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Synthesis of Antibacterial Activity of Pyrimidine-2-thiones and Acetylpyrimidine-2-thiols

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Pyrimidie-2-thiones were prepared by heating chalcones with thiourea in ethanolic petassium hydroxide. 1-Acetylpyrimidine-2-thiol derivatives were prepared by the reaction of pyrimidine-2-thiones with acetyl chloride. The structures of the compounds have been confirmed by elemental analysis and spectral analysis. The antibacterial activity of the compounds have also been screened.

Key Words: Synthesis, Antibacterial, Pyrimidine-2-thiones, Acetylpyrimidine-2-thiols.

INTRODUCTION

Chalcones have bactericidal-1,2-derivatives[1,2]. In the present work we report the synthesis of pyrimidine derivatives. In continuation of our work on pyrimidines, we report here the synthesis of some new pyrimidine-2-thiones and 1-acetylpyrimidine-2-thiols[3]. 2-Methyl-5-nitro-N-{4′(6″-aryl-pyrimidine-2″-thione)-phenyl}-benzenesulfonamide **[2(a–j)]** have been prepared by the reaction of chalcones **[1(a–j)]** with thiourea in ethanol in presence of potassium hydroxide, which on treatment with acetyl chloride yield 2-methyl-5-nitro-N-{4′-(1″-acetyl-6″-aryl-pyrimidine-2″-thiol)-phenyl}-benzenesulfonamide **[3(a–j)]**.

EXPERIMENTAL

All the melting points were taken in open capillary tube and are uncorrected. The IR spectra were recorded with KBr pellets on Parkin-Elmer 783 spectrophotometer. Starting materials **[1(a–j)]** were synthesized from the appropriate acetophenones and aromatic aldehydes according to known produces[3].

Synthesis of 2-methyl-5-nitro-N-{4′-(6″-aryl-pyrimidine-2″-thione)-phenyl}-benzene-sulfonamide[4] [2(a–j)]

A mixture of chalcone (0.01 mole), thiourea (0.01 mole) and potassium hydroxide (**1g**) in ethanol (95%, 30 mL) were refluxed on water bath at 70–80°C for 3 h. After keeping overnight, the solid obtained was collected and crystallized from benzene (Table-1) **(Scheme-1).**

IR (KBr): 1600–1580 cm^{-1} ν(C=N); 3350–3300 cm^{-1} ν(—NH) and 1250–1215 cm^{-1} ν(C=S).

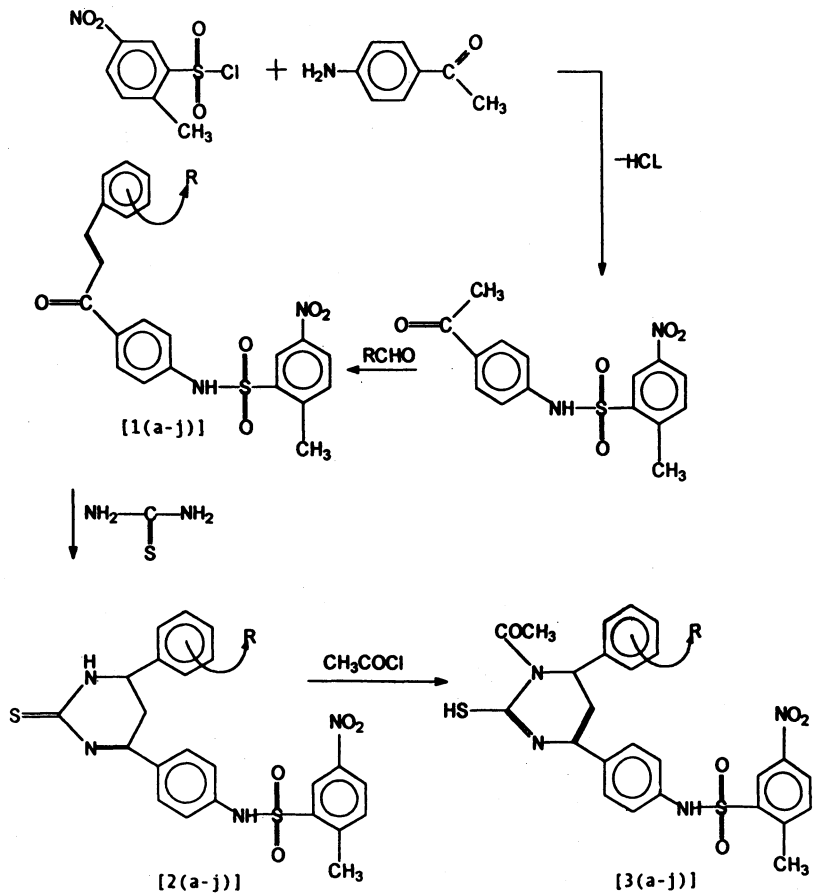
Synthesis of 2-methyl-5-nitro-N-{4′-(1″-acetyl-6″-aryl-pyrimidine-2″-thiol)-phenyl}-benzenesulfonamide [3(a–j)]

A mixture of pyrimidine-2-thione (0.0025 mole) and acetyl chloride (8.0 mL) were heated under reflux on a water-bath at 35–45°C for 2 h. Excess of acetyl chloride was evaporated and the oil obtained was treated with light petroleum ether and crystallized from benzene (Table-2).

IR (KBr): 1750–1700 cm^{-1} ν(N—C=O) and 160—1590 cm^{-1} ν(C=N).

TABLE-1
ANALYTICAL DATA OF PYRIMIDINE-2-THIONES [2(a–j)]

Compound	Substituent (R)	m.f.(m.w)	% Analysis, Found (Calcd.)		
			C	H	N
2a	H	$C_{23}H_{18}N_4O_4S_2$ (478)	57.74 (57.78)	3.76 (3.78)	11.71 (11.73)
2b	4-OCH_3	$C_{24}H_{20}N_4O_5S_2$ (508)	56.69 (56.72)	3.93 (3.97)	11.02 (11.05)
2c	2-OCH_3	$C_{24}H_{20}N_4O_5S_2$ (508)	56.69 (56.75)	3.93 (3.94)	11.02 (11.06)
2d	2-OH	$C_{23}H_{18}N_4O_5S_2$ (494)	55.87 (55.90)	3.64 (3.67)	11.33 (11.37)
2e	2-Cl	$C_{23}H_{17}N_4O_4S_2Cl$ (512)	53.90 (53.94)	3.32 (3.35)	10.93 (10.97)
2f	4-Cl	$C_{23}H_{17}N_4O_4S_2Cl$ (512)	53.90 (53.91)	3.32 (3.38)	10.93 (10.97)
2g	2-NO_2	$C_{23}H_{17}N_5O_6S_2$ (523)	52.77 (52.79)	3.25 (3.28)	13.38 (13.40)
2h	3-Br	$C_{23}H_{17}N_4O_4S_2Br$ (557)	49.58 (49.65)	3.05 (3.07)	10.05 (10.04)
2i	3,4(OCH_3)$_2$	$C_{25}H_{22}N_4O_6S_2$ (538)	55.76 (55.82)	4.08 (4.11)	10.40 (10.46)
2J	3,4,5(OCH_3)$_3$	$C_{26}H_{24}N_4O_7S_2$ (568)	54.92 (54.97)	4.22 (4.26)	9.85 (9.90)



SCHEME-1

TABLE-2
ANALYTICAL DATA OF ACETYLPYRIMIDINE-2-THIOLS [3(a–j)]

Compound	Substituent (R)	m.f.(m.w)	% Analysis, Found (Calcd.)		
			C	H	N
3a	H	$C_{25}H_{21}N_4O_5S_2$ (522)	57.47 (57.51)	4.02 (4.04)	10.72 (10.78)
3b	4-OCH_3	$C_{26}H_{23}N_4O_6S_2$ (552)	56.52 (56.56)	4.16 (4.19)	10.14 (10.16)
3c	2-OCH_3	$C_{26}H_{23}N_4O_6S_2$ (552)	56.52 (56.58)	4.16 (4.15)	10.14 (10.19)
3d	2-OH	$C_{25}H_{21}N_4O_6S_2$ (538)	55.76 (55.82)	3.90 (3.96)	10.40 (10.42)
3e	2-Cl	$C_{25}H_{20}N_4O_5S_2Cl_2$ (592)	50.67 (50.74)	3.37 (3.45)	9.45 (9.47)
3f	4-Cl	$C_{25}H_{20}N_4O_5S_2Cl_2$ (592)	50.67 (50.69)	3.37 (3.39)	9.45 (9.52)
3g	2-NO_2	$C_{25}H_{20}N_5O_5S_2$ (553)	54.24 (54.28)	3.61 (3.68)	10.12 (10.18)
3h	3-Br	$C_{25}H_{20}N_4O_5S_2Br$ (601)	49.91 (49.95)	3.22 (3.26)	9.31 (9.37)
3i	3,4(OCH_3)$_2$	$C_{27}H_{25}N_4O_7S_2$ (582)	55.67 (55.69)	4.29 (4.30)	9.62 (9.64)
3j	3,4,5(OCH_3)$_3$	$C_{25}H_{27}N_4O_8S_2$ (612)	54.90 (54.97)	4.41 (4.47)	9.15 (9.19)

Antibacterial activity

This part deals with the *in-vitro* screening of newly synthesised compounds for their antimicrobial activity by filter paper disc method at a concentration of 50 μg. The species gram +ve *Staphylococcus aureus* and gram –ve *Escherichia coli* have been taken for the antibacterial activity. Against *Staphylococcus aureus*, maximum activity was found in compounds **2g** (zone of inhibition is 13.0 mm) and **3h** (zone of inhibition is 14.0 mm) and minimum activity was found in compounds **2a** (zone of inhibition is 7.0 mm) and **3e** (zone of inhibition is 6.0 mm). Against *Esherichia coli*, maximum activity was found in compounds **2g** (zone of inhibition is 14.0 mm) and **3d** (zone of inhibition is 11.0 mm) and minimum activity was found in compounds **2d** (zone of inhibition is 6.0 mm) and **3a** (zone of inhibition is 6.0 mm) (Table-3).

TABLE-3
ANTIMICROBIAL ACTIVITIES OF COMPOUNDS

Compound	Zone of inhibition (mm)		Compound	Zone of inhibition (mm)	
	Staphylococcus aureus	*Escherichia coli*		*Staphylococcus aureus*	*Escherichia coli*
2a	7.0	9.0	**3a**	8.0	6.0
2b	7.0	8.0	**3b**	12.0	10.0
2c	8.0	10.0	**3c**	6.0	8.0
2d	9.0	6.0	**3d**	8.0	11.0
2e	10.0	12.0	**3e**	6.0	6.0
2f	12.0	10.0	**3f**	8.0	9.0
2g	13.0	14.0	**3g**	6.0	6.0
2h	12.0	12.0	**3h**	14.0	10.0
2i	7.0	8.0	**3i**	10.0	8.0
2j	9.0	9.0	**3j**	12.0	8.0

The compounds possess moderate to good activity against all stains in comparison with ampicillin, penicillin and tetracyline.

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