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Acid Promoted One Pot Synthesis of Some New Coumarinyl 3,4'-Bipyrazole and Their *In Vitro* Antimicrobial Evaluation

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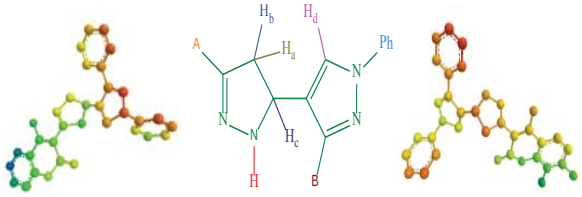
Abstract: A series of diversely substituted 3,4'-bipyrazole, functionalized with 4-hydroxy coumarinyl ring system, was synthesized via mild acid promoted one pot cyclization of chalcone precursors with hydrazine hydrate. In order to obtain a bipyrazole skeleton, pyrazole aldehydes were selected for Claisen-Schmidt condensation with 3-acetyl, 4-hydroxy coumarin ring system to make desired chalcone precursors. Hydrazine hydrate behaves like a bidentate nucleophile and reacts with coumarinyl chalcones in acetic acid media to yield desired 3,4' -bipyrazoles. The structures of all synthesized analogues were substantiated by diverse analytical spectroscopic data. Anti-microbial evaluation of all synthesized compounds was carried out via Broth Dilution method using standard microbial strains.

Keywords: 3,4'-Bipyrazole, Chalcone precursors, Acetic acid, Hydrazine hydrate, Microwave synthesizer, Parallel synthesizer, Antimicrobial evaluation

Introduction

Herein, we have reported some novel 3,4'-bipyrazole synthesized from coumarinyl chalcones. Coumarin derivatives are reported for exhibiting antioxidant[1], antiviral[2], anticancer[3], anti-inflammatory[4], antimicrobial & moluscicidal[5-6], anticoagulant[7] and cardiovascular[8] activities. Moreover, pyrazole derivatives, especially 4-functionalized 1,3-diphenyl pyrazoles are reported for their anti-inflammatory[9], antiparasitic[10] and antidiabetic properties[11]. The chalcone moiety, containing nitrogenous ring, has been reported as active compounds against herpes simplex virus-1(HSV-1) and human immunodeficiency virus 1(HIV-1)[12]. Our keen interest in synthesizing the highly attraction grabbing class of heterocycles, known as 'bipyrazoles', is due to their wide range of biological activities such as antimicrobial, cardiovascular,

antiallergic, diuretic, antitumor and antioxidant/ free radical scavenging activity[13]. At present, there is a fastidious significance of bipyrazoles derivatives in studies of intermolecular interactions, supramolecular complex formation[14] along with the contribution of pyrazoles and other heterocyclic ring systems. Application of bipyrazoles is also reported in paint & photography[15], polymer[16] and agrochemical industries[17]. According to the linking between two pyrazole ring systems, there are three main class of bipyrazoles: C-C bipyrazole, C-N bipyrazole and N-N bipyrazole[18]. 3,4'-bipyrazole is one type of C-C bipyrazoles which are already reported for several applications such as anticancer activity, catalysis, corrosion inhibition, liquid-liquid extraction, resins and polymer synthesis[19]. An anti-microbial is a stuff that kills or inhibits the growth of microorganisms such as bacteria, fungi or protozoa. The chemotherapy of microbial infections has become exigent problem due to the rising multiple drug-resistant organisms because they twist the administration of transmittable diseases more wobbly[20-22]. It is hypothesized that the enlargement of confrontation to recognized antimicrobials can be prevailed over by making out some new drug targets via genomics and by discovering new antimicrobial agents having new structure and mechanism of action[23]. In order to afford a vital need of a new class of antimicrobial agents, impassive by existing resistance mechanisms, an effort has been done to synthesize some new 3,4' -bipyrazoles. Our pre-planned use of pyrazole aldehydes can be proved as a facile route of synthesis of bipyrazoles from chalcon precursors which are synthesized via Claisen-Schmidt condensation[24].



Materials and Methods

Melting points of all the synthesized compounds were recorded by open capillary method. Reactions were monitored by thin layer chromatography technique using silica gel-G plates of 0.5 mm thickness and spots were observed using iodine and UV. All the chalcones were synthesized in Anton Parr Monowave-300 microwave synthesizer. All the bipyrazoles were synthesized in Radleys Carousel 6 Classic parallel synthesizer. The IR spectra were recorded on a Shimadzu FT-IR-8400 instrument using KBr pellet method. Mass spectra were recorded on Shimadzu GC-MS-QP-2010 model using Direct Injection Probe technique. ^{1}H NMR spectra were determined in DMSO-d_6 solution by a Bruker Ac 400 MHz spectrometer. Elemental analysis of the all the synthesized compounds was carried out on Elemental Vario EL III Carlo Erba 1108 model and the results are in agreements with the structures assigned. In-vitro antimicrobial evaluation was carried out by means of Broth Dilution method using common standard strains (MTCC — Micro Type Culture Collection) procured from Institute of Microbial Technology, Chandigarh. An MIC (Minimum Inhibitory Concentration) value was carried out for all newly synthesized compounds by Micro-Broth Dilution method in accordance with National Committee for Clinical Laboratory Standards (NCCLS).

Experimental Procedure

General method for preparation of 3-acetyl, 4-hydroxy coumarinyl chlcones (3a-r):

A mixture of 3-acetyl 4-hydroxy coumarin **1a-b** (0.01 mol) and substituted pyrazole aldehyde **2a-i** (0.01 mol) was dissolved in chloroform (10 ml). The catalytic amount of piperidine (0.02 ml) was added and the reaction mixture was subjected into the vial having cap and inserted into the microwave synthesizer for a specific time (3-9 min) at 80^{o}C. The progress of the

reaction was monitored by TLC examination at an interval of each minute using ethyl acetate: hexane (2:3) system. On completion of the reaction, the excess of chloroform was distilled out and the resulting mass was cooled and titurated with methanol. The solid separated was filtered and washed with methanol, dried and further used in the next step.

General method for preparation of 4-hydroxy coumarinyl 3,4'-bipyrazoles (5a-r):

All previously synthesized 4-hydroxy coumarinyl chalcones **3a-r** (0.01 mol) were mixed with hydrazine hydrate **4** (0.02 mol) and added carefully to refluxing acetic acid (CH_3COOH) (20 ml) in the reaction vessels of parallel synthesizer containing magnetic needle. Proper rotation per minute (rpm) and 130°C temperature were set in the parallel synthesizer. Reaction monitoring was continued at the interval of every 2 hours using ethyl acetate: hexane (3:7) system. After 3-4 hrs, a new spot generated in the TLC plate at the lower R_f value than that of the chalcone spot in all the reactions set in the parallel synthesizer. After 6-8 hrs, when the starting gets completely consumed, each reaction mass was poured into the crushed ice and kept stirring overnight. Then the solid precipitated was filtered, washed with Acetone, dried and recrystallized with dichloromethane to obtain chromatography free pure product. (Yield: 80-90%) (Some of the reactions complete faster whereas some take much time while synthesizing more than one bipyrazole simultaneously in parallel synthesizer, so TLC monitoring is must.)

***In vitro* Antimicrobial Screening Protocol**

For evaluation of *in vitro* antibacterial activity, we have used *Staphylococcus aureus* (MTCC 96) & *Streptococcus pyogenes* (MTCC 442) from gram positive group of bacteria and *Escherichia coli* (MTCC 443) & *Pseudomonas aeruginosa* (MTCC 1688) from gram negative group of bacteria. The *in vitro* antifungal activity of all compounds and standard drugs were evaluated against two fungi viz. *Aspergillus fumigates* (MTCC 3008) *and Candida albicans* (MTCC 227). Inoculum size for test strain was attuned to 108 $CFUmL^{-1}$ (Colony Forming Unit per milliliter) by comparing the turbidity (turbidimetric method). To cultivate and dilute the compound suspension for the microbial strains, Mueller Hinton Broth was used as fortifying medium for bacterial strains and Sabouraud Dextrose Broth was used for nutrition of fungal strains. Ampicillin, Norfloxacin, Ciprofloxacin and Chloramphenicol were used as standard antibacterial drugs, whereas Griseofulvin and Nystatin were used as standard antifungal drugs. DMSO was used as diluent/vehicle to get proper concentration of synthesized compounds and standard drugs were used to test upon standard microbial strains. Serial dilutions were prepared in primary and secondary screening. All compounds and standard drugs were diluted to obtain 2000μg/mL concentration, as a stock solution. In primary screening 1000, 500, and 250μg/mL concentrations of the synthesized compounds were used. The active compounds found in this primary screening were further diluted to obtain 200, 100, 62.5, 50, 25, 12.5 and 6.250μg/mL concentrations for secondary screening to test in a second set of dilution against all microbial strains. The control tube containing no antibiotic was immediately sub cultured [before inoculation] by spreading a loopful evenly over a quarter of plate of medium suitable for the growth of the test organism. The tubes were then put for incubation at 37◦C for 24 h for bacteria and 48 h for fungi. The highest dilution (lowest concentration) preventing appearance of turbidity was considered as minimal inhibitory concentration (MIC, μg/mL) i.e., the amount of growth from the control tube before incubation (representating the original inoculum) was compared. A set of tubes containing only seeded broth and the solvent controls were maintained under

Reaction Scheme

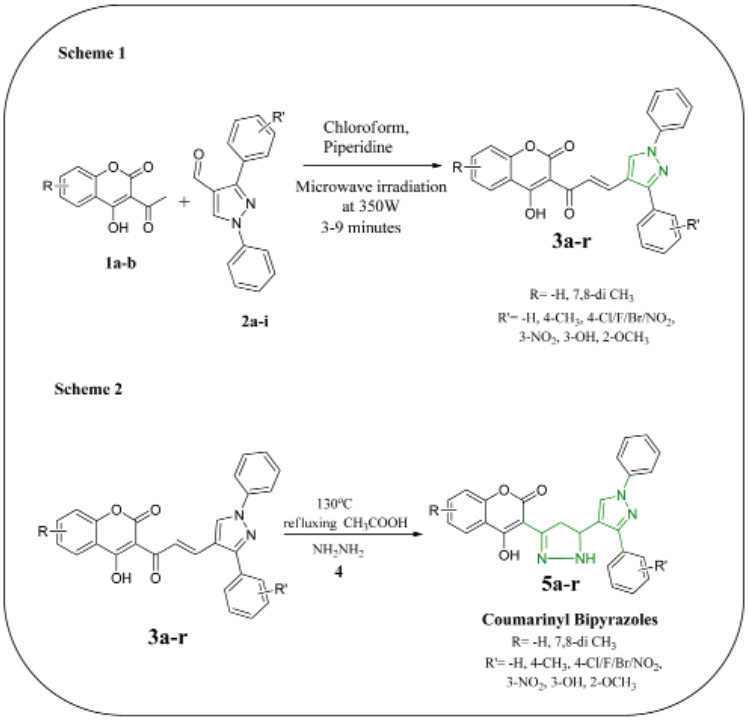


Table 1. Physical data table for the compounds **5a-r:**

Entry as	R	R'	M.F.	M.W. (g/ mole)	M.P. °C	Yield %	R_f
5a	H	H	$C_{27}H_{20}N_4O_3$	448.47	200-202	88	0.50
5b	H	4-CH_3	$C_{28}H_{22}N_4O_3$	462.50	210-212	90	0.54
5c	H	4-Cl	$C_{27}H_{19}ClN_4O_3$	482.92	232-234	80	0.56
5d	H	4-F	$C_{27}H_{19}FN_4O_3$	466.46	194-196	83	0.52
5e	H	4-Br	$C_{27}H_{19}BrN_4O_3$	527.37	206-208	81	0.55
5f	H	4-NO_2	$C_{27}H_{19}N_5O_5$	493.47	212-214	84	0.53
5g	H	3-NO_2	$C_{27}H_{19}N_5O_5$	493.47	224-226	85	0.54
5h	H	3-OH	$C_{27}H_{20}N_4O_4$	464.47	216-218	80	0.42
5i	H	2-OCH_3	$C_{28}H_{22}N_4O_4$	478.50	201-203	89	0.53
5j	7, 8-di Me	H	$C_{29}H_{24}N_4O_3$	476.53	218-220	82	0.50
5k	7, 8-di Me	4-CH_3	$C_{30}H_{26}N_4O_3$	490.55	226-228	88	0.51
5l	7, 8-di Me	4-Cl	$C_{29}H_{23}ClN_4O_3$	510.97	230-232	87	0.53
5m	7, 8-di Me	4-F	$C_{29}H_{23}FN_4O_3$	494.52	236-238	84	0.52
5n	7, 8-di Me	4-Br	$C_{29}H_{23}BrN_4O_3$	555.42	246-248	81	0.51
5o	7, 8-di Me	4-NO_2	$C_{29}H_{23}N_5O_5$	521.52	238-240	83	0.50
5p	7, 8-di Me	3-NO_2	$C_{29}H_{23}N_5O_5$	521.52	242-244	80	0.54
5q	7, 8-di Me	3-OH	$C_{29}H_{24}N_4O_4$	492.53	228-230	81	0.45
5r	7, 8-di Me	2-OCH_3	$C_{30}H_{26}N_4O_4$	506.55	198-200	90	0.53

Table 2. Antibacterial activity data table for compounds **5a-r:**

Minimum Inhibitory Concentration (MIC, *μg*/mL)					
Antibacterial Activity Table					
Minimum Bactericidal Concentration					
Microbial Strains Used					
Sr. No	**Entry as**	***E.Coli***	***P.Aeruginosa***	***S.Aureus***	***S.Pyogenus***
		MTCC 443 Gram Negative	**MTCC 1688 Gram Negative**	**MTCC 96 Gram Positive**	**MTCC 442 Gram Positive**
1	5a	**100**	250	**62.5**	200
2	5b	125	250	**100**	125
3	5c	200	200	**200**	250
4	5d	200	125	**200**	250
5	5e	500	250	500	250
6	5f	**100**	200	**250**	250
7	5g	200	200	**250**	250
8	5h	200	250	**250**	250
9	5i	250	250	**125**	**100**
10	5j	125	200	**62.5**	200
11	5k	**62.5**	100	**250**	250
12	5l	125	100	**250**	200
13	5m	500	250	**250**	125
14	5n	**100**	125	**250**	500
15	5o	250	200	**100**	200
16	5p	250	250	**125**	250
17	5q	250	200	**250**	250
18	5r	200	200	**200**	**100**
Ampicillin		**100**	**--**	**250**	**100**
Chloramphenicol		**50**	**50**	**50**	**50**
Ciprofloxacin		**25**	**25**	**50**	**50**
Norfloxacin		**10**	**10**	**10**	**t10**

Table 3. Antifungal activity data table for compounds **5a-r:**

Minimum Inhibitory Concentration (MIC, μg/mL)			
Antifungal Activity			
Sr. No.	Entry As	Microbial Strains Used	
		C.Albicans MTCC 227	*As.Fumigatus* MTCC 3008
1	5a	>1000	>1000
2	5b	**500**	500
3	5c	**250**	1000
4	5d	**250**	250
5	5e	**500**	>1000
6	5f	**250**	>1000
7	5g	>1000	500
8	5h	**200**	500
9	5i	**500**	500
10	5j	>1000	1000
11	5k	**200**	>1000
12	5l	1000	1000
13	5m	>1000	500
14	5n	**200**	500
15	5o	**500**	1000
16	5p	**200**	1000
17	5q	**250**	>1000
18	5r	**500**	>1000
Nystatin		**100**	**100**
Griseofulvin		**500**	**100**

identical conditions so as to make sure that the solvent had no influence on strain growth. The result of this was much affected by the size of the inoculum. The test mixture should contain 10^8 $CFUmL^{-1}$ organisms. The protocols mentioned in Table 2 and 3 can be considered as the minimal inhibitory concentration (MIC, μg/mL).

Evaluation of antimicrobial activity

The evaluation of the antimicrobial activity data (Table 2 and 3) proves that most of the compounds showed effective antibacterial and antifungal activity against used standard strains when compared with standard drugs Ampicillin, Norfloxacin, Ciprofloxacin, Chloramphenicol, Griseofulvin and Nystatin.

(1)Antibacterial activity: None of the synthesized compounds exhibited activity against the bacterial strains as compared to the standard antibacterial drugs other than the Ampicillin. Moreover, none of the compounds is found to be active as compared to the standard drugs against *P.Aeruginosa* (MTCC 1688). Compounds **5a, 5f** and **5n** are found to be equipotent to Ampicillin (MIC=250μg/mL) against *E. Coli* (MTCC 443). Compounds **5f, 5g, 5h, 5k, 5l, 5m, 5n** and **5q** are also found to be equipotent to Ampicillin (MIC=250μg/mL) against *S.Aureus* (MTCC 96). **5i** and **5r**, both compounds are found to have comparative inhibition effect to Ampicillin (MIC=250μg/mL) against *S.Pyogenus* (MTCC 442). The compound **5k** is found to be more active than the Ampicillin (MIC=250μg/mL) against *E. Coli*

(MTCC 443). The compounds **5a,5b, 5c, 5d, 5i, 5j, 5o, 5p** and **5r** are also found to be more active than the Ampicillin (MIC=250μg/mL) against *S.Aureus* (MTCC 96). **(2)Antifungal activity**: None of the compounds is found to be active against *As.Fumigatus* (MTCC 3008) as compared to both the standard antifungal drugs used. All the compounds are found to be less active as compared to the Nystatin (MIC=100μg/mL) against *C.Albicans* (MTCC 227). However, compounds **5b, 5e, 5i, 5o** and **5r** are found to be equipotent to the Griseofulvin (MIC=500μg/mL) against *C.Albicans* (MTCC 227). The compounds **5c, 5d, 5f, 5h, 5k, 5n, 5p and 5q** are found to be more active than the Griseofulvin (MIC=500μg/mL) against *C.Albicans* (MTCC 227).

Result and Discussion

While establishing the proper parameters of a reaction for the synthesis of these bipyrazoles, we tried the reactions using various solvents and compared the reaction time and % yield for each performed reaction. As a result, we found the use of acetic acid as reaction media, gave high yield within shorter reaction time than the other solvents. All the synthesized compounds were characterized by elemental analysis, Mass, IR, ^{1}H NMR and ^{13}C NMR. According to Tables 2 and 3, all newly synthesized compounds are found to possess antibacterial activity either identical or more potent than that of the Ampicillin (MIC=250μg/mL) except the compound **5e** against any of the antibacterial strains used in the test. Similarly in case of antifungal activity, all the compounds excluding **5a, 5g, 5j, 5l and 5m,** exhibit antifungal activity either equivalent or higher than that of the Griseofulvin (MIC=500μg/mL) against C.*Albicans* (MTCC 227).

Conclusion

The merit of the synthetic procedure is Chromatography free pure products with excellent yields, simple work-up and high number of functional group compatibility. For MIC determination **'Broth Dilution Method'** is proved to be advantageous due to the fact that it allows the option of providing both quantitative (MIC) and qualitative (group interpretation) results. In conclusion, out of all newly synthesized **18** compounds**(5a-r)**, **17** compounds exhibit antibacterial activity, **13** compounds revel antifungal activity and **12** compounds **(5b, 5c, 5d, 5f, 5h, 5i, 5k, 5n, 5o, 5p, 5q and 5r)** own both antibacterial as well as antifungal activity as per the *in vitro* antimicrobial assay. Thus this effort of synthesizing some new antimicrobial agents from coumarinyl chalcones is worth.

Spectral Data

3-(1',3'-diphenyl-3,4-dihydro-1'H,2H-[3,4'-bipyrazol]-5-yl)-4-hydroxy-2H-chromen-2-one (5a)

IR (KBr) cm^{-1}: 3207, 3173, 3051, 2908, 1679, 1608, 1513, 1456, 1344, 1230, 1134, 1062, 924, 867, 814, 758, 690, 635. ^{1}H NMR 400 MHz: (DMSO-d_6, δ ppm): 3.58-3.65 (dd, 1H, $\mathbf{H_a}$-CH_b), 4.06-4.13 (dd, 1H, $\mathbf{H_b}$-CH_a), 5.00-5.05 (t, 1H, **H**-C-CH_aH_b), 7.18 (s, 1H, **H**-N-), 7.30-7.34 (m, 3H, **H**-Ar), 7.41-7.45 (t, 1H, **H**-Ar), 7.49-7.53 (m, 4H, **H**-Ar), 7.61-7.63 (t, 1H, **H**-Ar), 7.80-7.81 (d, 2H, **H**-Ar), 7.91-7.96 (m, 3H, **H**-Ar), 8.75 (s, 1H, **H**-trisubstituted 1*H*-pyrazole), 13.28-13.29 (s, 1H, **H**-O-). ^{13}C NMR 400 MHz: (DMSO-d_6, δ ppm): 41.0, 46.4, 88.0, 114.8, 116.4, 117.2 119.9 123.0, 125.4, 127.5, 129.2, 133.0, 139.7, 149.9, 152.5, 155.6, 159.4, 166.2. MS: *m/z* 448; anal. Calcd. for $C_{27}H_{20}N_4O_3$: C, 72.31; H, 4.49; N, 12.49; O, 10.70; Found: C, 72.28; H, 4.44; N, 12.46; O, 10.66 %.

4-hydroxy-3-(1'-phenyl-3'-(p-tolyl)-3,4-dihydro-1'H,2H-[3,4'-bipyrazol]-5-yl)-2H-chromen-2-one (5b)

IR (KBr) cm^{-1}: 3836, 3703, 3196, 3065, 3019,

2914, 2742, 2299, 1923, 1673, 1454, 1341, 1288, 1195, 1128, 1025, 881, 816, 758, 686. ^{1}H NMR 400 MHz: (DMSO-d_6, δ ppm): 2.35 (s, 3H, -C**H**$_3$), 3.55-3.62 (dd, 1H, **H**$_a$-CH$_b$), 4.03-4.10 (dd, 1H, **H**$_b$-CH$_a$), 5.00-5.01 (t, 1H, **H**-C-CH$_a$H$_b$), 7.16 (s, 1H, **H**-N-), 7.28-7.32 (m, 5H, **H**-Ar), 7.48-7.52 (t, 2H, **H**-Ar), 7.60-7.62 (t, 1H, **H**-Ar), 7.67-7.69 (d, 2H, **H**-Ar), 7.89-7.96 (m, 3H, **H**-Ar), 8.71 (s, 1H, **H**-trisubstituted 1*H*-pyrazole), 13.24-13.29 (s, 1H, **H**-O-). ^{13}C NMR 400 MHz: (DMSO-d_6, δ ppm): 21.3, 41.0, 46.4, 88.0, 114.8, 116.4, 117.2, 119.9, 123.0, 123.3, 125.4, 125.7, 126.2, 128.3, 129.5, 130.3, 131.7, 139.7, 149.9, 152.5, 155.6, 159.4, 166.2. MS: *m/z* 462; anal. Calcd. for $C_{28}H_{22}N_4O_3$: C, 72.71; H, 4.79; N, 12.11; O, 10.38; Found C, 72.68; H, 4.70; N, 12.08; O, 10.34 %

3-(3'-(4-chlorophenyl)-1'-phenyl-3,4-dihydro-1'H,2H-[3,4'-bipyrazol]-5-yl)-4-hydroxy-2H-chromen-2-one (5c)

IR (KBr) cm^{-1}: 3210, 3178, 3055, 2910, 1680, 1610, 1520, 1440, 1348, 1260, 1140, 1070, 930, 870, 820, 710, 760, 694, 640. ^{1}H NMR 400 MHz: (DMSO-d_6, δ ppm): 3.59-3.62 (dd, 1H, **H**$_a$-CH$_b$), 4.06-4.12 (dd, 1H, **H**$_b$-CH$_a$), 5.02-5.04 (t, 1H, **H**-C-CH$_a$H$_b$), 7.19 (s, 1H, **H**-N-), 7.40-7.44 (m, 5H, **H**-Ar), 7.45-7.53 (t, 2H, **H**-Ar), 7.58-7.60 (t, 1H, **H**-Ar), 7.66-7.70 (d, 2H, **H**-Ar), 7.90-7.98 (m, 3H, **H**-Ar), 8.73 (s, 1H, **H**-trisubstituted 1*H*-pyrazole), 13.21-13.28 (s, 1H, **H**-O-). ^{13}C NMR 400 MHz: (DMSO-d_6, δ ppm): 41.0, 46.4, 88.0, 114.8, 116.4, 117.2, 119.9, 123.0, 123.3, 125.4, 126.2, 128.3, 128.9, 129.3, 131.1, 134.3, 139.7, 149.9, 152.5, 155.6, 159.4, 166.2. MS: *m/z* 482; anal. Calcd. for $C_{27}H_{19}ClN_4O_3$: C, 67.15; H, 3.97; Cl, 7.34; N, 11.60; O, 9.94; Found: C, 67.13; H, 3.94; Cl, 7.33; N, 11.57; O, 9.90%.

3-(3'-(4-fluorophenyl)-1'-phenyl-3,4-dihydro-1'H,2H-[3,4'-bipyrazol]-5-yl)-4-hydroxy-2H-chromen-2-one (5d)

IR (KBr) cm^{-1}: 3204, 3170, 3056, 2918, 1680, 1640, 1530, 1440, 1466, 1341, 1250, 1154, 1070, 930, 870, 820, 760, 650, 640. ^{1}H NMR 400 MHz: (DMSO-d_6, δ ppm): 3.52-3.58 (dd, 1H, **H**$_a$-CH$_b$), 4.02-4.09 (dd, 1H, **H**$_b$-CH$_a$), 5.02-5.05 (t, 1H, **H**-C-CH$_a$H$_b$), 7.14 (s, 1H, **H**-N-), 7.24-7.28 (m, 5H, **H**-Ar), 7.46-7.50 (t, 2H, **H**-Ar), 7.62-7.64 (t, 1H, **H**-Ar), 7.66-7.70 (d, 2H, **H**-Ar), 7.92-7.98 (m, 3H, **H**-Ar), 8.73 (s, 1H, **H**-trisubstituted 1*H*-pyrazole), 13.26-13.28 (s, 1H, **H**-O-). ^{13}C NMR 400 MHz: (DMSO-d_6, δ ppm): 41.0, 46.4, 88.0, 114.8, 116.0, 117.2, 119.9, 123.0, 123.3, 125.4, 126.2, 128.3, 128.6, 129.3, 130.6, 139.7, 149.9, 152.5, 155.6, 159.4, 162.9, 166.2**.** MS: *m/z* 466; anal. Calcd. for $C_{27}H_{19}FN_4O_3$: C, 69.52; H, 4.11; F, 4.07; N, 12.01; O, 10.29; Found: C, 69.51; H, 4.8; F, 4.05; N, 12.04; O, 10.26%.

3-(3'-(4-bromophenyl)-1'-phenyl-3,4-dihydro-1'H,2H-[3,4'-bipyrazol]-5-yl)-4-hydroxy-2H-chromen-2-one (5e)

IR (KBr) cm^{-1}: 3210, 3180, 3050, 2910, 1680, 1610, 1520, 1440, 1342, 1250, 1140, 1070, 930, 870, 820, 760, 650, 640, 520. ^{1}H NMR 400 MHz: (DMSO-d_6, δ ppm): 3.52-3.59 (dd, 1H, **H**$_a$-CH$_b$), 4.04-4.08 (dd, 1H, **H**$_b$-CH$_a$), 5.02-5.04 (t, 1H, **H**-C-CH$_a$H$_b$), 7.19 (s, 1H, **H**-N-), 7.28-7.32 (m, 5H, **H**-Ar), 7.49-7.53 (t, 2H, **H**-Ar), 7.62-7.64 (t, 1H, **H**-Ar), 7.65-7.69 (d, 2H, **H**-Ar), 7.89-7.96 (m, 3H, **H**-Ar), 8.73 (s, 1H, **H**-trisubstituted 1*H*-pyrazole), 13.26-13.29 (s, 1H, **H**-O-). ^{13}C NMR 400 MHz: (DMSO-d_6, δ ppm): 41.0, 46.4, 88.0, 114.8, 116.4, 117.2, 119.9, 123.0, 123.1, 123.3, 125.4, 126.2, 128.3, 129.3, 132.0, 132.1, 139.7, 149.9, 152.5, 155.6, 159.4, 166.2. MS: *m/z* 527; anal. Calcd. for $C_{27}H_{19}BrN_4O_3$: C, 61.49; H, 3.63; Br, 15.15; N, 10.62; O, 9.10; Found: C, 61.44; H, 3.61; Br, 15.12; N, 10.60; O, 9.8%.

4-hydroxy-3-(3'-(4-nitrophenyl)-1'-phenyl-3,4-dihydro-1'H,2H-[3,4'-bipyrazol]-5-yl)-2H-chromen-2-one (5f)

IR (KBr) cm^{-1}: 3210, 3120, 3055, 2920, 1680, 1625, 1530, 1420, 1354, 1330, 1245, 1140, 1068, 930, 854, 830, 760, 692, 640. ^{1}H NMR

400 MHz: (DMSO-d_6, δ ppm): 3.52-3.60 (dd, 1H, **H**$_a$-CH$_b$), 4.06-4.12 (dd, 1H, **H**$_b$-CH$_a$), 5.02-5.04 (t, 1H, **H**-C-CH$_a$H$_b$), 7.20 (s, 1H, **H**-N-), 7.29-7.35 (m, 3H, **H**-Ar), 7.48-7.52 (t, 2H, **H**-Ar), 7.60-7.63 (t, 1H, **H**-Ar), 7.68-7.72 (d, 2H, **H**-Ar), 8.12-8.24 (m, 5H, **H**-Ar), 8.75 (s, 1H, **H**-trisubstituted 1*H*-pyrazole), 13.27-13.29 (s, 1H, **H**-O-). ^{13}C NMR 400 MHz: (DMSO-d_6, δ ppm): 41.0, 46.4, 88.0, 114.8, 116.4, 117.2, 119.9, 123.0, 123.3, 124.4, 125.4, 126.2, 128.3, 129.3, 139.1, 139.7, 147.9, 149.9, 152.5, 155.6, 159.4, 166.2. MS: *m/z* 493; anal. Calcd. for $C_{27}H_{19}N_5O_5$: C, 65.72; H, 3.88; N, 14.19; O, 16.21; Found: C, 65.7; H, 3.84; N, 14.16; O, 16.20%.

4-hydroxy-3-(3'-(3-nitrophenyl)-1'-phenyl-3,4-dihydro-1'H,2H-[3,4'-bipyrazol]-5-yl)-2H-chromen-2-one (5g)

IR (KBr) cm^{-1}: 3210, 3170, 3052, 2918, 1675, 1620, 1510, 1450, 1341, 1330, 1260, 1150, 1068, 936, 872, 820, 760, 650, 640. ^{1}H NMR 400 MHz: (DMSO-d_6, δ ppm): 3.60-3.62 (dd, 1H, **H**$_a$-CH$_b$), 4.02-4.08 (dd, 1H, **H**$_b$-CH$_a$), 5.00-5.04 (t, 1H, **H**-C-CH$_a$H$_b$), 7.12 (s, 1H, **H**-N-), 7.30-7.35 (m, 3H, **H**-Ar), 7.48-7.52 (t, 2H, **H**-Ar), 7.62-7.78 (m, 4H, **H**-Ar), 8.34-8.46 (m,4H, **H**-Ar), 8.73 (s, 1H, **H**-trisubstituted 1*H*-pyrazole), 13.20-13.23 (s, 1H, **H**-O-). ^{13}C NMR 400 MHz: (DMSO-d_6, δ ppm): 41.0, 46.4, 88.0, 116.4, 117.2, 119.9, 123.0, 123.9, 125.4, 126.2, 128.3, 129.3, 130.6, 133.6, 133.9, 139.7, 148.4, 149.9, 152.5, 155.6, 159.4, 166.2. MS: *m/z* 493; anal. Calcd. for $C_{27}H_{19}N_5O_5$: C, 65.72; H, 3.88; N, 14.19; O, 16.21; Found: C, 65.7; H, 3.86; N, 14.16; O, 16.19%.

4-hydroxy-3-(3'-(3-hydroxyphenyl)-1'-phenyl-3,4-dihydro-1'H,2H-[3,4'-bipyrazol]-5-yl)-2H-chromen-2-one (5h)

IR (KBr) cm^{-1}: 3210, 3180, 3050, 2920, 2540, 1680, 1610, 1530, 1440, 1320, 1345, 1240, 1140, 1070, 930, 870, 820, 760, 650, 630. ^{1}H NMR 400 MHz: (DMSO-d_6, δ ppm): 3.58-3.60 (dd, 1H, **H**$_a$-CH$_b$), 4.04-4.08 (dd, 1H, **H**$_b$-CH$_a$), 5.02-5.05 (t, 1H, **H**-C-CH$_a$H$_b$), 5.42-5.44 (s, 1H, **H**-O-), 7.10 (s, 1H, **H**-N-), 7.20-7.36 (m, 5H, **H**-Ar), 7.42-7.50 (m, 4H, **H**-Ar), 7.60-7.62 (t, 1H, **H**-Ar), 7.70-7.81 (m, 3H, **H**-Ar), 8.70 (s, 1H, **H**-trisubstituted 1*H*-pyrazole), 13.23-13.25 (s, 1H, **H**-O-). ^{13}C NMR 400 MHz: (DMSO-d_6, δ ppm): 41.0, 46.4, 88.0, 114.8, 115.9, 117.2, 119.9, 120.1, 123.0, 123.3, 125.4, 126.2, 128.3, 129.3, 130.6, 134.4, 139.7, 149.9, 152.5, 155.6, 157.5, 159.4, 166.2. MS: *m/z* 464; anal. Calcd. for $C_{27}H_{20}N_4O_4$: C, 69.82; H, 4.34; N, 12.06; O, 13.78; Found: C, 69.80; H, 4.32; N, 12.02; O, 13.75%.

4-hydroxy-3-(3'-(2-methoxyphenyl)-1'-phenyl-3,4-dihydro-1'H,2H-[3,4'-bipyrazol]-5-yl)-2H-chromen-2-one (5i)

IR (KBr) cm^{-1}: 3340, 3110, 3080, 2940, 2830, 2350, 2320, 1724, 1650, 1580, 1550, 1460, 1350, 1330, 1060, 940, 870, 750, 620. ^{1}H NMR 400 MHz: (DMSO-d_6, δ ppm): 3.56-3.61 (dd, 1H, **H**$_a$-CH$_b$), 3.86 (s, 3H, -O-C**H**$_3$), 4.06-4.10 (dd, 1H, **H**$_b$-CH$_a$), 5.00-5.04 (t, 1H, **H**-C-CH$_a$H$_b$), 7.10-7.14 (t, 1H, **H**-Ar), 7.18 (s, 1H, **H**-N-), 7.21-7.30 (m, 5H, **H**-Ar), 7.42-7.48 (t, 2H, **H**-Ar), 7.58-7.61 (t, 1H, **H**-Ar), 7.64-7.68 (d, 2H, **H**-Ar), 7.80-7.84 (dd, 2H, **H**-Ar), 8.65 (s, 1H, **H**-trisubstituted 1*H*-pyrazole), 13.23 (s, 1H, **H**-O-). ^{13}C NMR 400 MHz: (DMSO-d_6, δ ppm): 41.0, 46.4, 56.1, 88.0, 111.1, 114.8, 116.4, 117.2, 118.9, 119.9, 121.5, 123.0, 123.3, 125.4, 126.2, 128.3, 129.3, 129.7, 131.1, 139.7, 149.9, 152.5, 155.6, 157.3, 159.4, 166.2. MS: *m/z* 478; anal. Calcd. for $C_{28}H_{22}N_4O_4$: C, 70.28; H, 4.63; N, 11.71; O, 13.37; Found: C, 70.25; H, 4.61; N, 11.68; O, 13.33 %.

3-(1',3'-diphenyl-3,4-dihydro-1'H,2H-[3,4'-bipyrazol]-5-yl)-4-hydroxy-7,8-dimethyl-2H-chromen-2-one (5j)

IR (KBr) cm^{-1}: 3206, 3148, 3066, 2358, 1928, 1680, 1615, 1550, 1420, 1230, 1144, 1068, 1020, 970, 850, 830, 758, 690. ^{1}H NMR 400 MHz: (DMSO-d_6, δ ppm): 2.28 (s, 3H, -C**H**$_3$), 2.35 (s, 3H, -C**H**$_3$), 3.52-3.58 (dd, 1H, **H**$_a$-CH$_b$),

4.00-4.04 (dd, 1H, $\mathbf{H_b}$-CH_a), 5.05 (t, 1H, **H**-C-CH_aH_b), 7.11-7.15 (d, 1H, **H**-Ar), 7.18 (s, 1H, **H**-N-), 7.36-7.42 (t, 2H, **H**-Ar), 7.46-7.50 (t, 2H, **H**-Ar), 7.60-7.68 (m, 3H, **H**-Ar), 7.75-7.84 (m, 4H, **H**-Ar), 8.80 (s, 1H, **H**-trisubstituted 1*H*-pyrazole), 13.21 (s, 1H, **H**-O-). ^{13}C NMR 400 MHz: (DMSO-d_6, δ ppm): 11.6, 18.8, 41.0, 46.4, 88.0, 114.3, 117.2, 119.9, 123.0, 123.7, 124.5, 126.2, 127.5, 129.2, 129.3, 133.0, 137.9, 139.7, 149.9, 155.6, 159.4, 166.2. MS: *m/z* 476; anal. Calcd. for $C_{29}H_{24}N_4O_3$: C, 73.09; H, 5.08; N, 11.76; O, 10.07; Found: C, 73.06; H, 5.06; N, 11.72; O, 10.04 %.

4-hydroxy-7,8-dimethyl-3-(1'-phenyl-3'-(p-tolyl)-3,4-dihydro-1'H,2H-[3,4'-bipyrazol]-5-yl)-2H-chromen-2-one (5k)

IR (KBr) cm^{-1}: 3207, 3157, 3068, 2916, 2861, 2359, 1925, 1682, 1609, 1500, 1450, 1337, 1228, 1141, 1066, 1019, 963, 877, 825, 754, 692. ^{1}H NMR 400 MHz: (DMSO-d_6, δ ppm): 2.23 (s, 3H, -C$\mathbf{H_3}$), 2.33 (s, 3H, -C$\mathbf{H_3}$), 2.35 (s, 3H, -C$\mathbf{H_3}$), 3.54-3.61 (dd, 1H, $\mathbf{H_a}$-CH_b), 4.01-4.08 (dd, 1H, $\mathbf{H_b}$-CH_a), 5.00 (t, 1H, **H**-C-CH_aH_b), 7.10-7.12 (d, 1H, **H**-Ar), 7.14 (s, 1H, **H**-N-), 7.29-7.33 (m, 3H, **H**-Ar), 7.48-7.52 (t, 2H, **H**-Ar), 7.66-7.70 (m, 3H, **H**-Ar), 7.90-7.92 (d, 2H, **H**-Ar), 8.72 (s, 1H, **H**-trisubstituted 1*H*-pyrazole), 13.21-13.23 (s, 1H, **H**-O-). ^{13}C NMR 400 MHz: (DMSO-d_6, δ ppm): 11.6, 18.8, 41.0, 46.4, 88.0, 114.3, 117.2, 119.9, 123.0, 123.7, 124.5, 126.2, 127.5, 129.2, 129.3, 133.0, 137.9, 139.7, 149.9, 155.6, 159.4, 166.2. MS: *m/z* 490; anal. Calcd. for $C_{30}H_{26}N_4O_3$: C, 73.45; H, 5.34; N, 11.42; O, 9.78; Found: C, 73.43; H, 5.33; N, 11.40; O, 9.74 %.

3-(3'-(4-chlorophenyl)-1'-phenyl-3,4-dihydro-1'H,2H-[3,4'-bipyrazol]-5-yl)-4-hydroxy-7,8-dimethyl-2H-chromen-2-one (5l)

IR (KBr) cm^{-1}: 3210, 3160, 3066, 2920, 2860, 2369, 1930, 1680, 1620, 1520, 1440, 1330, 1240, 1150, 1070, 1030, 970, 880, 830, 760, 730, 690. ^{1}H NMR 400 MHz: (DMSO-d_6, δ ppm): 2.22 (s, 3H, -C$\mathbf{H_3}$), 2.32 (s, 3H, -C$\mathbf{H_3}$), 3.56-3.60 (dd, 1H, $\mathbf{H_a}$-CH_b), 4.00-4.04 (dd, 1H, $\mathbf{H_b}$-CH_a), 5.08 (t, 1H, **H**-C-CH_aH_b), 7.08-7.10 (d, 1H, **H**-Ar), 7.12 (s, 1H, **H**-N-), 7.38-7.46 (m, 3H, **H**-Ar), 7.50-7.56 (t, 2H, **H**-Ar), 7.68-7.72 (m, 3H, **H**-Ar), 7.96-8.00 (d, 2H, **H**-Ar), 8.80 (s, 1H, **H**-trisubstituted 1*H*-pyrazole), 13.30 (s, 1H, **H**-O-). ^{13}C NMR 400 MHz: (DMSO-d_6, δ ppm): 11.6, 18.8, 41.0, 46.4, 88.0, 114.3, 117.2, 129.9, 123.0, 124.5, 126.2, 128.8, 128.9, 129.3, 131.1, 134.3, 137.9, 139.7, 149.9, 155.6, 159.4, 166.2. MS: *m/z* 510; anal. Calcd. for $C_{29}H_{23}ClN_4O_3$: C, 68.17; H, 4.54; Cl, 6.94; N, 10.96; O, 9.39; Found: C, 68.15; H, 4.53; Cl, 6.91; N, 10.94; O, 9.37%.

3-(3'-(4-fluorophenyl)-1'-phenyl-3,4-dihydro-1'H,2H-[3,4'-bipyrazol]-5-yl)-4-hydroxy-7,8-dimethyl-2H-chromen-2-one (5m)

IR (KBr) cm^{-1}: 3212, 3160, 3052, 2920, 2860, 2350, 1940, 1630, 1610, 1520, 1430, 1347, 1230, 1140, 1120, 1070, 1025, 970, 850, 830, 758, 698. ^{1}H NMR 400 MHz: (DMSO-d_6, δ ppm): 2.18 (s, 3H, -C$\mathbf{H_3}$), 2.30 (s, 3H, -C$\mathbf{H_3}$), 3.52-3.58 (dd, 1H, $\mathbf{H_a}$-CH_b), 3.98-4.02 (dd, 1H, $\mathbf{H_b}$-CH_a), 5.25 (t, 1H, **H**-C-CH_aH_b), 7.08-7.10 (d, 1H, **H**-Ar), 7.19 (s, 1H, **H**-N-), 7.40-7.45 (m, 3H, **H**-Ar), 7.50-7.53 (t, 2H, **H**-Ar), 7.68-7.72 (m, 3H, **H**-Ar), 7.98-8.00 (d, 2H, **H**-Ar), 8.75 (s, 1H, **H**-trisubstituted 1*H*-pyrazole), 13.33 (s, 1H, **H**-O-). ^{13}C NMR 400 MHz: (DMSO-d_6, δ ppm): 11.6, 18.8, 41.0, 46.4, 88.0, 114.3, 117.2, 116.0, 117.2, 119.9, 123.0, 123.7, 124.5, 126.2, 128.6, 129.3, 130.6, 137.9, 139.7, 150.3, 155.6, 159.4, 162.9, 166.2. MS: *m/z* 494; anal. Calcd. for $C_{29}H_{23}FN_4O_3$: C, 70.43; H, 4.69; F, 3.84; N, 11.33; O, 9.71; Found: C, 70.41; H, 4.66; F, 3.82; N, 11.31; O, 9.69%.

3-(3'-(4-bromophenyl)-1'-phenyl-3,4-dihydro-1'H,2H-[3,4'-bipyrazol]-5-yl)-4-hydroxy-7,8-dimethyl-2H-chromen-2-one (5n)

IR (KBr) cm-1: 3205, 3160, 3062, 2920, 2863, 2352, 1920, 1680, 1619, 1520, 1440, 1320, 1230, 1150, 1062, 1020, 970, 880, 830, 760, 690, 630. ^{1}H NMR 400 MHz: (DMSO-d_6, δ

ppm): 2.28 (s, 3H, -C**H**$_3$), 2.32 (s, 1H, -C**H**$_3$), 3.50-3.55 (dd, 1H, **H**$_a$-CH$_b$), 4.00-4.06 (dd, 1H, **H**$_b$-CH$_a$), 5.22 (t, 1H, **H**-C-CH$_a$H$_b$), 7.08-7.13 (d, 1H, **H**-Ar), 7.20 (s, 1H, **H**-N-), 7.44-7.50 (t, 2H, **H**-Ar), 7.53-7.59 (m, 3H, **H**-Ar), 7.62-7.68 (m, 3H, **H**-Ar), 7.94-7.99 (d, 2H, **H**-Ar), 8.78 (s, 1H, **H**-trisubstituted 1*H*-pyrazole), 13.32 (s, 1H, **H**-O-). ^{13}C NMR 400 MHz: (DMSO-d_6, δ ppm): 11.6, 18.8, 41.0, 46.4, 88.0, 114.3, 117.2, 119.9, 123.0, 123.1, 126.2, 128.3, 129.3, 132.0, 132,1, 137.9, 139.7, 150.3, 155.6, 159.4, 166.2. MS: *m/z* 555; anal. Calcd. for $C_{29}H_{23}BrN_4O_3$: C, 62.71; H, 4.17; Br, 14.39; N, 10.09; O, 8.64; Found: C, 62.68; H, 4.15; Br, 14.36; N, 10.05; O, 8.62%.

4-hydroxy-7,8-dimethyl-3-(3'-(4-nitrophenyl)-1'-phenyl-3,4-dihydro-1'H,2H-[3,4'-bipyrazol]-5-yl)-2H-chromen-2-one(5o)

IR (KBr) cm^{-1}: 3210, 3160, 3062, 2920, 2850, 2360, 1930, 1680, 1610, 1520, 1450, 1360, 1347, 1220, 1151, 1070, 1020, 973, 880, 835, 750, 690. ^{1}H NMR 400 MHz: (DMSO-d_6, δ ppm): 2.26 (s, 3H, -C**H**$_3$), 2.38 (s, 3H, -C**H**$_3$), 3.50-3.54 (dd, 1H, **H**$_a$-CH$_b$), 4.00-4.04 (dd, 1H, **H**$_b$-CH$_a$), 5.00-5.04 (t, 1H, **H**-C-CH$_a$H$_b$), 7.05-7.09 (d, 1H, **H**-Ar), 7.18 (s, 1H, **H**-N-), 7.44 (t, 1H, **H**-Ar), 7.55-7.59 (t, 2H, **H**-Ar), 7.68-7.72 (m, 3H, **H**-Ar), 7.94-7.98 (d, 2H, **H**-Ar), 8.18-8.22 (d, 2H, **H**-Ar), 8.80 (s, 1H, **H**-trisubstituted 1*H*-pyrazole), 13.25 (s, 1H, **H**-O-). ^{13}C NMR 400 MHz: (DMSO-d_6, δ ppm): 11.6, 18.8, 41.0, 46.4, 28.0, 114.3, 117.2, 119.9, 123.0, 123.7, 124.4, 124.5, 126.2, 126.8, 129.3, 137.9, 139.1, 139.7, 147.9, 149.9, 150.3, 155.6, 159.4, 166.2. MS: *m/z* 521; anal. Calcd. for $C_{29}H_{23}N_5O_5$: C, 66.79; H, 4.45; N, 13.43; O, 15.34; Found: C, 66.76; H, 4.43; N, 13.40; O, 15.32%.

4-hydroxy-7,8-dimethyl-3-(3'-(3-nitrophenyl)-1'-phenyl-3,4-dihydro-1'H,2H-[3,4'-bipyrazol]-5-yl)-2H-chromen-2-one (5p)

IR (KBr) cm^{-1}: 3217, 3167, 3062, 2920, 2862, 2360, 1920, 1680, 1610, 1520, 1530, 1460, 1330, 1328, 1220, 1142, 1070, 1020, 970, 880, 830, 758, 690. ^{1}H NMR 400 MHz: (DMSO-d_6, δ ppm): 2.23 (s, 3H, -C**H**$_3$), 2.35 (s, 3H, -C**H**$_3$), 3.52-3.55 (dd, 1H, **H**$_a$-CH$_b$), 4.02-4.06 (dd, 1H, **H**$_b$-CH$_a$), 5.02-5.05 (t, 1H, **H**-C-CH$_a$H$_b$), 7.09-7.13 (d, 1H, **H**-Ar), 7.13 (s, 1H, **H**-N-), 7.50 (t, 1H, **H**-Ar), 7.52-7.56 (t, 2H, **H**-Ar), 7.70-7.78 (m, 4H, **H**-Ar), 8.17-8.23 (d, 2H, **H**-Ar), 8.70 (s, 1H, **H**-trisubstituted 1*H*-pyrazole), 8.76 (s, 1H, **H**-Pyrazole), 13.20 (s, 1H, **H**-O-). ^{13}C NMR 400 MHz: (DMSO-d_6, δ ppm): 11.6, 18.8, 41.0, 46.4, 88.0, 114.3, 117.2, 119.9, 122.7, 123.0, 123.7, 123.9, 124.5, 126.2, 128.8, 129.3, 130.6, 133.6, 133.9, 137.9, 139.7, 148.4, 149.9, 155.6, 159.4, 166.2. MS: *m/z* 521; anal. Calcd. for $C_{29}H_{23}N_5O_5$: C, 66.79; H, 4.45; N, 13.43; O, 15.34; Found: C, 66.77; H, 4.43; N, 13.42; O, 15.32 %.

4-hydroxy-3-(3'-(3-hydroxyphenyl)-1'-phenyl-3,4-dihydro-1'H,2H-[3,4'-bipyrazol]-5-yl)-7,8-dimethyl-2H-chromen-2-one (5q)

IR (KBr) cm^{-1}: 3210, 3150, 3062, 2920, 2860, 2550, 2360, 1924, 1680, 1620, 1510, 1460, 1370, 1330, 1230, 1145, 1068, 1020, 965, 880, 830, 752, 690. ^{1}H NMR 400 MHz: (DMSO-d_6, δ ppm): 2.25 (s, 3H, -C**H**$_3$), 2.36 (s, 3H, -C**H**$_3$), 3.51-3.54 (dd, 1H, **H**$_a$-CH$_b$), 4.06-4.08 (dd, 1H, **H**$_b$-CH$_a$), 5.06-5.09 (t, 1H, **H**-C-CH$_a$H$_b$), 5.41-5.43 (s, 1H, **H**-O-), 6.96-6.98 (d, 1H, **H**-Ar), 7.04-7.08 (d, 1H, **H**-Ar), 7.16 (s, 1H, **H**-N-), 7.34-7.42 (m, 3H, **H**-Ar), 7.46 (t, 1H, **H**-Ar), 7.58-7.62 (t, 2H, **H**-Ar), 7.65-7.72 (m, 3H, **H**-Ar), 8.74 (s, 1H, **H**-trisubstituted 1*H*-pyrazole), 13.23 (s, 1H, **H**-O-). ^{13}C NMR 400 MHz: (DMSO-d_6, δ ppm): 11.6, 18.8, 41.0, 46.4, 88.0, 114.3, 115.9, 117.2, 119.9, 120.1, 123.0, 123.7, 124.5, 126.2, 128.8, 129.3, 130.6, 134.4, 137.9, 139.7, 149.9, 150.3, 155.6, 157.5, 159.4, 166.2. MS: *m/z* 492; anal. Calcd. for $C_{29}H_{24}N_4O_4$: C, 70.72; H, 4.91; N, 11.38; O, 12.99; Found: C, 70.70; H, 4.88; N, 11.36; O, 12.97 %.

4-hydroxy-3-(3'-(2-methoxyphenyl)-1'-phenyl-3,4-dihydro-1'H,2H-[3,4'-bipyrazol]-5-yl)-7,8-dimethyl-2H-chromen-2-one (5r)

IR (KBr) cm^{-1}: 3336, 3105, 3064, 2958, 2833, 2359, 2332, 1708, 1607, 1549, 1500, 1461, 1376, 1329, 1339, 1056, 1020, 961, 847, 757, 695. ^{1}H NMR 400 MHz: (DMSO-d_6, δ ppm): 2.23 (s, 3H, -C**H**$_3$), 2.33 (s, 3H, -C**H**$_3$), 3.82 (s, 3H, -O-C**H**$_3$), 3.46-3.53 (dd, 1H, **H**$_a$-CH$_b$), 3.84-3.92 (dd, 1H, **H**$_b$-CH$_a$), 4.67-4.68 (t, 1H, **H**-C-CH$_a$H$_b$), 6.92 (s, 1H, **H**-N-), 7.02-7.06 (t, 1H, **H**-Ar), 7.09-7.14 (t, 2H, **H**-Ar), 7.28-7.31 (t, 1H, **H**-Ar), 7.39-7.50 (m, 4H, **H**-Ar), 7.65-7.67 (d, 1H, **H**-Ar), 7.85-7.87 (d, 2H, **H**-Ar), 8.61 (s, 1H, **H**-trisubstituted 1*H*-pyrazole), 13.33 (s, 1H, **H**-O-). ^{13}C NMR 400 MHz: (DMSO-d_6, δ ppm): 11.6, 18.8, 41.0, 46.4, 56.1, 88.0, 111.1, 114.3, 117.2, 118.9, 119.9, 121.5, 123.0, 123.7, 124.5, 126.2, 129.3, 129.7, 131.1, 137.9, 139.7, 149.9, 155.6, 157.3, 159.4, 166.2. MS: *m/z* 506; anal. Calcd. for $C_{30}H_{26}N_4O_4$: C, 71.13; H, 5.17; N, 11.06; O, 12.63; Found: C, 71.11; H, 5.15; N, 11.03; O, 12.61 %.

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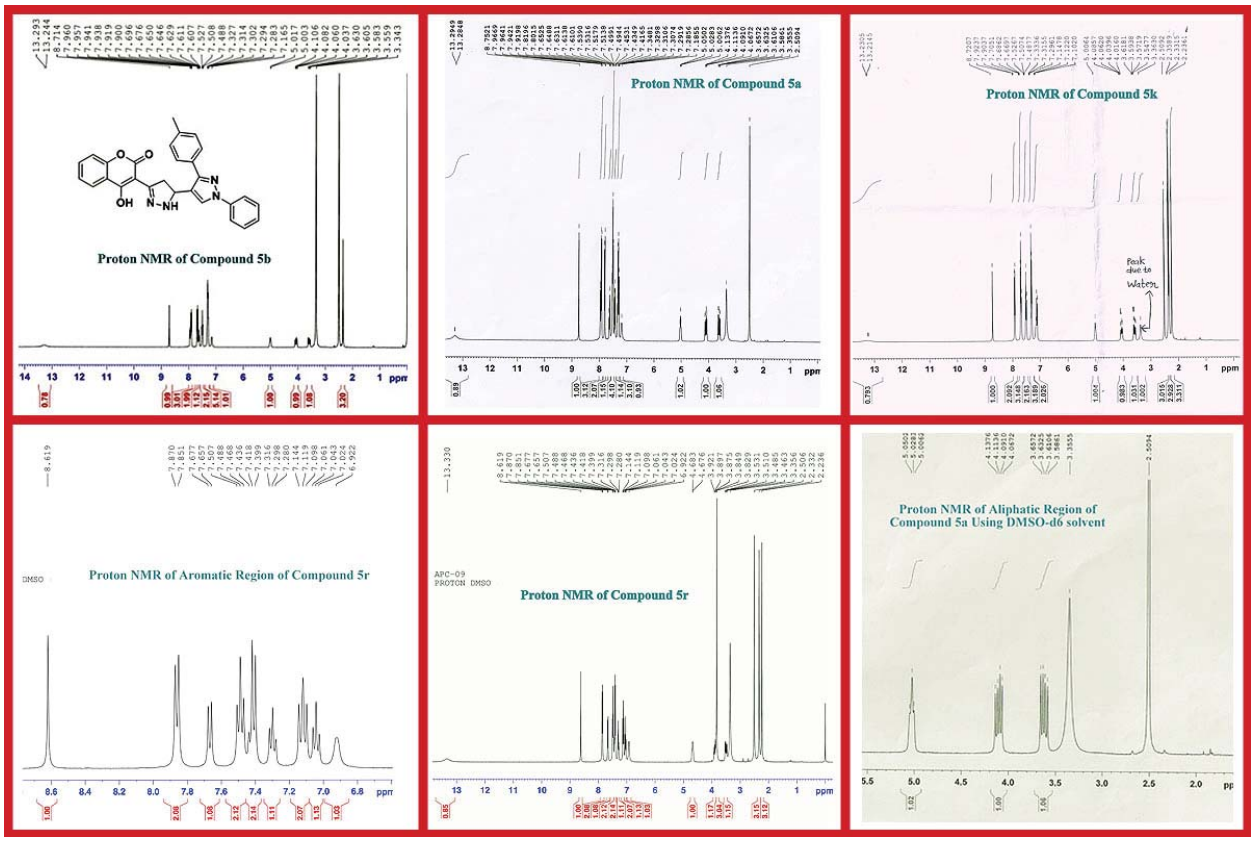
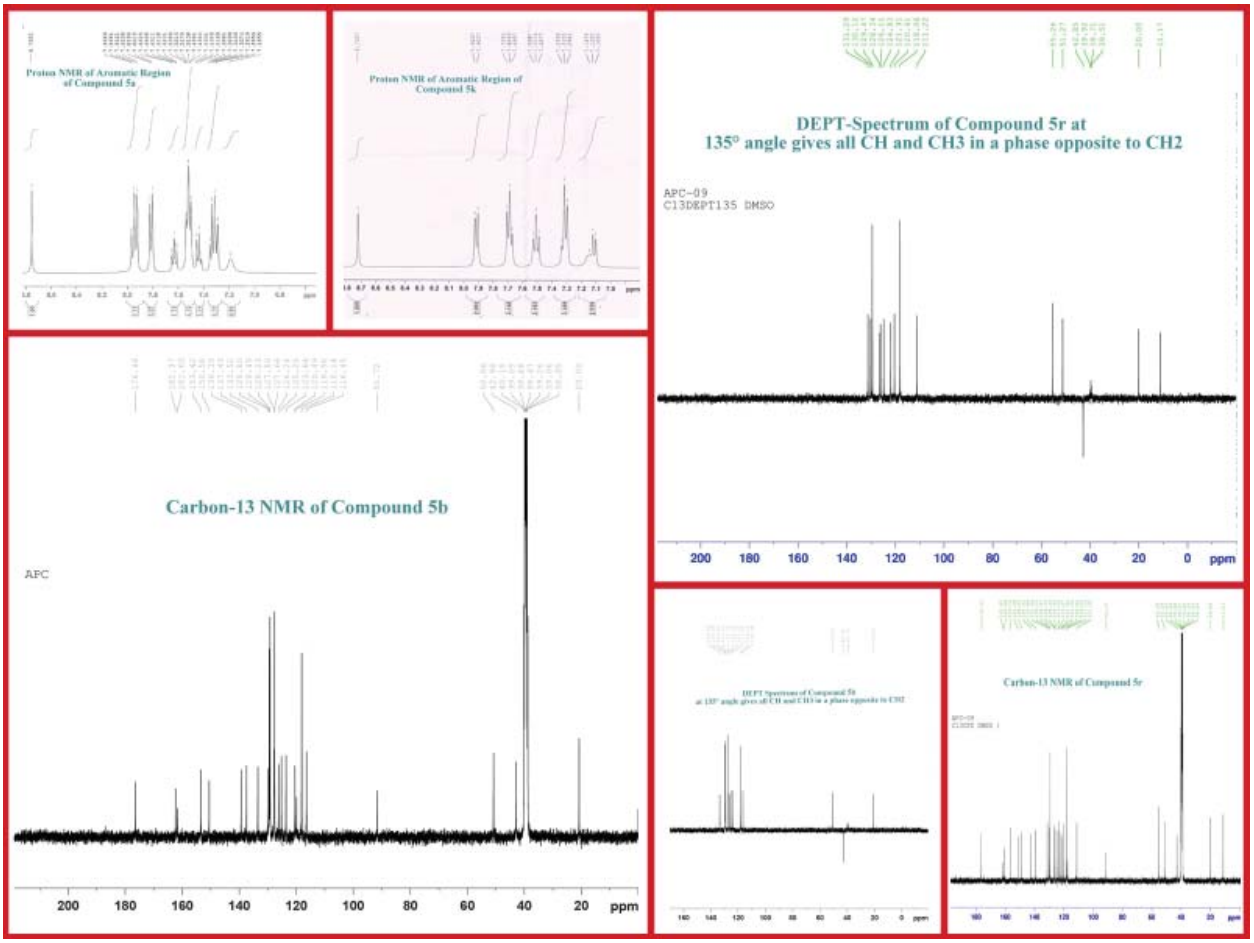
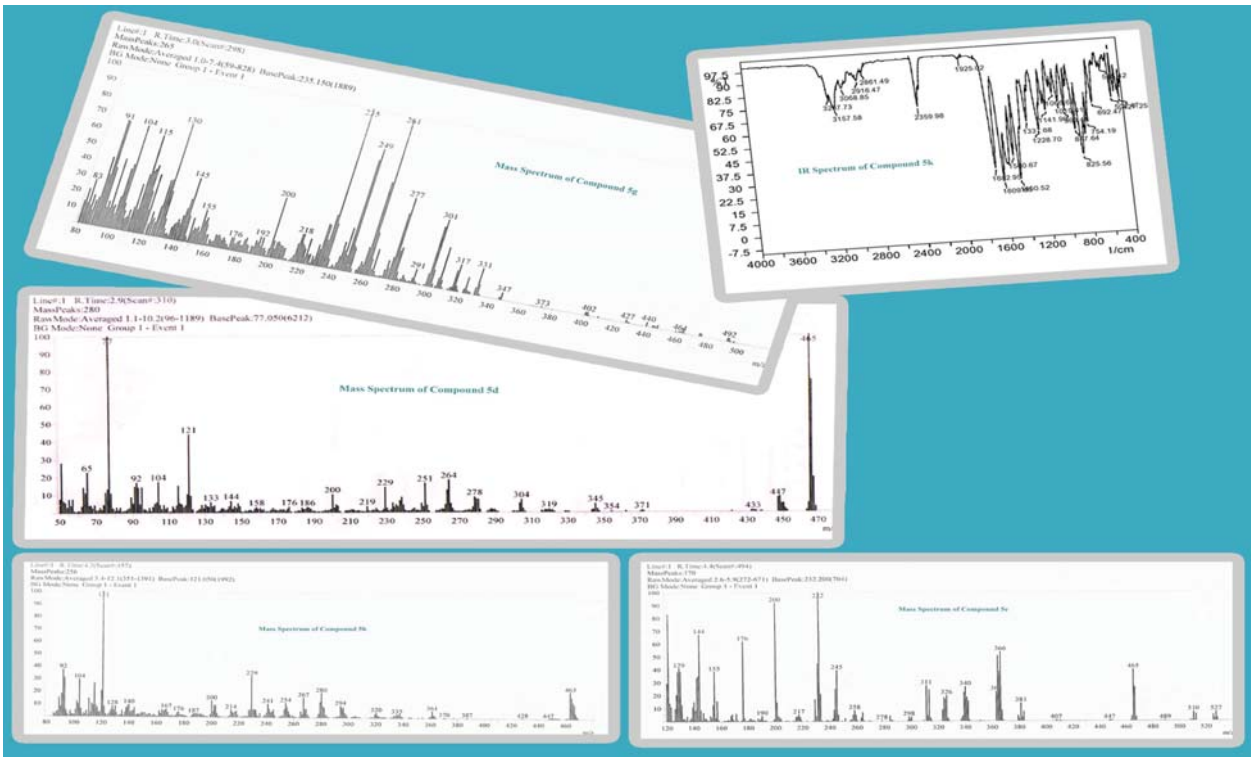



Proton NMR of Aromatic Region of Compound 5a
Proton NMR of Aromatic Region of Compound 5k
DEPT-Spectrum of Compound 5r at 135° angle gives all CH and CH3 in a phase opposite to CH2
APC-09
C13DEPT135 DMSO
200 180 160 140 120 100 80 60 40 20 0 ppm
Carbon-13 NMR of Compound 5b
APC
200 180 160 140 120 100 80 60 40 20 ppm
Carbon-13 NMR of Compound 5r


Mass Spectrum of Compound 5g
IR Spectrum of Compound 5k
4000 3600 3200 2800 2400 2000 1600 1200 800 400 1/cm
Mass Spectrum of Compound 5d

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