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A rapid and highly efficient microwave synthesis of highly functionalized chalcones derivatives

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Abstract: A new series of substituted coumarinyl chalcones were synthesized by microwave method. The reaction of 3-acetyl 4-hydroxy coumarin **1a-c** with substituted 1,3-diphenyl-1H-pyrazole-4-carbaldehyde **2a-h** in the presence of piperidine afforded novel chalcones **3a-x** under microwave irradiation. The main advantage of this reaction is very rapid, facile and high yielding. The structures of all synthesized compounds were well characterized by Mass, FT-IR, ^{1}H NMR and elemental analysis.
Key words: Chalcones, 3-Acetyl 4-hydroxy coumarin, Pyrazole aldehyde, piperidine, Microwave.

Introduction:

The chalcones are α, β unsaturated ketones containing the reactive keto ethylene group –CO– CH=CH-. Presence of α, β unsaturated carbonyl system in chalcone makes it biologically active. Many of the chalcones are highly biological active which have medicinal and pharmaceutical applications.[1-2] Chalcones are products of condensation of simple or substituted aromatic with simple or substituted acetophenone in presence of alkali. They have been reported to possess antioxidant,[3-6] antimalarial,[7] antileishmanial,[8] anti-inflammatory,[9] antitumor[10] and antibacterial activity.[11] Pyrazole and fused heterocyclic pyrazole derivatives constute an interesting class of heterocycles due to their synthetic versatility and effective biological activities.[12-14] Pyrazoles are also known for its antibacterial, anti HIV, anticancer anti-inflammatory, analgesic and hypoglycaemic activities.[15] Pyrazoles are used as insecticidal and pesticidal due to their herbicidal and fungicidal activity.[16] Recently, pyrazoles containing aryl substituted emerged as p38 Kinase inhibitors, antiparasitic activities.[17] These finding prompted us to synthesize pyrazole containing DHPs functionalized with dicyano groups for biological interest. Moreover, the Coumarin derivatives have been reported for anticoagulant, anti-inflammatory,[18] antimicrobial,[19] anti HIV,[20] antioxidant,[21] antiallergic, anticancer[22] and anti proliferative and antiviral[23] activities. These finding us to synthesize the pyrazole and Coumarin containing chalcones for biological interest. Our ongoing interest on the synthesis of highly functionalized chalcones by various methods,[24] as a continuation of these studies, herein we report a rapid and high yielding synthesis of chalcones by microwave method.

Experimental :

Melting points were determined in open capillary tubes and are uncorrected. Formation of the compounds was routinely checked by TLC on silica gel-G plates of 0.5 mm thickness and spots were located by iodine and UV. All the reactions were carried out in **Q-pro microwave synthesizer.** IR spectra were recorded in **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 was determined in $CDCl_3$/DMSO solution on a **Bruker Ac 400 MHz spectrometer**. Elemental analysis of the all the synthesized compounds was carried out on Elemental **Vario EL**

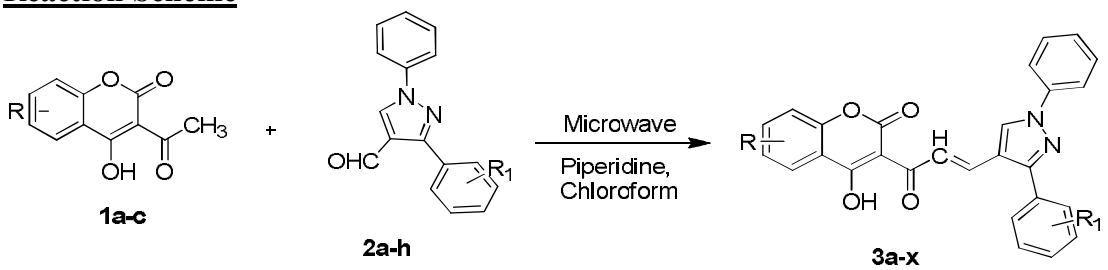
III Carlo Erba 1108 model and the results are in agreements with the structures assigned.

General procedure for preparation of 3a-x :
3-acetyl 4-hydroxy Coumarin **1a-c** was synthesized by reported method.[25] A mixture of 3-Acetyl 4-hydroxy coumarin (0.01mole) **1a-c** and substituted aromatic aldehyde (0.01mole) **2a-h** were dissolved in 30 ml of chloroform. The catalytic amount of piperidine+ (0.02 ml) was added and the reaction mixture was subjected to microwave for a specific time (**Table 1**) at lower power (320W). The progress of the reaction was monitored by TLC examination at an interval of every minutes. On completion of reaction distilled out excess of chloroform and cool it and add methanol to it, filter it and wash with methanol, dried.

Result and discussion:

All the synthesized compounds were characterized by TLC, Melting point, elemental analysis, IR and ^{1}HNMR. Analysis indicated by the symbols of the elements is very close to the theoretical values. During the reaction procedure we have observed that the time taken by **3b**, **3k**, **3l**, **3m** and **3p** is less as compare to other.
In conclusion, we have reported a rapid, facile and high yielding procedure for the synthesis of chalcones for biological interest. The present procedure is general and convenient for the synthesis of highly functionalized chalcones derivatives.

Reaction Scheme



R= H,8-CH_3, 5,8-diCH_3

R1=H,Cl,OH etc...

Physical data table -1

Entry	Substitution		M.P.	Time	Yield[a]
	R	R_1			
3a	H	H	186-188	8	84
3b	4-CH_3	H	172-174	**5**	88
3c	2-OCH_3	H	198-200	9	83
3d	4-NO_2	H	174-176	7	89
3e	2-OCH_3	H	172-174	11	83
3f	4-Cl	H	184-186	14	84
3g	3-NO_2	H	202-204	7	84
3h	4-F	H	192-194	9	88
3i	H	8-CH_3	218-220	8	84
3j	4-CH_3	8- CH_3	178-180	7	78
3k	4-Cl	8- CH_3	212-214	**5**	86
3l	4-NO_2	8- CH_3	166-168	**5**	82

3m	2-OH	8- CH_3	158-160	**3**	72
3n	2-OCH_3	8- CH_3	192-194	7	83
3o	3-NO_2	8- CH_3	200-202	8	79
3p	4-F	8- CH_3	218-220	**5**	85
3q	H	5,8-di CH_3	188-190	9	89
3r	4-CH_3	5,8-di CH_3	210-212	6	82
3s	4-Cl	5,8-di CH_3	204-206	8	85
3t	4-NO_2	5,8-di CH_3	186-188	7	78
3u	2-OH	5,8-di CH_3	176-178	**5**	83
3v	2-OCH_3	5,8-di CH_3	192-194	9	86
3w	3-NO_2	5,8-di CH_3	196-198	7	78
3x	4-F	5,8-di CH_3	202-204	8	81

[a] Isolated yield after purification

Analytical data:

4-Hydroxy-3-((E)-3-(1,3-di phenyl-1H-pyrazol-4-yl) acryloyl)-2H-chromen-2-one.(3a)

IR (cm^{-1}): 3587, 3101, 3015, 2978, 2898, 1708, 1497, 1433, 1363, 1291, 1236, 1215, 1134, 987, 933, 690, MS: *m/z:* 434.44(M^+); Anal. Calcd. for $C_{27}H_{18}N_2O_4$: C, 74.64; H, 4.18; N, 6.45; O,14.73; Found: C, 74.60; H, 4.06; N, 6.31; O, 14.69.

4-Hydroxy-3-((E)-3-(1-phenyl-3-p-tolyl-1H-pyrazol-4yl)acryloyl)-2H-chromen-2-one (3b)

IR (cm^{-1}): 3581, 3522, 3001, 2968, 2897, 1707, 1498, 1431, 1383, 1290, 1226, 1205, 1139, 997, 923, 731, ^{1}H NMR (DMSO-d_6) δ ppm: 2.16 (s, 1H), 7.04-7.07 (d, 1H) 7.08-7.09 (d, 2H), 7.23-7.27 (m, 3H), 7.38-7.40 (t, 2H), 7.44-7.46 (d,2H, J=8.0Hz), 7.51-7.56 (t, 1H), 7.59-7.63(d, 1H), 7.70-7.72 (d, 2H, J=8.0Hz), 8.08-8.10 (d, 1H), 8.46 (s, 1H), MS: *m/z:* 448.47(M^+); Anal. Calcd. for $C_{28}H_{20}N_2O_4$: C, 74.99; H, 4.50; N,6.25; O, 14.27 ; Found: C, 74.89; H, 4.40; N, 6.19; O, 14.18.

4-Hydroxy-3-((E)-3-(3-(2-hydroxypenyl)-1-phenyl-1H-pyrazol-4-yl)acryloyl)-2H-chromen-2-one. (3c)

IR (cm^{-1}): 3581, 3477, 3194, 3084, 3003, 2899, 1705, 1454, 1429, 1294, 1226, 1138, 1062, 819, 761, 756, 690, ^{1}H NMR (DMSO-d_6) δ ppm: 7.14 (s, 1H), 7.16 - 7.19 (t, 1H), 7.21 - 7.36 (m, 3H), 7.45 - 7.47 (d, 2H), 7.58 -7.76 (m, 4H), 7.77 - 7.79 (d, 2H), 7.95 – 7.99(d, 1H) , 8.06 – 8.08(d, 1H), 8.42(s, 1H), MS: *m/z:* 450.44(M^+); Anal. Calcd. for $C_{27}H_{18}N_2O_5$: C, 71.99; H, 4.03; N, 6.22; O,17.76 Found: C, 71.89; H, 4.01; N, 6.10; O,17.66.

4-Hydroxy-3-((E)-3-(3-(4-nitrophenyl)-1-phenyl-1H-pyrazol-4-yl)acryloyl)-2H-chromen-2-one. (3d)

IR (cm^{-1}): 3582, 3532, 3031, 3010, 2966, 2887, 1717, 1545, 1499, 1433, 1373, 1291, 1236, 996, 745, 689, MS: *m/z:* 479.44(M^+); Anal. Calcd. for $C_{27}H_{17}N_3O_6$: C, 67.64; H, 3.57; N, 8.76; O, 20.02 Found: C, 67.54; H, 3.45; N, 8.70; O, 20.00.

4-Hydroxy-3-((E)-3-(3-(2-methoxyphenyl)-1-phenyl-1H-pyrazol-4-yl)acryloyl)-2H-chromen-2-one (3e)

% IR (cm^{-1}): 3571, 3101, 3010, 2961, 2891, 1727, 1497, 1432, 1384, 1291, 1227, 1215, 1149, 987, 913, 731, 705, MS: *m/z:* 464.47(M^+); Anal. Calcd. for $C_{28}H_{20}N_2O_5$: C, 72.41; H, 4.34; N, 6.03; O,17.22 Found: C, 72.23; H, 4.29; N, 6.00; O, 17.13.

3-((E)-3-(3-(4-chlorophenyl)-1-phenyl-1H-pyrazol-4-yl)acryloyl)-4-hydroxy-2H-chromen-2-one. (3f)

IR (cm^{-1}): 3582, 3532, 3011, 2978, 2887, 1707, 1498, 1432, 1393, 1291, 1236, 1215, 1149, 987, 925, 755, 715, MS: *m/z:* 468 (M^+), 470 (M^{+2}); Anal. Calcd. for $C_{27}H_{17}ClN_2O_4$: C, 69.16; H, 3.65; N, 5.97; O, 13.65 Found: C, 69.11; H, 3.57; N, 5.85; O, 13.60.

4-Hydroxy-3-((E)-3-(3-(3-nitrophenyl)-1-phenyl-1H-pyrazol-4-yl)acryloyl)-2H-chromen-2-one (3g)

IR (cm^{-1}): 3561, 3532, 3121, 2969, 2890, 1717, 1551, 1499, 1432, 1373, 1291, 1236, 1215, 1149, 998, 943, 731, 688, MS: *m/z:* 479.44(M^+); Anal. Calcd. for $C_{27}H_{17}N_3O_6$: C, 67.64; H, 3.57; N, 8.76; O, 20.02 Found: C, 67.54; H, 3.46; N, 8.71; O, 20.00.

3-((E)-3-(3-(4-flourophenyl)-1-phenyl-1H-pyrazol-4-yl)acryloyl)-4-hydroxy-2H-chromen-2-one (3h)

IR (cm^{-1}): 3566, 3542, 3021, 2989, 2898, 1707, 1489, 1442, 1372, 1281, 1246, 1205, 1159, 988, 942, 739,

712, MS: *m/z:* 452(M^+), 454 (M^{+2}) ; Anal. Calcd. for $C_{27}H_{17}FN_2O_4$: C,71.68; H, 3.79; N,6.19; O,14.15 Found: C, 71.63; H, 3.59; N, 6.17; O,14.10.

4-Hydroxy-8-methyl-3-((E)-3-(1,3-diphenyl-1H-pyrazol-4-yl)acryloyl)-2H-chromen-2-one (3i)

IR (cm^{-1}): 3606, 3540, 3026, 2980, 2891, 1717, 1479, 1443, 1371, 1282, 1236, 1215, 998, 962, 704, MS: *m/z:* 448.47(M^+); Anal. Calcd. for $C_{28}H_{20}N_2O_4$: C,74.99; H, 4.50; N, 6.25; O,14.27 Found: C, 74.83; H, 4.41; N, 6.17; O,14.18.

4-Hydroxy-8-methyl-3-((E)-3-(1-phenyl-3-p-tolyl-1H-pyrazol-4-yl)acryloyl)-2H-chromen-2-one (3j)

IR (cm^{-1}): 3616, 3560, 3036, 2981, 2892, 1707, 1489, 1453, 1372, 1281, 1246, 1205, 997, 961, 735, MS: *m/z:* 462.50(M^+); Anal. Calcd. for $C_{29}H_{22}N_2O_4$: C, 75.31; H, 4.79; N, 6.06: O,13.84 Found: C, 75.23; H, 4.71; F, 6.01; O,13.79.

3-((E)-3-(3-(4-chlorophenyl)-1-phenyl-1H-pyrazol-4-yl)acryloyl)-4-hydroxy-8-methyl-2H-chromen-2-one (3k)

IR (cm^{-1}): 3616, 3560, 3036, 2981, 2892, 1707, 1489, 1453, 1372, 1281, 1246, 1205, 997, 961, 735, MS: *m/z:* 482(M^+), 484(M^{+2}) ; Anal. Calcd. for $C_{28}H_{19}ClN_2O_4$: C, 69.64; H, 3.97; Cl, 7.34; N, 5.80 ;O, 13.25 Found: C, 69.63; H, 3.81; Cl,7.27; N,579; O,13.19.

4-Hydroxy-8-methyl-3-((E)-3-(3-(4-nitrophenyl)-1-phenyl-1H-pyrazol-4-yl)acryloyl)-wH-chromen-2-one (3l)

IR (cm^{-1}): 3536, 3561, 3046, 2991, 2890, 1717, 1541, 1481, 1451, 1382, 1291, 1266, 1215, 996, 966, 731, MS: *m/z:* 493(M^+); Anal. Calcd. for $C_{28}H_{19}N_3O_6$: C,68.15; H, 3.88; N, 8.52; O,19.45 Found: C,68.13; H, 3.81; N,8.47; O,19.41.

4-Hydroxy-3-((E)-3-(3-(2-hydroxyphenyl)-1-phenyl-1H-pyrazolyl-4-yl)acrylolyl)-8-methyl-2H-chromen-2-one(3m)

IR (cm^{-1}): 3546, 3521, 3056, 2981, 2891, 1707, 1471, 1461, 1372, 1292, 1276, 1205, 997, 965, 745, MS: *m/z:* 464.47(M^+); Anal. Calcd. for $C_{28}H_{20}N_2O_5$: C,72.41; H, 4.34; N, 6.06; O,17.22 Found: C, 72.33; H, 4.31; N, 6.01; O,17.11.

4-Hydroxy-3-((E)-3-(3-(2-methoxyphenyl)-1-phenyl-1H-pyrazol-4-yl)acryloyl)-8-methyl-2H-chromen-2-one (3n)

IR (cm^{-1}): 3556, 3541, 3016, 2998, 2892, 1707, 1491, 1461, 1392, 1282, 1281, 1225, 997, 735, 698, MS: *m/z:* 478.50(M^+); Anal. Calcd. for $C_{29}H_{22}N_2O_5$: C, 72.79; H, 4.63; N, 5.85; O, 16.72 Found: C, 72.73; H, 4.61; N, 5.77; O,16.69.

4-Hydroxy-8-methyl-3-((E)-3-(3-(3-nitrophenyl)-1-phenyl-1H-pyrazol-4-yl)acryloyl)-2H-chromen-2-one (3o)

IR (cm^{-1}): 3576, 3521, 3016, 2996, 2881, 1711, 1556, 1491, 1442, 1372, 1272, 1256, 1235, 986, 741, 701, MS: *m/z:* 493.47(M^+); Anal. Calcd. for $C_{28}H_{19}N_3O_6$: C,68.15; H, 3.88; N, 8.52; O,19.45 Found: C, 68.13; H, 3.71; N, 4.77; O, 19.41.

3-((E)-3-(3-(4-flourophenyl)-1-phenyl-1H-pyrazol-4-yl)acryloyl)-4-hydroxy-8-methyl-2H-chromen-2-one (3p)

IR (cm^{-1}): 3606, 3561, 3006, 2998, 2891, 1701, 1498, 1452, 1371, 1273, 1246, 1215, 996, 745, 702, MS: *m/z:* 466(M^+), 468(M^{+2}) ; Anal. Calcd. for $C_{28}H_{19}FN_2O_4$: C,72.10; H, 4.11; N, 6.01; O, 13.72 Found: C, 72.03; H, 4.05; N,5.98; O,13.69.

4-Hydroxy-5,8-dimethyl-3-((E)-3-(1,3-diphenyl-1H-pyrazol-4-yl)acryloyl)-2H-chromen-2-one (3q)

IR (cm^{-1}): 3616, 3501, 3016, 2988, 2892, 1711, 1488, 1381, 1272, 1256, 1225, 997, 715, MS: *m/z:* 462.50(M^+) ; Anal. Calcd. for $C_{29}H_{22}N_2O_4$: C, 75.31; H, 4.79; N, 6.06; O,13.84 Found: C, 75.23; H, 4.71; N, 6.01; O,13.79.

4-Hydroxy-5,8-dimethyl-3-((E)-3-(1-phenyl-3-p-tolyl-1H-pyrazol-4-yl)acryloyl-2H-chromen-2-one (3r)

IR (cm^{-1}): 3661, 3521, 3046, 2981, 2899, 1715, 1498, 1382, 1271, 1257, 1235, 987, 732, MS: *m/z:* 476.52(M^+) ; Anal. Calcd. for $C_{30}H_{24}N_2O_4$: C, 75.61; H, 5.08; N, 5.88; O, 13.43 Found: C, 75.58; H, 5.01; N, 5.77; O,13.39.

3-((E)-3-(3-(4-chlorophenyl)-1-phenyl-1H-pyrazol-4-yl)acryloyl)-4-hydroxy-5,8-dimethyl-2H-chromen-2-one(3s)

IR (cm^{-1}): 3651, 3591, 3041, 2991, 2879, 1705, 1488, 1392, 1281, 1267, 1245, 989, 744, 701, MS: *m/z:* 496(M^+), 498(M^{+2}); Anal. Calcd. for $C_{29}H_{21}ClN_2O_4$: C,70.09; H, 4.26; N, 5.64; O,12.88 Found: C, 70.03; H, 4.11; N, 5.57; O,12.81.

4-Hydroxy-5,8-dimethyl-3-((E)-3-(3-(4-nitrophenyl)-1-phenyl-1H-pyrazol-4-yl)acryloyl)-2H-chromen-2-one (3t)

IR (cm^{-1}): 3601, 3581, 3011, 2998, 2899, 1715, 1542, 1498, 1382, 1282, 1245, 979, 755, 701, MS: *m/z:* 507.49(M^+) ; Anal. Calcd. for $C_{29}H_{21}N_3O_6$: C, 68.63; H, 4.17; N, 8.28; O, 18.92 Found: C, 68.56; H, 4.11; N, 4.07; O,18.90.

4-Hydroxy-3-((E)-3-(3-(2-hydroxyphenyl)-1-phenyl-1H-pyrazol-4-yl)acryloyl)-5,8-dimethyl-2H-chromen-2-one (3u)

IR (cm^{-1}): 3611, 3561, 3021, 2988, 2889, 1717, 1497, 1392, 1292, 1255, 989, 749, 711, MS: *m/z:* 478.50 (M^+); Anal. Calcd. for $C_{29}H_{22}N_2O_5$: C, 72.79; H, 4.63; N, 5.85; O, 16.72 Found: C, 72.73; H, 4.51; N, 5.77; O,16.68.

4-Hydroxy-3-((E)-3-(3-(2-methoxyphenyl)-1-phenyl-1H-pyrazol-4-yl)acryloyl)-5,8-dometyl-2H-chromen-2-one (3v)

IR (cm^{-1}): 3610, 3551, 3031, 2989, 2879, 1712, 1498, 1362, 1299, 1265, 979, 741, 698, MS: *m/z:* 492.52 (M^+); Anal. Calcd. for $C_{30}H_{24}N_2O_5$: C, 73.16; H, 4.91; N, 5.69; O, 16.24 Found: C, 73.13; H, 4.81; N, 5.67; O,16.20.

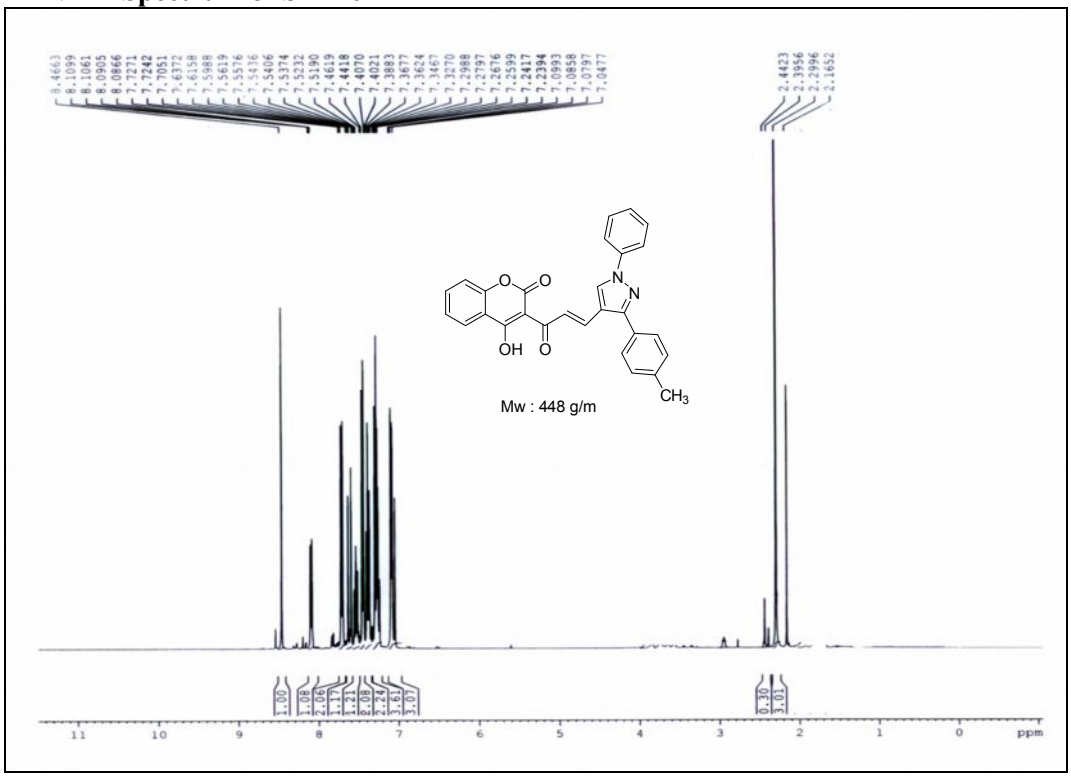
4-Hydroxy-5,8-dimethyl-3-((E)-3-(3-(-nitrophenyl)-1-phenyl-1H-pyrazol-4-yl)acryloyl)-2H-chromen-2-one (3w)

IR (cm^{-1}): 3610, 3541, 3041, 2928, 2859, 1727, 1551, 1491, 1390, 1293, 1235, 979, 739, MS: *m/z:* 507.49 (M^+); Anal. Calcd. for $C_{29}H_{21}N_3O_6$: C,68.63; H, 4.17; N, 8.28; O, 18.92 Found: C, 68.53; H, 4.11; N, 8.17; O, 18.88.

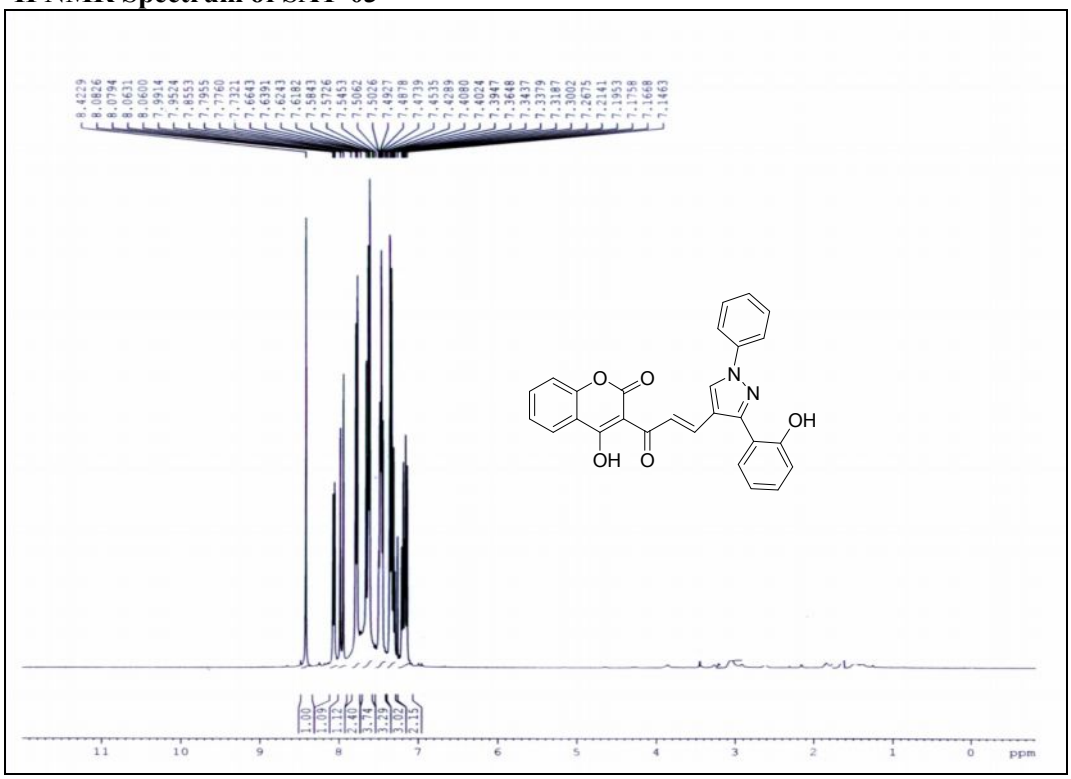
3-((E)-3-(3-(4-flourophenyl)-1-phenyl-1H-pyrazol-4-yl)acryloyl)-4-hydroxy-5,8-dimethyl-2H-chromen-2-one (3x)

IR (cm^{-1}): 3591, 3521, 3071, 2985, 2829, 1727, 1487, 1362, 1252, 1225, 969, 749, 689, MS: *m/z:* 480 (M^+), 482 (M^{+2}) ; Anal. Calcd. for $C_{29}H_{21}FN_2O_4$: C, 72.49; H, 4.41; N, 5.83; O, 13.32 Found: C, 72.43; H, 4.31; N, 5.77; O,13.28.

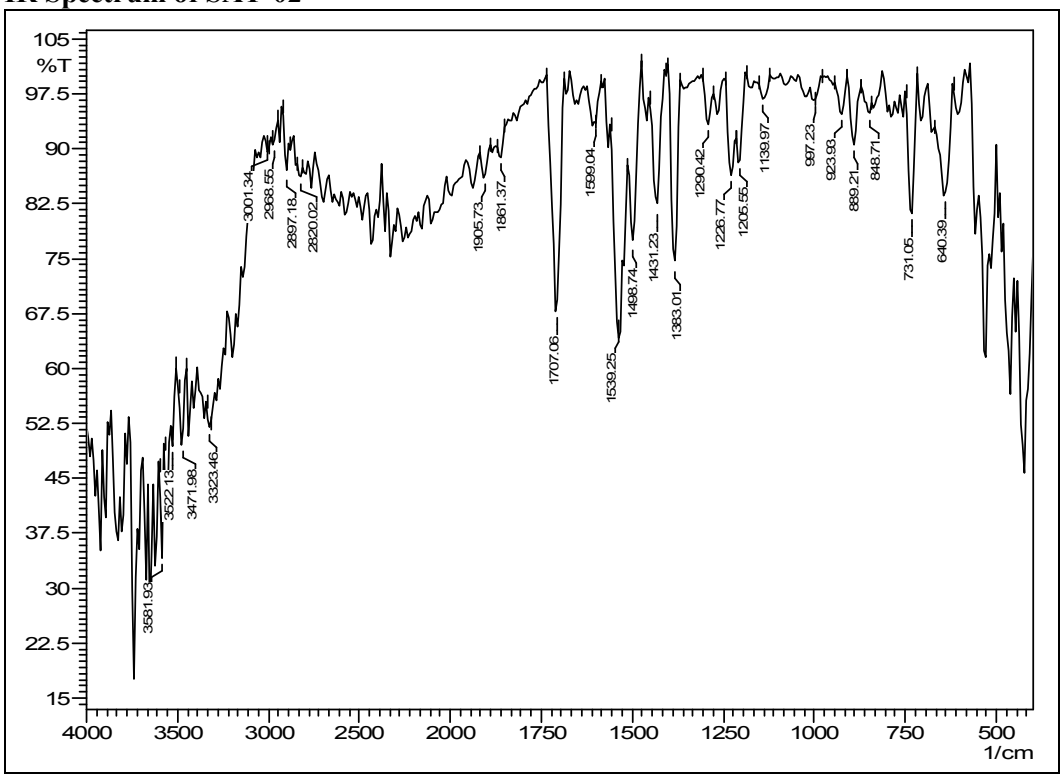
^{1}H NMR Spectrum of SAT-02



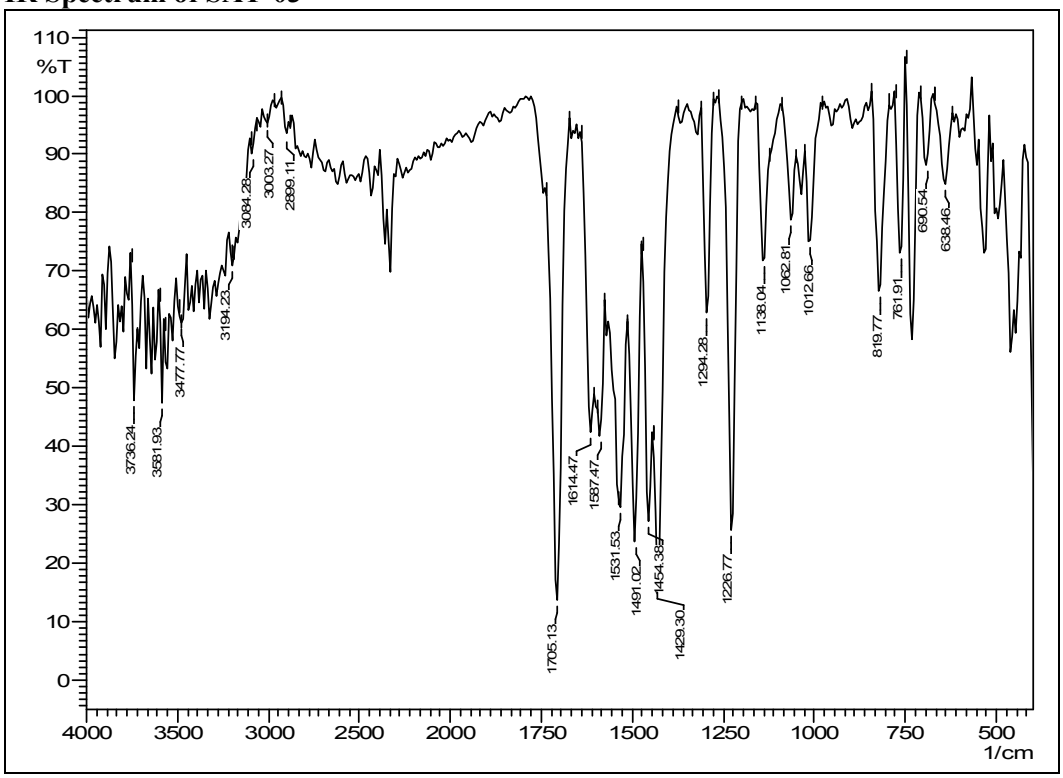
^{1}H NMR Spectrum of SAT-03



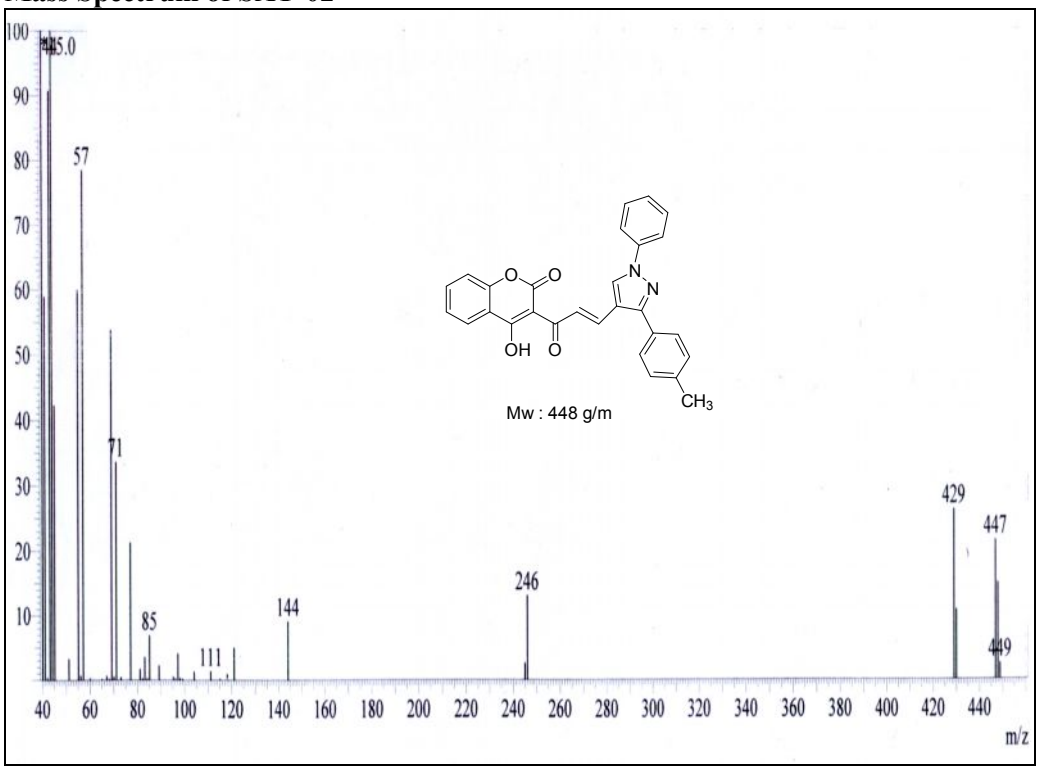
IR Spectrum of SAT-02



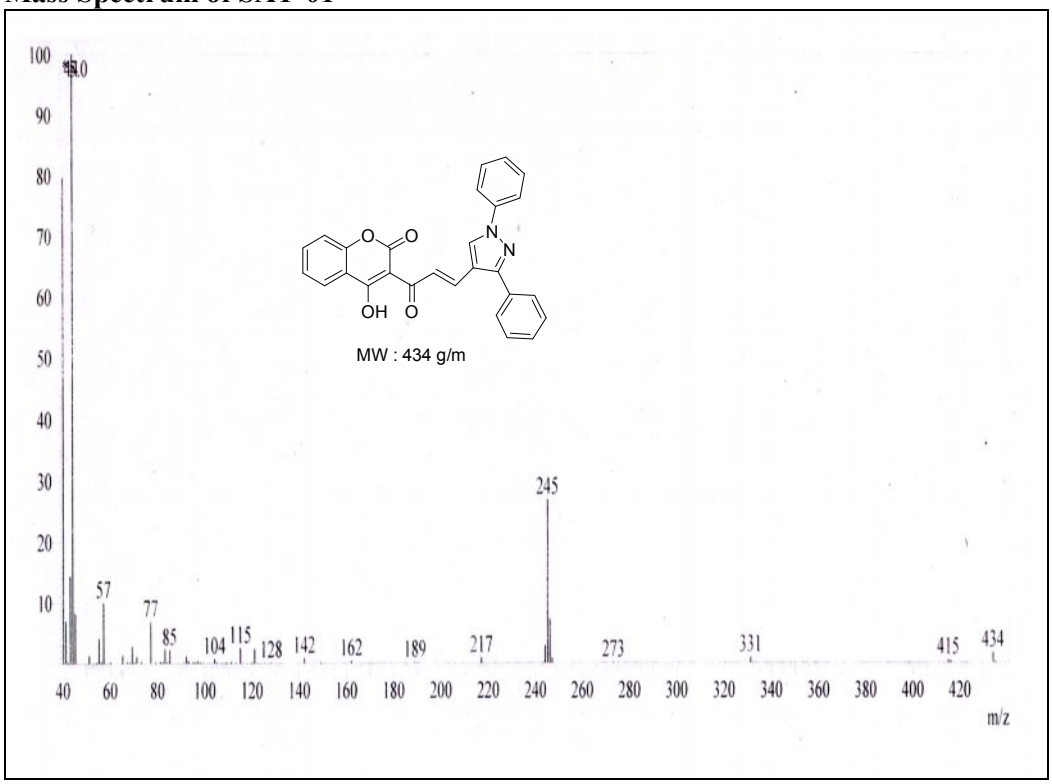
IR Spectrum of SAT-03



Mass Spectrum of SAT-02



Mass Spectrum of SAT-01



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References :

1. S.Caddick, Tetrahedron, 1995, 51, 10403.
2. R.K. Saini, A.S. Choudhary, Y.C.Joshi and P.Joshi, E.J. Chem, 2005, 2, 9.
3. John Anto R, Sukumaran K, Kuttan G, Rao M N A, Subbaraju V and Kuttan R,. Cancer Letters. 1995, 97, 33.
4. Vaya R, Belinky P A and Aviram M, Free Radic. Biol. Med. 1997, 23, 302.
5. Mukherjee S, Kumar V, Prasad A K, Raj H G, Brakhe M E, Olsen C E, Jain S C and Parmar V P, Bioorg. Med. Chem. 2001, 9, 337.
6. Indyah S A, Timmerman H, Samhoedi M, Sastrohami D, Sugiyanto H and Van Der Goot H, Eur. J. Med. Chem. 2000, 35, 449.
7. Chen M, Christensen S B, Zhai L, Rasmussen M H, Theander T G, Frokjaer S, Steffensen B, Davidson J and Kharazmi A, J. Infect. Dis. 1997, 176, 1327.
8. Nielsen S F, Christensen S B, Cruciani G, Kharazmi A and Liljefors T, J. Med. Chem. 1998, 41, 4819.
9. Hsin-kaw H, Tai-Hua L, Pyang Wang J, Jey-Jeng W and Chun-Nan L, Pharm. Res. 1998, 15, 39.
10. Kumar S K, Hager E, Catherine P, Gurulingappa H, Davidson N E and Khan S R, J. Med. Chem. 2003, 46, 2813.
11. Prasad Y R, Prasoona L, Rao A L, Lakshmi K, Kumar P R and Rao B, G. Int. J. Chem. Sci. 2005, 3(4), 685-689.
12. Goda, F. E.; Maarouf, A. R.; El-Bendary, E. R. Synthesis and Antimicrobial Evaluation of New Isoxazole and Pyrazole Derivatives. Saudi Pharm. J. 2003, 11, 111-117.
13. El-Emary, T. I. Synthesis and Biological Activity of Some New Pyrazolo[3,4-b] pyrazines. J. Chin. Chem. Soc. 2006, 53, 391-401.
14. Mansour, A. K.; Eid, M. M.; Khalil, N. S. A. M. Synthesis and Reactions of Some New Heterocyclic Carbohydrazides and Related

Compounds as Potential Anticancer Agents. Molecules 2003, 8, 744-755.

15. (a) Shin, K. D.; Lee, M. Y.; Shin, D. S.; Lee, S.; Son, K. H.;Koh, S.; Paik, Y. K.; Kwon, B. M.; Han, D. C. J. Biol. Chem. 2005, 280, 41439. (b) Demers, J.; Hageman, W.; Johnson,S.; Klaubert, D.; Look, R.; Moore, J. Bioorg. Med. Chem.Lett. 1994, 4, 2451. (c) Simoni, D.; Roberti, M.; Paolo, I. F.;Rondanin, R.; Baruchello, R.; Malagutti, C.; Mazzali, A.;Rossi, M.; Grimaudo, S.; Capone, F.; Dusonchet, L.; Meli, M.; Raimondi, M. V.; Landino, M.; D'Alessandro, N.; Tolomeo, M.; Arindam, D.; Lu, S.; Benbrook, D. M. J. Med. Chem. 2001, 44, 2308. (d) Liu, X. H.; Cui, P.; Song, B. A.; Bhadury, P. S.; Zhu, H. L.; Wang, S. F. Bioorg. Med. Chem. 2008, 16, 4075. (e) Velaparthi, S.; Brunsteiner, M.; Uddin, R.; Wan, B.; Franzblau, S. G.; Petukhov, P. A. J. Med. Chem. 2008, 51, 1999. (f) Magedov, I. V.; Manpadi, M.; Van slambrouck, S.; Steelant, W. F. A.; Rozhkova, E.; Przheval'skii, N. M.; Rogelj, S.; Kornienko, A. J. Med. Chem. 2007, 50, 5183.
16. (a) Pinho, E. M.; Teresa, M. V. D. Curr. Org. Chem. 2005, 9, 925. (b) Colliot, F.; Kukorowski, K. A.; Hawkins, D. W.; Roberts, D. A. Brighton Crop Prot. Conf. Pests Dis. 1992, 1, 29. (c) Chen, H. S.; Li, Z. M.; Han, Y. F. J. Agric. Food. Chem. 2000, 48, 5312. (d) Vicentini, C. B.; Romagnoli, C.; Reotti, E.; Mares, D. J. Agric. Food Chem. 2007, 55, 10331. (e) Vicentini, C. B.; Mares, D.; Tartari, A.; Manfrini, M.; Forlani, G. J. Agric. Food Chem. 2004, 52, 1898.
17. (a) Graneto, M. J.; Kurumbail, R. G.; Vazquez, M. L.; Shieh, H. S.; Pawlitz, J. L.; Williams, J. M.; Stallings, W. C.; Geng, L.; Naraian, A. S.; Koszyk, F. J.; Stealey, M. A.; Xu, X. D.; Weier, R. M.; Hanson, G. J.; Mourey, R. J.; Compton, R. P.; Mnich, S. J.; Anderson, G. D.; Monahan, J. B.; Devraj, R. J. Med. Chem. 2007, 50, 5712. (b) Kuettel, S.; Zambon, A.; Kaiser, M.; Brun, R.; Scapozza, L.; Perozzo, R. J. Med. Chem. 2007, 50, 5833.
18. Vogel AI and Tatchell AR. Vogel's Textbook of Practical Organic Chemistry. A.J. Hannaford AJ and Smith PWJ. 5thed, 1191-1192.
19. Mulwad VV and Shirodkhar JM. Indian Journal of Heterocyclic Chemistry. 2002, 11, 192-202.
20. Nachiket S Dighe, Shashikant R Pattan, Santosh S Dengale, Deepak S Musmade, Madhuri Shelar, Vishal Tambe and Mangesh B Hole Archives of Applied Science Research, 2010, 2 (2): 65-71
21. Manohar K, Manjunath G and Raviraj K. Indian Journal of Heterocyclic Chemistry. 2004, 13, 201-204.
22. RajeshwarRao V, Srimanth K and VijayaKumar P. Indian Journal of Heterocyclic chemistry. 2004, 14, 141-144.
23. Nofal ZM, El-Zahar MI and Abd El-Karim SS. Journal of Antimicrobial Chemotherapy. 2005, 5, 483–488.
24. Jalpa C. Trivedi, Jitender B. Bariwal, Kuldip D. Upadhyay, Yogesh T. Naliapara, Sudhir K. Joshi, Christophe C. Pannecouque, Erik De Clercq and Anamik K. Shah, Tetrahedron letters 2007, 48(48), 8472-8474.
25. Venkateshwara Rao V. and Sundaramurthy V. Proc. Indian. Acad. Sci., 1975, 81(3), 118-123.

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