175.0, 154.4, 135.1, 130.8, 128.0, 125.5, 124.6, 123.7, 117.9, 116.1, 52.8, 52.3, 29.6. ESI-MS: *m/z* $[M+H]^+$ 437, $[M+Na]^+$ 459.

Dimethyl 1-(4-Bromophenyl)-3-(6-methyl-4-oxo-4*H*-chromen-3-yl)-1*H*-pyrazole-4,5-dicarboxylate (5k)

Brownish solid. Yield 67%. M.p. 145–147 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.20 (s, 1H, imine), 8.06 (s, 1H, Ar-H), 7.61 (d, 2H, *J* = 9.0 Hz, Ar-H), 7.48 (dd, 1H, J_1 = 9.0 Hz, J_2 = 6.8 Hz, Ar-H), 7.40 (d, 2H, *J* = 2.2 Hz, Ar-H), 7.38–7.36 (m, 1H, Ar-H), 3.86 (s, 3H, OCH_3), 3.78 (s, 3H, OCH_3), 2.50 (s, 3H, CH_3). ESI-MS: *m/z* $[M+H]^+$ 497.

Dimethyl 3-(6-Chloro-4-oxo-4*H*-chromen-3-yl)-1-phenyl-1*H*-pyrazole-4,5-dicarboxylate (5l)

Colourless solid. Yield 77%. M.p. 152–154 °C. FT-IR (KBr): *ν* 2924, 2856, 1728, 1659, 1454, 1239, 1036 cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.23 (s, 1H, Ar-H), 8.09 (s, 1H, Ar-H), 7.53–7.45 (m, 6H, Ar-H), 7.40 (d, 1H, *J* = 8.6 Hz, Ar-H), 3.85 (s, 3H, OCH_3), 3.79 (s, 3H, OCH_3). ^{13}C NMR (75 MHz, $CDCl_3$): δ 175.2, 160.3, 157.3, 154.2, 144.4, 139.0, 136.5, 129.1, 129.0, 126.3, 124.4, 120.7, 119.0, 116.6, 107.0, 100.0, 53.0, 51.9. ESI-MS: *m/z* $[M+H]^+$ 439.

Dimethyl 3-(6-Chloro-4-oxo-4*H*-chromen-3-yl)-1-*m*-tolyl-1*H*-pyrazole-4,5-dicarboxylate (5m)

Pale brownish solid. Yield 61%. M.p. 154–156 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.24 (d, 1H, *J* = 2.4, Ar-H), 8.22 (s, 1H, imine), 7.63 (dd, 1H, J_1 = 9.0 Hz, J_2 = 6.8 Hz, Ar-H), 7.46 (d, 1H, *J* = 9.0 Hz, Ar-H), 7.36–7.30 (m, 2H, Ar-H), 7.24–7.18 (m, 2H, Ar-H), 3.84 (s, 3H, OCH_3), 3.80 (s, 3H, OCH_3), 2.45 (s, 3H, CH_3).

Dimethyl 3-(6-Chloro-4-oxo-4*H*-chromen-3-yl)-1-(4-methoxyphenyl)-1*H*-pyrazole-4,5-dicarboxylate (5n)

Pale yellow solid. Yield 72%. M.p. 158–160 °C. FT-IR (KBr): *ν* 2925, 1736, 1653, 1250, 1105, 763 cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.24 (d, 1H, *J* = 2.4 Hz, Ar-H), 8.20 (s, 1H, Ar-H), 7.60 (dd, 1H, J_1 = 9.0 Hz, J_2 = 6.8 Hz, Ar-H), 7.44 (d, 1H, *J* = 9.0 Hz, Ar-H), 7.40 (d, 2H, *J* = 9.0 Hz, Ar-H), 6.94 (d, 2H, *J* = 9.0 Hz, Ar-H), 3.86 (s, 3H, OCH_3), 3.84 (s, 3H, OCH_3), 3.78 (s, 3H, OCH_3). ESI-MS: *m/z* $[M+H]^+$ 469.

Dimethyl 3-(6-Bromo-4-oxo-4*H*-chromen-3-yl)-1-phenyl-1*H*-pyrazole-4,5-dicarboxylate (5o)

Colourless solid. Yield 46%. M.p. 169–171 °C. FT-IR (KBr): *ν* 2924, 1728, 1659, 1454, 1384, 1239, 1036, 758 cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.41 (d, 1H, *J* = 2.2 Hz, Ar-H), 8.24 (s, 1H, Ar-H), 7.76 (dd, 1H, J_1 = 7.6 Hz, J_2 = 6.0 Hz, Ar-H), 7.50–7.44 (m, 5H, Ar-H), 7.39 (d, 1H, *J* = 7.6 Hz, Ar-H), 3.85 (s, 3H, OCH_3), 3.79 (s, 3H, OCH_3). ^{13}C NMR (75 MHz, $CDCl_3$): δ 173.8, 172.4, 159.2, 155.0, 154.5, 138.9, 136.8, 132.3, 129.3, 128.9, 125.8, 124.4, 120.1, 119.0, 111.5, 108.1, 53.2, 52.1. ESI-MS: *m/z* $[M+H]^+$ 483.

Dimethyl 3-(6-Bromo-4-oxo-4*H*-chromen-3-yl)-1-*m*-tolyl-1*H*-pyrazole-4,5-dicarboxylate (5p)

Colourless solid. Yield 74%. M.p. 151–153 °C. FT-IR (KBr): *ν* 2925, 1724, 1655, 1493, 1328, 1233, 1155, 1070 cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.40 (d, 1H, *J* = 2.4 Hz, Ar-H), 8.20 (s, 1H, imine), 7.76 (dd, 1H, J_1 = 8.4 Hz, J_2 = 6.4 Hz, Ar-H), 7.40–7.30 (m, 3H, Ar-H), 7.23–7.14 (m, 1H, Ar-H), 3.84 (s, 3H, OCH_3), 3.78 (s, 3H, OCH_3), 2.58 (s, 3H, CH_3). ^{13}C NMR (75 MHz, $CDCl_3$): δ 174.5, 162.2, 160.2, 158.1, 150.7, 144.1, 139.2, 136.4, 129.7, 124.9, 121.1, 119.6, 118.3, 117.0, 110.2, 104.1, 52.9, 51.8, 21.2. ESI-MS: *m/z* $[M+H]^+$ 497, $[M+2]^+$ 499.

Dimethyl 3-(6-Bromo-4-oxo-4*H*-chromen-3-yl)-1-(4-methoxyphenyl)-1*H*-pyrazole-4,5-dicarboxylate (5q)

Pale yellow solid. Yield 68%. M.p. 164–166 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.40 (dd, 1H, J_1 = 9.0 Hz, J_2 = 2.2 Hz, Ar-H), 8.20 (s, 1H, Ar-H), 7.76 (dd, 1H, J_1 = 9.0 Hz, J_2 = 6.8 Hz, Ar-H), 7.40–7.33 (m, 3H, Ar-H), 6.94 (d, 2H, *J* = 9.0 Hz, Ar-H), 3.86 (s, 3H, OCH_3), 3.84 (s, 3H, OCH_3), 3.78 (s, 3H, OCH_3). ^{13}C NMR (75 MHz, $CDCl_3$): δ 174.4, 162.1, 159.9, 154.1, 144.4, 136.1, 133.6, 132.7, 126.6, 126.0, 125.4, 124.4, 118.1, 117.8, 117.4, 53.0, 52.0.

Diethyl 3-(4-Oxo-4*H*-chromen-3-yl)-1-phenyl-1*H*-pyrazole-4,5-dicarboxylate (5r)

Pale yellow solid. Yield 61%. M.p. 119–121 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.30 (dd, 1H, J_1 = 7.8 Hz, J_2 = 6.4 Hz, Ar-H), 8.22 (s, 1H, Ar-H), 7.68 (t, 1H, *J* = 2.5 Hz, Ar-H), 7.52–7.39 (m, 7H, Ar-H), 4.30 (q, 2H, *J* = 7.1 Hz, OCH_2), 4.24 (q, 2H, *J* = 3.5 Hz, OCH_2), 1.24 (t, 3H, *J* = 4.3 Hz, CH_3), 1.10 (t, 3H, *J* = 3.2 Hz, CH_3). ^{13}C NMR (300 MHz, $CDCl_3$): δ 174.9, 161.8, 159.9, 156.3, 154.2, 144.3, 139.0, 133.6, 126.4, 125.4, 124.4, 118.1, 62.3, 60.7, 13.9, 13.7. ESI-MS: *m/z* $[M+H]^+$ 433, $[M+Na]^+$ 455.

Dimethyl 3-(5-Oxo-5*H*-furo[3,2-*g*]chromen-6-yl)-1-phenyl-1*H*-pyrazole-4,5-dicarboxylate (5s)

Brown solid. Yield 77%. M.p. 176–178 °C. FT-IR (KBr): *ν* 2953, 1733, 1651, 1457, 1162 cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.52 (s, 1H, Ar-H), 8.26 (s, 1H, Ar-H), 7.72 (d, 1H, *J* = 1.6 Hz, Ar-H), 7.57 (s, 1H, Ar-H), 7.52–7.41 (m, 5H, Ar-H), 6.90 (d, 1H, *J* = 1.6 Hz, Ar-H), 3.84 (s, 3H, OCH_3), 3.76 (s, 3H, OCH_3). ^{13}C NMR (75 MHz, $CDCl_3$): δ 175.2, 157.3, 154.5, 147.5, 144.4, 139.0, 129.3, 126.3, 124.4, 120.7, 119.0, 116.6, 107.0, 53.0, 51.9. ESI-MS: *m/z* $[M+H]^+$ 445.

Dimethyl 3-(5-Oxo-5*H*-furo[3,2-*g*]chromen-6-yl)-1-*m*-tolyl-1*H*-pyrazole-4,5-dicarboxylate (5t)

Colourless solid. Yield 68%. M.p. 192–194 °C. FT-IR (KBr): *ν* 2949, 1721, 1650, 1589, 1460, 1165, 1037 cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.52 (s, 1H, Ar-H), 8.26 (s, 1H,

Ar-H), 7.72 (s, 1H, Ar-H), 7.58 (s, 1H, Ar-H), 7.36–7.20 (m, 4H, Ar-H), 6.90 (s, 1H, Ar-H), 3.86 (s, 3H, OCH_3), 3.76 (s, 3H, OCH_3), 2.44 (s, 3H, CH_3). ^{13}C NMR (75 MHz, $CDCl_3$): δ 162.6, 160.6, 154.6, 154.2, 147.7, 144.4, 139.6, 138.8, 136.7, 129.9, 128.9, 126.4, 125.0, 121.2, 118.9, 107.0, 53.1, 52.0, 29.3. ESI-MS: *m/z* $[M+H]^+$ 459.

Diethyl 3-(5-Oxo-5*H*-furo[3,2-*g*]chromen-6-yl)-1-phenyl-1*H*-pyrazole-4,5-dicarboxylate (5u)

Brown solid. Yield 64%. M.p. 162–164 °C. FT-IR (KBr): *ν* 2949, 1721, 1650, 1589, 1460, 1165, 1037, 795 cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.50 (s, 1H, Ar-H), 8.22 (s, 1H, Ar-H), 7.70 (d, 1H, *J* = 2.2 Hz, Ar-H), 7.58–7.39 (m, 5H, Ar-H), 6.90 (s, 1H, Ar-H), 4.29 (q, 2H, *J* = 7.5 Hz, OCH_2), 4.23 (q, 2H, *J* = 4.5 Hz, OCH_2), 1.23 (t, 3H, *J* = 6.7 Hz, CH_3), 1.19 (t, 3H, *J* = 5.2 Hz, CH_3). ^{13}C NMR (75 MHz, $CDCl_3$): δ 174.6, 161.4, 159.5, 153.9, 147.1, 138.9, 128.7, 125.9, 124.1, 120.5, 118.8, 116.7, 106.7, 99.7, 95.8, 61.8, 60.3, 13.8. ESI-MS: *m/z* $[M+H]^+$, 473 $[M+Na]^+$ 495.

Dimethyl 3-(4-Oxo-4*H*-furo[2,3-*h*]chromen-3-yl)-1-phenyl-1*H*-pyrazole-4,5-dicarboxylate (5v)

Colourless solid. Yield 79%. M.p. 173–175 °C. FT-IR (KBr): *ν* 2953, 1733, 1651, 1588, 1457, 1269, 1039, 758 cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.30 (s, 1H, Ar-H), 8.21 (d, 1H, *J* = 8.6 Hz, Ar-H), 7.74 (s, 1H, Ar-H), 7.58–7.42 (m, 6H, Ar-H), 7.12 (s, 1H, Ar-H), 3.86 (s, 3H, OCH_3), 3.78 (s, 3H, OCH_3). ^{13}C NMR (75 MHz, $CDCl_3$): δ 174.6, 162.3, 160.3, 158.2, 153.3, 150.8, 145.7, 144.2, 139.0, 136.4, 129.1, 128.9, 125.7, 124.4, 122.4, 119.6, 118.3, 116.7, 110.4, 104.2, 53.0, 51.9. ESI-MS: *m/z* $[M+H]^+$ 445.

Dimethyl 3-(4-Oxo-4*H*-furo[2,3-*h*]chromen-3-yl)-1-*m*-tolyl-1*H*-pyrazole-4,5-dicarboxylate (5w)

Pale yellow solid. Yield 82%. M.p. 189–191 °C. FT-IR (KBr): *ν* 2952, 1732, 1652, 1588, 1456, 1234, 1039, 763 cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.28 (s, 1H, Ar-H), 8.18 (dd, 1H, J_1 = 8.4 Hz, J_2 = 6.4 Hz, Ar-H), 7.72 (s, 1H, Ar-H), 7.52 (d, 1H, *J* = 8.6 Hz, Ar-H), 7.36–7.18 (m, 4H, Ar-H), 7.08 (s, 1H, Ar-H), 3.84 (s, 3H, OCH_3), 3.76 (s, 3H, OCH_3), 2.42 (s, 3H, CH_3). ^{13}C NMR (75 MHz, $CDCl_3$): δ 174.5, 162.2, 160.2, 158.1, 153.2, 150.7, 145.6, 144.1, 139.2, 136.4, 129.7, 128.8, 124.9, 122.3, 121.1, 119.6, 118.3, 117.0, 110.2, 104.1, 52.9, 51.8, 21.2. ESI-MS: *m/z* $[M+H]^+$ 459.

Diethyl 3-(4-Oxo-4*H*-furo[2,3-*h*]chromen-3-yl)-1-phenyl-1*H*-pyrazole-4,5-dicarboxylate (5x)

Colourless solid. Yield 78%. M.p. 167–169 °C. FT-IR (KBr): *ν* 2926, 1731, 1657, 1464, 1221, 762 cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.26 (s, 1H, Ar-H), 8.20 (d, 1H, *J* = 8.3 Hz, Ar-H), 7.73 (d, 1H, *J* = 2.2 Hz, Ar-H), 7.58–7.42 (m, 6H, Ar-H), 7.10 (s, 1H, Ar-H), 4.29 (q, 2H, *J* = 6.7 Hz, OCH_2), 4.23 (q, 2H, *J* = 4.5 Hz, OCH_2), 1.24 (t, 3H, *J* = 4.5 Hz, CH_3), 1.19 (t, 3H, *J* = 6.5 Hz, CH_3). ^{13}C NMR (75 MHz, $CDCl_3$): δ 174.8, 161.8, 159.9, 158.1, 153.3, 150.7, 145.7, 144.3, 138.9, 137.1, 129.1, 124.4, 119.6, 118.4, 117.0, 110.3, 104.1, 62.3, 60.7, 13.8, 13.9. ESI-MS: *m/z* $[M+H]^+$ 473.

4. 4. General Procedure for the Preparation of Pyrazolylmethanones 6a–u

K_2CO_3 (0.276 g, 2 mmol) was added to a stirred solution of (*E*)-3-((2-phenylhydrazono)methyl)-4*H*-chromen-4-one **3a** (0.264 g, 1 mmol) in acetonitrile (3 mL) at room temperature. The reaction mixture was refluxed for 12 h and after completion of the reaction (TLC), the solvent was removed under reduced pressure. The crude product was purified by column chromatography using silica gel (60–120, hexane–ethyl acetate, 97:3) affording **6a**. Similarly, the compounds **6b–u** were prepared by treating the (*E*)-3-((2-phenylhydrazono)methyl)-4*H*-chromen-4-ones **3a–h**, **3k–s**, **3u–v** with K_2CO_3.

(2-Hydroxyphenyl)(1-phenyl-1*H*-pyrazol-4-yl)methanone (6a)

Pale yellow solid. Yield 88%. M.p. 113–114 °C. FT-IR (KBr): *ν* 3129, 1622, 1589, 1482, 1293 cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$): δ 12.02 (s, 1H, ArOH), 8.48 (s, 1H, pyrazole H_3), 8.18 (s, 1H, pyrazole H_5), 7.92 (dd, 1H, J_1 = 7.9 Hz, J_2 = 1.1 Hz, Ar-H), 7.75 (d, 2H, *J* = 7.7 Hz, Ar-H), 7.56–7.48 (m, 3H, Ar-H), 7.39 (t, 1H, *J* = 7.3 Hz, Ar-H), 7.07 (d, 1H, *J* = 8.3 Hz, Ar-H), 6.97 (t, 1H, *J* = 7.9 Hz, Ar-H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 192.0, 162.6, 142.3, 139.1, 135.9, 131.1, 130.4, 129.6, 127.8, 123.3, 120.0, 119.7, 119.0, 118.4. ESI-MS: *m/z* $[M+H]^+$ 265.

(2-Hydroxyphenyl)(1-*m*-tolyl-1*H*-pyrazol-4-yl)methanone (6b)

Yellow thick liquid. Yield 76%. FT-IR (KBr): *ν* 3447, 1622, 1539, 1483, 1238, 903, 771 cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$): δ 11.95 (s, 1H, ArOH), 8.39 (s, 1H, pyrazole H_3), 8.09 (s, 1H, pyrazole H_5), 7.84 (dd, J_1 = 8.1 Hz, J_2 = 1.7 Hz, 1H, Ar-H), 7.52–7.41 (m, 3H), 7.30 (t, 1H, *J* = 7.7 Hz, Ar-H), 7.12 (d, 1H, *J* = 7.5 Hz, Ar-H), 6.99 (d, 1H, *J* = 8.4 Hz, Ar-H), 6.89 (t, 1H, *J* = 7.1 Hz, Ar-H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 192.0, 162.6, 142.2, 139.8, 139.0, 135.9, 131.1, 130.4, 129.4, 128.6, 123.2, 120.4, 120.0, 119.0, 118.4, 116.7, 21.4. ESI-MS: *m/z* $[M+H]^+$ 279.

(2-Hydroxyphenyl)(1-(4-methoxyphenyl)-1*H*-pyrazol-4-yl)methanone (6c)

Yellow thick liquid. Yield 73%. FT-IR (KBr): *ν* 3422, 2924, 1722, 1590, 1237, 771 cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$): δ 12.04 (s, 1H, ArOH), 8.39 (s, 1H, pyrazole H_3), 8.15 (s, 1H, pyrazole H_5), 7.91 (dd, 1H, J_1 = 7.9 Hz, J_2 = 1.3 Hz, Ar-H), 7.64 (d, 2H, *J* = 9.0 Hz, Ar-H), 7.52 (t, 1H, *J* = 6.9 Hz, Ar-H), 7.09–6.93 (m, 4H, Ar-H), 3.86 (s, 3H, OCH_3). ^{13}C NMR (75 MHz, $CDCl_3$): δ 192.0, 162.5, 159.1, 142.0, 135.9, 132.6, 131.1, 130.3, 123.0, 121.3, 120.0, 118.9, 118.4, 114.6, 55.5. ESI-MS: *m/z* $[M+H]^+$ 295.

(1-(2-Fluorophenyl)-1*H*-pyrazol-4-yl)(2-hydroxyphenyl)methanone (6d)

Pale yellow solid. Yield 63%. M.p. 150–152 °C. FT-IR (KBr): *ν* 3067, 1675, 1501, 1219, 765 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$) δ 10.02 (s, 1H, ArOH), 8.32 (s, 1H, pyrazole H_3), 7.89 (d, J = 8.1 Hz, 1H, pyrazole H_5), 7.66 (dd, 1H, J_1 = 7.5 Hz, J_2 = 1.5 Hz, Ar-H), 7.54 (td, 1H, J_1 = 9.6 Hz, J_2 = 1.7 Hz, Ar-H), 7.44–7.30 (m, 5H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 184.4, 158.7, 152.2, 143.7, 142.2, 132.7, 132.1, 131.5, 129.5, 126.2, 125.9, 124.9, 124.1, 121.7, 121.6, 120.1. ESI-MS: *m*/*z* $[M+H]^+$ 283.

(1-(3-Fluorophenyl)-1*H*-pyrazol-4-yl)(2-hydroxyphenyl)methanone (6e)

Pale yellow solid. Yield 69%. M.p. 104–106 °C. FT-IR (KBr): *ν* 3127, 1602, 1542, 1245, 757 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ 11.98 (s, 1H, ArOH), 8.48 (s, 1H, pyrazole H_3), 8.18 (s, 1H, pyrazole H_5), 7.90 (dd, J_1 = 8.3 Hz, J_2 = 1.5 Hz, 1H, Ar-H), 7.58–7.46 (m, 4H, Ar-H), 7.14–7.06 (m, 2H, Ar-H), 6.98 (dt, 1H, J_1 = 8.3 Hz, J_2 = 1.5 Hz, Ar-H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 191.9, 164.8, 162.7, 161.5, 142.5, 140.3, 136.1, 131.0, 130.4, 123.6, 119.9, 119.0, 118.5, 114.8, 114.5, 107.7, 107.4. ESI-MS: *m*/*z* $[M+H]^+$ 283.

(1-(3-Chlorophenyl)-1*H*-pyrazol-4-yl)(2-hydroxyphenyl)methanone (6f)

Yellow solid. Yield 66%. M.p. 94–96 °C. FT-IR (KBr): *ν* 3127, 1581, 1464, 1215, 752 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ 11.97 (s, 1H, ArOH), 8.47 (s, 1H, pyrazole H_3), 8.18 (s, 1H, pyrazole H_5), 7.89 (dd, J_1 = 7.9 Hz, J_2 = 1.5 Hz, 1H, Ar-H), 7.64 (dd, J = 3.0 Hz, 1H, Ar-H), 7.53 (dt, 1H, J_1 = 8.4 Hz, J_2 = 1.5 Hz, Ar-H), 7.44 (t, 1H, J = 8.1 Hz, Ar-H), 7.36 (d, J = 7.9 Hz, 1H, Ar-H), 7.07 (d, 1H, J = 7.5 Hz, Ar-H), 6.98 (dt, 1H, J_1 = 8.1 Hz, J_2 = 1.0 Hz, Ar-H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 191.8, 162.6, 142.5, 140.0, 136.1, 135.5, 131.0, 130.6, 127.8, 123.6, 120.0, 119.1, 118.5, 117.5. ESI-MS: *m*/*z* $[M+H]^+$ 299.

(1-(4-Fluorophenyl)-1*H*-pyrazol-4-yl)(2-hydroxyphenyl)methanone (6g)

Pale yellow solid. Yield 74%. M.p. 112–114 °C. FT-IR (KBr): *ν* 3067, 1675, 1501, 1219, 765 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ 12.00 (s, 1H, ArOH), 8.43 (s, 1H, pyrazole H_3), 8.17 (s, 1H, pyrazole H_5), 7.91 (dd, J_1 = 8.1 Hz, J_2 = 1.7 Hz, 1H, Ar-H), 7.75–7.70 (m, 2H, Ar-H), 7.53 (td, 1H, J_1 = 7.3 Hz, J_2 = 1.7 Hz, Ar-H), 7.21 (t, 2H, J = 9.0 Hz, Ar-H), 7.07 (dd, J_1 = 8.4 Hz, J_2 = 1.2 Hz, 1H, Ar-H), 6.98 (dt, 1H, J_1 = 8.1 Hz, J_2 = 1.1 Hz, Ar-H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 191.9, 162.6, 160.2, 142.3, 136.0, 135.4, 131.1, 130.5, 123.4, 121.7, 121.6, 120.0, 119.0, 118.5, 116.7, 116.4. ESI-MS: *m*/*z* $[M+H]^+$ 283.

(1-(4-Bromophenyl)-1*H*-pyrazol-4-yl)(2-hydroxyphenyl)methanone (6h)

Pale yellow solid. Yield 68%. M.p. 115–117 °C. FT-IR (KBr): *ν* 3112, 2924, 1626, 1542, 1243, 905, 756 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ 11.98 (s, 1H, ArOH), 8.46 (s, 1H, pyrazole H_3), 8.18 (s, 1H, pyrazole H_5), 7.90 (dd, J_1 = 7.9 Hz, J_2 = 1.3 Hz, 1H, Ar-H), 7.65 (s, 4H, Ar-H), 7.54 (td, 1H, J_1 = 8.4 Hz, J_2 = 1.3 Hz, Ar-H), 7.08 (d, 1H, J = 8.3 Hz, Ar-H), 6.98 (t, 1H, J = 7.9 Hz, Ar-H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 191.9, 162.6, 142.5, 138.0, 136.1, 132.7, 131.0, 130.2, 121.0, 119.0, 118.5.

(2-Hydroxy-5-methylphenyl)(1-*m*-tolyl-1*H*-pyrazol-4-yl)methanone (6i)

Yellow thick liquid. Yield 73%. FT-IR (KBr): *ν* 3127, 1629, 1541, 1227, 783 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ 11.82 (s, 1H, ArOH), 8.45 (s, 1H, pyrazole H_3), 8.16 (s, 1H, pyrazole H_5), 7.68 (d, J = 1.3 Hz, 1H, Ar-H), 7.58 (d, J = 1.5 Hz, 1H, Ar-H), 7.51 (d, J = 7.9 Hz, 1H, Ar-H), 7.39 (t, J = 7.7 Hz, 1H, Ar-H), 7.33 (dd, J_1 = 8.6 Hz, J_2 = 2.2 Hz, 1H, Ar-H), 7.19 (d, J = 7.5 Hz, 1H, Ar-H), 6.97 (d, J = 8.4 Hz, 1H, Ar-H), 2.44 (s, 3H, CH_3), 2.34 (s, 3H, CH_3). ^{13}C NMR (75 MHz, $CDCl_3$): δ 192.0, 160.4, 142.1, 139.8, 139.0, 136.9, 130.9, 130.3, 129.3, 128.5, 128.0, 123.2, 120.4, 119.7, 118.1, 116.7, 21.3, 20.5. ESI-MS: *m*/*z* $[M+H]^+$ 293.

(2-Hydroxy-5-methylphenyl)(1-(4-methoxyphenyl)-1*H*-pyrazol-4-yl)methanone (6j)

Yellow solid. Yield 61%. M.p. 128–130 °C. FT-IR (KBr): *ν* 3131, 1585, 1539, 1225 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ 11.83 (s, 1H, ArOH), 8.38 (s, 1H, pyrazole H_3), 8.14 (s, 1H, pyrazole H_5), 7.69 (d, 1H, J = 1.2 Hz, Ar-H), 7.64 (d, 2H, J = 9.0 Hz, Ar-H), 7.33 (dd, 1H, J_1 = 8.3 Hz, J_2 = 1.5 Hz, Ar-H), 7.03 (d, 2H, J = 9.0 Hz, Ar-H), 6.97 (d, 1H, J = 8.3 Hz, Ar-H), 3.86 (s, 3H, OCH_3), 2.34 (s, 1H, CH_3). ^{13}C NMR (75 MHz, $CDCl_3$): δ 192.0, 160.4, 159.1, 142.0, 136.9, 132.7, 130.9, 130.3, 128.1, 123.1, 121.3, 119.7, 118.2, 114.6, 55.5, 20.5. ESI-MS: *m*/*z* $[M+H]^+$ 309.

(1-(2-Fluorophenyl)-1*H*-pyrazol-4-yl)(2-hydroxy-5-methylphenyl)methanone (6k)

Pale yellow solid. Yield 73%. M.p. 115–117 °C. FT-IR (KBr): *ν* 3063, 1630, 1592, 1230, 757 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ 11.80 (s, 1H, ArOH), 8.54 (d, J = 2.2 Hz, 1H, pyrazole H_3), 8.20 (s, 1H, pyrazole H_5), 7.94 (dt, 1H, J_1 = 8.4 Hz, J_2 = 2.0 Hz, Ar-H), 7.68 (d, J = 1.3 Hz, 1H, Ar-H), 7.42–7.28 (m, 4H, Ar-H), 6.97 (d, 1H, J = 8.4 Hz, Ar-H), 2.34 (s, 3H, CH_3). ^{13}C NMR (75 MHz, $CDCl_3$): δ 191.9, 160.4, 151.8, 142.0, 137.0, 134.3, 134.1, 130.9, 129.0, 128.1, 125.1, 124.5, 119.6, 118.1, 117.0, 116.8, 20.5. ESI-MS: *m*/*z* $[M+H]^+$ 297.

(1-(3-Fluorophenyl)-1*H*-pyrazol-4-yl)(2-hydroxy-5-methylphenyl)methanone (6l)

Yellow solid. Yield 82%. M.p. 136–138 °C. FT-IR (KBr): *ν* 3141, 1630, 1543, 1228, 759 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ 11.77 (s, 1H, ArOH), 8.48 (s, 1H, pyrazole H_3), 8.17 (s, 1H, pyrazole H_5), 7.67 (d, J = 1.3 Hz, 1H, Ar-H), 7.58–7.46 (m, 3H, Ar-H), 7.35 (dd, J_1 = 8.4 Hz, J_2 = 2.0 Hz, 1H, Ar-H), 7.14–7.06 (m, 1H, Ar-H), 6.99 (d, J = 8.3

Hz, 1H, Ar-H), 2.35 (s, 3H, CH_3). ^{13}C NMR (75 MHz, $CDCl_3$): δ 191.9, 164.8, 160.5, 142.5, 137.2, 131.1, 130.9, 130.8, 130.3, 128.2, 119.6, 118.3, 114.7, 114.5, 107.7, 107.3, 20.6. ESI-MS: *m*/*z* $[M+H]^+$ 297.

(1-(4-Fluorophenyl)-1*H*-pyrazol-4-yl)(2-hydroxy-5-methylphenyl)methanone (6m)

Pale yellow solid. Yield 74%. M.p. 125–127 °C. FT-IR (KBr): *ν* 3120, 1631, 1583, 1222, 836 cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$): δ 11.79 (s, 1H, ArOH) 8.42 (s, 1H, pyrazole H_3), 8.16 (s, 1H, pyrazole H_5), 7.76–7.70 (m, 2H, Ar-H), 7.67 (d, 1H, *J* = 1.2 Hz, Ar-H), 7.34 (dd, J_1 = 8.3 Hz, J_2 = 1.9 Hz, 1H, Ar-H), 7.21 (t, 2H, *J* = 8.1 Hz, Ar-H), 6.97 (d, 1H, *J* = 8.4 Hz, Ar-H), 2.34 (s, 3H, CH_3). ^{13}C NMR (75 MHz, $CDCl_3$): δ 191.9, 160.5, 142.3, 137.1, 135.4, 130.8, 130.4, 128.1, 123.5, 121.5, 119.6, 118.2, 116.6, 116.3, 20.5. ESI-MS: *m*/*z* $[M+H]^+$ 297.

(1-(4-Bromophenyl)-1*H*-pyrazol-4-yl)(2-hydroxy-5-methylphenyl)methanone (6n)

Pale yellow solid. Yield 82%. M.p. 142–144 °C. FT-IR (KBr): *ν* 3132, 1592, 1539, 1229 cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$): δ 11.77 (s, 1H, ArOH), 8.46 (s, 1H, pyrazole H_3), 8.17 (s, 1H, pyrazole H_5), 7.65 (brs, 5H, Ar-H), 7.35 (dd, 1H, J_1 = 8.4 Hz, J_2 = 2.0 Hz, Ar-H), 6.98 (d, 1H, *J* = 8.4 Hz, Ar-H), 2.34 (s, 3H, CH_3). ^{13}C NMR (75 MHz, $CDCl_3$): δ 191.8, 160.5, 142.4, 138.1, 137.1, 132.7, 130.8, 130.1, 128.1, 123.7, 115.0, 119.6, 118.2, 20.5. ESI-MS: *m*/*z* $[M+H]^+$ 357.

(5-Chloro-2-hydroxyphenyl)(1-phenyl-1*H*-pyrazol-4-yl)methanone (6o)

Pale yellow solid. Yield 67%. M.p. 142–144 °C. FT-IR (KBr): *ν* 3127, 1581, 1464, 1215, 752 cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$): δ 11.90 (s, 1H, ArOH), 8.50 (s, 1H, pyrazole H_3), 8.20 (s, 1H, pyrazole H_5), 7.88 (d, 1H, *J* = 2.2 Hz, Ar-H), 7.76 (d, 2H, *J* = 7.5 Hz, Ar-H), 7.57–7.39 (m, 4H, Ar-H), 7.04 (d, 1H, *J* = 9.0 Hz, Ar-H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 190.9, 161.0, 142.2, 139.0, 135.8, 130.4, 130.2, 129.6, 128.0, 123.7, 122.8, 120.6, 120.1, 119.8. ESI-MS: *m*/*z* $[M+H]^+$ 299.

(5-Chloro-2-hydroxyphenyl)(1-*m*-tolyl-1*H*-pyrazol-4-yl)methanone (6p)

Yellow solid. Yield 81%. M.p. 105–107 °C. FT-IR (KBr): *ν* 3127, 1624, 1539, 1228 cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$): δ 11.90 (s, 1H, ArOH), 8.47 (s, 1H, pyrazole H_3), 8.18 (s, 1H, pyrazole H_5), 7.87 (d, 1H, *J* = 2.4 Hz, Ar-H), 7.59 (d, *J* = 1.5 Hz, 1H, Ar-H), 7.53 (d, 1H, *J* = 8.1 Hz, Ar-H), 7.46 (dd, 1H, J_1 = 8.8 Hz, J_2 = 2.6 Hz, Ar-H), 7.40 (t, 1H, *J* = 7.7 Hz, Ar-H), 7.62–7.51 (m, 3H, Ar-H), 7.40 (t, 1H, *J* = 7.7 Hz, Ar-H), 7.22 (d, 1H, *J* = 7.5 Hz, Ar-H), 7.03 (d, 1H, *J* = 8.8 Hz, Ar-H), 2.46 (s, 1H, CH_3). ^{13}C NMR (75 MHz, $CDCl_3$): δ 190.9, 161.0, 142.1, 139.8, 138.8, 135.7, 130.4, 130.1, 129.4, 128.7, 123.7, 122.6, 120.5, 120.0, 116.8, 21.4. ESI-MS: *m*/*z* $[M+H]^+$ 313.

(5-Chloro-2-hydroxyphenyl)(1-(4-methoxyphenyl)-1*H*-pyrazol-4-yl)methanone (6q)

Yellow thick liquid. Yield 87%. FT-IR (KBr): *ν* 3232, 1584, 1517, 1219, 773 cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$): δ 11.91 (s, 1H, ArOH), 8.39 (s, 1H, pyrazole H_3), 8.16 (s, 1H, pyrazole H_5), 7.87 (d, *J* = 3.0 Hz, 1H, Ar-H), 7.65 (d, 2H, *J* = 9.0 Hz, Ar-H), 7.46 (dd, 1H, J_1 = 8.3 Hz, J_2 = 2.2 Hz, Ar-H), 7.02 (d, 3H, *J* = 9.0 Hz, Ar-H), 3.87 (s, 3H, OCH_3). ^{13}C NMR (75 MHz, $CDCl_3$): δ 191.0, 161.0, 159.3, 142.0, 135.7, 132.6, 130.4, 130.2, 123.7, 122.6, 121.5, 120.1, 114.7, 55.6. ESI-MS: *m*/*z* $[M+H]^+$ 329.

(5-Bromo-2-hydroxyphenyl)(1-*m*-tolyl-1*H*-pyrazol-4-yl)methanone (6r)

Pale yellow solid. Yield 68%. M.p. 122–124 °C. FT-IR (KBr): *ν* 3118, 1630, 1542, 1225, 823 cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$): δ 11.91 (s, 1H, ArOH), 8.47 (s, 1H, pyrazole H_3), 8.17 (s, 1H, pyrazole H_5), 8.01 (d, 1H, *J* = 2.2 Hz, Ar-H), 7.62–7.51 (m, 3H, Ar-H), 7.40 (t, 1H, *J* = 7.7 Hz, Ar-H), 6.98 (d, 1H, *J* = 8.8 Hz, Ar-H), 2.46 (s, 1H, CH_3). ^{13}C NMR (75 MHz, $CDCl_3$): δ 190.9, 161.4, 142.1, 139.9, 138.9, 138.5, 133.2, 130.5, 129.4, 128.8, 122.6, 121.2, 120.4, 116.8, 110.6, 21.4. ESI-MS: *m*/*z* $[M+H]^+$ 357.

(5-Bromo-2-hydroxyphenyl)(1-(4-methoxyphenyl)-1*H*-pyrazol-4-yl)methanone (6s)

Pale yellow solid. Yield 87%. M.p. 128–130 °C. FT-IR (KBr): *ν* 3122, 1615, 1581, 1249, 818 cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$): δ 11.93 (s, 1H, ArOH), 8.39 (s, 1H, pyrazole H_3), 8.16 (s, 1H, pyrazole H_5), 8.02 (d, *J* = 2.2 Hz, 1H, Ar-H), 7.66 (d, 2H, *J* = 9.0 Hz, Ar-H), 7.60 (dd, 1H, J_1 = 9.0 Hz, J_2 = 3.0 Hz, Ar-H), 7.03 (d, 2H, *J* = 9.0 Hz, Ar-H), 6.98 (d, 1H, *J* = 9.0 Hz, Ar-H), 3.88 (s, 3H, OCH_3). ^{13}C NMR (75 MHz, $CDCl_3$): δ 190.0, 161.4, 159.3, 142.0, 138.5, 133.2, 132.5, 130.4, 122.5, 121.4, 120.4, 114.7, 110.6, 55.6. ESI-MS: *m*/*z* $[M+H]^+$ 373

(6-Hydroxybenzofuran-5-yl)(1-*m*-tolyl-1*H*-pyrazol-4-yl)methanone (6t)

Yellow thick liquid. Yield 83%. FT-IR (KBr): *ν* 3121, 1634, 1541, 1247, 785 cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$): δ 12.14 (s, 1H, ArOH), 8.47 (s, 1H, pyrazole H_3), 8.18 (s, 1H, pyrazole H_5), 8.14 (s, 1H, Ar-H), 7.61–7.51 (m, 3H, Ar-H), 7.39 (t, *J* = 7.5 Hz, 1H, Ar-H), 7.20 (d, 1H, *J* = 7.5 Hz, Ar-H), 6.75 (d, 1H, *J* = 1.5 Hz, Ar-H), 2.45 (s, 3H, CH_3). ^{13}C NMR (75 MHz, $CDCl_3$): δ 192.1, 161.1, 159.2, 145.6, 142.2, 139.8, 139.1, 130.4, 129.4, 128.6, 124.6, 123.4, 120.4, 120.2, 117.4, 116.7, 106.7, 100.0, 21.4. ESI-MS: *m*/*z* $[M+H]^+$ 319.

(2-Hydroxy-6-methylphenyl)(1-phenyl-1*H*-pyrazol-4-yl)methanone (6u)

Yellow solid. Yield 77%. M.p. 111–113 °C. FT-IR (KBr): *ν* 3447, 1622, 1539, 1483, 1238, 903, 771 cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$): δ 12.13 (s, 1H, ArOH), 8.47 (s, 1H, pyrazole H_3), 8.17 (s, 1H, pyrazole H_5), 7.80 (d, 1H, *J* = 8.1 Hz, Ar-H), 7.75 (d, *J* = 8.1 Hz, 2H, Ar-H), 7.52 (t, 2H, *J*

= 7.3 Hz, Ar-H), 7.40 (d, *J* = 7.5 Hz, 1H, Ar-H), 6.88 (s, 1H, Ar-H), 6.78 (d, *J* = 8.1 Hz, 1H, Ar-H), 2.39 (s, 3H, CH_3). ^{13}C NMR (75 MHz, $CDCl_3$): δ 191.6, 162.9, 147.7, 142.2, 139.2, 131.1, 130.2, 129.6, 127.8, 125.0, 123.4, 120.3, 119.7, 119.5, 118.6, 117.7, 21.9. ESI-MS: *m*/*z* $[M+H]^+$ 279.

5. Anti-proliferative Assay

5. 1. Cell Proliferation Assay

This assay is a quantitative colorimetric method for determination of cell survival and proliferation. The assessed parameter is the metabolic activity of viable cells.[13] Metabolically active cells reduce pale yellow tetrazolium salt (MTT) to a dark blue water-insoluble formazan, which can be directly quantified after solubilisation with DMSO. The absorbance of the formazan directly correlates with the number of viable cells. The cells were plated in 96-well plates at a density of 2.0 × 104 in 100 µL of medium per well of 96-well plate. Cultures were incubated with test compounds (10 µM) and incubated for 48 h. The medium was replaced with fresh medium containing 100 µg/mL of 3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide (MTT) for 2–3 h. The supernatant was aspirated and MTT-formazan crystals dissolved in 100 µL DMSO; OD measured at λ 540 nm (reference wavelength, λ 620 nm) on ELISA reader cell viability % was calculated by comparing the absorbance of treated versus untreated cells.

6. Conclusion

In conclusion, 4*H*-chromone-based hydrazones, pyrazolecarboxylates and pyrazolylmethanones were synthesized and evaluated for their anti-proliferative activity against four human cancer cell lines. The compounds **5p–q**, **5w**, **6e** and **6j** displayed potent anti-proliferative activity, however, compounds **3s** and **5g–h** have shown promising activity.

7. Acknowledgments

The authors thank Dr. S. Chandrasekhar, Director, CSIR-IICT for constant encouragement. Financial assistance to R. N. R from CSIR, New Delhi is gratefully acknowledged. B. China Raju acknowledges CSIR, New Delhi for financial support through the programme "ORIGIN" (CSC-0108) of XII five year plan.

8. References

1. S. Fustero, M. Sanchez-Rosello, P. Barrio, A. Simon-Fuentes, *Chem. Rev.* **2011**, *111*, 6984–7034. **DOI:**10.1021/cr2000459
2. S. Ulloora, R. Shabaraya, R. Ranganathan, A. V. Adhikari, *Eur. J. Med. Chem.* **2013**, *70*, 341–349. **DOI:**10.1016/j.ejmech.2013.10.010
3. M. D. Altintop, A. Ozdemir, G. Turan-Zitouni, *Eur. J. Med. Chem.* **2012**, *58*, 299–307. **DOI:**10.1016/j.ejmech.2012.10.011
4. A. M. Pieczonka, A. Strzelczyk, B. Sadowska, G. Mloston, P. Stączek, *Eur. J. Med. Chem.* **2013**, *64*, 389–395. **DOI:**10.1016/j.ejmech.2013.04.023
5. M. B. Bhalerao, S. T. Dhumal, A. R. Deshmukh, *Bioorg. Med. Chem. Lett.* **2017**, *27*, 288–294. **DOI:**10.1016/j.bmcl.2016.11.056
6. T. Yoshioka, T. Fujita, T. Kanai, Y. Aizawa, T. Kurumada, K. Hasegawa, H. Horikoshi, *J. Med. Chem.* **1989**, *32*, 421–428. **DOI:**10.1021/jm00122a022
7. M. Rinaldi-Carmona, F. Barth, M. Heaulme, D. Shire, B. Calandra, C. Congy, S. Martinez, J. Maruani, G. Neliat, D. Caput, P. Ferrara, P. Soubrie, J. C. Breliere, G. Le Fur, *FEBS Lett.* **1994**, *350,* 240–244. **DOI:**10.1016/0014-5793(94)00773-X
8. Ch. Dayakar, B. S. Kumar, G. Sneha, G. Sagarika, K. Meghana, S. Ramakrishna, R. S. Prakasham, B. C. Raju, *Bioorg. Med. Chem.* **2017**, *25*, 5678–5691. **DOI:**10.1016/j.bmc.2017.08.042
9. B. C. Raju, A. K. Tiwari, J. A. Kumar, A. Z. Ali, Sachin B. Agawane, G. Saidachary, K. Madhusudana, *Bioorg. Med. Chem.* **2010**, *18*, 358–365. **DOI:**10.1016/j.bmc.2009.10.047
10. G. Saidachary, K. Veera Prasad, D. Divya, A. Singh, U. Ramesh, B. Sridhar, B. C. Raju, *Eur. J. Med. Chem.* **2014**, *76*, 460–469. **DOI:**10.1016/j.ejmech.2014.02.042
11. P. Suman, T. R. Murthy, K. Rajkumar, D. Srikanth, Ch. Dayakar, C. Kishor, A. Addlagatta, S. V. Kalivendi, B. C. Raju, *Eur. J. Med. Chem.* **2015**, *90*, 603–619. **DOI:**10.1016/j.ejmech.2014.11.063
12. P. Suman, Ch. Dayakar, K. Rajkumar, B. Yashwanth, P. Yogeeswari, D. Sriram, J. V. Rao, B. C. Raju, *Bioorg. Med. Chem. Lett.* **2015**, *25*, 2390–2394. **DOI:**10.1016/j.bmcl.2015.04.009
13. B. C. Raju, R. N. Rao, P. Suman, P. Yogeeswari, D. Sriram, T. B. Shaik, S. V. Kalivendi, *Bioorg. Med. Chem. Lett.* **2011**, *21*, 2855–2859. http://doi.org/10.1016/j.bmcl.2011.03.079
14. K. Rajkumar, P. Suman, B. C. Raju, *RSC Adv.* **2015**, *5*, 73850–73858. **DOI:**10.1039/c5ra10185a
15. W. Guangcheng, C. Ming, W. Jing, P. Yaping, L. Luyao, Z. X. Zhen, D. Bing, C. Shan, L. Wenbiao, *Bioorg. Med. Chem. Lett.* **2017**, *27*, 2957–2961. **DOI:**10.1016/j.bmcl.2017.05.007
16. L. Deng, W. Wang, C. Hu, C. Wu, CN103554123, **2016**.
17. L. Deng, W. Wang, G. Chen, Q. Yang, X. Gao, Y. Zhou, C. Hu, C. Wu, R. Shen, Y. Wu, CN106083884, **2016**.
18. A. Lazarenkow, J. Nawrot-Modranka, E. Brzezinska, U. Krajewska, M. Rozalski, *Med. Chem. Res.* **2012**, *21*, 1861–1868. **DOI:**10.1007/s00044-011-9703-4
19. B. A. Kumar, P. Dipak, S. J. Singh, *Tetrahedron* **1988**, *44*, 1241–1246. **DOI:**10.1016/S0040-4020(01)85904-4
20. M. A. Ibrahim, N. M. El-Gohary, *Heterocycles* **2014**, *89*, 413–425. **DOI:**10.3987/COM-13-12899

Povzetek

Sintetizirali smo serijo hidrazonov **3a**–**z**, pirazolkarboksilatov **5a**–**x** in pirazolilmetanonov **6a**–**u**, temelječih na ogrodju 4*H*-kromona. Za vse pripravljene spojine smo preučili anti-proliferativne lastnosti proti celičnim linijam A549, HeLa, DU145 in MDAMB 231. Hidrazon **3s** s kloro substituentom na kromanonskem skeletu in z metoksi skupino na fenilnem obroču je izkazoval obetavno aktivnost na celične linije A549, HeLa in DU145. Spojina **5p** z bromo substituentom na kromanonskem skeletu in metilno skupino na fenilnem obroču je izkazala veliko aktivnost proti celični liniji DU145. Furopirazolkarboksilat **5w**, ki vsebuje metilni substituent na fenilnem obroču, je izkazal močno aktivnost proti HeLa celični liniji. Pirazolilmetanon **6e** s fluoro substituentom na fenilnem obroču in spojina **6j** z metilnim substituentom na kromanonskem skeletu ter metoksi skupino na fenilnem obroču sta izkazali obetavne anti-proliferativne lastnosti proti HeLa celični liniji.