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Synthesis and antimicrobial screening of novel 2-(5-(4-(allyloxy)-3-methoxyphenyl)-1*H*-pyrazol-3-yl)phenols analogues of 2-(4-(allyloxy)-3-methoxyphenyl)-4*H*-chromen-4-ones

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Abstract: A series of novel 2-(5-(4-(allyloxy)-3-methoxyphenyl)-1*H*-pyrazol-3-yl)phenols derivatives have been synthesized *via* the ring opening of 2-(4-(allyloxy)-3-methoxyphenyl)-4*H*-chromen-4-ones in ethanol and hydrazine hydrate under reflux condition. The synthesized compounds were screened for antibacterial and antifungal activity against bacteria *Staphylococcus aureus* (MRSA E710) and *Escherichia coli* (ATCC 25922) and fungi *Candida albicans* and *Aspergillus fumigates* respectively. Some of the tested compounds showed significant antimicrobial activity. ^{1}H NMR, IR, Mass spectral data and elemental analysis elucidated the structures of the all newly synthesized compounds.

Keywords: Pyrazoles; chromones; chalcones; antimicrobial activity.

1. Introduction

Compounds incorporating heterocyclic ring systems continue to attract considerable interest due to the wide range of biological activities. Amongst them five member heterocyclic compounds particularly azoles occupy a unique place in the realm of natural and synthetic organic chemistry. Antibacterial and antifungal activities of the azoles are most widely studied and some of them are in clinical practice as antimicrobial agents. However, the azole resistant strains led to develop a new antimicrobial compounds. In particular pyrazole derivatives are extensively studied and used as antimicrobial agents.[1–21] Pyrazole is an important class of heterocyclic compound and many pyrazole derivatives are reported to have the broad spectrum of biological activities, such as anti-inflammatory,[22,23] antifungal,[24] herbicidal,[25,26] antitumor, cytotoxic, molecular modelling,[27–29] and antiviral[30,31] activities. Pyrazole derivatives also acting as antiangiogenic agents,[32] A3 adenosine receptor antagonists,[33] neuropeptide YY5 receptor antagonists,[34] kinase inhibitor for treatment of type 2 diabetes, hyperlipidemia, obesity,[35] and thrombopiotinmimetics.[36] George Mihai Nitulescu *et al.* [37]

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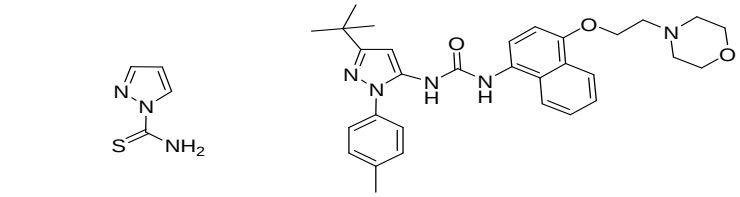
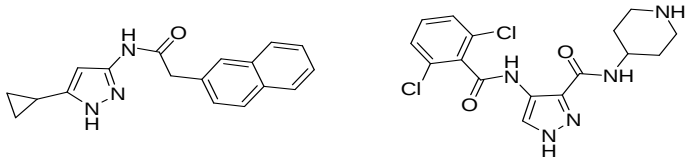
designed and synthesized some chimeric thiourea-pyrazole derivatives. **Fig. 1** shows relevant antitumor pyrazole derivatives.



1-thyocabamoylpyrazole

AT9283
Aurora kinases inhibitor



PNU 292137
CDK2/ cyclin A inhibitor

AT 7519
CDK inhibitor

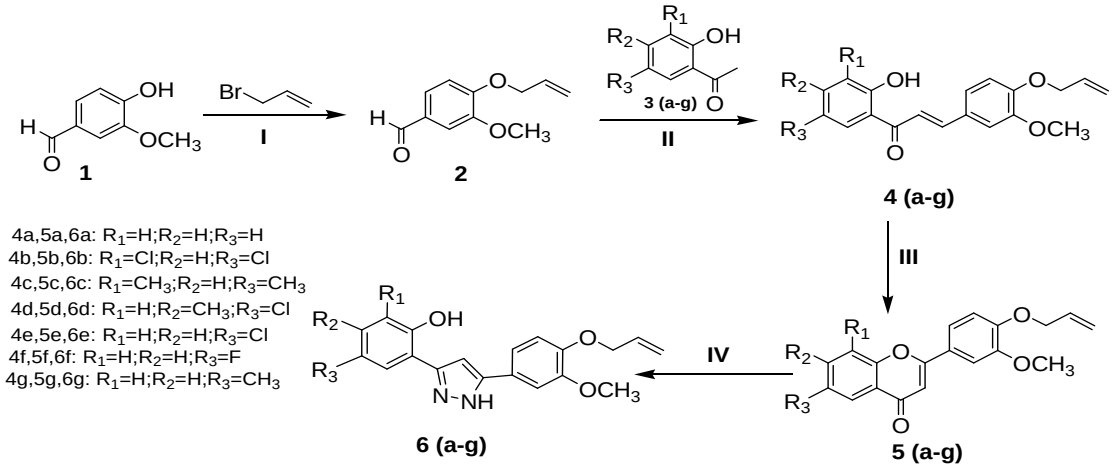
Figure 1. Structure of antitumor pyrazoles as rational compounds design template

Much attention was paid to pyrazole as a potential antimicrobial agent after the discovery of the natural pyrazole C-glycoside, pyrazofurin which demonstrated a broad spectrum of antimicrobial activity.[38] Herein, in continuation to our research work on pyrazole.[39-41] So, we report the synthesis of novel pyrazole derivatives and their microbial activities.

2. Results and discussion

2.1. Chemistry

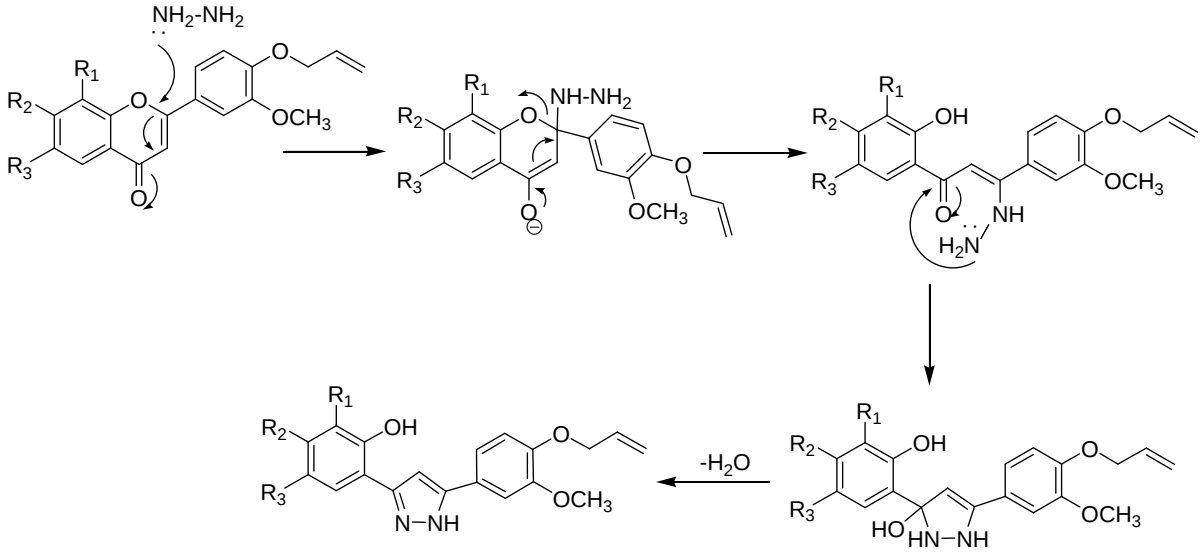
The synthetic route for the preparation of **6(a-g)** analogues of **5(a-g)** are shown in **Scheme 1**. Allyl bromide was treated with 4-hydroxy-3-methoxybenzaldehyde **(1)** in DMF and K_2CO_3 at 65°C under ultrasonication to yield **(2)**. The 4-(allyloxy)-3-methoxybenzaldehyde **(2)** was subjected to a base catalysed Claisen-Schmidt condensation reaction[42] with appropriate *o*-hydroxy acetophenones **3(a-g)** generating **4(a-g). 5(a-g)** were prepared by the oxidative cyclization of corresponding **4(a-g)** in dimethyl sulphoxide and catalytic a amount of iodine at 120°C. The compounds **5(a-g),** on treatment with hydrazine hydrate in ethanol and under reflux condition yielded **6(a-g)**.



Scheme 1. Reagents and Conditions: (I) K_2CO_3/DMF, under ultrasonication 65°C; (II) Etha nol/KOH at room temperature; (III) DMSO/I_2, reflux 120°C; (IV) Hydrazine hydrate in Ethanol under reflux condition.

2.2. Spectral analysis

Analytical and spectral data (^{1}H NMR, IR, Mass and elemental analysis) of the newly synthesized compounds were in full agreement with the proposed structures. The structure of **4d** is interpreted from spectroscopic data. Its IR spectrum showed a characteristic absorption band at 3427 cm^{-1} due to -OH stretching and 1654 due to C=O. Its ^{1}H NMR spectrum exhibited the presence of olefinic protons as a doublet at δ = 7.41 and 7.90 regions with a mutual coupling constant value (*J* = 15.32 & 16.16 Hz) due to trans coupling of olefinic protons i.e H-3 (alpha) and H-2 (beta). These observed coupling constant values indicate the presence of the *E*,*E*'-configuration form the structure, the CH_3 and OCH_3 show the singlet at 2.37 and 3.91 ppm and the remaining aromatic protons appear at their respective positions. The phenolic -OH is highly deshielded and appears at δ = 12.58 ppm. The mass spectrum of **4a** showed (M+1) peak at 359.2 and (M+3) at 361.2. IR spectrum of compound **5a** did not reveal any absorption of the –OH group due to ring cyclization and also showed a characteristic absorption band at 1669 cm^{-1} respectively due to C=O stretching. The ^{1}H NMR spectrum of **5a** revealed the characteristic CH proton of the chromone ring appearing at δ = 7.26 ppm as a singlet and the rest of the aromatic protons appear at their respective position. The mass spectrum of **5a** showed (M+1) peak at 309.7. The IR spectrum of **6d** showed a characteristic absorption band at 3282 cm^{-1} due to -OH stretching and the band at 3072 cm^{-1} and 1525 cm^{-1} corresponds to the -NH and C=N stretching. Its ^{1}H NMR spectrum exhibited two singlets at δ = 2.41 & 3.94 ppm characteristic to one CH_3 proton and one OCH_3 respectively and in turn the pyrazol proton singlet at δ = 7.02 and -NH proton of the pyrazol was found at δ = 12.58 ppm as a broad band and also showed one singlet at δ = 11.03 ppm of –OH due to ring opening of chromone. The mass spectrum of **6d** showed (M+1) peak at 371.2 and (M+3) at 373.2.



Scheme 2. Proposed mechanism for the construction of the pyrazole.

Table 1. Physical data of the compounds **4(a-g), 5(a-g)** and **6(a-g)**

Comp. No.	R_1	R_2	R_3	M. P. (^oC)	Yield (%)
4a	H	H	H	72-74	78
4b	Cl	H	Cl	89-91	80
4c	CH_3	H	CH_3	97-99	81
4d	H	CH_3	Cl	68-70	83
4e	H	H	Cl	84-86	82
4f	H	H	F	82-84	78
4g	H	H	CH_3	115-117	76
5a	H	H	H	95-97	76
5b	Cl	H	Cl	104-107	69
5c	CH_3	H	CH_3	106-108	74
5d	H	CH_3	Cl	189-190	72
5e	H	H	Cl	102-105	67
5f	H	H	F	115-117	73
5g	H	H	CH_3	110-112	74
6a	H	H	H	98-100	89
6b	Cl	H	Cl	140-143	88
6c	CH_3	H	CH_3	130-132	86
6d	H	CH_3	Cl	138-140	89
6e	H	H	Cl	108-112	88
6f	H	H	F	110-113	86
6g	H	H	CH_3	116-118	85

2.3. Antimicrobial activity

The standardized agar well diffusion method [43-48] was followed to determine the activity of the synthesized compounds against the sensitive organisms *Staphylococcus aureus* (MRSA E710) and *Escherichia coli* (ATCC 25922) as a gram positive bacteria, and two species of fungi, *Candida albicans* and *Aspergillus fumigates*. The *Amphotericin B* was used as reference in the case of antibacterial, while *Vancomycin* was used in the case of antifungal reference. The methanol was used as solvent control. The culture strains of bacteria were maintained on nutrient agar slant at 37^{o}C for 24h. The wells of 6 diameters were filled with 0.1 mL of solution at fixed concentration 20 ug/mL separately for each bacterial strain. All the plates were incubated at 37^{o}C for 24h. The zone of inhibition of compounds was measured using mm scale. Antimicrobial activity was determined by measuring the diameter of inhibition zone. Activity of each compound was compared with *Amphotericin B* (for antibacterial) and *Vancomycin* (for antifungal) as standards. The observed data of antimicrobial activity of compounds and the standard drugs is given in **Table 2**. Among all the compounds screened **5a, 5c, 5e, 6c, 6d** and **6e** showed highest antibacterial activity and **5a, 5b, 5c, 5f, 6b, 6e** and **6f** against antifungal activity was found to be comparable with that of standard drug tested. Although with respect to standard drugs, all the tested compounds were found to moderate activity, so result of all preliminary study indicated that the substituted 2-(4-(allyloxy)-3-methoxyphenyl)-4*H*-chromen-4-one and 2-(5-(4-(allyloxy)-3-methoxyphenyl)-1*H*-pyrazol-3-yl)phenol moiety represent a new class of pharmacophore for broad spectrum antibacterial and antifungal activity.

Table 2. Antimicrobial activity of compounds **5(a-g)** and **6(a-g)**

Compd. No	Conc. (µg/mL)	Antibacterial activity		Antifungal Activity	
		S. aureus (MRSA E710) [a]	*E. coli* (ATCC 25922) [a]	*C. albicans*[a]	*A. fumigates*[a]
5a	**200**	16	33	27	40
	100	10	25	16	26
5b	**200**	25	26	30	48
	100	15	16	14	32
5c	**200**	27	39	30	36
	100	13	26	19	26
5d	**200**	21	34	22	41
	100	14	23	17	30
5e	**200**	23	36	19	30
	100	12	24	13	20
5f	**200**	18	29	31	42
	100	19	28	26	25
5g	**200**	15	27	22	30
	100	11	17	10	20
6a	**200**	18	26	19	31
	100	8	20	11	23
6b	**200**	13	20	27	42
	100	8	10	18	26
6c	**200**	22	33	14	23
	100	14	21	9	16
6d	**200**	30	36	22	37
	100	19	25	12	26
6e	**200**	37	40	26	33
	100	11	19	15	23
6f	**200**	17	28	29	28
	100	12	13	18	19
6g	**200**	14	27	23	29
	100	7	13	12	15
Vancomycin	**20 µg/mL**	**NA**	**NA**	**15**	**19**
Amphotericin B	**20 µg/mL**	**20**	**21**	**NA**	**NA**

[a]Zone of inhibition

3. Conclusion

In summary, we have synthesized the series of vanillin incorporated novel 2-(5-(4-(allyloxy)-3-methoxyphenyl)-1*H*-pyrazol-3-yl)phenols analogues of 2-(4-(allyloxy)-3-methoxyphenyl)-4*H*-chromen-4-ones derivatives and their antimicrobial activities have been evaulated. All the compounds demostrated potent inhibition against all the tested strains. The importance of such work lies in the possibility that the new compounds might be more efficacious drugs against bacteria and fungi, which could be helpful in designing more potent antibacterial and antifungal agent for therapeutic use.

4. Experimental

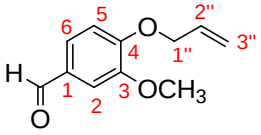
The melting points of all synthesized compounds were determined in open capillary tubes and are uncorrected. The purity of all compounds was checked by TLC. IR spectra were recorded on Jasco FT-IR-4100, Japan, in KBr disc, ^{1}H NMR spectra were recorded on a Varian As 400 MHz spectrometer in $CDCl_3$/DMSO-d_6; chemical shifts (δ) are in ppm relative to TMS and coupling

constant (*J*) are expressed in hertz (Hz). Mass spectra were recorded on a Macro mass spectrometer (Water) by electro-spray method (ES). Elemental analysis was performed on Perkin-Elmer EAL-240 elemental analyzer.

General procedure for the Synthesis of 4-(allyloxy)-3-methoxybenzaldehyde (2)

In a clean and dry RBf (1.0 g, 0.006 mmole) of 4-hydroxy-3-methoxybenzaldehyde was dissolved in 5 mL of DMF to this reaction mixture (0.99 g, 0.0072 mmole) of K_2CO_3 was added. The resultant reaction mixture was irradiated under ultrasonication at 65 °C for 5-10 min. followed by addition of (0.798 g, 0.0066 mmole) of allyl bromide and continue the reaction for 46 min under ultrasonication. After the completion of reaction, monitored by TLC. The reaction mass was poured over ice-cold water and extracted with ethyl acetate and washed with sodium sulphate, a liquid compound of 4-(allyloxy)-3-methoxybenzaldehyde **(2)** was obtained in 92% yield. The obtained liquid was directly used for next reaction without any purification. Purity of sample was checked by spectral data.

4-Allyloxy-3-methoxybenzaldehyde:

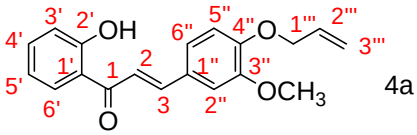


^{1}H NMR (400 MHz, $CDCl_3$): δ 3.86 (s, 3H, OCH_3), 4.70 (dt, *J* = 5.6 Hz, 2H, H-1’’), 5.38 (m, *J* = 1.4 & 10.2 Hz, 1H, H-3’’(cis)),5.41 (m, *J* = 1.2 & 15.5 Hz, 1H, H-3’’(trans)), 6.06 (m, 1H, H-2’’), 6.96 (d, *J* = 8.4 Hz, 1H, H-2), 7.43 (AB system, 2H, H-5 & H-6), 9.87 (s, 1H, CHO); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 69.9 (OCH_2), 72.8 (C-1’’), 114.3 (C-2 and C-5), 115.9 (C-3’’), 119.3 (C-5), 124.3 (C-6), 130.7 (C-1), 131.8 (C-2’’), 146.2 (C-3), 150.7 (C-4), 191.0 (-CHO).

General procedure for the synthesis of (E)-3-(4-(allyloxy)-3-methoxyphenyl)-1-(5-chloro-2-hydroxy-4-methylphenyl)prop-2-en-1-ones 4(a-g)

Alcoholic KOH (0.18 g, 0.0032 mmole) was added to a suspension of 1-(5-chloro-2-hydroxy-4-methylphenyl)ethanone **(3d)** (0.272 g, 0.0016 mmole) and 4-(allyloxy)-3-methoxybenzaldehyde **(2)** (0.3 g, 0.0016 mmole) in 10 mL ethanol. The mixture was stirred at room temperature for overnight. The reaction was monitored by TLC. After the completion of reaction, mixture was poured into crushed ice and acidified with HCl (2M) till pH = 4. The solid product separated out was filtered off and crystallized from ethanol to afford **4(a-g)**. The physical data of the compounds **4(a-g)** were recorded in **Table 1**. Their structures have been confirmed by ^{1}H NMR, Mass and IR spectra.

(E)-3-(4-(allyloxy)-3-methoxyphenyl)-1-(2-hydroxyphenyl)prop-2-en-1-ones (4a):

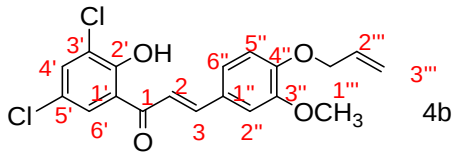


4a

^{1}H NMR (400 MHz $CDCl_3$): δ = 3.75 (s, 3H, OCH_3), 4.64 (dt, *J* = 2.0 & 5.3 Hz, 2H, 2x H-1’’’), 5.25 (dd, *J* = 1.5 Hz & *J* = 10.0 Hz, 1H, H-3’’’(cis)), 5.27 (dd, *J* = 1.5 Hz & *J* = 15.5 Hz, 1H, H-3’’’(trans)), 5.90 (m, 1H, H-2’’’), 6.67-6.81 (m, 3H, Ar-H), 6.94-7.67 (m, 4H, Ar-H) , 7.52 (d, *J* = 16.10 Hz, H-2), 7.89 (d, *J* = 15.15 Hz, H-3), 12.14 (s, 1H, OH); IR (KBr): ν (cm^{-1}): 3321 (OH), 1695 (C=O), 1295 (CH=CH); MS :*m/z* (%) 311.5 (M+1) (80.0), 305.1 (20.9), 302.1 (10.9); Anal. Calcd for $C_{19}H_{18}O_4$: C, 73.53; H, 5.85. Found C, 73.64; H, 5.91; ^{13}C NMR ($CDCl_3$, 100 MHz): δ 54.8 (OCH_3),

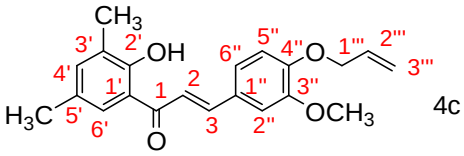
71.9 (C-1’’’), 112.3 (C-2’’), 115.5 (C-5’’), 116.3 (C-3’’’), 118.9 (C-6’’), 122.2 (C-2 & C-5’), 127.9 (C-1’’), 130.5 (C-6’), 135.9 (C-4’), 144.8 (C-3), 148-6 (C-3’’ & C-4’’), 161.3 (C-2’), 190.2 (C-1).

(E)-3-(4-(allyloxy)-3-methoxyphenyl)-1-(3,5-dichloro-2-hydroxyphenyl)prop-2-en-1-one (4b):



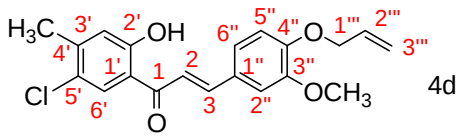
^{1}H NMR (300 MHz, DMSO-d_6) : δ = 3.78 (s, 3H, OCH_3), 4.63 (dt, *J* = 1.5 & 5.2 Hz, 2H, 2x H-1’’’), 5.27 (dd, *J* = 2.0 Hz & *J* = 10.5 Hz, 1H, H-3’’’(cis)),), 5.28 (dd, *J* = 1.5 Hz & *J* = 15.3 Hz, 1H, H-3’’’(trans)), 5.92 (m, 1H, H-2’’’), 7.54 (d, *J* = 15.00 Hz, H-2), 6.66-6.85 (m, Ar-H), 7.40 (d, 1H, Ar-H), 7.56 (d, 1H,Ar-H), 7.91 (d, *J* = 16.15 Hz, H-3), 11.78 (s, 1H, OH); IR (KBr): ν (cm^{-1}): 3328 (OH), 1695 (C=O), 1295 (CH=CH); MS: *m/z* (%) 380.4 (M+1) & 382.10 (M+3), 378.0 (66.7), 365.0 (20.9), 281.0 (13.4), 242.0 (12.1), 183.0 (2.3); Anal. Calcd for $C_{19}H_{16}Cl_2O_2$: C, 60.17; H, 4.25. Found C, 60.25; H, 4.31; ^{13}C NMR ($CDCl_3$, 100 MHz): δ 56.2 (OCH_3), 72.3 (C-1’’’), 112.4 (C-2’’), 115.3 (C-5’’), 116.9 (C-3’’’), 119.2 (C-6’’), 124.9 (C-2 & C-5’), 127.5 (C-1’’), 129.2 (C-6’), 137.1 (C-4’), 148.5 (C-3’’ & C-4’’), 159.1 (C-2’), 189.2 (C-1).

(E)-3-(4-(allyloxy)-3-methoxyphenyl)-1-(2-hydroxy-3,5-dimethylphenyl)prop-2-en-1-one (4c):



^{1}H NMR (300 MHz, DMSO-d_6):δ = 2.36 (s, 3H, CH_3), 2.38 (s, 3H, CH_3), 3.81 (s, 3H, OCH_3), 4.65 (dt, *J* = 1.6 &5.6 Hz, 2H, 2xH-1’’’), 5.29 (dd, *J* = 1.5 Hz & *J* = 10.0 Hz, 1H, H-3’’’(cis)), 5.31 (dd, *J* = 1.5 Hz & *J* = 15.3 Hz, 1H, H-3’’’(trans)), 5.90 (m, 1H, H-2’’’), 7.91 (d, *J* = 16.10 Hz, H-2), 6.77-6.89 (m, 3H, Ar-H), 6.98 (d, 1H, Ar-H), 7.30 (d, 1H,Ar-H), 7.54 (d, *J* = 15.30 Hz, H-3), 12.00 (s, 1H, OH); IR (KBr): ν (cm^{-1}): 3324 (OH), 1695 (C=O), 1295 (CH=CH). MS :*m/z* 339.8 (M+1) 339.8 (100.0), 330 (80), 290 (65), 239.2 (23.1), 214.2 (13.4); Anal. Calcd for $C_{21}H_{22}O_4$: C, 74.54; H, 6.55. Found: C, 74.61; H, 6.51; ^{13}C NMR ($CDCl_3$, 100 MHz): 15.2 (CH_{3a}), 25.3 (CH_{3b}), 56.3 (OCH_3), 72.9 (C-1’’), 113.2 (C-2’’),115.4 (C-5’’), 116.3 (C-3’’’), 119.2 (C-6’’), 120.9 (C-2), 122.2 (C-1’), 125.8 (C-3’), 128.5 (C-1’’ & C-6’), 131.2 (C-5’), 149.0 (C-3’’ & C-4’’), 158.2 (C-2’), 190.2 (C-1).

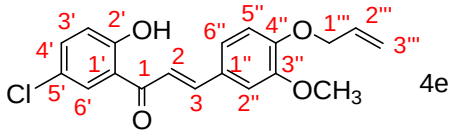
(E)-3-(4-(allyloxy)-3-methoxyphenyl)-1-(5-chloro-2-hydroxy)-4-methylphenyl)prop-2-en-1-one (4d):



^{1}H NMR (400 MHz, $CDCl_3$-d_6) : δ = 2.37 (s, 3H, CH_3), 3.91 (s, 3H, OCH_3), 4.67 (dt, *J* = 1.8 & 5.3 Hz, 2H, 2xH-1’’’), 5.32 (dd, *J* = 1.3 Hz & *J* = 10.3 Hz, 1H, H-3’’’(cis)), 5.41 (dd, *J* = 1.4 Hz & *J* = 17.3 Hz, 1H, H-3’’’(trans)), 6.04 (m, 1H, H-2’’’), 6.91 (s, 1H, Ar-H), 7.18 (s, 1H, Ar-H), 7.41 (d, *J* = 15.32 Hz, H-2), 7.90 (d, *J* = 16.16 Hz, H-3), 6.10-7.86 (m, 3H, Ar-H), 12.58 (s, 1H, -OH). EC-MS: 359.2 (M+1, 54) and 361.2 (M+3, 32), 356.1 (65.1), 352.1 (100.0), 320 (73.1), 261.1 (47.4), 228.1 (11.0). IR (KBr) cm^{-1}: 3427 (OH); 1654 (C=O); 1510 (C=C); 1020 (Ar-Cl). Anal. Calcd for

$C_{14}H_8NO_2$. C, 69.71; H, 3.34; N, 5.81. Found: C, 70.10; H, 2.99; N, 5.53; ^{13}C NMR ($CDCl_3$, 100 MHz): δ 15.8 (CH_3), 55.8 (OCH_3), 71.8 (C-1''), 112.1 (C-2''),114.8 (C-5''), 116.8 (C-3'''), 120.8 (C-6''), 127.3 (C-3'), 143.5 (C-4'), 148.3(C-3'' & C-4''), 159.1 (C-2'), 190.3 (C-1).

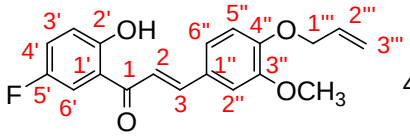
(E)-3-(4-(allyloxy)-3-methoxyphenyl)-1-(5-chloro-2-hydroxyphenyl)prop-2-en-1-one (4e):



4e

^{1}H NMR (300 MHz, $CDCl_3$-d_6) :δ = 3.77 (s, 3H, OCH_3), 4.61 (dt, *J* = 1.5 & 5.1 Hz, 2H, 2xH-1'''), 5.27 (dd, *J* = 1.5 Hz & *J* = 10.0 Hz, 1H, H-3'''(cis)), 5.28 (dd, *J* = 1.5 Hz & *J* = 17.5 Hz, 1H, H-3'''(trans)), 5.92 (m, 1H, H-2'''), 6.43 (d, 1H, H-3') , 6.53-6.95 (m, 4H, Ar-H), 7.53 (d, *J* = 15.30 Hz, H-3), 7.96 (d, 1H, H-6') , 7.98 (d, 1H, *J* = 15.16 Hz, H-2), 11.85 (s, 1H, OH); IR (KBr): ν (cm^{-1}): 1679 (C=O), 1298 (CH=CH), 3327 (OH); MS :*m/z* 344.18 (M+1, 50) & 346.21 (M+3, 36), 332 (72), 315.1 (20.9), 290 (34), 247.1 (7.0), 158(17.4); Anal. Calcd for $C_{19}H_{17}ClO_4$: C, 66.16; H, 4.96; Found C, 66.22; H, 5.02; ^{13}C NMR ($CDCl_3$, 100 MHz): δ 56.3 (OCH_3), 73.2 (C-1'''), 112.3 (C-2''),115.4 (C-5''), 116.8 (C-3'''), 119.2 (C-6''), 121.5 (C-2), 123.8 (C-1'), 127.2 (C-3'), 128.3 (C-1''), 131.5 (C-6'), 133.9 (C-2'''), 135.8 (C-4'), 148.2 (C-3'' & C-4''), 160.3 (C-2'), 189.2 (C-1).

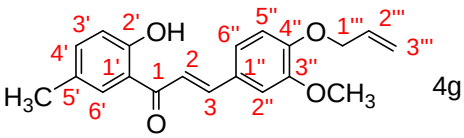
(E)-3-(4-(allyloxy)-3-methoxyphenyl)-1-(5-fluoro-2-hydroxyphenyl)prop-2-en-1-one (4f):



4f

^{1}H NMR (300 MHz, DMSO-d_6):δ = 3.79 (s, 3H, OCH_3), 4.58 (dt, *J* = 1.2 & 5.4 Hz, 2H, 2xH-1'''), 5.20 (dd, *J* = 1.3 Hz & *J* = 8.30 Hz, 1H, H-3'''(cis)), 5.31 (dd, *J* = 1.5 Hz & *J* = 17.0 Hz, 1H, H-3'''(trans)), 5.98 (m, 1H, H-2'''), 7.58 (d, *J* = 15.00 Hz, H-3), 7.03-7.95 (m, 6H, Ar-H), 7.93 (d, 1H, *J* = 15.10 Hz, H-2), 12.05 (s, 1H, OH); IR (KBr): ν (cm^{-1}): 1668 (C=O), 1285 (CH=CH), 3318 (OH); MS :*m/z* 328.11 (M+1, 87), 320.1 (100.9), 302 (68.6), 295 (56), 252 (45.6), 230.1 (12.9), 196 (42); Anal. Calcd for $C_{19}H_{17}FO_4$: C, 69.50; H, 5.22; Found C, 69.61; H, 5.31; ^{13}C NMR ($CDCl_3$, 100 MHz): δ 56.5 (OCH_3), 73.6 (C-1'''), 111.3 (C-2''), 115.7 (C-5''), 116.1 (C-3'''), 119.3 (C-6''), 122.5 (C-2), 123.8 (C-1'), 127.2 (C-3'), 128.3(C-1''), 130.5 (C-6'), 132.9(C-2'''), 135.2 (C-4'), 148.8 (C-3'' & C-4''), 155.8 (C-5'), 160.3 (C-2'), 189.2 (C-1).

(E)-3-(4-(allyloxy)-3-methoxyphenyl)-1-(2-hydroxy-5-methylphenyl)prop-2-en-1-one (4g):



4g

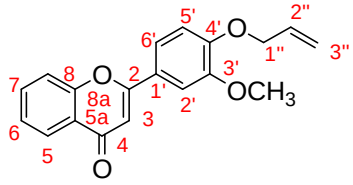
^{1}H NMR (300 MHz, DMSO-d_6) :δ = 2.37 (s,3H, CH_3), 3.87 (s,3H, OCH_3), 4.60 (dt, *J* = 1.5 & 5.3 Hz, 2H, 2xH-1'''), 5.33 (dd, *J* = 1.5 Hz & *J* = 10.3 Hz, 1H, H-3'''(cis)), 5.37 (dd, *J* = 1.6 Hz & *J* = 15.3 Hz, 1H, H-3'''(trans)), 5.96 (m, 1H, H-2'''), 7.51 (d, *J* = 15.00 Hz, H-3), 6.79 (d, 1H, H-6), 6.86-7.89 (m, 5H, Ar-H), 7.96 (d, 1H, *J* = 16.10 Hz, H-2), 11.09 (s, 1H, OH); IR (KBr): ν (cm^{-1}): 1670 (C=O), 1290 (CH=CH), 3319 (OH); MS :*m/z* 324.14 (M+1, 65), 320.1 (72.0), 302.1 (63.1), 294 (100), 258 (74), 232 (65), 195 (23.6), 145 (50.4); Anal. Calcd for $C_{20}H_{20}O_4$: C, 74.06; H, 6.21; Found C, 74.16;

H, 6.31; ^{13}C NMR ($CDCl_3$, 100 MHz): δ 24.8 (CH_3), 55.9 (OCH_3), 72.2 (C-1'''), 111.3 (C-2''), 115.8 (C-5''), 116.1 (C-3'''), 119.1 (C-6''), 122.5 (C-2), 123.3 (C-1'), 127.8 (C-3'),128.0 (C-1''), 132.5 (C-2'''), 135.6 (C-4'), 145.7 (C-3), 149.2 (C-3'' & C-4''), 159.3 (C-2'), 190.2 (C-1).

General procedure for the synthesis of 2-(4-(allyloxy)-3-methoxyphenyl)-4H-chromen-4-one 5(a-g)

(0.25 g, 0.0007 mmole) of chalcone **4a** was dissolved in 15 mL of DMSO. To this reaction mixture catalytic amount of iodine (I_2) was added. The reaction mixture was heated in an oil bath for 2 hr at 120°C. After completion of reaction (monitored by TLC), reaction mass was left for overnight. 10 mL cold water was slowly added to the flask and the separated product was filtered, washed with water followed by dil. sodium thiosulphate solution for several times. It was again washed with water, dried under vacuum and crystallized from ethanol to afford **5(a-g)**. The physical data of the compounds **5(a-g)** were recorded in **Table 2**. Their structures have been confirmed by ^{1}H NMR, Mass and IR spectra.

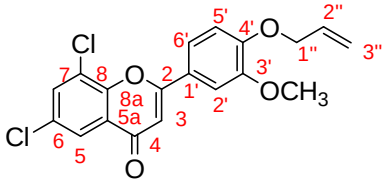
2-(4-(allyloxy)-3-methoxyphenyl)-4H-chromen-4-one (5a):



5a

^{1}H NMR (400 MHz $CDCl_3$): δ = 3.91 (s, 3H, OCH_3), 4.69 (dt, *J* = 1.4 & 5.7 Hz, 2H, 2xH-1''), 5.35 (dd, *J* = 1.3 & *J* = 10.52 Hz, 1H, H-3''(cis)), 5.43 (dd, *J* = 1.5 & *J* = 10.62 Hz, H-3''(trans)), 6.06 (m, 1H, H-2''), 7.26 (s, 1H, H-3), 6.70-7.92 (m, 7H, Ar-H); IR (KBr): ν (cm^{-1}): 1669 (C=O), 1610 &1573 (C=C); MS: *m/z* 309.7 (M+1, 80.0), 304.1 (48.9), 300.1 (62.9), 278 (74.4); Anal. Calcd for $C_{19}H_{16}O_4$: C, 74.01; H, 5.23; Found: C, 73.98; H, 5.27; ^{13}C NMR ($CDCl_3$, 100 MHz): δ 55.3 (OCH_3), 72.8 (C-1''), 103.9 (C-3), 111.8 (C-2'), 115.5 (C-3''), 118.5 (C-6'), 123.5 (C-1' & C-6), 125.4 (C-5a), 129.8 (C-5), 132.8 (C-2''), 134.9 (C-7), 149.5 (C-3' & C-4'), 156.8 (C-2), 181.8 (C-4).

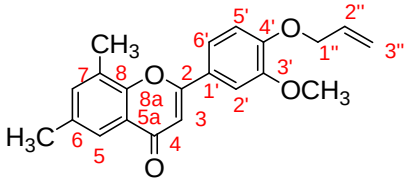
2-(4-(allyloxy)-3-methoxyphenyl)-6,8-dichloro-4H-chromen-4-one (5b):



5b

^{1}H NMR (400 MHz $CDCl_3$): δ = 3.91 (s, 3H, OCH_3), 4.70 (dt, *J* = 1.5 & 5.6 Hz, 2H, 2xH-1''), 5.36 (d, *J* = 1.5 & *J* = 10.52 Hz, 1H, H-3''(cis)), 5.43 (d, *J* = 2.0 & *J* = 10.62 Hz, 1H, H-3''(trans)), 6.07 (m, 1H, H-2''), 6.81 (s, 1H, H-3), 6.85-7.22 (m, 3H, Ar-H), 7.24 (d, *J* = 2.1 Hz, 1H, H-6), 7.30 (d, *J* = 2.1 Hz, 1H, H-7); IR (KBr): ν (cm^{-1}): 1665 (C=O), 1613 &1570 (C=C); MS: *m/z* 377.7 (M+1, 75.0) & 379.6 (M+3, 66.8), 372.0 (20.9), 279.0 (13.6), 260.0 (12.1), 243.0 (32.3), 221 (42.7); Anal. Calcd for $C_{19}H_{14}Cl_2O_4$: C, 60.50; H, 3.74. Found: C, 75.95; H, 6.02; ^{13}C NMR ($CDCl_3$, 100 MHz): δ 55.8 (OCH_3), 71.8 (C-1''), 104.5 (C-3), 112.1(C-2'), 115.8 (C-3''), 126.5 (C-5a), 128.9 (C-5), 132.8 (C-2''), 136.5 (C-7), 149.2 (C-3'), 150.1 (C-5'), 162.8 (C-2), 181.5 (C-4).

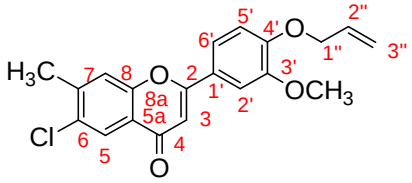
2-(4-(allyloxy)-3-methoxyphenyl)-6,8-dimethyl-4H-chromen-4-one (5c):



5c

^{1}H NMR (400 MHz $CDCl_3$): δ = 2.43 (s, 3H, CH_3), 2.57 (s, 3H, CH_3), 3.88 (s, 3H, OCH_3), 4.63 (dt, *J* = 1.5 & 5.4 Hz, 2H, 2xH-1''),5.23 (dd, *J* = 2 & *J* = 10.50 Hz, 1H, H-3''(cis)), 5.33 (dd, *J* = 2.0 & *J* = 10.60 Hz, 1H, H-3''(trans)), 6.00 (m, 1H, H-2''), 6.80 (s, 1H, H-3), 6.88-7.26 (m, 3H, Ar-H), 7.27 (d, *J* = 2.0 Hz, 1H, H-6), 7.31 (d, *J* = 2.1 Hz, 1H, H-7); IR (KBr): ν (cm^{-1}): 1665 (C=O), 1615 &1575 (C=C); MS: *m/z* 337.7 (M+1, 80.0), 332.1 (53.1), 321 (75), 305 (44), 278.1 (33.4); Anal. Calcd for $C_{21}H_{20}O_4$: C, 74.98; H, 5.99. Found: C, 60.47; H, 3.78; ^{13}C NMR ($CDCl_3$, 100 MHz): δ 15.7 (CH_{3a}), 25.3 (CH_{3b}), 55.8 (OCH_3), 72.1(C-1''), 103.8 (C-3), 118.8 (C_5[1]), 114.7 (C-3''), 123.5 (C_7), 127.1 (C-5a), 132.4 (C-2''), 133.5, 137.1 (C-7), 148.2 (C-3'), 150.0 (C-5'), 153.8 (C-8), 181.2 (C-4).

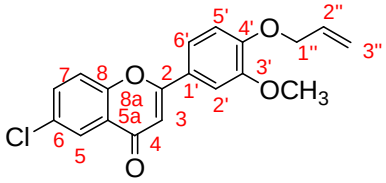
2-(4-(allyloxy)-3-methoxyphenyl)-6-chloro-7-methyl-4H-chromen-4-one (5d):



5d

^{1}H NMR (400 MHz $CDCl_3$): δ = 2.41 (s, 3H, CH_3), 3.76 (s, 3H, OCH_3), 4.65 (dt, *J* = 1.5 & 5.3 Hz, 2H, 2xH-1''), 5.26 (dd, *J* = 2 & *J* = 10 Hz, 1H, H-3''(cis)), 5.29 (dd, *J* = 1.4 & *J* = 10.50 Hz, 1H, H-3''(trans)), 5.92 (m, 1H, H-2''), 6.67 (s, 1H, H-3), 6.69 (s, 1H, H-5), 6.72 -7.26 (m, 3H, Ar-H), 7.55 (s, 1H, H-8); IR (KBr): ν (cm^{-1}): 1667 (C=O), 1570 (C=C); MS: *m/z* 357.06 (M+1, 70.0), 359.1 (M+3, 55.1), 347.1 (100.0), 339.1 (57.4%), 224.1 (41.0), 198 (80); Anal. Calcd for $C_{20}H_{17}ClO_4$: C, 67.13; H, 5.07, Found: C, 67.05; H, 5.15. ^{13}C NMR ($CDCl_3$, 100 MHz): δ 16.5 (CH_3), 54.9 (OCH_3), 71.3 (C-1''), 104.9 (C-3), 116.3 (C-3''), 117.2 (C-7), 121.8 (C_7), 127.8 (C-5a), 130.3 (C-5), 132.9 (C-2'') 148.8 (C-3'), 154.8 (C-8), 162.8 (C-2), 181.7 (C-4).

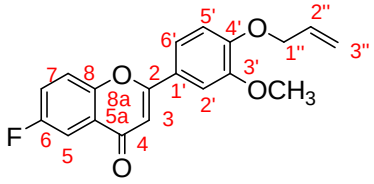
2-(4-(allyloxy)-3-methoxyphenyl)-6-chloro-4H-chromen-4-one (5e):



5e

^{1}H NMR (400 MHz $CDCl_3$): δ = 3.71 (s, 3H, OCH_3), 4.61 (dt, *J* = 1.5 & 5.5 Hz, 2H, 2xH-1''), 5.25 (dd, *J* = 1.4 & *J* = 10.50 Hz, 1H, H-3''(cis)), 5.33 (dd, *J* = 1.5 & *J* = 10.60 Hz, 1H, H-3''(trans)),5.96 (m, 1H, H-2''), 6.89 (s, 1H, H-3), 7.26 (d, 1H, H-5), 7.28-7.52 (m, 3H, Ar-H), 7.55 (dd, *J* = 2.0 & *J* = 8 Hz, 1H, H-7), 7.64 (d, 1H, H-8); IR (KBr): ν (cm^{-1}): 1660 (C=O), 1617 &1575 (C=C); MS: *m/z* 343.06 (M+1, 54.9), 343.6 (M+3, 35.0), 332.1 (42.9), 315.1 (100.0), 301 (55), 295 (42), 255 (32); Anal. Calcd for $C_{19}H_{15}ClO_4$: C, 66.58; H, 4.41. Found: C, 66.53; H, 4.43; ^{13}C NMR ($CDCl_3$, 100 MHz): δ 56.8 (OCH_3), 72.9 (C-1'') 110.9 (C-2'), 115.8 (C-3''), 118.9 (C-7), 123.8 (C-6), 124.8 (C-5a), 129.5 (C-5), 133.5 (C-2'') 135.4 (C-7), 141.2 (C-2'') 155.1 (C-8), 182.3 (C-4).

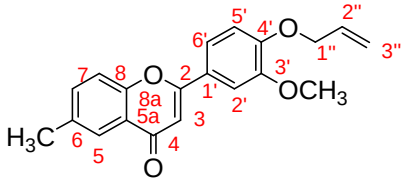
2-(4-(allyloxy)-3-methoxyphenyl)-6-fluoro-4H-chromen-4-one (5f):



5f

^{1}H NMR (400 MHz $CDCl_3$): δ = 3.77 (s, 3H, OCH_3), 4.61 (dt, *J* = 1.5 & 5.6 Hz, 2H, 2xH-1''), 5.24 (dd, *J* = 1.5 & *J* = 10.50 Hz, 1H, H-3''(cis)), 5.30 (dd, *J* = 1.5 & *J* = 10.60 Hz, 1H, H-3''(trans)), 5.98 (m, 1H, H-2''), 6.75 (s, 1H, H-3), 6.80-7.05 (m, 3H, Ar-H), 7.09 (d, *J* = 6.0 Hz, 1H, H-5), 7.18 (dd, *J* = 2 & *J* = 8.0 Hz,1H, H-7), 7.45 (d, *J* = 2.08 Hz, 1H, H-8); IR (KBr): ν (cm^{-1}): 1669 (C=O), 1627 &1571 (C=C); MS: *m/z* 327.16 (M+1, 56), 321.1 (80.9), 315.1 (62.9), 305 (45), 290 (76), 254 (32), 205 (15); Anal. Calcd for $C_{19}H_{15}FO_4$: C, 69.93; H, 4.63. Found: C, 74.48; H, 5.66; ^{13}C NMR ($CDCl_3$, 100 MHz): δ 56.5 (OCH_3), 71.2 (C-1'') 103.5 (C-3), 114.9 (C-5'), 118.3 (C-6'), 122.1 (C-6), 123.5 (C-1'), 133.1 (C-2'') 150.2 (C-4'), 150.8 (C-3'), 152.3 (C-8), 162.8 (C-2), 181.9 (C-4).

2-(4-(allyloxy)-3-methoxyphenyl)-6-methyl-4H-chromen-4-one (5g):



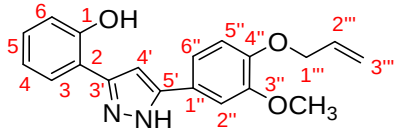
5g

^{1}H NMR (400 MHz $CDCl_3$): δ = 2.56 (s, 3H, CH_3), 3.70 (s, 3H, OCH_3), 4.60 (dt, *J* = 2.0 & 5.8 Hz, 2H, 2xH-1''), 5.25 (dd, *J* = 1.5 & *J* = 9.5 Hz, 1H, H-3''(cis)),5.35 (dd, *J* = 2.0 & *J* = 10.60 Hz, 1H, H-3''(trans)), 5.95 (m, 1H, H-2''), 6.83 (s, 1H, H-3), 6.85-7.00 (m, 3H, Ar-H), 7.05 (d, *J* = 6.5 Hz, 1H, H-5), 7.21 (dd, *J* = 1.5 & *J* = 8.0 Hz,1H, H-7), 7.50 (d, *J* = 2.0 Hz, 1H, H-8); IR (KBr): ν (cm^{-1}): 1666 (C=O), 1625 &1578 (C=C); MS: *m/z* 323.4 (M+1, 75.0), 315.1 (100.0), 307(60), 288 (51), 224.1 (33.1); Anal. Calcd for $C_{20}H_{18}O_4$: C, 74.52; H, 5.63. Found: C, 69.90; H, 4.60; ^{13}C NMR ($CDCl_3$, 100 MHz): δ 25.7 (CH_3), 55.9 (OCH_3), 73.1 (C-1'') 104.3 (C-3), 111.9 (C-2'), 115.3 (C-5'), 117.5 (C-6'), 124.1 (C-1'), 130.4 (C-5), 133.9 (C-2'') 148.2 (C-3'), 149.0 (C-4'), 153.2 (C-8), 161.4 (C-2), 182.3 (C-4).

General procedure for the synthesis of 2-(5-(4-(allyloxy)-3-methoxyphenyl)-1H-pyrazol-3-yl)phenol 6(a-g)

To the solution of (0.25 g, 0.0007 mmole) of chromone **5a** in 10 mL of ethanol was added (0.035 mL, 0.0007 mmole) of hydrazine hydrate. The reaction mixture was heated for 5-6 hr. After completion of reaction (monitored by TLC). In the reaction mass 10 mL cold water was added and the product was filtered, dried over under vacuum and crystallized from ethanol to afford **6(a-g)**. The physical data of the compounds **6(a-g)** were recorded in **Table 1**. Their structures have been confirmed by ^{1}H NMR, Mass and IR spectra.

2-(5-(4-(allyloxy)-3-methoxyphenyl)-1H-pyrazol-3-yl)phenol (6a):

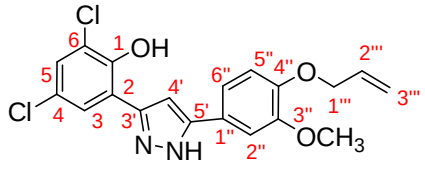


6a

^{1}H NMR (400 MHz $CDCl_3$): δ = 3.84 (s, 3H, OCH_3), 4.63 (dt, *J* = 4.01 & 6.1 Hz, 2H, 2xH-1'''), 5.25 (dd, *J* = 2.1 & *J* =14.2 Hz, 1H, H-3'''(cis)), 5.30 (dd, *J* = 2.0 & *J* = 10.0 Hz, 1H, H-3'''(trans)), 6.00

(m, 1H, H-2’’’), 6.82 (br s, 1H, -NH), 6.85-6.90 (m, 3H, Ar-H), 7.00 (s, 1H, H-4’), 7.29- 7.40 (m, 4H, Ar-H), 11.13 (s, 1H, OH), 12.16 (br s, 1H, -NH); IR (KBr): ν (cm^{-1}): 3280 (OH), 3075 (-NH), 1614 (C=C), 1522 (C=N); MS: *m/z* 323.5 (M+1, 84), 318.1 (52.6), 214.1 (32.8), 168 (60); Anal. Calcd for $C_{19}H_{18}N_2O_3$: C, 70.79; H, 5.63; N, 8.69. Found: C, 70.74; H, 5.60; N, 8.63; ^{13}C NMR ($CDCl_3$, 100 MHz): δ 30.1 (C-3’), 56.1 (OCH_3), 72.4 (C-1’’’) 94.1 (C-4’), 112.4 (C-2’’), 115.8 (C-5’’), 116.3 (C-3’’), 116.7 (C-6), 120.1 (C-6’’), 121.3 (C-4), 128.5 (C-6 & C-1’’), 129.4 (C-2), 130.1 (C-3), 133.2 (C-2’’), 148.1 (C-3’’ & C-4’’), 151.2 (C-5’), 155.2 (C-1).

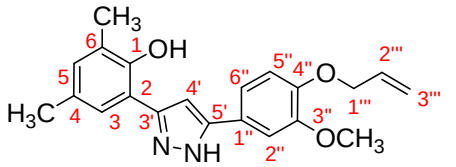
2-(5-(4-(allyloxy)-3-methoxyphenyl)-1H-pyrazol-3-yl)-4,6-dichlorophenol (6b):



6b

^{1}H NMR (400 MHz $CDCl_3$): δ = 3.88 (s, 3H, OCH_3), 4.56 (dt, *J* = 1.94 & 5.5 Hz, 2H, 2xH-1’’’), 5.29 (dd, *J* = 2.1 & *J* =14.2 Hz, 1H, H-3’’’(cis)), 5.31 (dd, *J* = 2.2 & *J* = 10.0 Hz, 1H, H-3’’’(trans)), 5.98 (m, 1H, H-2’’’), 6.83 (br s, 1H, -NH), 6.88-6.98 (m, 3H, Ar-H), 7.07 (s, 1H, H-4’), 7.23 (d, *J* = 1.5 Hz,1H, H-4), 7.27 (d, *J* = 2.0 Hz,1H, H-5), 11.59 (s, 1H, OH), 12.63 (br s, 1H, -NH); IR (KBr): ν (cm^{-1}): 3280 (OH), 3068 (-NH), 1613 (C=C), 1522 (C=N), 751 (C-Cl); MS: *m/z* 391.3 (M+1, 80.0) and 393.6 (M+3, 66.8), 291.1 (21.6), 288.1 (73.6), 272.0 (40.2), 255.1 (52.3), 224.1 (21.8); Anal. Calcd for $C_{19}H_{16}Cl_2N_2O_3$: C, 58.33; H, 4.12; Cl, 18.12; N, 7.16. Found: C, 71.94; H, 6.37; N, 7.92; ^{13}C NMR ($CDCl_3$, 100 MHz): δ 30.2 (C-3’), 56.5 (OCH_3), 72.6 (C-1’’’) 95.2 (C-4’), 115.4 (C-5’’), 116.6 (C-3’’), 116.9 (C-6), 123.1 (C-4), 126.3 (C-6), 126.7 (C-1’’), 128.4 (C-2), 131.1 (C-3), 148.3 (C-3’’ & C-4’’), 151.2 (C-5’), 154.2 (C-1).

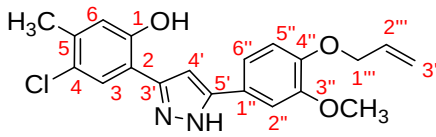
2-(5-(4-(allyloxy)-3-methoxyphenyl)-1H-pyrazol-3-yl)-4,6-dimethylphenol (6c):



6c

^{1}H NMR (400 MHz $CDCl_3$): δ = 2.43 (s, 3H, CH_3), 2.50 (s, 3H, CH_3), 3.81 (s, 3H, OCH_3), 4.56 (dt, *J* = 2.2 & 5.2 Hz, 2H, 2xH-1’’’), 5.29 (dd, *J* = 2.0 & *J* =15.0 Hz, 1H, H-3’’’(cis)), 5.30 (dd, *J* = 2.0 & *J* = 10.2 Hz, 1H, H-3’’’(trans)), 5.92 (m, 1H, H-2’’’), 6.85-6.99 (m, 3H, Ar-H), 7.12 (s, 1H, H-4’), 7.15 (d, *J* = 2.0 Hz, 1H, H-3), 7.20 (d, *J* = 2.0 Hz,1H, H-5), 11.23 (s, 1H, OH), 12.61 (br s, 1H, -NH); IR (KBr): ν (cm^{-1}): 3278 (OH), 3074 (-NH), 1615 (C=C), 1527 (C=N); MS: *m/z* 351.9 (M+1, 92), 341.2 (83.8), 325.2 (65), 311 (58.6), 294 (45), 252.2 (13.3); Anal. Calcd for $C_{21}H_{22}N_2O_3$: C, 71.98; H, 6.33; N, 7.99. Found: C, 58.37; H, 4.17; N, 7.19; ^{13}C NMR ($CDCl_3$, 100 MHz): δ 15.3 (CH_{3a}), 14.6 (CH_{3b}), 29.2 (C-3’), 55.8 (OCH_3), 71.9 (C-1’’’) 98.7 (C-4’), 112.3 (C-5’’), 116.2 (C-3’’), 120.2 (C-6’’), 126.5 (C-6), 131.9 (C-3), 133.5 (C-2’’), 147.9 (C-3’’ & C-4’’), 149.4 (C-5’), 155.1 (C-1).

2-(5-(4-(allyloxy)-3-methoxyphenyl)-1H-pyrazol-3-yl)-4-chloro-5-methylphenol (6d):

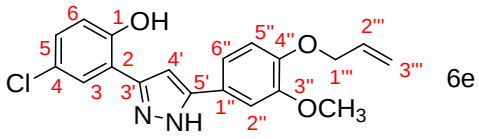


6d

^{1}H NMR (400 MHz $CDCl_3$): δ = 2.52 (s, 3H, CH_3), 3.94 (s, 3H, OCH_3), 4.60 (dt, *J* = 2.1 & 5.6 Hz, 2H, 2xH-1’’’), 5.27 (dd, *J* = 2.0 & *J* =14.0 Hz, 1H, H-3’’’(cis)), 5.33 (dd, *J* = 2.0 & *J* = 10.0 Hz, 1H, H-3’’’(trans)), 6.01 (m, 1H, H-2’’’), 6.83-6.88 (m, 3H, Ar-H), 7.02 (s, 1H, H-6), 7.27 (s, 1H, H-4’),

7.32 (s, 1H, H-3), 11.03 (s, 1H, OH), 12.58 (br s, 1H, -NH); IR (KBr): ν (cm^{-1}): 3282 (OH), 3072 (-NH), 1610 (C=C), 1525 (C=N), 748 (C-Cl); MS: *m/z* 371.2 (M+1, 90.0) and 373.2 (M+3, 65.0), 365.1 (42.7), 343.1 (57.6), 324.1 (41.0), 255 (32), 205 (56.6); Anal. Calcd for $C_{20}H_{19}ClN_2O_3$: C, 64.78; H, 5.16; Cl, 9.56; N, 7.55. Found: C, 64.82; H, 5.22; N, 7.59; ^{13}C NMR ($CDCl_3$, 100 MHz): δ 14.8 (CH_{3a}), 31.2 (C-3'), 55.3 (OCH_3), 71.4 (C-1''') 98.3 (C-4'), 115.4 (C-5''), 116.2 (C-3''), 118.8 (C-6''), 126.1 (C-6), 128.3 (C-5), 131.2 (C-2 & C-3), 132.9 (C-2''), 148.2 (C-3'' & C-4''), 150.4 (C-5'), 152.3 (C-1).

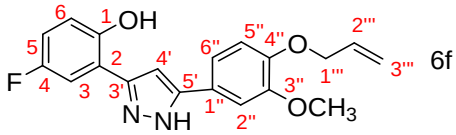
2-(5-(4-(allyloxy)-3-methoxyphenyl)-1H-pyrazol-3-yl)-4-chlorophenol (6e):



6e

^{1}H NMR (400 MHz $CDCl_3$): δ = 3.90 (s, 3H, OCH_3), 4.62 (dt, *J* = 2.0 & 5.6 Hz,1H, 2xH-1'''), 5.32 (dd, *J* = 2.0 & *J* =14.0 Hz, 1H, H-3'''(cis)), 5.33 (dd, *J* = 2.0 & *J* = 10.0 Hz, 1H, H-3'''(trans)), 6.01 (m, 1H, H-2'''), 6.88 (s, 1H, H-4'), 6.83-7.03 (m, 3H, Ar-H), 7.27-7.33 (m, 3H, H-3, H-5 & H-6), 11.88 (s, 1H, -OH), 13.18 (br s, 1H, -NH)); IR (KBr): ν (cm^{-1}): 3282 (OH), 3072 (-NH), 1610 (C=C), 1525 (C=N); 746 (C-Cl); MS: *m/z* 371.2 (M+1, 78) and 373.2 (M+3, 53), 356.1 (100.0), 358.1 (74.8), 351.1 (55.6), 330.1 (47.2), 318 (37), 265 (43); Anal. Calcd for $C_{19}H_{17}ClN_2O_3$: C, 63.96; H, 4.80; N, 7.85. Found: C, 66.92; H, 5.00; N, 8.18; ^{13}C NMR ($CDCl_3$, 100 MHz): δ 28.2 (C-3'), 55.7 (OCH_3), 72.9 (C-1''') 98.8 (C-4'), 115.8 (C-5''), 117.1 (C-6''), 120.3 (C-4), 127.3 (C-5), 128.0 (C-2), 130.8 (C-3), 148.5 (C-3'' & C-4''), 149.2 (C-5'), 152.7 (C-1).

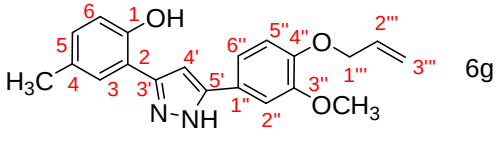
2-(5-(4-(allyloxy)-3-methoxyphenyl)-1H-pyrazol-3-yl)-4-fluorophenol (6f):



6f

^{1}H NMR (400 MHz $CDCl_3$): δ = 3.92 (s, 3H, OCH_3), 4.66 (dt, *J* = 2.5 & 5.8 Hz,1H, 2xH-1'''), 5.35 (dd, *J* = 2.0 & *J* =14.5 Hz, 1H, H-3'''(cis)), 5.31 (dd, *J* = 2.0 & *J* = 10.2 Hz, 1H, H-3'''(trans)), 6.00 (m, 1H, H-2'''), 6.83 (s, 1H, H-4'), 6.85-7.00 (m, 3H, Ar-H), 7.25 (dd, *J* = 2.0 & *J* = 8.0 Hz, 1H, H-5), 7.27-7.32 (dd, 2H, H-3 & H-6), 11.62 (s, 1H, -OH), 13.10 (br s, 1H, -NH)); IR (KBr): ν (cm^{-1}): 3276 (OH), 3067 (-NH), 1664 (C=C), 1520 (C=N), 748 (C-Cl); MS: *m/z* 341.7 (M+1.88), 332 (78), 305 (65.6), 294 (45), 255 (62), 241 (34.4), 202 (40); Anal. Calcd for $C_{19}H_{17}FN_2O_3$: C, 67.05; H, 5.03; N, 8.23. Found: C, 75.02; H, 6.32; N, 8.80; ^{13}C NMR ($CDCl_3$, 100 MHz): δ 28.8 (C-3'), 56.8 (OCH_3), 72.7 (C-1'''), 98.4 (C-4'), 111.9 (C-2''), 115.7 (C-5''), 116.5 (C-6), 118.3 (C-6''), 120.1 (C-4), 127.4 (C-2 & C-5), 132.7 (C-3), 148.1 (C-3'' & C-4''), 150.4 (C-5'), 155.7 (C-1).

2-(5-(4-(allyloxy)-3-methoxyphenyl)-1H-pyrazol-3-yl)-4-methylphenol (6g):



6g

^{1}H NMR (400 MHz $CDCl_3$): δ = 3.87 (s, 3H, OCH_3), 4.61 (dt, *J* = 2.1 & 6.0 Hz,1H, 2xH-1'''), 5.33 (dd, *J* = 2.0 & *J* =14 Hz, 1H, H-3'''(cis)), 5.34 (dd, *J* = 2.0 & *J* = 10.2 Hz, 1H, -3'''(trans)), 5.97 (m, 1H, H-2'''), 6.75-6.92 (m, 3H, Ar-H), 6.98 (s, 1H, H-4'), 7.15 (dd, *J* = 1.5 & *J* = 8.0 Hz, 1H, H-5), 7.22-7.30 (dd, 2H, H-3 & H-6), 11.56 (s, 1H, -OH), 12.88 (br s, 1H, -NH)); IR (KBr): ν (cm^{-1}): 3268

(OH), 3061 (-NH), 1660 (C=C), 1522 (C=N); MS: *m/z* 337.5 (M+1, 75), 325.2 (62.0), 311 (70), 298 (66), 275 (46), 228 (16); Anal. Calcd for $C_{20}H_{20}N_2O_3$: C, 71.41; H, 5.99; N, 8.33. Found: C, 70.40; H, 5.33; N, 8.60; ^{13}C NMR ($CDCl_3$, 100 MHz): δ 23.3 (CH_3), 30.1 (C-3'), 56.1 (OCH_3), 71.8 (C-1'''), 99.3 (C-4'), 112.8 (C-2''), 114.7 (C-5''), 116.1 (C-6), 121.5 (C-4), 126.4 (C-2 & C-5), 130.8 (C-1''), 133.7 (C-3), 148.1 (C-3'' & C-4''), 150.4 (C-5'), 151.8 (C-1).

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