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SYNTHESIS AND ANTIMICROBIAL ACTIVITY STUDIES OF 3-(7-HYDROXY-4-METHYL-2-OXO-2H-CHROMEN-8-YL)-1-H-PYRAZOLE-4-CARBALDEHYDE COUMARIN DERIVATIVES

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ABSTRACT
Synthesis, spectral analysis and Antimicrobial activity of new coumarin derivatives are described in this paper. Eight new coumarin derivatives were synthesized in moderate to good yields by N,N-Dimethylformamide and $POCl_3$ via Vilsmeier-Haack Reaction method. The structures of all the newly synthesized molecules were assigned by elemental analysis and spectral data. The synthesized compounds were screened for their Antimicrobial activities strains using Cup plate method.

KEYWORDS: Antimicrobialactivity, N,N-Dimethylformamide, $POCl_3$, Vilsmeier-Haack Reaction.

INTRODUCTION

Heteroaromatic compounds have attracted considerable attention in the design of biologically active molecules and advanced organic materials. Hence a practical method for the preparation of such compounds is of great interest in synthetic organic chemistry, Pyrazole is a five member heterocyclic compound containing two nitrogen atoms adjacent to each other. In 1883, Knorr et al[1] gave the generic name pyrazole to the compounds, which is a five member unsaturated ring compound with two adjacent nitrogen atoms. Pyrazoles and its derivatives, a class of well known nitrogen containing heterocyclic compounds, occupy an important position in pharmaceutical and agrochemical industry due to their antimicrobial[2], anti-inflammatory[3] and antitumor[4] activities, antibacterial[5], antifungal[6], antiviral[7], antitubercular[8], antioxidant[9], antiandrogenic[10] etc. On the other hand, sulfonamides and their different derivatives are extensively used in medicine due to their pharmacological properties such as antibacterial activity.[11,12]

Formation of 3-substituted 1-aryl-4-formylpyrazoles from N-arylhydrazones in presence of DMF-$POC1_3$ is known as Vilsmeier-Haack (VH) reaction. These formylation of a variety of both aromatic and heteroaromatic substrates.is well documented.[13] Besides this, the reagent has also been extensively used for effecting various chemical transformations from other classes of compounds. Many of these reactions have led to novel and convenient routes for the synthesis of various heterocyclic compounds.[14] A notable example that finds significant application in heterocylic chemistry is the synthesis of 4-formylpyrazoles from the double formylation of hydrazones with VH reagent.[15,16] These observations, coupled with the recent developments on the simple synthesis of pyrazole derivatives[17], especially 4-functionalized 1,3-diphenylpyrazoles as antibacterial[18], anti-inflammatory[19], antiparasitic[20] and antidiabetic[21] drugs, prompted us to undertake the synthesis of 1,3-disubstituted pyrazole-4-carbaldehyde derivatives using Vilsmeier-Haack (VH) reaction.

RESULTS AND DISCUSSION

Chemistry

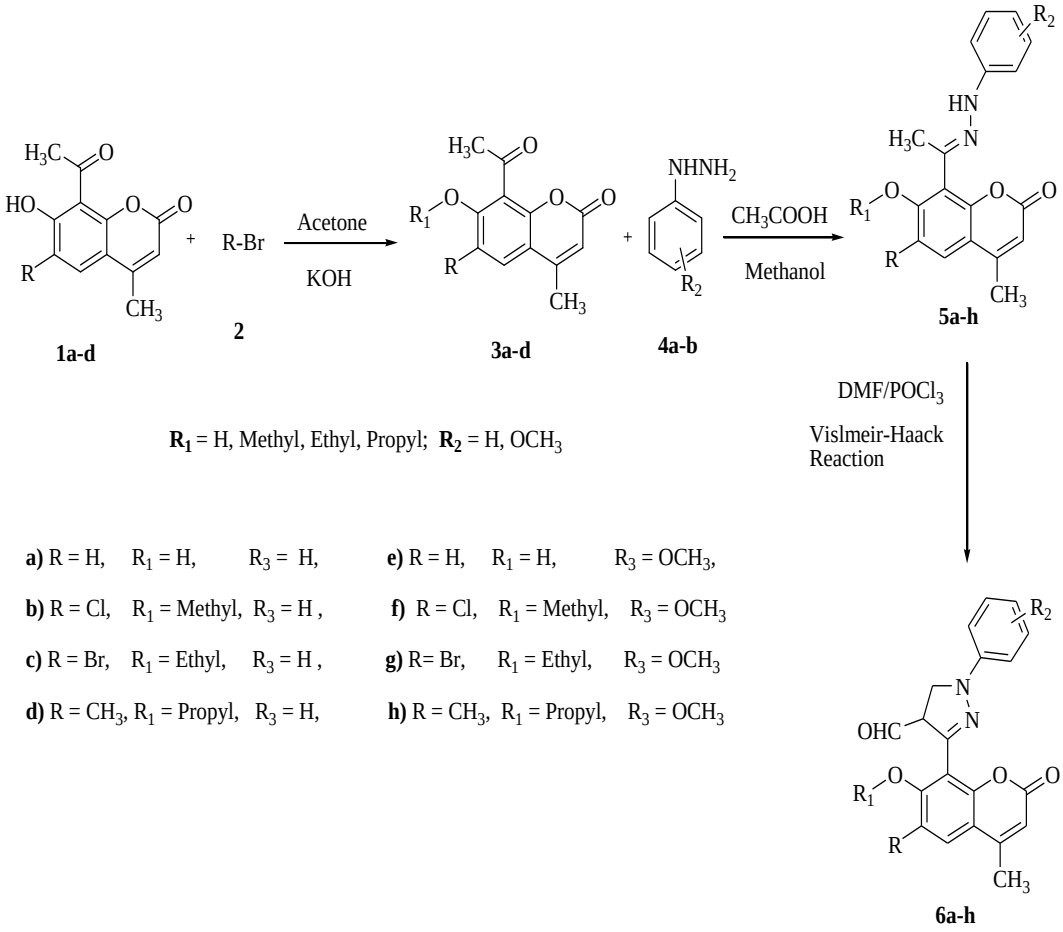
We have successfully eight novel compounds (**6a-h**) in good yields via 7-hydroxy-4-methyl-8-(l-(2-phenylhydrazono) ethyl)-2H-chromen-2-one(**5a-h**) by employing the reaction sequences shown in various schemes (**scheme 1).**

Synthesis of 3-(7-hydroxy-4-methyl-2-oxo-2H-chromen-8-yl)-l-phenyl-lH-pyrazole-4-carbaldehydes (6a-h)

7-hydroxy-4-methyl-8-(l-(2-phenylhydrazono) ethyl)-2H-chromen-2-one **(5a)** was treated with a mixture of Dry N,N-Dimethylformamide and $POC1_3$ in a round bottom flask under Vilsmeier Haack Formylation reaction conditions, the completion of reaction was monitored by TLC and poured into ice cold water. The

solid separated on neutralization with $NaHCO_3$ was filtered, washed with water and crystallized from aq. Methanol which formed 3-(7-hydroxy-4-methyl-2-oxo-2H-chromen-8-yl)-l-phenyl-lH-pyrazole-4-carbaldehyde **(6a)**.

3-(7-hydroxy-4-methyl-2-oxo-2H-chromen-8-yl)-l-phenyl-lH-pyrazole-4-carbaldehyde **(6a)** is characterized from its spectral data. In the IR spectrum (KBr): O-H showed absorption at 3150 cm^{-1}, C-H of aldehyde at 2780 cm^{-1}, C=O of aldehyde at 1724 cm^{-1}, C=O of coumarin at 1690 cm^{-1} and C=C of coumarin at 1597 cm^{-1}. In the ^{1}H-NMR ($CDC1_3$, 400MHz): Aldehyde proton appeared at δ10.02 as singlet and remaining at δ 8.13 (s, 5'-H), 7.73 (d, J=8.0Hz, 5-H), 7.61-7.63 (m, 2"-H, 6"-H), 7.54-7.58 (m, 3"-H, 4"-H, 5"-H), 7.45 (d, J=8.0Hz, 6-H), 6.18 (s, 3-H), 2.47 (s, 4-CH_3).^{13}C-NMR ($CDC1_3$, 100MHz): δ 187.0 (CHO), 160.7 (C-2), 158.6 (C-7), 152.5 (C-4), 148.5 (3'-C), 132.8 (C-8a), 128.9 (1"-C), 124.7 (5'-C), 121.0 (3"-C, 5"-C), 116.6 (C-8), 116.0 (2"-C, 6"-C), 115.6 (C-5), 113.1 (4"-C), 112.4 (C-4a), 110.1 (C-3): 106.5(4'-C), 105.2 (C-6) and 19.2 (4-CH_3).In the Mass spectra (ES):$[M+H]^+$ peak appeared at m/z 347. Anal. Calcd for: C, 69.36; H, 4.07; N, 8.09%. Found: C, 69.03; H, 3.88; N, 8.40 %. M.P:168°C, Yield: 72%.



Synthesis of Final Compounds Scheme-1.

Antimicrobial Activity

In view of developing new class of antimicrobial agents, synthesized novel compounds were screened for their In vitro antimicrobial activities to determine zone of inhibition at 100 µg/mL against two Gram-positive bacteria (Staphylococcus aureus (MTCC 096), Bacillus subtilis (MTCC 441) and two Gram-negative bacteria (Escherichia coli (MTCC 443), Pseudomonas aeruginosa (MTCC 424), as well as two fungi (Aspergillus niger (MTCC 282), Aspergillus fumigates (MTCC 343), strains using Cup plate method[22,23] where inoculated Muller-Hilton agar for bacteria and Sabouraud dextrose agar for fungi was poured onto the sterilized petri dishes (25–30 mL each petri dish). The poured material was allowed to set (30 min.) and thereafter the 'CUPS' (06mm diameter) was made by punching into the agar surface with a sterile cork borer and scooping out the punched part of the agar. Into these cups the test compound solution (0.1mL) was added with the help of a micro pipette. The plates were incubated at 37 °C for 14h for bacteria and 30 h for fungi and the results were noted. The test solution was prepared by DMSO as solvent. Clinically antimicrobial drugs Ciprofloxacin and Miconazole were used as the positive control and DMSO was used for blank.

The obtained results, depicted in Table 1, revealed that all the synthesized compounds, **6a-h** could effectively, to

some extent, inhibit the growth of all tested strains In vitro. In antibacterial studies, all the compounds tested were found less active towards Bacillus subtilis, as compared to other three strains of bacteria. Most of the compounds showed moderate to good activity against Staphylococcus aureus. Compounds, **6h** and **6g** have shown good antibacterial activity against Staphylococcus aureus. **6a**, **6b** and **6d** have shown moderate activity against Escherichia coli. Out of two strains of fungi, these compounds were found to be less active against Aspergillus niger whereas showed moderate to good activity against Aspergillus fumigatus. Compounds, **6a**, **6d, 6e, 6f, 6g** and **6h** possessed good antifungal activity against Aspergillus fumigates.

Table-1: Antimicrobial activity of title compounds 6a-h.

Compound	Gram positive bacteria		Gram negative bacteria		Fungi	
	Staphylococcus aureus	Bacillus subtilis	Escherichia coli	Pseudomonas aeruginosa	Aspergillus Niger	Aspergillus fumigatus
6a	17	14	12	13	10	17
6b	13	12	15	12	10	18
6c	15	11	16	12	11	17
6d	13	11	12	10	12	18
6e	13	10	10	11	11	18
6f	14	11	10	13	13	19
6g	13	11	12	12	13	18
6h	16	10	14	14	14	18
std	20	21	22	20	29	22

Standard drug for bacteria: Ciprofloxacin; Standard drug for fungi: Miconazole Zone of Inhibition (Internal diameter: 6mm) All the compounds were screened at 100µg/mL concentration.

EXPERIMENTAL

All the reagents were obtained commercially (SD fine, India) and used with further purification. Melting points were determined by open capillary method. The IR spectra (in KBr pellets) were recorded on a" Perkin-Elmer FTIR spectrophotometer".^{1}H NMR ($CDCl_3$ 400 MHz) and ^{13}C NMR (DMSO-d_6, 100.6 MHz) were recorded on spectrometer TMS as internal standard (chemical shifts and ppm). Mass spectra were recorded on a VG micromass70-70H instrument. The purity of the compounds were checked by TLC on silica gel plates using a mixture of n-hexane and ethyl acetate.

I. General procedure for the synthesis of 7-hydroxy-4-methyl-8-(l-(2-phenylhydrazono) ethyl)-2H-chromen-2-ones(5a-h)

(i) 7-hydroxy-4-methyl-8-(l-(2-phenylhydrazono) ethyl)-2H-chromen-2-one (5a)

A mixture of 8-acetyl-7-hydroxy-4-methyl-2H-chromen-2-one **(3a)** (1gr, 0.004 mmol) and phenylhydrazine **(5a)** (0.5ml, 0.004 mmol) in methanol (30 ml) containing few drops of glacial acetic acid was refluxed for 1 hour on a water bath to get 7-hydroxy-4-methyl-8-(l-(2-phenylhydrazono) ethyl)-2H-chromen-2-one **(5a)**. IR (KBr): v 3336 (N-H), 3100 (O-H), 1735 (C=O of coumarin), 1602 (C=C of coumarin) cm^{-11}H-NMR: ($CDC1_3$, 400MHz): µ 12.07 (s, NH), 7.45 (d, J=8.0Hz, 5-H), 7.30-7.34 (m, 2"-H, 6"-H), 7.06 (d, J=8.0Hz, 6-H), 6.94-6.97 (m, 3"-H, 4"-H, 5"-H), 6.13 (d, J=1.2Hz, 3-H), 2.58 (s, 2(-CH_3), 2.41 (d, J-1.2HZ, 4-CH=).^{13}C-NMR: ($CDC1_3$ 100MHz): µ 161.0, 160.1, 153.3, 152.6, 143.6, 129.6, 125.3, 121.4, 113.8, 113.2, 112.8, 110.9, 110.7, 110.5, 19.1 and 17.0.Mass (ES): m/z 309 $[M+H]^+$. M.P: 190 °C, Yield: 92%.

(ii) 6-Chloro-7-methoxy-4-methyl-8-(l-(2-phenylhydrazono) ethyl)-2H-chromen-2-one (5b)

IR (KBr): v 3342 (N-H), 3116 (O-H), 1741 (C=O of coumarin), 1613 (C=C of coumarin) cm^{-1} ^{1}H-NMR: ($CDC1_3$, 400MHz): δ 12.04 (s, NH), 7.51 (d, J=8.2Hz, 5-H), 7.34-7.39 (m, 2"'-H, 6"' H), 7.12 (d, J=8.2Hz, 6-H), 6.96-7.08 (m, 3"'-H, 4"'-H, 5"'-H), 6.20 (s, 3-H), 4.01 (s, l'-CH_3) 2.62 (s, 2n-CH_3), 2.28 (s, 4-CH_3).^{13}C-NMR: ($CDCl_3$ 100MHz): δ 166.3,. 160.9, 159.4, 153.8, 152.1, 144.4,129.9, 125.9, 121.7, 113.7, 112.4, 112.0, 110.4, 109.4, 53.l', 19.7 and 16.0. Mass (ES): m/z 342 $[M+H]^+$. M.P: 187 °C, Yield: 91%.

(iii) 6-Bromo-7-ethoxy-4-methyl-8-(l-(2-phenylhydrazono)ethyl)-2H-chromen-2-one (5c)

IR (KBr): v 3338 (N-H), 3104 (O-H), 1739 (C=O of coumarin), 1589 (C=C of coumarin) cm^{-1} ^{1}H-NMR: ($CDC1_3$, 400MHz): δ 12.02 (s, NH), 7.49 (d, J=8.0Hz, 5-H), 7.32-7.37 (m, 2"'-H, 6"'-H), 7.11 (d, J=8.0Hz, 6-H), 6.95- 7.10 (m, 3"'-H, 4"'-H, 5"'-H), 6.18 (d, J=1.2Hz, 3-H), 4.13 (q, J=7.2Hz, l'-CH_3) 2.60 (s, 2"- CH_3), 2.31 (d, J-1.2HZ, 4-CH_3), 2.16 (t, J=7.2Hz, 2'-CH_3).^{13}C-NMR: ($CDCl_3$ 100MHz): δ 165.9, 159.7, 155.9, 153.2, 149.7, 143.9, 128.7, 125.1, 122.1, 113.9, 112.9, 112.7, 110.6, 109.0, 63.7, 20.1, 16.8 and 15.5. Mass (ES): m/z 386 $[M+H]^+$. M.P: 182°C, Yield: 91%.

(iv) 6,4-dimethyl-8-(l-(2-phenylhydrazono)ethyl)- 7-propoxy-2H-chromen-2-one (5d)

IR (KBr): v 3328 (N-H), 3108 (O-H), 1737 (C=O of coumarin), 1594 (C=C of coumarin) cm^{-1} ^{1}H-NMR: ($CDC1_3$, 400MHz): δ 12.23 (s, NH), 7.42 (d, J=8.2Hz, 5-H), 7.31-7.37 (m, 2"'-H, 6"'-H), 7.14 (d, J=8.2Hz, 6-H), 6.98- 7.12 (m, 3"'-H, 4m-H, 5"'-H), 6.11 (s, 3-H), 4.34 (t, J=7.2Hz, 1'- CH_2) 2.61 (s, 2"-CH_3), 2.43 (s, 4-CH_3), 2.06 (m, 2'-CH_2), 1.90 (t, J=7.2Hz, 3'-CH_3).^{13}C-NMR:

($CDC1_3$, 100MHz): δ 165.4, 160.7, 159.5, 153.7, 149.2, 144.7, 129.4, 125.4, 122.4, 114.2, 113.1, 112.9, 110.7, 109.3, 64.2, 24.6, 20.8, 16.9 and 16.2. Mass (ES): m/z 322 $[M+H]^{+\cdot}$ M.P:168°C, Yield: 92%.

(v) 7-hydroxy-8-(l-(2-(4-methoxyphenyl) hydrazono) ethyl)-4-methyl-2H-chromen-2-one (5e)

IR (KBr): v 3336 (N-H), 3102 (O-H), 1737 (C=O of coumarin), 1605 (C=C of coumarin) cm^{-1} ^{1}H-NMR: ($CDC1_3$, 400MHz): δ 12.80 (s, NH), 7.66 (d, J=8.2Hz, 5-H), 7.44-7.50 (m, 2"-H, 6"-H), 7.22 (d, J=8.2Hz, 6-H), 6.99-7.12 (m, 3"-H, 5"-H), 6.23 (s, 3-H), 4.07 (s, 4"-OCH_3); 2.62 (s, 2'-CH_3), 2.32 (s, 4-CH_3).^{13}C-NMR: ($CDC1_3$, 100MHz): δ 167.2, 160.8, 158.4, 153.0, 151.2, 149.7, 136.0, 132.1,119.7, 117.0, 116.2, 114.7,113.1,112.4, 54.8, 22.2 and 16.3.Mass (ES): m/z 308 $[M+H]^+$. M.P: 200-202 °C, Yield: 86%.

(vi) 6-Chloro-7-methoxy-8-(l-(2-(4-methoxyphenyl) hydrazono) ethyl)-4-methyl-2H-chromen-2-one (5f)

IR (KBr): v 3341 (N-H), 3111 (O-H), 1744 (C=O of coumarin), 1603 (C=C of coumarin) cm^{-1} ^{1}H-NMR: ($CDC1_3$, 400MHz): δ 13.42 (s, NH), 7.41 (d, J=8.2Hz, 5-H), 7.31-7.37 (m, 2"'-H, 6"'-H), 7.26 (d, J=8.2Hz, 6-H), 6.98-7.11 (m, 3"'-H, 5"'-H), 6.22 (s, 3-H), 4.04 (s, l'-CH_3), 3.85 (s, 4"'-OCH_3), 2.49 (s, 2"-CH_3), 2.27 (s, 4-CH_3).^{13}C-NMR: ($CDC1_3$, 100MHz): δ 166.1, 161.3, 158.2, 153.9, 150.5, 149.1, 135.8, 132.7, 119.4, 117.2, 116.7, 114.5, 113.4, 112.6, 55.5, 55.3, 20.8 and 17.2. Mass (ES): m/z 341$[M+H]^+$. M.P:192 °C, Yield: 86%.

(vii) 6-Bromo-7-ethoxy-8-(l-(2-(4-methoxyphenyl) hydrazono) ethyl)-4-methyl-2H-chromen-2-one (5g)

IR (KBr): v 3334 (N-H), 3120 (O-H), 1750 (C=O of coumarin), 1607 (C=C of coumarin) cm^{-1} ^{1}H-NMR: ($CDC1_3$, 400MHz): δ 13.68 (s, NH), 7,42-7.52 (m, 5-H, 6-H, 2"'-H, 6"'-H, 3"'-H, 5"'-H), 6.20 (d, J=0.8Hz, 3-H), 4.14 (q, J=7.6Hz, l'-CH_2), 3.79 (s, 4"'-OCH_3), 2.88 (s, 2"-CH_3), 2.00 (d, J-0.8Hz, 4-CH_3), 1.77 (t, J=7.6Hz, 2'-CH_3).^{13}C-NMR: ($CDC1_3$, 100MHz): δ 167.7, 161.7, 157.9, 153.7, 150.9, 148.7, 135.3, 132.1, 119.7,117.3,116.4, 114.2, 113.2, 112.4, 65.2, 54.6, 20.2, 17.8 and 17.1.Mass (ES): m/z 385 $[M+H]^+$. M.P:177 °C, Yield: 89%.

(viii) 8-(l-(2-(4-methoxyphenyl) hydrazono) ethyl)-6,4-dimethyl-7-propoxy-2H-chromen-2-one (5h)

IR (KBr): v 3329 (N-H), 3106 (O-H), 1718 (C=O of coumarin), 1588 (C=C of coumarin) cm^{-1} ^{1}H-NMR: ($CDC1_3$, 400MHz): δ 2.45 (s, NH), 7.27-7.39 (m, 5-H, 6-H, 2"'-H, 6"'-H, 3"'-H, 5"VH), 6.22 (s, 3-H), 4.18 (t, J=7.6Hz, l'-CH_2), 3.83 (s, 4"'-OCH_3); 2.69 (s, 2"-CH_3), 2.20 (s, 4-CH_3), 1.90-1.97 (m, 2'-CH_3), 1.52 (t, J-7.6Hz, 3'-CH_3).^{13}C-NMR: ($CDC1_3$ 100MHz): δ 167.1, 160.4, 157.2, 154.1, '151.4, 149.5, 134.7, 132.0, 120.1, 117.6, 116.8, 115.1, 113.2, 111.7, 68.8, 55.2, 21.5,20.0, 17.2 and 16.8. Mass (ES): m/z 321 $[M+H]^+$. M.P: 170 °C, Yield: 88%.

II. General procedure for the synthesis of -(7-hydroxy-4-methyl-2-oxo-2H-chromen-8-yl)-l-phenyl-lH-pyrazole-4-carbaldehyde comarin derivatives (6a-h)

(ix) 3-(7-hydroxy-4-methyl-2-oxo-2H-chromen-8-yl)-l-phenyl-lH-pyrazole-4-carbaldehyde (6a)

Dry N,N-Dimethylformamide (4ml) was cooled to 0 °C in a round bottom flask and $POC1_3$ (3ml) was added slowly under stirring over 15-20 minutes, and stirring was continued for another 15 minutes at the same temperature. To this mixture 7-hydroxy-4-methyl-8-(l-(2-phenylhydrazono) ethyl)-2H-chromen-2-one (**5a**) (0.001mmol) was added as solid directly in small aliquots at a time, remove the ice bath, the resulting reaction mixture was, stirred at room temperature for 6 hours, completion of reaction was monitored by TLC and poured into ice cold water. The solid separated on neutralization with $NaHCO_3$ was filtered, washed with water and purified on column chromatography with ethyl acetate: pet ether (15:85) to obtain 3-(7-hydroxy-4-methyl-2-oxo- 2H-chromen-8-yl)-l-phenyl-lH-pyrazole-4-carbaldehyde **(6a)**.

IR (KBr): v 3150 (O-H), 2780 (C-H of aldehyde), 1724 (C=O of aldehyde), 1690 (C=O of coumarin), 1597 (C=C of coumarin) cm^{-11}H-NMR: ($CDC1_3$, 400MHz): δ 10.02 (s, CHO), 8.13 (s, 5'-H), 7.73 (d, J=8.0Hz, 5-H), 7.61-7.63 (m, 2"-H, 6"-H), 7.54-7.58 (m, 3"-H, 4"-H, 5"-H), 7.45 (d, J=8.0Hz, 6-H), 6.18 (s, 3-H), 2.47 (s, 4-CH_3).^{13}C-NMR: ($CDC1_3$ 100MHz): δ 187.0, 160.7, 158.6, 152.5, 148.5, 132.8, 128.9, 124.7, 121.0, 116.6, 116.0,115.6, 113.1, 112.4, 110.1, 106.5, 105.2 and 19.2.Mass (ES): m/z 347 $[M+H]^+$. Anal. Calcd for: C, 69.36; H, 4.07; N, '8.09%. Found: C, 69.03; H, 3.88; N, 8.40%. M.P:168 °C, Yield: 72%. .

(x) 6-Chloro-3-(7-methoxy-4-methyl-2-oxo-2H-chromen-8-yl)-l-phenyl~lH-pyrazole-4-carbaldehyde (6b)

IR (KBr): v 3166 (O-H), 2777 (C-H of aldehyde), 1731 (C=6 of aldehyde), 1698 (C=O of coumarin), 1602 (C=C of coumarin) cm^{-1} ^{1}H-NMR: ($CDC1_3$, 400MHz): δ 10.00 (s, CHO), 8.24 (s, 5"-H), 7.68 (d, J-8.2Hz, 5-H), 7.62-7.66 (m, 2"'-H, 6"'-H), 7.54-7.60 (m, 3"'-H, 4"'-H, 5"'-H), 7.47 (d, J=8.2Hz, 6-H), 6.24 (s, 3-H), 3.94 (s, l'-CH_3), 2.39 (s, 4-CH_3).^{13}C-NMR: ($CDC1_3$, 100MHz): δ 189.8, 159.6, 157.4, 150.7, 149.2, 146.0, 138.2, 130.8, 128.2, 127.6, 124,2, 118.5, 112.9, 112.1, 110.8, 105.7, 101.3, 55.4 and 18.1.Mass (ES): m/z 381 $[M+H]^+$. Anal. Calcd for: C, 69.99; H, 4.48; N, 7.77%. Found: C, 69.73;H, 4.32; N, 8.06%. M.P: 162 °C, Yield: 72%.

(xi) 6-Bromo-3-(7-ethoxy-4-methyl-2-oxo-2H-chromen-8-yl)-l-phenyl-lH-pyrazole-4-carbaldehyde (6c)

IR (KBr): v 3172 (O-H),-2748 (C-H of aldehyde), 1718 (C=O of aldehyde), 1682 (C=O of coumarin), 1585 (C-C of coumarin) cm^{-1} ^{1}H-NMR: ($CDC1_3$, 400MHz): δ 9.95 (s, CHO), 8.80 (s, 5"-H), 7.69 (d, J=8.4Hz, 5-H), 7.59-7.63 (m, 2"'-H, 6"'-H), 1.52-1.51 (m, 3"'-H, 4"'-H, 5"'-H),

7.48 (d, J=8.4Hz, 6-H), 6.21 (s, 3-H), 4.01 (q, J-7.6Hz, l'-CH_2) 2.63 (s, 4-CH_3), 2.02 (t, J=7.6Hz, 2'-CH_3).^{13}C-NMR: ($CDC1_3$, 100MHz): δ 190.0, 159.3, 157.9, 150.4, 149.9, 146.2, 138.6, 130.2, 127.9,126.3, 124.8, 118.9, 113.2, 112.8, 110.2, 105.1, 101.9, 62.2, 18.4 and 16.3.Mass (ES): m/z 425 $[M+H]^+$. Anal. Calcd for: C, 70.58; H, 4.85; N, 7.48 %. Found: C, 70.24; H, 4.72; N, 7.71 %. M.P:157 °C, Yield: 74%.

(xii) 3-(6,4-dimethyl-2-oxo-7-propoxy-2H-chromen-8-yl)-l-phenyl~lH-pyrazole-4-carbaldehyde (6d)

IR (KBr): v 3162 (O-H), 2754 (C-H of aldehyde), 1714 (C=O of aldehyde), 1677 (C=O of coumarin), 1584 (C=C of coumarin) cm^{-1} ^{1}H-NMR: ($CDC1_3$, 400MHz): δ 10.10 (s, CHO), 8.44 (s, 5"-H), 7.69 (d, J=7.8Hz: 5-H) 7.64-7.67 (m, 2"'-H, 6"'-H), 7.55-7.59 (m, 3m-H; 4"'-H? 5"-H), 7.42 (d, J=7.8Hz, 6-H), 6.10 (d, J=0.8Hz, 3-H), 433 (t, J=7.8Hz, l'-CH_2), 2.41 (d, J=0.8Hz, 4-CH_3), 2.02 (m, 2'-CH_2), 1.83 (t, J=7.8Hz, 3'-CH_3).^{13}C-NMR: ($CDC1_3$, 100MHz): δ 191.2, 160.2, 158.1, 150.9, 150.0, 146:9, 138.9, 131.0, 127.6,126.5, 124.9, 118.1, 113.1, 112.2, 110.7, 105.9, 102.2, 64.9, 23.0, 19.2 and 14.6.Mass (ES): m/z 361 $[M+H]^+$. Anal. Calcd for: C, 71.12; H, 5.19; N, 7.21 %. Found: C, 70.85; H, 4.86; N, 7.39 %. M.P:154 °C, Yield: 78%.

(xiii) 3-(7-hydroxy-4-methyl-2-oxo-2H-chromen-8-yl)-l-(4-methoxyphenyl)-lH-pyrazole-4-carbaldehyde (6e)

IR (KBr): v 3175 (O-H), 2788 (C-H of aldehyde), 1724 (C=O. of aldehyde), 1674 (C=O of coumarin), 1588 (C=C of coumarin) cm^{-11}H-NMR: ($CDC1_3$, 400MHz): δ 10.21 (s, CHO), 8.66 (s, 5'-H), 7.14-7.26 (m, 5-H, 6-H, 2"-H, 6"-H, 3"-H, 5"-H), 6.22 (d, J=0.8Hz, 3-H), 3.92 (s, 4"-OCH_3), 2.60 (d, J=0.8Hz, 4-CH_3).^{13}C-NMR: ($CDC1_3$ 100MHz): δ 190.2, 161.0, 160.2, 158.7, 153.4, 152.3, 147.6, 132.7, 130.5, 127.7, 124.7, 120.8, 115.3, 114.7, 112.5, 110.8, 105.2, 55.6 and 19.1. Mass (ES): m/z 347 $[M+H]^+$. Anal. Calcd for: C, 67.02; H, 4.28; N, 7.44 %. Found: C, 66.68; H, 4.16; N, 7.62 %. M.P:180 °C, Yield: 68%.

(xiv) 6-Chloro-3-(7-methoxy-4-methyl-2-oxo-2H-chromen-8-yl)-l-(4-methoxyphenyl)-lH-pyrazole-4-carbaldehyde (6f)

IR (KBr): u 3153 (O-H), 2782 (C-H of aldehyde), 1735 (C=O of aldehyde), 1698 (C=O of coumarin), 1597 (C-C of coumarin) cm^{-11}H-NMR: ($CDC1_3$, 400MHz): δ 9.88 (s, CHO), 8.46 (s, 5"-H), 7.18-7.27 (m, 5-H, 6-H, 2"'-H, 6"'-H, 3"'-H, 5"'-H), 6.24 (s, 3- H), 4.03 (s, l'-CH_3), 3,74 (s, 4"'-OCH_3);2.12 (s, 4-CH_3).^{13}C-NMR: ($CDC1_3$ 100MHz): δ 190.3, 161.2, 160.4, 158.4, 153.9, 151.7, 146.9, 133.0, 130.6, 127.2, 124.3, 120.0, 115.8, 114.2, 112.5, 110.2, 105.4, 55.8, 52.7 and 18.8.Mass (ES): m/z 381 $[M+H]^+$. Anal. Calcd for: C, 67.69; H, 4.65; N, 7.18 %. Found: C, 67.44; H, 4.49; N, 7.52 %. M.P:181 °C, Yield: 68%.

(xv) 6-Bromo-3-(7-ethoxy-4-methyl-2-oxo~2H-chromen-8-yl)-l-(4-methoxyphenyl)-lH-pyrazole-4-carbaldehyde (6g)

IR (KBr): v 3180 (O-H), 2793 (C-H of aldehyde), 1743 (C=O of aldehyde), 1678 (C=O of coumarin), 1594 (C=C of coumarin) cm^{-11}H-NMR: ($CDC1_3$, 400MHz): δ 10.06 (s, CHO), 8.62 (s, 5"-H), 7.21-7.34 (m, 5-H, 6-H, 2"'-H, 6"'-H, 3"'-H, 5"'-H), 6.27 (d, J=1.2Hz, 3-H), 4.07 (q, J=7.2Hz, l'-CH_2), 3.84 (s, 4"'-OCH_3), 1.99 (d, J=1.2Hz, 4-CH_3), 1.76 (t, J=7.2Hz, 2'-CH_3).^{13}C-NMR: ($CDC1_3$ 100MHz): δ 189.9, 161.7, 160.8, 158.1, 153.9, 151.4, 146.7, 132.9, 130.4, 127.3,124.1, 120.7,115.4, 114.4, 113.1, 110.4, 104.9,64.5,56.1, 19.4 and 16.2. Mass (ES): m/z 426 $[M+H]^+$. Anal. Calcd for: C, 68.31; H, 4.98; N, 6.93 %. Found: C, 68.07; H, 4.81; N, 7.24 %. M.P: 172 °C, Yield: 71%.

(xvi) 1 -(4-methoxyphenyl)-3-(6,4-dimethyl-2-oxo- 7-propoxy-2H-chromen-8-yl)-lH-pyrazole-4-carbaldehyde (6h)

IR (KBr): v 3179 (O-H), 2785 (C-H of aldehyde), 1741 (C=O of aldehyde), 1691 (C=O of coumarin), 1592 (C=C of coumarin) cm^{-11}H-NMR: ($CDC1_3$, 400MHz): δ 10.11 (s, CHO), 8.68 (s, 5"- H), 7.16-7.29 (m, 5-H, 6-H, 2m-H, 6"'-H, 3m-H, 5m-H), 6.33 (d, J-0.8Hz, 3-H), 4.02 (t, J=7.6Hz, l'-CH_2), 3.77 (s, 4"'- OCH_3), 2.22 (d, J=0.8Hz, 4-CH_2), 1.87-1.91 (m, 2'-CH_2), 1.46(t,J=7.6Hz, 3'-CH_3). ^{13}C-NMR: ($CDC1_3$, 100MHz): δ 190.2, 161.1, 160.3, 158.1, 153.1, 152.0, 147.1, 133.1, 130.9, 127.7, 124.1, 120.1, 115.9, 114.7, 112.8, 109.2, 104.7, 65.3, 56.7, 23.7, 19.8 and 16.4. Mass (ES): m/z 361 $[M+H]^+$. Anal. Calcd for: C 68.89; H, 5.30; N, 6.69 %. Found: C, 68.56; H, 5.02; N, 6.98 %. M.P: 164 °C, Yield: 71%.

CONCLUSION

We have successfully synthesized eight novel 3-(7-hydroxy-4-methyl-2-oxo-2H-chromen-8-yl)-l-phenyl-lH-pyrazole-4-carbaldehyde **(6a-h)** Via 7-Hydroxy-4-methyl-coumarin-8-carbaldehyde **(3a-d)** 7-hydroxy-4-methyl-8-(l-(2-phenylhydrazono) ethyl)-2H-chromen-2-one (**5a**), in good yields. The structures of all the compounds were confirmed by their spectral data. All the newly synthesized compounds were screened for their MIC and zone of inhibition against three strains of bacteria. Amongst the compounds screened, most of the compounds have shown moderate to good Antimicrobial properties where as some compounds have shown promising antifungal properties, which were further used to determine MBC and MFC against some selected strains of bacteria and fungi.

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