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Synthesis, Characterization & Antimicrobial Activity of some new Dihydropyrimidinethione Derivatives

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Abstract: Thiopyrimidinone ring system has a prominent feature in medicinal chemistry and possesses biological activities such as analgesic, insecticidal, antibacterial, ant diabetic, anticonvulsant, etc. Some new Thiopyrimidinone derivatives like 4-Aryl-6-isopropyl-5-[N-(3-nitrophenyl)amino carbonyl]-3,4-dihydro pyrimidine-2(1H)-thione of type (2a-l) have been prepared by the cyclization of 2-Arylidene-4-methyl-N-(3-nitrophenyl)-3-oxopentanamide derivatives of type (1a-l) with thiourea in presence of potassium bicarbonate. All the prepared compounds were characterized byspectral(I.R.,N.M.R. andMass) data and screened for their antimicrobial activities.

Keywords:2-Arylidene-4-methyl-N-(3-nitrophenyl)-3-oxopentanamide, dihydropyrimidinethiones , antimicrobial activities.

I. INTRODUCTION

Generally pyrimidine derivatives such as 1,4dihydrothiopyrimidinone, In the area of drug development, dihydroazines show great promise, particularly since the 4-aryldihydropyridines exhibit powerful vasodilation activity via modifying the calcium ion membrane channel1-2additionally,dihydropyridines have been found to be actively transport medication across biological membranes3. Thiopyrimidinone ring system have a prominent feature in medicinal chemistry and possess biological activities such as insecticidal, antibacterial, anti diabetic, anticonvulsant, etc. antilukemic4 ,Adrenergic receptor antagonist5-6, antitumor7 , cardiovascular8-9 , Blood platelet aggregation inhibitor10 , antiinflammatory11, Anticarcinogenic12, calcium channel modulator13, antihypertensive14 , Vasodialative15 , anti carcinogenic activity16, analgesic 17 antimicrobial activities18etc.

II. EXPERIMENTAL SECTION

Melting points were taken in open capillary tubes are uncorrected. IR spectra (cm-1) were recorded on Shimadzu-435-IR Spectrophotometer and ,1H-NMR spectra on Bruker spectrometer (300MHz) using TMS as an internal standard, chemical shift in δ ppm.

A. General procedure for the preparation of synthesis 2-(2-Chlorobenzylidene)-4-methyl-N-(3-nitrophenyl)-3-oxopentanamide (1a-l)

To the mixture of 2-Chloro benzaldehyde 1.40gm (0.01mol) and 4-Methyl-N-(3-nitrophenyl)-3-oxopentanamide 2.50gm (0.01mol), morpholine, acetic acid and toluene were added and refluxed for 22 hrs with continuous removal of water by dean and stark apratus. After completion of the reaction, cooled it at room temperature, filtered the material and washed with toluene. Make slurry of the material into the solution of sodium meta bisulphite and remove excess aryl aldehyde.

B. General procedure for the preparation of 4-(2-Chlorophenyl)-6-isopropyl-5-[N-(3-nitrophenyl) amino carbonyl]-3,4-dihydropyrimidine-2(1H)-thione (2a-l) :

To the mixture of 2-(2-Chlorobenzylidene)-4-methyl-N-(3-nitrophenyl)-3-oxopentanamide 3.72gm (0.01mol) and thiourea 0.76gm (0.01mol) in DMSO, potassium bicarbonate was added and the mixture was stirred at 45-55 oC temperature for 20 hrs. After completion of the reaction, cool down the reaction mixture at room temperature. Slowly pour the reaction mixture into a mixture of crushed ice, dil. HCl and toluene. Stir it for 1 hr then separate water layer and adjust pH 9-10 using liq NH3. Filter the material and wash it with water. Recrystallized from isopropyl alcohol. Yield 56%, m.p.dec250oC ,Elemental analysis calculated for C20H19ClN4O3S Requires : C-55.75%, H-4.44%, N-13.00%.Found : C-55.73%, H-4.45%, N-13.11%. Similarly, other 4-Aryl-6-isopropyl-5-[N-(3-nitrophenyl)amino carbonyl]-3,4-dihydropyrimidine-2(1H)-thiones were prepared.

C. 4-(2-Chlorophenyl)-6-isopropyl-5-[N-(3-nitrophenyl) amino carbonyl]-3,4-dihydropyrimidine-2(1H)-thione (2a-l) :

Yield 59%, m.p. 250 0C; IR(KBr) : ν 2922,2860,1435,1390(Alkane-CH3), 1346 (-NO2) ,1207(-C=S);1666 (C=O) ,3091,1531,821 (Aromatic), 1120C-H i.p.,1616(-NH) def.,3255 (-NH-)cm-1; 1H-NMR (CDCl3) : δ 3.89(s,1H-CH-),5.55-5.56 (d,1H-Ar-H-), 7.25-7.27 (d,2H,-Ar-H) ,7.49-7.54 (t,1H, ArH),8.12-8.15(d,1H, ArH) ,8.60 (s,1H,-NHCO,k) ,8.78-8.79(d,1H-NH), 9.22 (s,1H-NH).Mass m/z 430.5 . M.F.:C20H19ClN4O3S .

Scheme-1

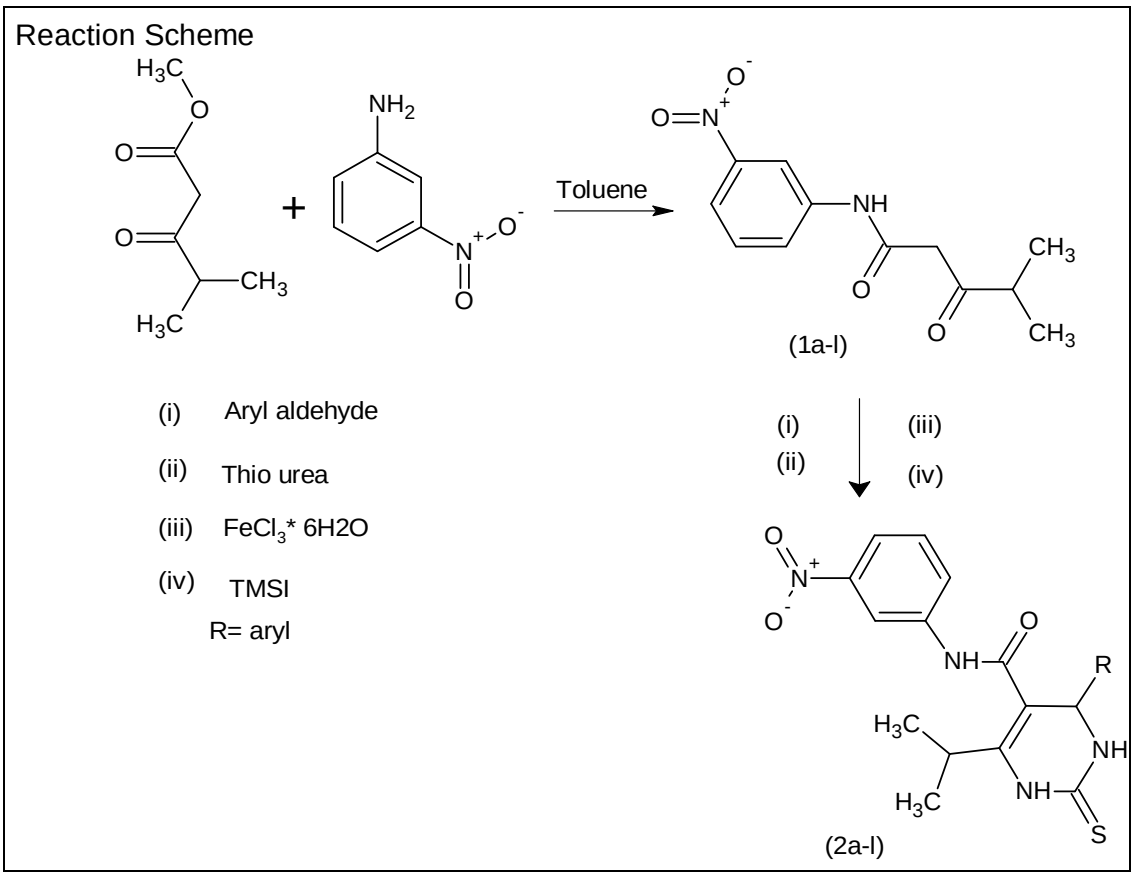


Table-1

Characterization data of the compounds (2a-l)

compd no.	R	Molecular formula	Mole.Wt.	M.P. (0C)	Nitrogen %	
					Found	Calcd
2a	-C6H5	C20H20N4O3S	396	122	14.14	14.12
1b	-4-OCH3-C6H4-	C21H22N4O4S	426	168	13.14	13.12
1c	3,4-(OCH3)2-C6H3-	C22H24N4O5S	456	135	12.28	12.19
1d	-4(OH)-3-(OCH3)C6H3-	C21H22N4O5S	442	239	12.66	12.72
1e	4-OH- C6H4-	C20H20N4O4S	412	174	13.59	13.57
1f	2-OH-C6H4-	C20H20N4O4S	412	178	13.59	13.61
1g	4-F- C6H4-	C20H19FN4O3S	414	244	13.52	13.57
1h	-4-Cl C6H4-	C20H19ClN4O3S	430.5	172	13.02	12.97
1i	2Cl- C6H4-	C20H19ClN4O3S	430.5	dec.250	13.02	13.08
1j	3,4-(Cl)2-C6H3-	C20H18Cl2N4O3S	465	190	12.04	12.07
1k	-3-Br-C6H4-	C20H19BrN4O3S	475	142	11.78	11.81
1l	-3-NO2- C6H4-	C20H19N5O5S	441	170	15.87	15.89

D. Antibacterial activity

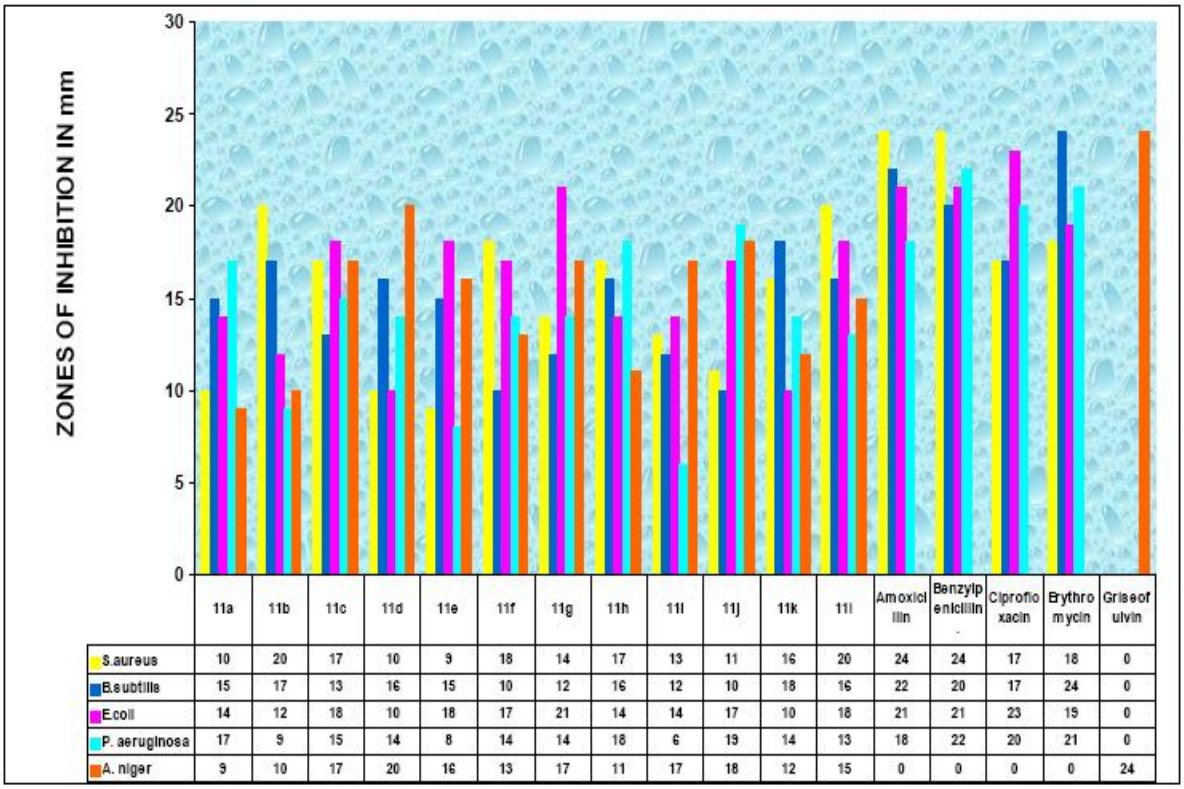
It has been observed from the microbiological data that all compounds (2a-l) were found to be mild to moderately active against Gram positive and Gram negative bacterial strains. However the maximum activity was observed in compounds (2b),(2l) against S.aureus. The significant activity was observed in compounds (2b),(2k) against B.subtillis. The maximum activity was displayed by the compounds (2g),(2e), against E.coli. The compounds (2j), and (2g) were comparatively more effective against P.aeruginosa.

E. Antifungal Activity

The antifungal data revealed that compounds were least toxic to the fungal strain. However mild activity was shown by the compounds (2d),(2j), against A.niger.

The antibacterial activity was compared with standard drug viz. Amoxicillin, Ciprofloxacin, Benzyl Penicillin , Erythromycin and antifungal activity was compared with standard drug viz. Griseofulvin.

Table-2 Antibacterial activity (zone of inhibition in mm):



	11a	11b	11c	11d	11e	11f	11g	11h	11i	11j	11k	11l	Amoxicillin	Benzylpenicillin	Ciprofloxacin	Erythromycin	Griseofulvin
S.aureus	10	20	17	10	9	18	14	17	13	11	16	20	24	24	17	18	0
B.subtilis	15	17	13	16	15	10	12	16	12	10	18	16	22	20	17	24	0
E.coli	14	12	18	10	18	17	21	14	14	17	10	18	21	21	23	19	0
P. aeruginosa	17	9	15	14	8	14	14	18	6	19	14	13	18	22	20	21	0
A. niger	9	10	17	20	16	13	17	11	17	18	12	15	0	0	0	0	24

III. RESULTS AND DISCUSSION

Thiopyrimidinone play a vital role owing to their range of biological and physiological activities. In the light of these biological activities and variety of industrial applications, some new 4-Aryl-6-isopropyl-5-[N-(3-nitrophenyl)amino carbonyl]-3,4-dihydro pyrimidine-2(1H)-thione of type (2a-l) have been prepared by the cyclocondensation of 2-Arylidene-4-methyl-N-(3-nitrophenyl)-3-oxopentanamide derivatives of type (1a-l) with in presence of potassium bicarbonate. The formulas of the selected compounds were confirmed by the elemental analysis and their structures were determined by IR ,1 H-NMR , and mass spectral data.

IV. CONCLUSION

The present study leads to a convenient synthetic method for the synthesis of new compounds. Which show significant antibacterial and antifungal activity. Further investigation with appropriate structural modification of the above compounds may result in therapeutically useful products.

V. ACKNOWLEDGMENT

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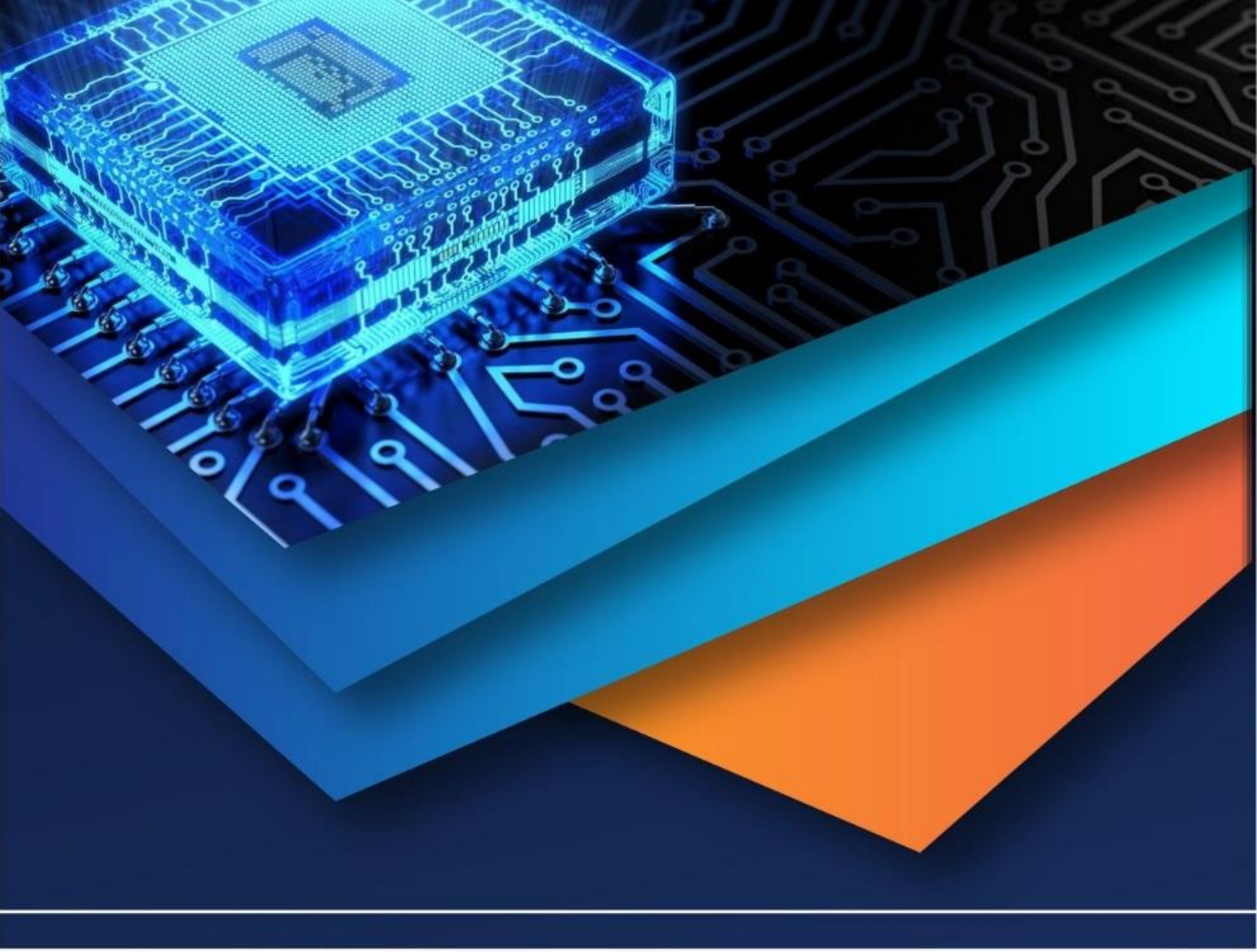

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