International Journal of Scientific Research in Science and Technology
Print ISSN: 2395-6011 | Online ISSN: 2395-602X (www.ijsrst.com)
© 2021 | IJSRST | Volume 8 - Issue 1

Microwave Assisted Synthesis and Antimicrobial Activity of Some New Thiopyrimidine Derivatives

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ABSTRACT

4-(4-chlorophenylamino)-6-(4-substitutedphenyl)-5,6-dihydropyrimidin-2-thiones(3a-d) were synthesized by condensation of (E)-N-(4-chlorophenyl) 3-(4-substitutedphenyl) acryl amide (2a-d) with thiourea in the presence of catalytic amount of 40% KOH respectively. The antimicrobial evolutions have been performed for their antibacterial activity and antifungal activities.

Keywords: - Microwave Synthesis, Thiopyrimidine Antimicrobial.

I. INTRODUCTION

In the last decade much interest has been focused on the study of oxopyrimidine and thiopyrimidine derivatives. Several publications have been pointed out the values of Oxopyrimidines and thiopyrimidines[1-2]. They have potential bioactive agents Due to their wide spectrum of pharmacological activities like anti-inflammatory[3], amimicrobial[4],calcium chanel blockes[5], antihypertensive[6], analgesic[7],antitumor[8], antiviral[9],antibacterial[10],anti HIV[11]. Looking to versatile activities exhibited and in continuation to our work on the biological active heterocyclics.

In our last publication we were reported the synthesis of thiopyrimidine derivatives (3a-e). in continuation to that we are reported here the biological study of some newly synthesized thiopyrimidine derivatives (3a-e).
All the synthesized compounds were screened for their antimicrobial activity against various microbs under condition, the standard antibiotics were used for comparison purpose like amoxicillin, benzyl penicillin ciprofloxacin and erythromycin against bacterial strain against *Aspergillus niger.* All the newly synthesized compound have been screened for in *vitro* antimicrobial activity.

II. EXPERIMENTAL

The melting points of all synthesized compound were recorded using hot paraffin bath and are uncorrected. ^{1}H NMR spectra ($CDCl_3$) were recorded on Bruker Advance II 400 NMR spectrophotometer using TMS as internal standard. IR spectra were recorded on Perkin-Elmer-1800 FTIR spectrophotometer in the frequency range 4000-450 cm^{-1} in Nujol mull and as KBr pellets. Mass spectra were recorded on a LC-MS Q-Tof Micro, Mass analyzer (Shimadzu). Chemicals used were of AR grade. The purity of the compound was checked on silica gel-G plates by TLC.

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Synthesis of 4-(4-chlorophenylamino)-6-(4-hydroxyphenyl)-5,6-dihydropyrimidine-2-thione(3a-d).

A mixture of (E)-N-(4-chlorophenyl) 3-(4-hydroxyphenyl)acryl amide **(2 a-d)** (0.01 mol) and thiourea (0.01 mol) was moist with ethanol containing KOH (1 mL) and refluxed for 60sec. in microwave oven. The excess solvent was distilled off and the residue was neutralized with dilute HCl. The separated solid was filtered out and crystallized from ethanol to afford compound **(3a-d).**

Spectral data of compound (IVa): IR (KBr, cm^{-1}): 3550 (O-H), 1670 (C=S), 1580 (C=N), 3290 (N-H), 3100 Ar (C-H), 1450(C-N), 1360 (C-Cl), 680-750 (monosubstituted benzene ring); ^1H NMR (EtOH): δ 1.3 (s, 1H, OH), 2.45 (s, 2H, CH), 4.35 (s, 1H NH), 7.78 (d, 2H, Ar-H), 7.68 (d, 2H, Ar-H), 7.90 (d, 2H, Ar-H), 7.58 (d, 2H, Ar-H).Mass :- m/e 330.81.

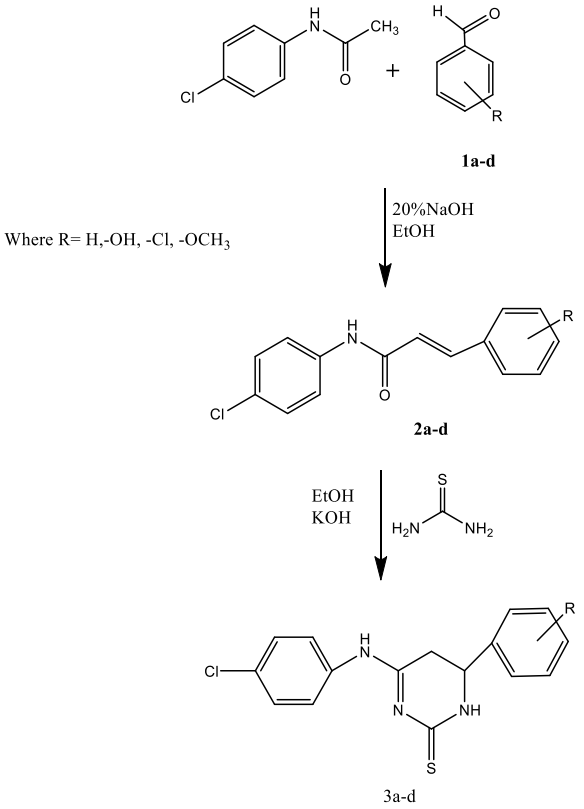
Synthesis of 4-(4-chlorophenylamino)-6-(4-chlorophenyl)-5,6-dihydropyrimidine -2-thione.

A mixture of (E)-N-(4-chlorophenyl)-3-(4-chlorophenyl)acryl amide (0.01 mol) and thiourea (0.01 mol) was moist with alcoholic KOH (1 mL)and the refluxed for 1min in microwave oven. The excess solvent was distilled off and the residue was neutralized with dilute with HCl. The separated solid was filtered out and crystallized from ethanol to afford compound.

Spectral data of compound (Va): IR (KBr, cm^{-1}): 3300 (N-H), 3050 (Ar C-H), 1690(C=S), 1510 (Ar C=C), 1560 (C=N), 1335 (C-N), 810 (p-disubstituted benzene ring), 780(C-Cl); ^1H NMR ($CDCl_3$): δ 4.4 (s,1H, NH), 7.89 (d,2H,Ar -H), 7.90 (d,2H,Ar -H), 7.95 (d,2H,Ar-H),7.67 (d,2H,Ar-H),2.25 (s,2H,Allylic-H).Mass:- m/e -350.0.

All other compounds (2a,2c-d) were prepared in similar manner by the reaction of 4-chloroacetanlide with aromatic aldehyde (1a, 1c-d) respectively.

REACTION SCHEME



III. RESULTS AND DISCUSSION

In present work we argue the antimicrobial and antifungal activity of 4-(4-chlorophenylamino)-6-(4-substitutedphenyl)-5,6-dihydropyrimidin-2-thione (3a-d) by the condensation of (E)-N-(4-chlorophenyl) 3-(4-substitutedphenyl) acryl amide (2a-d) with thiourea in the presence of catalytic amount of 40% KOH respectively. The starting material (E)-N-(4-chlorophenyl) 3-(4-substitutedphenyl) acryl amide

(2a-d) were prepared by condensation of 4-chloroacetanilide with different aromatic aldehyde (1a-d). All these synthesized compounds were screened for their antimicrobial activity using the cup-plate agar diffusion method[12] by measuring the zone of inhibition in mm. All the compound were screened for their in vitro antimicrobial activity against different bacteria strain *Bacillus megaterium, Staphylococcus aureus, Pasteurella aerogenes and fungi Aspergillus niger at 40 µg/ml concentration. Standard drug like* amoxicillin, benzyl penicillin, ciprofloxacin and erythromycin were used for the comparison purpose. **(Table no. 1)**

Table 1. Antimicrobil screeing result of compound 3a-d

Zone of inhibition (mm)					
		Antimicrobial activity			Antifungal activity
Compound	**R**	***B. megaterium***	***S. aureus***	***P. aerogenes***	***A. niger***
3a	-H	12	14	16	25
3b	-OH	19	11	22	17
3c	-Cl	10	16	11	17
3d	$-OCH_3$	18	21	20	21
Amoxicillin		25	23	8	19
Benzyl penicillin		15	22	21	18
Ciprofloxacin		22	21	19	17
Erythromycin		18	23	24	21

IV. AKNOLEGEMENT

Authors are thanks full to ***Dr.V.G. Thakare*** , Principal Shri Shivaji Science College, Amravati for providing all necessary facilities to research works and also thanks fully to Director, R.S.I.C.(SAIF), Punjab University, Chandigarh for providing IR, NMR & Mass spectra. Microbiology laboratory of Shri Shivaji Science College Amravti for anti microbial evolutions.

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