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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, antidiabetic, 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 by spectral (I.R., N.M.R. and Mass) 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 1,4-dihydrothiopyrimidinone, 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 channel¹⁻² additionally, dihydropyridines have been found to be actively transport medication across biological membranes³. Thiopyrimidinone ring system has a prominent feature in medicinal chemistry and possess biological activities such as insecticidal, antibacterial, antidiabetic, anticonvulsant, etc. antileukemic⁴, Adrenergic receptor antagonist⁵⁻⁶, antitumor⁷, cardiovascular⁸⁻⁹, Blood platelet aggregation inhibitor¹⁰, antiinflammatory¹¹, Anticarcinogenic¹², calcium channel modulator¹³, antihypertensive¹⁴, Vasodilative¹⁵, anticarcinogenic activity¹⁶, analgesic¹⁷ antimicrobial activities¹⁸ etc.

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 apparatus. 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. dec 250 oC, 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 oC; IR(KBr) : ν 2922, 2860, 1435, 1390 (Alkane-CH₃), 1346 (-NO₂), 1207 (-C=S); 1666 (C=O), 3091, 1531, 821 (Aromatic), 1120 C-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

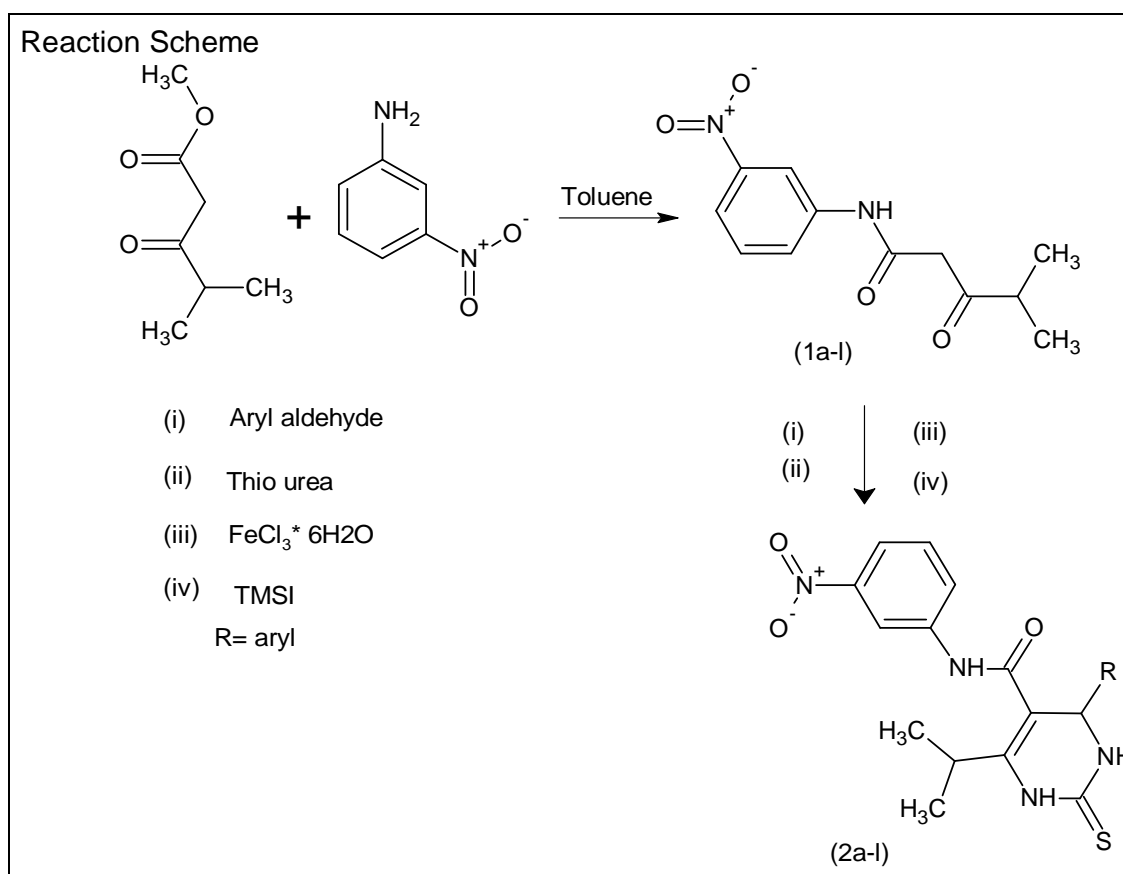


Table-1

Characterization data of the compounds (2a-l)						
compd no.	R	Molecular formula	Mole.Wt.	M.P. (0C)	Nitrogen %	
					Found	Calcd
2a	-C ₆ H ₅	C ₂₀ H ₂₀ N ₄ O ₃ S	396	122	14.14	14.12
1b	-4-OCH ₃ -C ₆ H ₄ -	C ₂₁ H ₂₂ N ₄ O ₄ S	426	168	13.14	13.12
1c	3,4-(OCH ₃) ₂ -C ₆ H ₃ -	C ₂₂ H ₂₄ N ₄ O ₅ S	456	135	12.28	12.19
1d	-4(OH)-3-(OCH ₃)C ₆ H ₃ -	C ₂₁ H ₂₂ N ₄ O ₅ S	442	239	12.66	12.72
1e	4-OH- C ₆ H ₄ -	C ₂₀ H ₂₀ N ₄ O ₄ S	412	174	13.59	13.57
1f	2-OH-C ₆ H ₄ -	C ₂₀ H ₂₀ N ₄ O ₄ S	412	178	13.59	13.61
1g	4-F- C ₆ H ₄ -	C ₂₀ H ₁₉ N ₄ O ₃ S	414	244	13.52	13.57
1h	-4-Cl C ₆ H ₄ -	C ₂₀ H ₁₉ ClN ₄ O ₃ S	430.5	172	13.02	12.97
1i	2Cl- C ₆ H ₄ -	C ₂₀ H ₁₉ ClN ₄ O ₃ S	430.5	dec.250	13.02	13.08
1j	3,4-(Cl) ₂ -C ₆ H ₃ -	C ₂₀ H ₁₈ Cl ₂ N ₄ O ₃ S	465	190	12.04	12.07
1k	-3-Br-C ₆ H ₄ -	C ₂₀ H ₁₉ BrN ₄ O ₃ S	475	142	11.78	11.81
1l	-3-NO ₂ - C ₆ H ₄ -	C ₂₀ H ₁₉ N ₅ O ₅ S	441	170	15.87	15.89

D. Antibacterial activity

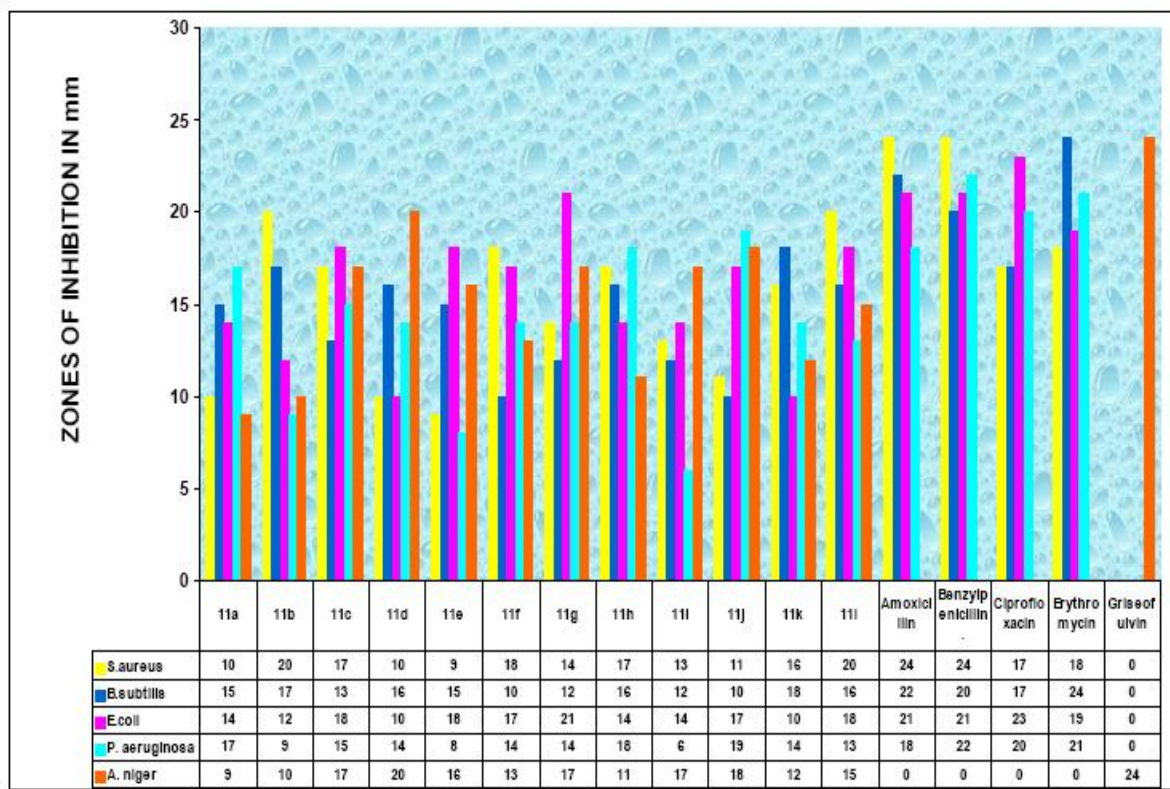
It has been observed from the microbiological data that all compounds (2a-l) were found to be mild to moderately active against Gram positive and Gram negative bacterial strains. However the maximum activity was observed in compounds (2b),(2l) against S.aureus. The significant activity was observed in 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):



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 ,¹H-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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