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Microwave-assisted synthesis and antimicrobial evaluation of novel pyrazolines

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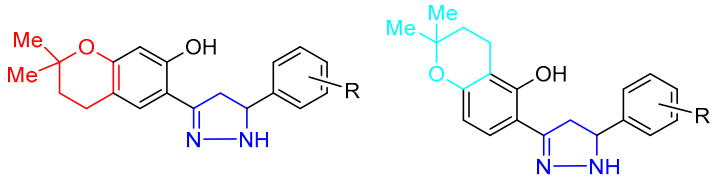


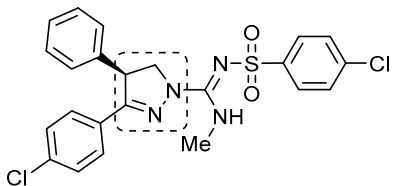
18 examples

A series of 6-(5-aryl-4,5-dihydro-1*H*-pyrazol-3-yl)-2,2-dimethylchroman-7-ol and 6-(5-aryl-4,5-dihydro-1*H*-pyrazol-3-yl)-2,2-dimethylchroman-5-ol derivatives have been synthesized from the corresponding chalcones and hydrazine hydrate in the presence of sodium acetate under microwave irradiation involving the Michael addition followed by cycloaddition. All the newly synthesized 18 compounds were screened for their *in vitro* antimicrobial activity. Most of the compounds displayed very good to excellent antimicrobial activity in comparison to standard drugs streptomycin and nystatin.

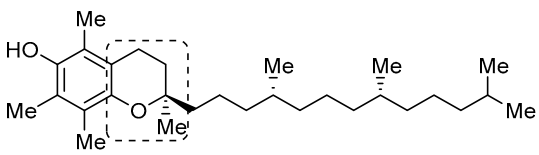
Keywords: chalcones, pyrazolines, antimicrobial activity, Michael addition, microwave irradiation.

Since resistance of pathogenic bacteria towards available antibiotics is rapidly becoming a worldwide problem, the design of new compounds to deal with resistant bacteria has become one of the most important areas of antibacterial research today. In addition, it is known that antifungal drugs do not have selective activity because of the biochemical similarity between human cell and fungi forms.[1] Therefore there are many studies focused on antibacterial and antifungal compounds.[2–3] Heterocyclic compounds such as pyrazolines and chromans are well known for their significant biological activities. Pyrazolines and their derivatives have attracted considerable attention due to their extensive biological activities such as antimicrobial,[4,5] antiamoebic,[6] antidepressant,[7] anticonvulsant,[8] anti-inflammatory,[9] and antitumor.[10] Ibipinabant (Fig. 1), a commercially available drug containing pyrazoline nucleus, is a potent and highly selective CB1 antagonist.[11] On the other hand, chromans are important oxygen-containing fused heterocycles frequently encountered in many natural products and exhibit significant biological activities such as anticancer,[12] neuroprotective,[13] HIV inhibitory,[14] antimicrobial,[15] and antioxidant.[16] Vitamin E (Fig. 1), a naturally occurring chroman, is very effective in suppression of cellular membrane phospholipid degradation.[17] Microwave-assisted organic synthesis is becoming very popular and is widely practiced by chemists,[18] as the rate of the reaction is accelerated under microwave (MW) irradiation compared to conventional heating.

Inspired by the biological profile of pyrazolines, their increasing importance in pharmaceutical and biological fields, and in connection with our previous research on the design and synthesis of pharmacologically important new



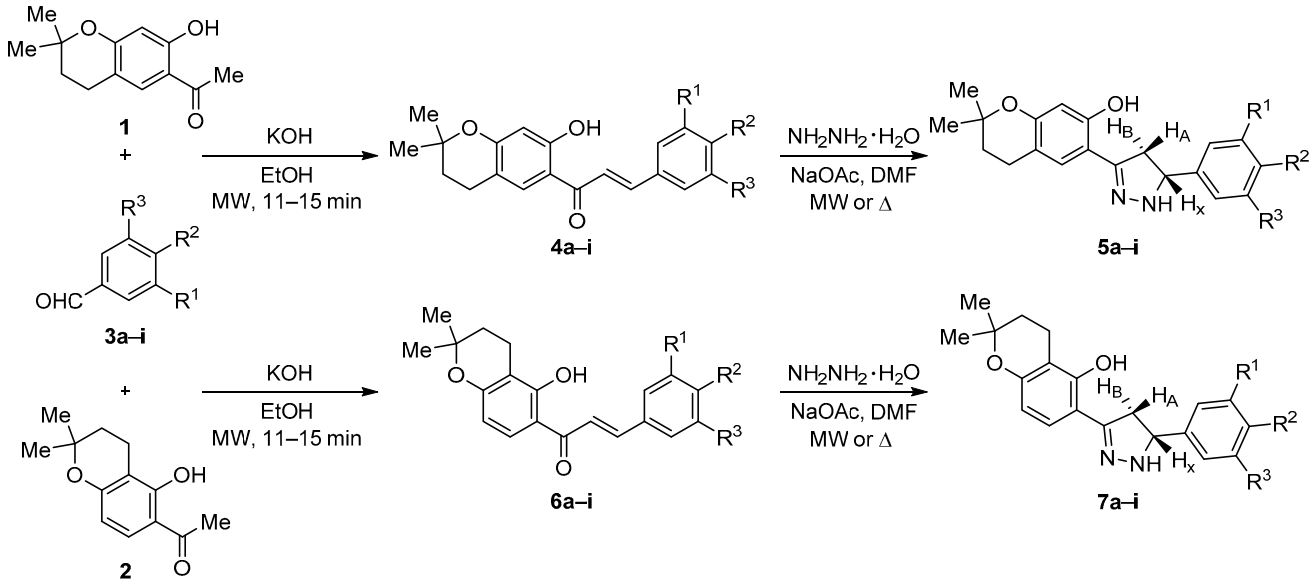
Ibipinabant



Vitamin E (γ-tocopherol)

Figure 1. Examples of commercially available drug containing pyrazoline moiety and a natural product containing chroman ring.

Scheme 1



heterocycles[19–22] linked to chroman ring system, we planned to synthesize pyrazoline compounds containing chroman moiety by conventional and microwave irradiation methods (Scheme 1). The constitution of all the compounds was characterized using elemental analysis, FT-IR, ^{1}H, ^{13}C NMR, and mass spectroscopy. The synthesized pyrazoline compounds were evaluated for their *in vitro* antimicrobial activity.

In the present investigation we have synthesized novel pyrazolines from the respective precursor chalcones. The synthesis of new derivatives of pyrazoline was carried out as outlined in Scheme 1. The starting materials 1-(7-hydroxy-2,2-dimethylchroman-6-yl)ethanone (**1**) and 1-(5-hydroxy-2,2-dimethylchroman-6-yl)ethanone (**2**) were prepared from resacetophenone and isoprene using Amberlyst-15 as catalyst in THF and heptane.[23] The Claisen–Schmidt condensation of compounds **1** and **2** with the selected aryl aldehydes **3a**–**i** in the presence of powdered KOH under MW irradiation produced chalcones – (*E*)-3-aryl-1-(7-hydroxy-2,2-dimethylchroman-6-yl)prop-2-en-1-ones **4a**–**i** and (*E*)-1-(5-hydroxy-2,2-dimethylchroman-6-yl)-3-phenylprop-2-en-1-ones **6a**–**i**, respectively.[24] The reaction of chalcones **4a**–**i** and **6a**–**i** with hydrazine hydrate in DMF in the presence of sodium acetate under thermal conditions gave the target pyrazolines 6-(5-aryl-4,5-dihydro-1*H*-pyrazol-3-yl)-2,2-dimethylchroman-7-ols **5a**–**i** and 6-(5-aryl-4,5-dihydro-1*H*-pyrazol-3-yl)-2,2-dimethylchroman-5-ols **7a**–**i** in low yields, and it took several hours to complete the reaction (Table 1). Hence, to investigate the advantages of microwave-assisted synthesis,

Table 1. Substituents and yields of compounds **5a**–**i** and **7a**–**i** obtained with conventional heating and microwave irradiation

Compound	R^1	R^2	R^3	Conventional method*		Microwave method**	
				Time, h	Yield, %	Time, min	Yield, %
5a	H	H	H	4.0	68	2.0	90
5b	H	Me	H	5.0	62	2.5	86
5c	H	OMe	H	5.0	64	3.0	88
5d	OMe	OMe	OMe	7.0	56	3.5	86
5e	H	Cl	H	7.0	62	3.0	86
5f	H	Cl	Cl	6.0	62	3.0	86
5g	H	*i*-Pr	H	7.0	60	3.0	88
5h	H	H	NO_2	8.0	58	5.0	60
5i	H	NMe_2	H	7.0	66	3.5	85
7a	H	H	H	4.0	66	2.5	90
7b	H	Me	H	5.0	64	3.0	88
7c	H	OMe	H	5.0	62	3.0	88
7d	OMe	OMe	OMe	6.0	58	3.5	86
7e	H	Cl	H	7.0	60	3.5	86
7f	H	Cl	Cl	7.0	64	3.0	88
7g	H	*i*-Pr	H	6.0	62	2.5	84
7h	H	H	NO_2	8.0	58	5.0	80
7i	H	NMe_2	H	7.0	64	3.5	82

* Chalcone **4** or **6** (1.0 mmol), hydrazine hydrate (1.0 mmol), NaOAc (1.0 mmol) in DMF (5 ml) heated at 80–90°C.
** Chalcone **4** or **6** (1.0 mmol), hydrazine hydrate (1.0 mmol), NaOAc (1.0 mmol) in DMF (5 ml) irradiated with MW (180 W).

we synthesized the target pyrazolines under MW irradiation. Chalcones **4a**–**i** and **6a**–**i** and hydrazine hydrate in DMF in the presence of sodium acetate were irradiated at 180 W power for 2–5 min to give pyrazole derivatives **5a**–**i** and **7a**–**i** in high yields. Therefore, investigation results revealed that applying MW irradiation to the reaction mixture provides better yields and lesser reaction times.

The ^{1}H NMR spectrum of the representative compound **5a** in $CDCl_3$ solution showed three characteristic signals due to the diastereotopic protons CH_A and CH_B, as well as CH_X proton at the chiral carbon atom of the pyrazoline ring.[25,26] The CH_A proton, which is *cis*-oriented relative to CH_X proton resonated as doublet of doublets at a higher field (3.10 ppm, J_{AB} = 16.4, J_{AX} = 8.8 Hz) than the CH_B proton which is *trans*-oriented (3.51 ppm, J_{BA} = 16.4, J_{BX} = 10.8 Hz). The CH_X proton (4.83 ppm) signal had both matching vicinal spin-spin interaction constants (8.8 and 10.8 Hz).

The proposed structure of compound **5a** was further supported by the ^{13}C NMR spectrum, in which the signals at 41.7 and 61.9 ppm could be attributed to C-4 and C-5 carbons of the pyrazoline ring, respectively, based on the close agreement of those values with the reported values for the respective carbons in analogous structures.[27,28] The ESI mass spectrum of **5a** showed the principal ion peak at the expected *m*/*z* value (323) for protonated molecular ion $[M+H]^+$. The combination of ^{1}H and ^{13}C NMR and mass spectral data thus provides a strong evidence in support of the structures assigned to pyrazoline derivatives **5a**–**i**, **7a**–**i**.

All new 18 pyrazoline compounds **5a**–**i**, **7a**–**i** were screened for their antibacterial and antifungal activity by the cup-plate agar diffusion method.[29] Antibacterial activity was tested against two Gram-positive bacteria viz., *Bacillus subtilis* (MTCC 441), *Staphylococcus aureus* (MTCC 737), and two Gram-negative bacteria viz., *Pseudomonas aeruginosa* (MTCC 741), *Escherichia coli* (MTCC 443). Nutrient agar medium was used for the antibacterial screening. The zone of inhibition (in mm) was compared with standard drug streptomycin sulfate. Antifungal activity was carried out against three fungi viz., *Aspergillus niger* (ATCC 9029), *Candida albicans* (ATCC 2091), and *Aspergillus foetidus* (NCIM 505). Sabouraud's agar medium was used for the antifungal screening. Nystatin was used as standard. The results are presented in Tables 2 and 3.

The investigation of antibacterial activity (Table 2) revealed that compounds **5a**,**c**,**g**, **7a**,**d**,**g**,**i** (inhibition zone >26 mm) showed excellent growth inhibition against *Bacillus subtilis* as compared to streptomycin (21 mm) at 100 μg/ml concentration. In the case of *Staphylococcus aureus*, compounds **5a**,**g**, **7a**,**d** (>27 mm) were found to be exceedingly potent in comparison with the standard (20 mm). Compounds **5b**,**d**,**f**,**i**, **7b**,**c**,**d**,**f**,**g** were found to exhibit good activity against both Gram-positive bacterial strains used in the test.

On the other hand, antibacterial activity evaluation against Gram-negative bacteria *Pseudomonas aeruginosa* revealed that all the tested compounds except **5e**,**h**, **7e**,**h** showed excellent to moderate activity compared to the standard drug streptomycin. Compounds **5b**,**c**,**g**, **7a**,**d**,**f**,**g**,**i** (inhibition zone >27 mm) were found to exhibit higher activity than the standard drug. Compounds **5c**,**g**,**i**, **7a**,**d**,**f**,**g**,**i** (>27 mm) were significantly more active than the standard drug streptomycin (21 mm) against *Escherichia coli*. Compounds **5b**, **7b**,**c** demonstrated activity comparable with that of streptomycin against *Escherichia coli*.

Table 2. Antibacterial activity of compounds **5a**–**i** and **7a**–**i** expressed as zone of inhibition (mm)*

Compound	Gram-positive strains		Gram-negative strains	
	Bacillus subtilis (MTCC 441)	*Staphylococcus aureus* (MTCC 737)	*Pseudomonas aeruginosa* (MTCC 741)	*Escherichia coli* (MTCC 443)
5a	26	28	26	25
5b	25	24	27	23
5c	26	26	27	27
5d	25	24	24	26
5e	–**	–	–	–
5f	25	26	26	25
5g	28	27	28	30
5h	–	–	–	–
5i	25	24	26	28
7a	29	27	28	28
7b	25	24	26	24
7c	22	22	22	22
7d	27	27	30	29
7e	–	–	–	–
7f	24	26	27	27
7g	26	25	29.5	28
7h	–	–	–	–
7i	28	2	27	28
Streptomycin	21	20	23	21

* The compounds were tested at 200 μg/ml concentration.
** Not active.

Overall, among the target molecules, only four compounds **5e**,**h**, **7e**,**h** did not respond to any of the bacterial strains, whereas compounds **5a**,**c**,**d**,**g**,**i** and **7a**,**c**,**d**,**g**,**i** showed excellent zones of inhibition against all bacterial strains.

All the synthesized pyrazolines **5a**–**i**, **7a**–**i** were screened *in vitro* for their antifungal activity against *Aspergillus niger* (ATCC 9029), *Candida albicans* (ATCC 2091), and *Aspergillus foetidus* (NCIM 505). Sabouraud's agar medium was used for the antifungal screening. Zone of inhibition (in mm) was compared with that of standard drug nystatin. The results are presented in Table 3.

From the antifungal activity data it can be observed that compounds **5a**,**c**,**d**,**g**, **7a**,**b**,**c**,**d**,**g**,**i** (inhibition zone >25 mm) exhibited excellent zone of inhibition when employed against *Aspergillus niger* as compared to the standard drug nystatin (22 mm). Other compounds **5b**,**f**, **7f** showed moderate zone of inhibition values, while compounds **5e**,**h**, **7e**,**h** were showing no activity against *Aspergillus niger*. When the synthesized compounds were tested against *C. albicans*, compounds **5a**,**g**,**i**, **7a**–**d**,**g**,**i** (>25 mm) were found to exhibit excellent zone of inhibition values compared to the standard drug (21 mm). Compounds **5b**–**d**,**f**, **7f** were also found to exhibit good to moderate zone of inhibition against *C. albicans* compared to the standard drug. Compounds **5a**,**g**, **7a**,**d**,**g** (>27 mm) were significantly more active against *Aspergillus foetidus* compared to nystatin (20 mm). Compounds **5b**–**d**,**i**, **7b**,**c**,**i** also showed higher activity compared to the standard while compounds **5e**,**f**,**h**, **7e**,**f**,**h** showed moderate to low activity against the fungal strain *Aspergillus foetidus.*

The structure–activity relationship analysis revealed the effect of different substituents at phenyl ring on the activity of the compounds against on various bacterial and fungal strains. Different electronic environments on the phenyl ring were produced by combination of different functional groups. Both electron-donating and electron-withdrawing groups were chosen as substituents for the design and synthesis of the target molecules (Table 1).

From the antibacterial and antifungal data available in the report, it can be concluded that, as a trend, electron-donating functional groups like OMe, Me, *i*-Pr, and *N*,*N*-dimethylamino in the *para*-position of the phenyl group, as well as 3,4,5-trimethoxyphenyl group, caused larger zone of inhibition than the electron-withdrawing groups like 4-Cl, 3-NO_2 on the phenyl group, or 3,4-dichlorophenyl group. Compounds **5b**,**c**,**d**,**g**,**i** and **7b**,**c**,**d**,**g**,**i** possesing electron-donating groups at *para*-position showed excellent activity against all bacterial strains and moderate activity against fungal strains. It was also observed that compounds **5e**,**f**,**h** and **7e**,**f**,**h** possesing electron-withdrawing groups showed moderate to poor inhibition of the growth of bacterial with respect to the standard. The antibacterial, as well as antifungal activities for the compounds **5a** and **7a** are well pronounced even in the absence of any substitution in the phenyl ring. Compounds without substituent(s) on phenyl ring showed very good antimicrobial activity compared to those with substituent(s) (electron-donating or electron-withdrawing) on the phenyl ring. Overall, the presence of electron-donating groups like methyl or methoxy group as substituents on phenyl ring in the synthesized molecules helps to increase the antimicrobial potency. From these results, we hypothesized that the compounds with electron-donating groups are predominantly involved in the

Table 3. Antifungal activity of compounds **5a**–**i** and **7a**–**i** expressed as zone of inhibition (mm)*

Compound	*Aspergillus niger* (ATCC 9029)	*Candida albicans* (ATCC 2091)	*Aspergillus foetidus* (NCIM 505)
5a	26	26	27
5b	22	22	25
5c	26	24	25
5d	28	24	24
5e	–**	–	–
5f	16	20	17
5g	26	27	27
5h	–	–	–
5i	22	26	24
7a	28	27	28
7b	25	26	25
7c	27	26	24
7d	29	28	28
7e	–	–	–
7f	15	21	14
7g	29	29	28
7h	–	–	–
7i	25	25	23
Nystatin	22	21	20

* The compounds were tested at 200 μg/ml concentration.
** Not active.

inhibition of protein synthesis of the bacteria and thus stop or slow down the growth or proliferation of bacterial cells.[22] Thus, in the future combination of different electron-donating groups on the phenyl ring together with pyrazoline moiety will be tried out for generating better lead entities as potent antibacterial and antifungal agents.

We have reported an easy, high yielding, and convenient method for the synthesis of 2,2-dimethyl-6-(5-aryl-4,5-dihydro-1*H*-pyrazol-3-yl)chroman-7-ol derivatives and 2,2-dimethyl-6-(5-aryl-4,5-dihydro-1*H*-pyrazol-3-yl)chroman-5-ol derivatives from suitable chalcones (*E*)-3-aryl-1-(7-hydroxy-2,2-dimethylchroman-6-yl)prop-2-en-1-ones and (*E*)-3-aryl-1-(5-hydroxy-2,2-dimethylchroman-6-yl)prop-2-en-1-ones under microwave irradiation method. All the final compounds were investigated for their *in vitro* antimicrobial activity. Several compounds showed promising antibacterial activity when compared to streptomycin and good antifungal activity compared to nystatin. We observed that compounds with electron-donating groups on phenyl ring showed better antimicrobial activity than those with electron-withdrawing groups.

Experimental

IR spectra were recorded on a Shimadzu FT-IR 8400 S spectrometer in KBr pellets. ^{1}H and ^{13}C NMR spectra were recorded on a Bruker Avance-400 spectrometer (400 and 100 MHz, respectively) in $CDCl_3$ using TMS as internal standard. Mass spectra (ESI) were recorded on a Shimadzu GCMS-QP 1000 spectrometer. Elemental analyses were recorded on a Karlo Erba 1106 elemental analyzer. Melting points were taken in open capillary tubes and are uncorrected. Microwave reactions were carried out in a Milestone multi SYNTH series ATC-FO 300 multimode microwave reactor with a twin magnetron (2×800 W, 2.45 GHz) with a maximum delivered power of 1000 W in 10 W increments (pulsed irradiation). Analytical TLC was performed on Merck precoated 60 F254 silica gel plates. Visualization was done by exposing to iodine vapor and UV. All the reagents and solvents were purchased from commercial sources.

Synthesis of chalcones 4a–i and 6a–i (General method). A mixture of 1-(7-hydroxy-2,2-dimethylchroman-6-yl)-ethanone (**1**) or 1-(5-hydroxy-2,2-dimethylchroman-6-yl)-ethanone (**2**) (0.194 g, 1.0 mmol), an aromatic aldehyde **3a–i** (1.0 mmol), and powdered KOH (0.224 g, 4 mmol) in ethanol (10 ml) was taken into a quartz tube and inserted into a screw-capped Teflon vial and then subjected to microwave irradiation for 2 or 3 periods of 5 min at 180 W (90°C) with 30 s time interval between them. The progress of the reaction was monitored by TLC (eluent petroleum ether–AcOEt, 4:1). After completion of the reaction, the reaction mixture was neutralized with dilute HCl, the solid obtained was filtered off, washed with water, dried, and recrystallized from chloroform to yield pure chalcones **4a–i** or **6a–i**.

(*E*)-1-(7-Hydroxy-2,2-dimethylchroman-6-yl)-3-phenylprop-2-en-1-one (4a). Yield 98%, pale-yellow solid, mp 192–193°C (mp 194–195°C[30]). IR spectrum, ν, cm^{-1}: 2938, 2855, 1637, 1570, 1357, 1151, 973. ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 1.36 (6H, s, 2CH_3); 1.85 (2H, t, *J* = 6.8, CH_2); 2.78 (2H, t, *J* = 6.8, CH_2); 6.37 (1H, s, H-5); 7.42–7.65 (6H, m, H Ar, α-CH); 7.66–7.88 (2H, m, H-8, β-CH); 13.00 (1H, s, OH). ^{13}C NMR spectrum, δ, ppm: 22.3; 26.8; 32.7; 79.8; 103.4; 112.5; 118.2; 119.3; 126.8; 127.8; 128.5; 131.5; 134.8; 144.5; 161.1; 164.3; 191.4. Mass spectrum, *m*/*z* (I_{rel}, %): 309 $[M+H]^+$ (100). Found, %: C 70.85; H 6.59. $C_{20}H_{20}O_3$. Calculated, %: C 70.90; H 6.54.

(*E*)-1-(7-Hydroxy-2,2-dimethylchroman-6-yl)-3-(4-methylphenyl)prop-2-en-1-one (4b). Yield 96%, pale-yellow solid, mp 164–166°C (mp 167–168°C[30]). IR spectrum, ν, cm^{-1}: 2934, 2853, 1638, 1568, 1356, 1289, 1151, 818. ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 1.37 (6H, s, 2CH_3); 1.85 (2H, t, *J* = 6.8, CH_2); 2.42 (3H, s, CH_3); 2.79 (2H, t, *J* = 6.8, CH_2); 6.39 (1H, s, H-5); 7.18–7.26 (2H, m, H Ar); 7.54–7.68 (4H, m, α-CH, H-8, H Ar); 7.88 (1H, d, *J* = 15.8, β-CH); 13.00 (1H, s, OH). ^{13}C NMR spectrum, δ, ppm: 21.3; 22.3; 26.8; 32.7; 76.8; 104.1; 112.5; 119.3; 126.8; 128.5; 129.4; 131.5; 132.6; 138.5; 144.5; 161.1; 164.3; 192.4. Mass spectrum, *m*/*z* (I_{rel}, %): 323 $[M+H]^+$ (100). Found, %: C 78.26; H 6.83. $C_{21}H_{22}O_3$. Calculated, %: C 78.23; H 6.88.

(*E*)-1-(7-Hydroxy-2,2-dimethylchroman-6-yl)-3-(4-methoxyphenyl)prop-2-en-1-one (4c). Yield 97%, pale-yellow solid, mp 145–146°C (mp 146–147°C[30]). IR spectrum, ν, cm^{-1}: 2929, 1634, 1602, 1558, 1423, 1358, 1293, 1247, 1151, 1028, 831, 761; ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 1.30 (6H, s, 2CH_3); 1.70 (2H, t, *J* = 6.8, CH_2); 2.75 (2H, t, *J* = 6.8, CH_2); 6.39 (1H, s, H-5); 3.64 (3H, s, OCH_3); 6.87–6.92 (2H, m, H Ar); 7.59–7.62 (3H, m, H Ar, α-CH); 7.76 (1H, s, H-8); 7.83 (1H, d, *J* = 15.8, β-CH); 13.1 (1H, s, OH). ^{13}C NMR spectrum, δ, ppm: 22.3; 26.8; 32.7; 56.2; 75.8; 108.8; 111.6; 112.5; 118.5; 126.8; 128.5; 129.5; 131.5; 139.5; 144.5; 161.1; 164.3; 191.4. Mass spectrum, *m*/*z* (I_{rel}, %): 339 $[M+H]^+$ (100). Found, %: C 74.50; H 6.51. $C_{21}H_{22}O_4$. Calculated, %: C 74.54; H 6.55.

(*E*)-1-(7-Hydroxy-2,2-dimethylchroman-6-yl)-3-(3,4,5-trimethoxyphenyl)prop-2-en-1-one (4d). Yield 98%, pale-yellow solid, mp 107–110°C. IR spectrum, ν, cm^{-1}: 2926, 2865, 1647, 1565, 1376, 1268, 1150, 889, 762. ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 1.37 (6H, s, 2CH_3); 1.85 (2H, t, *J* = 6.8, CH_2); 2.79 (2H, t, *J* = 6.8, CH_2); 3.91 (3H, s, OCH_3); 3.93 (6H, s, 2OCH_3); 6.37 (1H, s, H-5); 6.87 (2H, s, H Ar); 7.43 (1H, d, *J* = 15.8, α-CH); 7.62 (1H, s, H-8); 7.78 (1H, d, *J* = 15.8, β-CH); 13.20 (1H, s, OH). ^{13}C NMR spectrum, δ, ppm: 22.4; 27.0; 32.9; 56.7; 60.7; 75.9; 108.8; 111.6; 112.5; 118.5; 120.3; 126.8; 131.5; 139.5; 144.5; 156.6; 161.1; 164.3; 191.4. Mass spectrum, *m*/*z* (I_{rel}, %): 399 $[M+H]^+$ (100). Found %: C 69.35; H 6.55. $C_{23}H_{26}O_6$. Calculated, %: C 69.33; H 6.58.

(*E*)-3-(4-Chlorophenyl)-1-(7-hydroxy-2,2-dimethylchroman-6-yl)prop-2-en-1-one (4e). Yield 98%, pale-yellow solid, mp 170–172°C. IR spectrum, ν, cm^{-1}: 2928, 2864, 1632, 1566, 1358, 1209, 1086, 811. ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 1.37 (6H, s, 2CH_3); 1.83 (2H, t, *J* = 6.8, CH_2); 2.72 (2H, t, *J* = 6.8, CH_2); 6.38 (1H, s, H-5); 7.36–7.39 (2H, m, H Ar); 7.53–7.58 (3H, m, H Ar, α-CH); 7.68 (1H, s, H-8); 7.78 (1H, d, *J* = 15.8, β-CH); 12.90 (1H, s, OH). ^{13}C NMR spectrum, δ, ppm: 22.3; 26.7; 32.3; 76.9;

109.3; 112.7; 114.5; 118.9; 128.5; 129.4; 130.5; 133.4; 133.6; 145.2; 161.0; 165.2; 192.4. Mass spectrum, *m/z* (I_{rel}, %): 343 $[M+H]^+$ (100). Found, %: C 70.12; H 5.65. $C_{20}H_{19}ClO_3$. Calculated, %: C 70.07; H 5.59.

(*E*)-3-(3,4-Dichlorophenyl)-1-(7-hydroxy-2,2-dimethylchroman-6-yl)prop-2-en-1-one (4f). Yield 98%, pale-yellow solid, mp 100–102°C. IR spectrum, ν, cm^{-1}: 2929, 2858, 1590, 1433, 1360, 1295, 1157, 1090, 821. ^1H NMR spectrum, δ, ppm (*J*, Hz): 1.30 (6H, s, $2CH_3$); 1.77 (2H, t, *J* = 6.8, CH_2); 2.74 (2H, t, *J* = 6.8, CH_2); 6.68 (1H, s, H-5); 7.24 (1H, s, H Ar); 7.36–7.59 (3H, m, H Ar, α-CH); 7.94 (1H, s, H-8); 8.06 (1H, d, *J* = 15.8, β-CH); 13.40 (1H, s, OH). ^{13}C NMR spectrum, δ, ppm: 22.3; 26.8; 32.7; 76.5; 104.3; 112.7; 119.8; 127.3; 127.5; 128.5; 129.2; 130.1; 132.4; 133.5; 135.3; 145.2; 161.0; 164.2; 190.4. Mass spectrum, *m/z* (I_{rel}, %): 378 $[M+H]^+$ (100). Found, %: C 63.60; H 4.78. $C_{20}H_{18}Cl_2O_3$. Calculated, %: C 63.67; H 4.81.

(*E*)-1-(7-Hydroxy-2,2-dimethylchroman-6-yl)-3-(4-isopropylphenyl)prop-2-en-1-one (4g). Yield 98%, pale-yellow solid, mp 95–98°C. IR spectrum, ν, cm^{-1}: 2932, 2854 1598, 1463, 1352, 1260, 1167, 1108, 1032, 759. ^1H NMR spectrum, δ, ppm (*J*, Hz): 1.26 (6H, d, *J* = 7.0, $(C\underline{H}_3)_2$)CH); 1.36 (6H, s, $2CH_3$); 1.84 (2H, t, *J* = 6.8, CH_2); 2.78 (2H, t, *J* = 6.8, CH_2); 2.91–2.93 (1H, m, $(CH_3)_2C\underline{H}$); 6.37 (1H, s, H-5); 7.28–7.30 (2H, m, H Ar); 7.52–7.60 (3H, m, H Ar, α-CH); 7.62 (1H, s, H-8); 7.85 (1H, d, *J* = 15.6, β-CH); 13.00 (1H, s, OH). ^{13}C NMR spectrum, δ, ppm: 22.3; 23.3; 26.8; 32.3; 33.5; 76.6; 109.3; 112.7; 118.6; 119.8; 126.5; 128.6; 131.4; 135.3; 145.2; 147.8; 161.0; 164.2, 192.4. Mass spectrum, *m/z* (I_{rel}, %): 351 $[M+H]^+$ (100). Found, %: C 78.85; H 7.45. $C_{23}H_{26}O_3$. Calculated, %: C 78.83; H 7.48.

(*E*)-1-(7-Hydroxy-2,2-dimethylchroman-6-yl)-3-(3-nitrophenyl)prop-2-en-1-one (4h). Yield 98%, pale-yellow solid, mp 145–147°C (mp 147–148°C[30]). IR spectrum, ν, cm^{-1}: 2926, 2852, 1641, 1570, 1354, 1275, 1154, 890. ^1H NMR spectrum, δ, ppm (*J*, Hz): 1.32 (6H, s, $2CH_3$); 1.77 (2H, t, *J* = 6.8, CH_2); 2.75 (2H, t, *J* = 6.8, CH_2); 6.39 (1H, s, H-5); 7.69–7.72 (2H, m, H Ar, β-CH); 7.82 (1H, s, H-8); 8.00–8.08 (3H, m, H Ar, α-CH); 8.25 (1H, s, H Ar); 13.00 (1H, s, OH). ^{13}C NMR spectrum, δ, ppm: 22.3; 27.0; 32.4; 78.5; 104.5; 112.7; 118.5; 119.7; 123.5; 124.6; 128.5; 129.4; 131.1; 137.7; 142.2; 148.0; 162.0; 163.2; 192.5. Mass spectrum, *m/z* (I_{rel}, %): 354 $[M+H]^+$ (100). Found, %: C 67.94; H 5.36. $C_{20}H_{19}NO_5$. Calculated, %: C 67.98; H 5.42.

(*E*)-3-[4-(Dimethylamino)phenyl]-1-(5-hydroxy-2,2-dimethylchroman-6-yl)prop-2-en-1-one (4i). Yield 98%, pale-yellow solid, mp 170–172°C. IR spectrum, ν, cm^{-1}: 2928, 1589, 1432, 1355, 1164, 1108, 1062, 846. ^1H NMR spectrum, δ, ppm (*J*, Hz): 1.36 (6H, s, $2CH_3$); 1.84 (2H, t, *J* = 6.8, CH_2); 2.78 (2H, t, *J* = 6.8, CH_2); 3.06 (3H, s, NCH_3); 6.41 (1H, s, H-5); 6.61–6.64 (2H, m, H Ar); 7.58–7.62 (3H, m, H Ar, α-CH); 7.61 (1H, s, H-8); 7.85 (1H, d, *J* = 15.8, β-CH); 13.10 (1H, s, OH). ^{13}C NMR spectrum, δ, ppm: 22.3; 26.8; 33.0; 41.5; 77.1; 108.3; 111.7; 112.7; 115.3; 118.8; 122.5; 128.5; 130.1; 145.2; 156.2; 163.0; 165.2; 191.3. Mass spectrum, *m/z* (I_{rel}, %): 352 $[M+H]^+$ (100). Found, %: C 75.25; H 7.20. $C_{22}H_{25}NO_3$. Calculated, %: C 75.19; H 7.17.

(*E*)-1-(5-Hydroxy-2,2-dimethylchroman-6-yl)-3-phenylprop-2-en-1-one (6a). Yield 98%, pale-yellow solid, mp 129–130°C (mp 128–129°C[30]). IR spectrum, ν, cm^{-1}: 2979, 1633, 1571, 1359, 1279, 1220, 1112, 867. ^1H NMR spectrum, δ, ppm (*J*, Hz): 1.36 (6H, s, $2CH_3$); 1.83 (2H, t, *J* = 6.8, CH_2); 2.78 (2H, t, *J* = 6.8, CH_2); 6.39 (1H, d, *J* = 8.8, H-7); 6.86–6.92 (2H, m, H Ar); 7.33–7.43 (3H, m, H Ar); 7.59–7.62 (1H, m, H Ar, α-CH); 7.66 (1H, d, *J* = 8.6, H-8); 7.94 (1H, d, *J* = 15.5, β-CH); 13.00 (1H, s, OH). ^{13}C NMR spectrum, δ, ppm: 16.3; 26.9; 32.7; 79.8; 108.4; 112.5; 115.2; 119.3; 127.3; 128.5; 129.5; 131.5; 135.8; 144.5; 163.1; 165.3; 192.4. Mass spectrum, *m/z* (I_{rel}, %): 309 $[M+H]^+$ (100). Found, %: C 70.85; H 6.59. $C_{20}H_{20}O_3$. Calculated, %: C 70.90; H 6.54.

(*E*)-1-(5-Hydroxy-2,2-dimethylchroman-6-yl)-3-(4-methylphenyl)prop-2-en-1-one (6b). Yield 97%, pale-yellow solid, mp 150–151°C (mp 152–153°C[30]). IR spectrum, ν, cm^{-1}: 2934, 2856, 1625, 1573, 1363, 1284, 1220, 1109, 883. ^1H NMR spectrum, δ, ppm (*J*, Hz): 1.37 (6H, s, $2CH_3$); 1.85 (2H, t, *J* = 6.8, CH_2); 2.42 (3H, s, CH_3); 2.79 (2H, t, *J* = 6.8, CH_2); 6.40 (1H, d, *J* = 8.8, H-7); 7.20–7.24 (2H, m, H Ar); 7.44–7.63 (3H, m, α-CH, H Ar); 7.69 (1H, d, *J* = 8.6, H-8); 7.86 (1H, d, *J* = 15.1, β-CH); 14.00 (1H, s, OH). ^{13}C NMR spectrum, δ, ppm: 16.3; 21.5; 26.7; 31.8; 75.8; 109.1; 109.3; 112.8; 119.5; 128.5; 129.7; 129.8; 132.2; 141.0; 143.9; 160.8; 164.1; 191.9. Mass spectrum, *m/z* (I_{rel}, %): 323 $[M+H]^+$ (100). Found, %: C 78.26; H 6.83. $C_{21}H_{22}O_3$. Calculated, %: C 78.23; H 6.88.

(*E*)-1-(5-Hydroxy-2,2-dimethylchroman-6-yl)-3-(4-methoxyphenyl)prop-2-en-1-one (6c). Yield 98%, pale-yellow solid, mp 107–109°C (mp 106–107°C[30]). IR spectrum, ν, cm^{-1}: 2926, 2853, 1598, 1514, 1354, 1286, 1224, 1171, 1111, 891, 764. ^1H NMR spectrum, δ, ppm (*J*, Hz): 1.30 (6H, s, $2CH_3$); 1.70 (2H, t, *J* = 6.8, CH_2); 2.75 (2H, t, *J* = 6.8, CH_2); 3.65 (3H, s, OCH_3); 6.39 (1H, d, *J* = 8.8, H-7); 6.87 (2H, d, *J* = 8.7, H Ar); 7.49 (1H, d, *J* = 15.5, α-CH); 7.61 (2H, d, *J* = 8.7, H Ar); 7.72 (1H, d, *J* = 8.6, H-8); 7.82 (1H, d, *J* = 15.5, β-CH); 14.00 (1H, s, OH). ^{13}C NMR spectrum, δ, ppm: 16.2; 26.8; 32.7; 55.8; 76.8; 107.1; 114.6; 115.5; 123.3; 129.5; 130.4; 131.4; 132.2; 139.5; 144.5; 156.6; 160.1; 191.4. Mass spectrum, *m/z* (I_{rel}, %): 339 $[M+H]^+$ (100). Found, %: C 74.50; H 6.51. $C_{21}H_{22}O_4$. Calculated, %: C 74.54; H 6.55.

(*E*)-1-(5-Hydroxy-2,2-dimethylchroman-6-yl)-3-(3,4,5-trimethoxyphenyl)prop-2-en-1-one (6d). Yield 98%, pale-yellow solid, mp 98–100°C. IR spectrum, ν, cm^{-1}: 2979, 1635, 1578, 1498, 1359, 1221, 1112, 867. ^1H NMR spectrum, δ, ppm (*J*, Hz): 1.38 (6H, s, $2CH_3$); 1.85 (2H, t, *J* = 6.8, CH_2); 2.74 (2H, t, *J* = 6.8, CH_2); 3.87 (3H, s, OCH_3); 3.90 (6H, s, $2OCH_3$); 6.38 (1H, d, *J* = 8.8, H-7); 6.87 (2H, s, H Ar); 7.47 (1H, d, *J* = 15.2, α-CH); 7.71 (1H, d, *J* = 8.6, H-8); 7.80 (1H, d, *J* = 15.2, β-CH); 13.80 (1H, s, OH). ^{13}C NMR spectrum, δ, ppm: 16.3; 26.8; 32.7; 56.6; 60.7; 75.8; 103.8; 107.1; 112.6; 115.5; 118.5; 131.5; 139.5; 144.5; 155.7; 156.6; 161.1; 164.3; 191.4. Mass spectrum, *m/z* (I_{rel}, %): 399 $[M+H]^+$ (100). Found, %: C 69.33; H 6.55. $C_{23}H_{26}O_6$. Calculated, %: C 69.30; H 6.58.

(*E*)-3-(4-Chlorophenyl)-1-(5-hydroxy-2,2-dimethylchroman-6-yl)prop-2-en-1-one (6e). Yield 98%, pale-yellow solid, mp 138–140°C. IR spectrum, ν, cm^{-1}: 2943, 1638, 1585, 1488, 1223, 1112, 874, 792. ^1H NMR spectrum, δ, ppm (*J*, Hz): 1.39 (6H, s, $2CH_3$); 1.83 (2H, t, *J* = 6.8, CH_2); 2.78 (2H, t, *J* = 6.8, CH_2); 6.38 (1H, d, *J* = 8.8, H-7); 7.40–7.49 (2H, m, H Ar); 7.52–7.68 (4H, m, H Ar, α-CH, H-8); 7.80 (1H, d, *J* = 15.6, β-CH); 12.90 (1H, s, OH). ^{13}C NMR spectrum, δ, ppm: 16.1; 26.7; 33.0; 76.9; 108.3; 112.7; 114.5; 118.9; 128.5; 129.4; 130.5; 133.4; 133.6; 145.2; 161.0; 165.2; 192.4. Mass spectrum, *m*/*z* (I_{rel}, %): 343 $[M+H]^+$ (100). Found, %: C 70.12; H 5.65. $C_{20}H_{19}ClO_3$. Calculated, %: C 70.07; H 5.59.

(*E*)-3-(3,4-Dichlorophenyl)-1-(5-hydroxy-2,2-dimethylchroman-6-yl)prop-2-en-1-one (6f). Yield 98%, pale-yellow solid, mp 92–94°C. IR spectrum, ν, cm^{-1}: 2979, 1627, 1526, 1426, 1212, 1108, 792. ^1H NMR spectrum, δ, ppm (*J*, Hz): 1.30 (6H, s, $2CH_3$); 1.77 (2H, t, *J* = 6.8, CH_2); 2.74 (2H, t, *J* = 6.8, CH_2); 6.69 (1H, d, *J* = 8.8, H-7); 7.23 (1H, s, H Ar); 7.36–7.55 (3H, m, H Ar, α-CH); 7.88 (1H, d, *J* = 8.8, H-8); 8.06 (1H, d, *J* = 15.5, β-CH); 13.4 (1H, s, OH). ^{13}C NMR spectrum, δ, ppm: 16.3; 26.8; 32.9; 76.5; 107.5; 112.7; 114.5; 119.8; 127.5; 128.6; 129.2; 129.6; 130.1; 132.4; 133.5; 135.3; 145.2; 161.0; 164.2; 190.4. Mass spectrum, *m*/*z* (I_{rel}, %): 377 $[M+H]^+$ (100). Found, %: C 63.60; H 4.78. $C_{20}H_{18}Cl_2O_3$. Calculated, %: C 63.67; H 4.81.

(*E*)-1-(5-Hydroxy-2,2-dimethylchroman-6-yl)-3-(4-isopropylphenyl)prop-2-en-1-one (6g). Yield 98%, yellow solid, mp 90–92°C. IR spectrum, ν, cm^{-1}: 2930, 1594, 1430, 1351, 1157, 1114, 1058, 671. ^1H NMR spectrum, δ, ppm (*J*, Hz): 1.27 (6H, d, *J* = 7.0, $(C\underline{H}_3)_2$)CH); 1.36 (6H, s, $2CH_3$); 1.84 (2H, t, *J* = 6.8, CH_2); 2.78 (2H, t, *J* = 6.8, CH_2); 2.91–2.93 (1H, m, $(CH_3)_2C\underline{H}$); 6.39 (1H, d, *J* = 8.8, H-7); 7.24–7.28 (2H, m, H Ar); 7.56–7.60 (3H, m, H Ar, α-CH); 7.64 (1H, d, *J* = 8.7, H-8); 7.85 (1H, d, *J* = 15.5, β-CH); 13.00 (1H, s, OH). ^{13}C NMR spectrum, δ, ppm: 16.1; 23.3; 26.9; 32.8; 33.0; 77.1; 108.3; 112.7; 115.3; 119.8; 127.5; 129.2; 130.1; 132.4; 145.2; 147.5; 163.0; 165.2; 191.3. Mass spectrum, *m*/*z* (I_{rel}, %): 351 $[M+H]^+$ (100). Found, %: C 78.80; H 7.44. $C_{23}H_{26}O_3$. Calculated, %: C 78.83; H 7.48.

(*E*)-1-(5-Hydroxy-2,2-dimethylchroman-6-yl)-3-(3-nitrophenyl)prop-2-en-1-one (6h). Yield 98%, yellow solid, mp 128–130°C. IR spectrum, ν, cm^{-1}: 2924, 2855, 1643, 1565, 1342, 1154, 844. ^1H NMR spectrum, δ, ppm (*J*, Hz): 1.34 (6H, s, $2CH_3$); 1.82 (2H, t, *J* = 6.8, CH_2); 2.75 (2H, t, *J* = 6.8, CH_2); 6.38 (1H, d, *J* = 8.5, H-7); 7.75–7.78 (2H, m, H Ar, β-CH); 7.86 (1H, d, *J* = 8.5, H-8); 7.99–8.13 (3H, m, H Ar, α-CH); 8.25 (1H, s, H Ar); 13.0 (1H, s, OH). ^{13}C NMR spectrum, δ, ppm: 16.1; 26.9; 32.3; 76.5; 109.3; 111.7; 114.6; 118.7; 122.5; 123.6; 129.4; 130.1; 135.3; 137.7; 141.2; 147.8; 161.0; 164.2; 192.4. Mass spectrum, *m*/*z* (I_{rel}, %): 354 $[M+H]^+$ (100). Found, %: C 67.90; H 5.38. $C_{20}H_{19}NO_5$. Calculated, %: C 67.98; H 5.42.

(*E*)-3-[4-(Dimethylamino)phenyl]-1-(5-hydroxy-2,2-dimethylchroman-6-yl)prop-2-en-1-one (6i). Yield 98%, pale-yellow solid, mp 135–136°C (mp 136–137°C[31]). IR spectrum, ν, cm^{-1}: 2912, 2853, 1609, 1555, 1364, 1228, 1109, 791. ^1H NMR spectrum, δ, ppm (*J*, Hz): 1.36 (6H, s, $2CH_3$); 1.84 (2H, t, *J* = 6.8, CH_2); 2.78 (2H, t, *J* = 6.8, CH_2); 3.06 (6H, s, $N(CH_3)_2$); 6.42 (1H, d, *J* = 8.8, H-7); 6.61–6.64 (2H, m, H Ar); 7.56–7.60 (3H, m, H Ar, α-CH); 7.64 (1H, d, *J* = 8.6, H-8); 7.84 (1H, d, *J* = 15.8, β-CH). 13.0 (1H, s, OH). ^{13}C NMR spectrum, δ, ppm: 16.4; 26.7; 31.9; 40.1; 75.6; 108.8; 109.2; 111.8; 113.0; 114.9; 122.7; 128.2; 130.4; 144.8; 152.0; 160.2; 163.9; 191.9. Mass spectrum, *m*/*z* (I_{rel}, %): 352 $[M+H]^+$ (100). Found, %: C 75.25; H 7.20. $C_{22}H_{25}NO_3$. Calculated, %: C 75.19; H 7.17.

Synthesis of pyrazolines 5a–i and 7a–i (General method). Conventional method. Sodium acetate (0.08 g, 1.0 mmol) and hydrazine hydrate (0.03 g, 1.0 mmol) were added to a solution of an appropriate chalcone **4a–i**, **6a–i** (1.0 mmol) in DMF (5 ml), and the reaction mixture was heated at 80–90°C for 4–8 h. The progress of the reaction was monitored by TLC (hexane–AcOEt, 4:1). After the completion of the reaction, ice water was added. The separated solid product was filtered off, washed with water, dried, and recrystallized from the mixture $CHCl_3$–MeOH, 1:1.

Microwave method. A mixture of an appropriate chalcone **4a–i**, **6a–i** (1.0 mmol), hydrazine hydrate (0.03 g, 1.0 mmol), and sodium acetate (0.08 g, 1.0 mmol) in DMF (5 ml) was taken in a quartz tube (10 ml) and inserted into a screw-capped Teflon vial and then subjected to microwave irradiation for 2–5 min using an irradiation power of 180 W (90°C). The progress of the reaction was monitored by TLC for every 30 s. After completion of the reaction, ice water was added. The separated solid product was filtered off, washed with water, dried, and recrystallized from mixture $CHCl_3$–MeOH, 1:1.

2,2-Dimethyl-6-(5-phenyl-4,5-dihydro-1*H*-pyrazol-3-yl)-chroman-7-ol (5a). Pale-yellow solid, mp 120–122° C. IR spectrum, ν, cm^{-1}: 3422, 2927, 1632, 1493, 1294, 1118, 822, 700. ^1H NMR spectrum, δ, ppm (*J*, Hz): 1.33 (3H, s, CH_3); 1.35 (3H, s, CH_3); 1.78 (2H, t, *J* = 6.7, CH_2); 2.68 (2H, t, *J* = 6.7, CH_2); 3.10 (1H, dd, J_{AB} = 16.4, J_{AX} = 8.8, $C\underline{H}_AH_B$); 3.51 (1H, dd, J_{BA} = 16.4, J_{BX} = 10.8, $CH_A\underline{H}_B$); 4.83 (1H, dd, J_{XA} = 8.8, J_{XB} = 10.8, CH_X); 6.42 (1H, s, H-5); 6.83 (1H, s, H-8); 7.30–7.35 (5H, m, H Ar). ^{13}C NMR spectrum, δ, ppm: 21.8; 26.9; 33.0; 41.7; 61.9; 74.8; 104.8; 109.8; 112.0; 114.3; 126.5; 127.5; 128.5; 134.5; 156.0; 157.6; 159.3. Mass spectrum, *m*/*z* (I_{rel}, %): 323 $[M+H]^+$ (100). Found, %: C 74.45; H 6.83; N 8.64. $C_{20}H_{22}N_2O_2$. Calculated, %: C 74.51; H 6.88; N 8.69.

2,2-Dimethyl-6-[5-(4-methylphenyl)-4,5-dihydro-1*H*-pyrazol-3-yl]chroman-7-ol (5b). White solid, mp 125–129°C. IR spectrum, ν, cm^{-1}: 3342, 2937, 1634, 1509, 1260, 1151, 751. ^1H NMR spectrum, δ, ppm (*J*, Hz): 1.34 (6H, s, $2CH_3$); 1.80 (2H, t, *J* = 6.8, CH_2); 2.39 (3H, s, CH_3); 2.73 (2H, t, *J* = 6.8, CH_2); 3.10 (1H, dd, J_{AB} = 16.4, J_{AX} = 8.8, $C\underline{H}_AH_B$); 3.51 (1H, dd, J_{BA} = 16.4, J_{BX} = 10.8, $CH_A\underline{H}_B$); 4.83 (1H, dd, J_{XA} = 8.8, J_{XB} = 10.8, CH_X); 6.40 (1H, s, H-5); 6.79 (2H, d, *J* = 8.5, H Ar); 6.94 (1H, s, H-8); 7.23–7.24 (2H, m, H Ar); 11.40 (1H, s, OH). ^{13}C NMR spectrum, δ, ppm: 21.8; 22.3; 26.9; 33.0; 41.7; 61.9; 74.8; 104.6; 109.4; 112.0; 114.3; 127.5; 128.5; 134.5; 152.6;

156.1; 157.6; 159.3. Mass spectrum, *m/z* (I_{rel}, %): 337 $[M+H]^+$ (100). Found, %: C 74.85; H 7.15; N 8.30. $C_{21}H_{24}N_2O_2$. Calculated, %: C 74.97; H 7.19; N 8.33.

6-[5-(4-Methoxyphenyl)-4,5-dihydro-1*H*-pyrazol-3-yl]-2,2-dimethylchroman-7-ol (5c). White solid, mp 140–142°C. IR spectrum, ν, cm^{-1}: 3340, 2936, 1636, 1509, 1250, 1151, 827, 747. ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 1.33 (6H, s, $2CH_3$); 1.79 (2H, t, *J* = 6.8, CH_2); 2.69 (2H, t, *J* = 6.8, CH_2); 3.75 (1H, dd, J_{AB} = 16.4, J_{AX} = 8.8, $C\underline{H}_AH_B$); 3.46 (1H, dd, J_{BA} = 16.4, J_{BX} = 10.8, $CH_A\underline{H}_B$); 3.80 (3H, s, OCH_3); 4.78 (1H, dd, J_{XA} = 8.8, J_{XB} = 10.8, CH_X); 5.75 (1H, br. s, NH); 6.42 (1H, s, H-5); 6.85 (2H, d, *J* = 7.9, H Ar); 6.88 (1H, s, H-8); 7.27 (2H, d, *J* = 8.1, H Ar); 11.00 (1H, br. s, OH). ^{13}C NMR spectrum, δ, ppm: 21.7; 26.8; 32.9; 41.7; 55.3; 61.8; 74.7; 104.3; 109.8; 111.9; 114.2; 127.4; 128.4; 134.4; 154.5; 156.1; 157.5; 159.3. Mass spectrum, *m/z* (I_{rel}, %): 353 $[M+H]^+$ (100). Found, %: C 71.52; H 6.84; N 7.92. $C_{21}H_{24}N_2O_3$. Calculated, %: C 71.57; H 6.86; N 7.95.

2,2-Dimethyl-6-[5-(3,4,5-trimethoxyphenyl)-4,5-dihydro-1*H*-pyrazol-3-yl]chroman-7-ol (5d). Yellow solid, mp 155–157°C. IR spectrum, ν, cm^{-1}: 3457, 2943, 1656, 1596, 1534, 1439, 1116, 846. ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 1.50 (6H, s, $2CH_3$); 1.95 (2H, t, *J* = 6.8, CH_2); 2.85 (2H, t, *J* = 6.8, CH_2); 3.22 (1H, dd, J_{AB} = 16.4, J_{AX} = 8.8, $C\underline{H}_AH_B$); 3.68 (1H, dd, J_{BA} = 16.4, J_{BX} = 10.8, $CH_A\underline{H}_B$); 3.89 (3H, s, OCH_3); 4.02 (6H, s, $2OCH_3$); 4.95 (1H, dd, J_{XA} = 8.8, J_{XB} = 10.8, CH_X); 6.59 (1H, s, H-5); 6.78 (1H, s, H-8); 7.00 (1H, s, H Ar); 7.43 (1H, s, H Ar). ^{13}C NMR spectrum, δ, ppm: 21.7; 26.8; 32.9; 42.2; 56.2; 60.8; 62.8; 74.7; 103.2; 104.3; 109.6; 112.0; 128.4; 137.8; 150.4; 153.5; 156.1; 157.5; 159.4. Mass spectrum, *m/z* (I_{rel}, %): 413 $[M+H]^+$ (100). Found, %: C 66.91; H 6.80; N 6.75. $C_{23}H_{28}N_2O_5$. Calculated, %: C 66.97; H 6.84; N 6.79.

6-[5-(4-Chlorophenyl)-4,5-dihydro-1*H*-pyrazol-3-yl]-2,2-dimethylchroman-7-ol (5e). White solid, mp 160–162°C. IR spectrum, ν, cm^{-1}: 3344, 2947, 1630, 1496, 1275, 1170, 1045, 815. ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 1.34 (6H, s, $2CH_3$); 1.79 (2H, t, *J* = 6.8, CH_2); 2.69 (2H, t, *J* = 6.8, CH_2); 3.04 (1H, dd, J_{AB} = 16.4, J_{AX} = 8.8, $C\underline{H}_AH_B$); 3.52 (1H, dd, J_{BA} = 16.4, J_{BX} = 10.8, $CH_A\underline{H}_B$); 4.81 (1H, dd, J_{XA} = 8.8, J_{XB} = 10.8, 1-CH_X); 5.86 (1H, br. s, NH); 6.43 (1H, s, H-5); 6.83 (1H, s, H-8); 7.31–7.33 (4H, m, H Ar); 10.80 (1H, br. s, OH). ^{13}C NMR spectrum, δ, ppm: 21.8; 26.9; 27.1; 32.8; 41.5; 74.8; 104.5; 109.6; 112.0; 114.3; 127.8; 128.3; 129.2; 133.6; 153.4; 156.1; 159.2. Mass spectrum, *m/z* (I_{rel}, %): 357 $[M+H]^+$ (100). Found, %: C 67.30; H 5.90; N 7.83. $C_{20}H_{21}ClN_2O_2$. Calculated, %: C 67.32; H, 5.93; N 7.85.

6-[5-(3,4-Dichlorophenyl)-4,5-dihydro-1*H*-pyrazol-3-yl]-2,2-dimethylchroman-7-ol (5f). Yield 86%, yellow solid, mp 142–145°C. IR spectrum, ν, cm^{-1}: 3346, 2934, 1636, 1596, 1485, 1285, 1175, 845. ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 1.34 (6H, s, $2CH_3$); 1.80 (2H, t, *J* = 6.8, CH_2); 2.73 (2H, t, *J* = 6.8, CH_2); 3.02 (1H, dd, J_{AB} = 16.4, J_{AX} = 8.8, $C\underline{H}_AH_B$); 3.52 (1H, dd, J_{BA} = 16.4, J_{BX} = 10.8, $CH_A\underline{H}_B$); 4.78 (1H, dd, J_{XA} = 8.8, J_{XB} = 10.8, CH_X); 6.40 (1H, s, H-5); 6.80 (1H, s, H-8); 7.21 (1H, d, *J* = 7.8, H Ar); 7.40–7.46 (2H, m, H Ar); 11.40 (1H, s, OH). ^{13}C NMR spectrum, δ, ppm: 21.8; 27.0; 33.0; 41.5; 61.9; 74.7; 104.6; 108.9; 112.0; 114.3; 127.5; 128.2; 128.5; 129.4; 130.1; 134.7; 156.0; 156.9; 159.3. Mass spectrum, *m/z* (I_{rel}, %): 392 $[M+H]^+$ (100). Found, %: C 61.30; H 5.13; N 7.15. $C_{20}H_{20}Cl_2N_2O_2$. Calculated, %: C 61.39; H 5.15; N 7.16.

6-[5-(4-Isopropylphenyl)-4,5-dihydro-1*H*-pyrazol-3-yl]-2,2-dimethylchroman-7-ol (5g). Yellow solid, mp 139–142°C. IR spectrum, ν, cm^{-1}: 3346, 2962, 1636, 1512, 1276, 1156, 805. ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 1.25 (6H, d, *J* = 6.6 $(C\underline{H}_3)_2CH$); 1.34 (6H, s, $2CH_3$); 1.80 (2H, t, *J* = 6.8, CH_2); 2.73 (2H, t, *J* = 6.8, CH_2); 2.95–2.97 (1H, m, $(CH_3)_2C\underline{H}$); 3.11 (1H, dd, J_{AB} = 16.4, J_{AX} = 8.8, $C\underline{H}_AH_B$); 3.51 (1H, dd, J_{BA} = 16.4, J_{BX} = 10.8, $CH_A\underline{H}_B$); 4.80 (1H, dd, J_{XA} = 8.8, J_{XB} = 10.8, CH_X); 6.40 (1H, s, H-5); 6.80 (1H, s, H-8); 7.15–7.20 (3H, m, H Ar); 7.28 (1H, s, H Ar); 11.40 (1H, s, OH). ^{13}C NMR spectrum, δ, ppm: 21.7; 23.8; 27.0; 32.9; 33.8; 41.7; 61.9; 74.8; 104.5; 108.6; 112.3; 114.5; 127.3; 128.4; 134.5; 156.1; 156.3; 157.6. Mass spectrum, *m/z* (I_{rel}, %): 365 $[M+H]^+$ (100). Found, %: C 75.72; H 7.72; N 7.64. $C_{23}H_{28}N_2O_2$. Calculated, %: C 75.79; H 7.74; N 7.69.

2,2-Dimethyl-6-[5-(3-nitrophenyl)-4,5-dihydro-1*H*-pyrazol-3-yl]chroman-7-ol (5h). Yellow solid, mp 157–160°C. IR spectrum, ν, cm^{-1}: 3342, 2935, 1645, 1536, 1501, 1350, 1281, 1160, 794. ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 1.34 (6H, s, $2CH_3$); 1.81 (2H, t, *J* = 6.8, CH_2); 2.79 (2H, t, *J* = 6.8, CH_2); 3.05 (1H, dd, J_{AB} = 16.4, J_{AX} = 8.8, $C\underline{H}_AH_B$); 3.62 (1H, dd, J_{BA} = 16.4, J_{BX} = 10.8, $CH_A\underline{H}_B$); 4.97 (1H, dd, J_{XA} = 8.8, J_{XB} = 10.8, CH_X); 6.40 (1H, s, H-5); 6.91 (1H, d, *J* = 8.8, H Ar); 7.53 (1H, t, *J* = 8.8, H Ar); 7.65 (1H, s, H-8); 8.16 (1H, d, *J* = 8.1, H Ar); 8.25 (1H, s, H Ar). ^{13}C NMR spectrum, δ, ppm: 21.8; 26.9; 32.8; 41.7; 61.9; 74.8; 104.5; 112.0; 114.3; 126.4; 127.5; 1280.1; 128.5; 129.8; 130.5; 134.5; 156.1; 157.6; 159.3. Mass spectrum, *m/z* (I_{rel}, %): 368 $[M+H]^+$ (100). Found, %: C 65.30; H, 5.72; N 11.40. $C_{20}H_{21}N_3O_4$. Calculated, %: C 65.38; H 5.76; N 11.44.

6-{5-[4-(Dimethylamino)phenyl]-4,5-dihydro-1*H*-pyrazol-3-yl}-2,2-dimethylchroman-7-ol (5i). Yield 85%, yellow solid, mp 118–120°C. IR spectrum, ν, cm^{-1}: 3344, 2927, 1634, 1521, 1285, 1152, 880, 758. ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 1.33 (6H, s, $2CH_3$); 1.79 (2H, t, *J* = 6.8, CH_2); 2.69 (2H, t, *J* = 6.8, CH_2); 2.94 (6H, s, $2CH_3$); 3.10 (1H, dd, J_{AB} = 16.4, J_{AX} = 8.8, $C\underline{H}_AH_B$); 3.43 (1H, dd, J_{BA} = 16.4, J_{BX} = 10.8, $CH_A\underline{H}_B$); 4.74 (1H, dd, J_{XA} = 8.8, J_{XB} = 10.8, CH_X); 5.85 (1H, br. s, NH); 6.42 (1H, s, H-5); 6.69 (2H, d, *J* = 8.2, H Ar); 6.85 (1H, s, H-8); 7.19 (2H, d, *J* = 8.2, H Ar); 10.90 (1H, s, OH). ^{13}C NMR spectrum, δ, ppm: 21.7; 26.8; 32.9; 40.5; 41.4; 61.9; 74.6; 104.3; 111.9; 112.7; 125.4; 127.8; 128.3; 130.0; 150.3; 154.6; 156.0; 157.5. Mass spectrum, *m/z* (I_{rel}, %): 366 $[M+H]^+$ (100). Found, %: C 72.26; H 7.43; N 11.42. $C_{22}H_{27}N_3O_2$. Calculated, %: C 72.30; H 7.45; N 11.50.

2,2-Dimethyl-6-(5-phenyl-4,5-dihydro-1*H*-pyrazol-3-yl)-chroman-5-ol (7a). White solid, mp 97–100°C. IR spectrum, ν, cm^{-1}: 3335, 2931, 1627, 1595, 1498, 1350, 1275, 1232, 1162, 761. ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 1.34 (6H, s, $2CH_3$); 1.82 (2H, t, *J* = 6.8, CH_2); 2.75 (2H, t, *J* = 6.8, CH_2); 3.12 (1H, dd, J_{AB} = 16.4, J_{AX} = 8.8, $C\underline{H}_AH_B$); 3.52

(1H, dd, J_{BA} = 16.4, J_{BX} = 10.8, $CH_A\underline{H}_B$); 4.82 (1H, dd, J_{XA} = 8.8, J_{XB} = 10.8, CH_X); 5.86 (1H, br. s, NH); 6.36 (1H, d, *J* = 8.5, H-7); 6.94 (1H, d, *J* = 8.8, H-8); 7.29–7.31 (1H, m, H Ar); 7.34–7.35 (4H, m, H Ar); 11.40 (1H, s, OH). ^{13}C NMR spectrum, δ, ppm: 16.9; 26.6; 26.7; 32.2; 41.7; 62.3; 74.6; 108.2; 108.4; 109.1; 125.9; 126.3; 127.9; 128.9; 142.4; 155.0; 156.0; 156.7. Mass spectrum, *m/z* (I_{rel}, %): 323 $[M+H]^+$ (100). Found, %: C 74.45; H 6.83; N 8.64. $C_{20}H_{22}N_2O_2$. Calculated, %: C 74.51; H 6.88; N 8.69.

2,2-Dimethyl-6-[5-(4-methylphenyl)-4,5-dihydro-1*H*-pyrazol-3-yl]chroman-7-ol (7b). Pale-yellow solid, mp 115–117°C. IR spectrum, ν, cm^{-1}: 3327, 2931, 1627, 1503, 1275, 1161, 795. ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 1.33 (3H, s, CH_3); 1.34 (3H, s, CH_3); 1.82 (2H, t, *J* = 6.8, CH_2); 2.33 (3H, s, CH_3); 2.75 (2H, t, *J* = 6.8, CH_2); 3.10 (1H, dd, J_{AB} = 16.4, J_{AX} = 8.8, $C\underline{H}_AH_B$); 3.49 (1H, dd, J_{BA} = 16.4, J_{BX} = 10.8, $CH_A\underline{H}_B$); 4.79 (1H, dd, J_{XA} = 8.8, J_{XB} = 10.8, CH_X); 6.35 (1H, d, *J* = 8.5, H-7); 6.94 (1H, d, *J* = 8.6, H-8); 7.14 (2H, d, *J* = 8.1, H Ar); 7.23 (2H, d, *J* = 8.11, H Ar); 11.40 (1H, br. s, OH). ^{13}C NMR spectrum, δ, ppm: 16.8; 22.4; 26.5; 33.0; 41.7; 61.9; 74.5; 108.2; 108.4; 109.5; 125.5; 127.5; 128.5; 142.5; 155.1; 156.6; 156.9. Mass spectrum, *m/z* (I_{rel}, %): 337 $[M+H]^+$ (100). Found, %: C 74.85; H 7.15; N 8.30. $C_{21}H_{24}N_2O_2$. Calculated, %: C 74.97; H 7.19; N 8.33.

6-[5-(4-Methoxyphenyl)-4,5-dihydro-1*H*-pyrazol-3-yl]-2,2-dimethylchroman-7-ol (7c). Yellow solid, mp 138–140°C. IR spectrum, ν, cm^{-1}: 3133, 2935, 1626, 1597, 1512, 1245, 1164, 811. ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 1.34 (6H, s, $2CH_3$); 1.82 (2H, t, *J* = 6.8, CH_2); 2.75 (2H, t, *J* = 6.8, CH_2); 3.08 (1H, dd, J_{AB} = 16.4, J_{AX} = 8.8, $C\underline{H}_AH_B$); 3.48 (1H, dd, J_{BA} = 16.4, J_{BX} = 10.8, $CH_A\underline{H}_B$); 3.80 (3H, s, OCH_3); 4.78 (1H, dd, J_{XA} = 8.8, J_{XB} = 10.8, CH_X); 6.36 (1H, d, *J* = 8.5, H-7); 6.87 (2H, d, *J* = 8.0, H Ar); 6.94 (1H, d, *J* = 8.8, H-8); 7.25–7.28 (2H, m, H Ar). ^{13}C NMR spectrum, δ, ppm: 16.9; 26.9; 32.2; 41.6; 55.3; 61.8; 74.5; 108.3; 109.1; 125.9; 127.5; 128.6; 129.1; 130.5; 142.1; 155.2; 156.6; 156.8. Mass spectrum, *m/z* (I_{rel}, %): 353 $[M+H]^+$ (100). $C_{21}H_{24}N_2O_3$. Found, %: C 71.52; H 6.84; N 7.92. Calculated, %: C 71.57; H 6.86; N 7.95.

2,2-Dimethyl-6-[5-(3,4,5-trimethoxyphenyl)-4,5-dihydro-1*H*-pyrazol-3-yl]chroman-7-ol (7d). White solid, mp 120–122°C. IR spectrum, ν, cm^{-1}: 3431, 2934, 1665, 1593, 1504, 1419, 1126, 801. ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 1.36 (6H, s, $2CH_3$); 1.85 (2H, t, *J* = 6.8, CH_2); 2.77 (2H, t, *J* = 6.8, CH_2); 3.24 (1H, dd, J_{AB} = 16.4, J_{AX} = 8.8, $C\underline{H}_AH_B$); 3.80 (3H, s, OCH_3); 3.82 (6H, s, $2OCH_3$); 3.87 (1H, dd, J_{BA} = 16.4, J_{BX} = 10.8, $CH_A\underline{H}_B$); 5.46 (1H, dd, J_{XA} = 8.8, J_{XB} = 10.8, CH_X); 6.40–6.42 (3H, m, H Ar, H-7); 6.97 (1H, d, *J* = 8.8, H-8); 10.67 (1H, s, OH). ^{13}C NMR spectrum, δ, ppm: 16.8; 26.6; 26.7; 31.9; 42.9; 56.1; 58.3; 60.7; 75.1; 102.5; 103.3; 109.3; 109.5; 126.8; 137.1; 153.6; 156.7; 157.0; 157.6; 167.7. Mass spectrum, *m/z* (I_{rel}, %): 413 $[M+H]^+$ (100). Found, %: C 66.91; H 6.80; N 6.75. $C_{23}H_{28}N_2O_5$. Calculated, %: C 66.97; H 6.84; N 6.79.

6-[5-(4-Chlorophenyl)-4,5-dihydro-1*H*-pyrazol-3-yl]-2,2-dimethylchroman-7-ol (7e). Yield 86%, yellow solid, mp 170–173°C. IR spectrum, ν, cm^{-1}: 3308, 2932, 1626, 1595, 1272, 1162, 1058, 874. ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 1.34 (6H, s, $2CH_3$); 1.82 (2H, t, *J* = 6.8, CH_2); 2.75 (2H, t, *J* = 6.8, CH_2); 3.04 (1H, dd, J_{AB} = 16.4, J_{AX} = 8.8, $C\underline{H}_AH_B$); 3.52 (1H, dd, J_{BA} = 16.4, J_{BX} = 10.8, $CH_A\underline{H}_B$); 4.80 (1H, dd, J_{XA} = 8.8, J_{XB} = 10.8, CH_X); 5.84 (1H, br. s, NH); 6.36 (1H, d, *J* = 8.53, H-7); 6.93 (1H, d, *J* = 8.78, H-8); 7.28–7.33 (4H, m, H Ar); 11.30 (1H, s, OH). ^{13}C NMR spectrum, δ, ppm: 16.8; 26.8; 33.0; 41.7; 61.9; 74.8; 108.4; 109.7; 126.5; 127.4; 128.1; 128.5; 130.9; 142.2; 153.4; 156.2; 156.6. Mass spectrum, *m/z* (I_{rel}, %): 357 $[M+H]^+$ (100). Found, %: C 67.30; H 5.90; N 7.83. $C_{20}H_{21}ClN_2O_2$. Calculated, %: C 67.32; H 5.93; N 7.85.

6-[5-(3,4-Dichlorophenyl)-4,5-dihydro-1*H*-pyrazol-3-yl]-2,2-dimethylchroman-7-ol (7f). Yield 88%, white solid, mp 125–127°C. IR spectrum, ν, cm^{-1}: 3328, 2925, 1627, 1593, 1471, 1274, 1161, 797. ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 1.34 (3H, s, CH_3); 1.36 (3H, s, CH_3); 1.84 (2H, t, *J* = 6.8, CH_2); 2.75 (2H, t, *J* = 6.8, CH_2); 3.02 (1H, dd, J_{AB} = 16.4, J_{AX} = 8.8, $C\underline{H}_AH_B$); 3.53 (1H, dd, J_{BA} = 16.4, J_{BX} = 10.8, $CH_A\underline{H}_B$); 4.78 (1H, dd, J_{XA} = 8.8, J_{XB} = 10.8, CH_X); 6.36 (1H, d, *J* = 8.8, H-7); 6.91 (1H, d, *J* = 8.8, H-8); 7.21 (1H, d, *J* = 8.7, H Ar); 7.40–7.48 (2H, m, H Ar); 11.20 (1H, s, OH). ^{13}C NMR spectrum, δ, ppm: 16.9; 26.6; 32.1; 42.0; 61.3; 74.7; 107.9; 108.5; 109.2; 124.5; 125.9; 128.5; 130.8; 131.8; 132.9; 142.5; 154.9; 156.2; 156.7. Mass spectrum, *m/z* (I_{rel}, %): 392 $[M+H]^+$ (100). Found, %: C 61.30; H 5.13; N 7.15. $C_{20}H_{20}Cl_2N_2O_2$. Calculated, %: C 61.39; H 5.15; N 7.16.

6-[5-(4-Isopropyphenyl)-4,5-dihydro-1*H*-pyrazol-3-yl]-2,2-dimethylchroman-7-ol (7g). Pale-yellow solid, mp 170–172°C. IR spectrum, ν, cm^{-1}: 3340, 2957, 1630, 1503, 1275, 1161, 795. ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 1.25 (6H, d, *J* = 6.6, $(C\underline{H}_3)_2CH$); 1.34 (3H, s, CH_3); 1.35 (3H, s, CH_3); 1.82 (2H, t, *J* = 6.8, CH_2); 2.75 (2H, t, *J* = 6.8, CH_2); 2.86–2.92 (1H, m, $(CH_3)_2C\underline{H}$); 3.11 (1H, dd, J_{AB} = 16.4, J_{AX} = 8.8, $C\underline{H}_AH_B$); 3.49 (1H, dd, J_{BA} = 16.4, J_{BX} = 10.8, $CH_A\underline{H}_B$); 4.79 (1H, dd, J_{XA} = 8.8, J_{XB} = 10.8, CH_X); 5.81 (1H, br. s, NH); 6.35 (1H, d, *J* = 8.5, H-7); 6.94 (1H, d, *J* = 8.8, H-8); 7.18–7.20 (3H, m, H Ar); 7.27 (1H, s, H Ar); 11.43 (1H, s, OH). ^{13}C NMR spectrum, δ, ppm: 16.9; 23.9; 26.6; 26.7; 29.7; 32.2; 33.8; 41.6; 62.1; 74.8; 108.3; 109.1; 125.9; 126.2; 126.9; 139.7; 148.7; 155.0; 156.0; 156.7. Mass spectrum, *m/z* (I_{rel}, %): 365 $[M+H]^+$ (100). Found, %: C 75.72; H 7.72; N 7.64. $C_{23}H_{28}N_2O_2$. Calculated, %: C 75.79; H 7.74; N 7.69.

2,2-Dimethyl-6-[5-(3-nitrophenyl)-4,5-dihydro-1*H*-pyrazol-3-yl]-chroman-7-ol (7h). Orange solid, mp 120–122°C. IR spectrum, ν, cm^{-1}: 3328, 2927, 1626, 1531, 1496, 1348, 1273, 1160, 802. ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 1.34 (3H, s, CH_3); 1.36 (3H, s, CH_3); 1.82 (2H, t, *J* = 6.8, CH_2); 2.75 (2H, t, *J* = 6.8, CH_2); 3.05 (1H, dd, J_{AB} = 16.4, J_{AX} = 8.8, $C\underline{H}_AH_B$); 3.62 (1H, dd, J_{BA} = 16.4, J_{BX} = 10.8, $CH_A\underline{H}_B$); 4.97 (1H, dd, J_{XA} = 8.8, J_{XB} = 10.8, CH_X); 6.36 (1H, d, *J* = 8.5, H-7); 6.91 (1H, d, *J* = 7.1, H Ar); 7.54 (1H, t, *J* = 8.8, H Ar); 7.75 (1H, d, *J* = 8.8, H-8); 8.16 (1H, d, *J* = 7.1, H Ar); 8.26 (1H, s, H Ar). ^{13}C NMR spectrum, δ, ppm: 16.9; 26.6; 26.7; 29.6; 32.1; 42.2; 61.6; 74.6; 107.8; 108.5; 109.2; 121.7; 122.8; 125.9; 129.9; 132.5; 144.3; 154.9; 156.3; 156.7. Mass spectrum, *m/z* (I_{rel}, %): 368 $[M+H]^+$ (100). Found, %: C 65.30; H 5.72; N 11.40. $C_{20}H_{21}N_3O_4$. Calculated, %: C 65.38; H 5.76; N 11.44.

6-{5-[4-(Dimethylamino)phenyl]-4,5-dihydro-1*H*-pyrazol-3-yl}-2,2-dimethylchroman-7-ol (7i). Yellow solid, mp 140–143°C. IR spectrum, ν, cm^{-1}: 3318, 2927, 1622, 1523, 1351, 1275, 1163, 795. ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 1.34 (6H, s, $2CH_3$); 1.82 (2H, t, *J* = 6.8, CH_2); 2.75 (2H, t, *J* = 6.8, CH_2); 2.93 (6H, s, $N(CH_3)_2$); 3.10 (1H, dd, J_{AB} = 16.4, J_{AX} = 8.8, CH_AH_B); 3.44 (1H, dd, J_{BA} = 16.4, J_{BX} = 10.8, CH_AH_B); 4.59 (1H, dd, J_{XA} = 8.8, J_{XB} = 10.8, CH_X); 5.83 (1H, br. s, NH); 6.35 (1H, d, *J* = 8.5, H-7); 6.68 (2H, d, *J* = 8.1, H Ar); 6.95 (1H, d, *J* = 8.8, H-8); 7.20 (2H, d, *J* = 8.1, H Ar); 11.44 (1H, s, OH). ^{13}C NMR spectrum, δ, ppm: 16.9; 26.6; 26.7; 30.9; 32.2; 40.6; 41.4; 61.9; 74.5; 108.3; 108.5; 109.0; 112.8; 125.9; 127.1; 150.3; 155.2; 155.9; 156.7. Mass spectrum, *m*/*z* (I_{rel}, %): 366 $[M+H]^+$ (100). Found, %: C 72.25; H 7.48; N 11.45. $C_{22}H_{27}N_3O_2$. Calculated, %: C 72.30; H 7.45; N 11.50.

Antibacterial activity investigation. The test solutions of the samples were prepared in dimethyl formamide. The commercial drug streptomycin, used as standard, was dissolved in sterile distilled water. The microorganisms employed in this study were two Gram-positive bacteria such as *Bacillus subtilis* (MTCC 441), *Staphylococcus aureus* (MTCC 737), and two Gram-negative bacteria such as *Pseudomonas aeruginosa* (MTCC 741), *Escherichia coli* (MTCC 443). Nutrient broth (pH 7.2) was used for the preparation of inoculum of bacteria. Nutrient agar medium used for the antibacterial screening contained 20.0 g of agar in addition to the composition of nutrient broth. The agar medium was sterilized by autoclaving at 120°C for 15 min. The Petri dishes and pipettes were sterilized by dry heat in a hot-air oven at 150°C for 1 h. The molten agar medium (about 20 ml) was poured in each of sterilized Petri dishes and 24 h old broth cultures (0.5 ml each) of bacterial strains were added to the respective Petri dishes. The contents of the Petri dishes were mixed thoroughly by rotary motion. After solidification of the medium, four cups (diameter 8 mm) were made with the help of a sterile borer at equal distances. Accurately measured test samples (200 μg/ml, 0.1 ml) and standard antibiotics (200 μg/ml, 0.1 ml) were added into the cups and labelled accordingly. The dishes were kept undisturbed in a cool place for 1 h to allow the solutions to diffuse into the medium. The nutrient agar dishes were then incubated at 37°C for 24 h. . The presence of a definite zone of inhibition surrounding the cups indicated antibacterial activity. The diameter of the zone of inhibition[31] was recorded. The experiments were performed at least in triplicate.

Antifungal activity investigation. The test solutions of the samples were prepared in dimethyl formamide. The commercial drug nystatin, used as standard, was dissolved in buffered 70% propanol. The fungal strains employed in this study were *Aspergillus niger* (ATCC 9029), *Candida albicans* (ATCC 2091), and *Aspergillus foetidus* (NCIM 505). For antifungal screening, inoculum was prepared by transferring a loopful of fungal stock culture to a 100-ml conical flask containing Sabouraud's broth (50 ml). The composition of the broth was glucose (40 g), peptone (10 g), distilled water (1000 ml). Sabouraud's agar medium used for the antifungal screening contained 20.0 g of agar in addition to the composition of Sabouraud's broth. The corning sterile Petri dishes were used for investigation. The molten Sabouraud's agar medium (about 20 ml) was poured in each of the sterilized Petri dishes and 24 h old broth cultures of fungal strains (0.5 ml each) was added to the respective Petri dishes. The contents of the Petri dishes were mixed thoroughly by rotary motion. After solidification of the medium, four cups (diameter 8 mm) were made with the help of a sterile borer at equal distances. the Sabouraud's agar dishes were incubated at 28°C for 48 h. The presence of a definite zone of inhibition surrounding the cups indicated antifungal activity. The diameter of the zone of inhibition[31] was recorded. The experiments were performed at least in triplicate.

Supporting material to this article containing of ^{1}H NMR, ^{13}C NMR, and mass spectra of the synthesized compounds is available online at http://link.springer.com/journal/10593.

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