SYNTHESIS AND ANTIBACTERIAL ASSAY OF SOME OF SUBSTITUTED 1,3-THIAZINES

CHHAYA D. BADNAKHE[1] , P. R. RAJPUT[2] , ASHISH V. GAJBHIYE[3]

[1] Department of Chemistry, Dr.Manorama and Prof.H.S.Pundkar, Arts, Commerce and Science College, Balapur, Dist. Akola.
[2]Department of Chemistry,Vidyabharti Mahavidyalaya, Amravati-444604. India,
[3]S.P.H Arts,Science and Commerce college, Nampur, Dist: Nashik.

Abstract :-

The synthesis, spectral analysis and biological activities of 4-phenyl-2-hydroxy-chlorosubstituted-2-imino-1,3 thiazines have been carried out. In this case 4-(2'-hydroxy-3',5'-dichlorophenyl)-6-(4''-nitrophenyl)-2- iminophenyl-3,6-dihydro-1,3-thiazine (B), and has been screened. The compound B was synthesized from 2'-hydroxy-3,5-dichlorophenyl-4-(4”-nitrophenyl) chalcone (a) by the action of phenylthiourea. The compound (a) was synthesized from 2'-hydroxy-3',5'-dichloroacetophenone by the action of p-nitrobenzaldehyde in ethanol and 40% NaOH. The nanoparticles of the compound B has been prepared by using ultrasonic technique. The newly synthesized titled compound and it’s nanoparticles were screened for their antibacterial activities against some *Gram positive Staphylococcus aureus and Streptococcus sp.* and *Gram negative Pseudomonas sp.* and *Solmonella typhi* pathogens. All the newly synthesized compounds were found to be active against test pathogens.

Keywords : Chalcone, thiazine, , phenylthiourea, antibacterial assay.

INTRODUCTION :

Thiazine is a six membered ring system, which contains two hetero atoms [N and S] placed in a heterocyclic ring at 1, 3 positions. Many workers have synthesized different 1,3-thiazines. The researchers have reported the synthesis of several thiazines[1-6] and also their potent biological activities such as blood platelet aggregation inhibitors[7], antibacterial[8-9] antiallergic[10], anticholesterenic[11] and antifungal[12]**.** Moreover thiazine nucleus is a pharmacophore of cephalosporin that occupy a very important place in the field, of antibiotics and drug chemistry. Chalcones and their analogues having α, β-unsaturated carbonyl system are very versatile substrates for the evolution of various reactions and physiologically active compounds. The reaction of thiourea with α, β-unsaturated ketones also results in the formation of 1,3-thiazines.The chlorosubstituted thiazines with amino group at position 2 in the ring exhibit promising biological activities[13-16].

In the present study, the chlorosubstituted 1,3-thiazine (B) have been prepared along with its nanoparticles and were screened for their antibacterial activities against some *Gram positive Staphylococcus aureus and Streptococcus sp.* and *Gram negative Pseudomonas sp.* and *Solmonella typhi* pathogens. All the newly synthesized compounds were found to be active against test pathogens.

EXPERIMENTAL :-

All the glassware's used in the present work were of pyrex quality. Melting points were determined in hot paraffin bath and are uncorrected.The purity of compounds was monitored on silica gel coated TLC plate. IR spectra were recorded on Perkin-Elmer spectrophotometer in KBr pelletes, H^1 NMR spectra on spectrophotometer in $CDCl_3$ with TMS as internal standard. UV spectra were recorded in nujol medium. The analytical data of the titled compounds was highly satisfactory. All the chemicals used were of analytical grade. All the solvents used were purified by standard methods. Physical characterisation data of all the compounds is given in Table 1.

Table 1 : Characterisation data of newly synthesized compounds :

Compounds	Molecular formula	M.P. in ^0C	% of yield	% of element			
				C	H	N	S
	$C_8H_6O_2Cl_2$	54	80	47.90/48	2.95/3		
a	$C_{15}H_9O_4NCl_2$	250	70	53.10/53.25	2.40/2.66	3.98/4.18	
B	$C_{22}H_{15}O_3N_3Cl_2S$	100	75	55.93/56.01	3.177/3.285	8.89/8.92	6.77/6.82

2'-Hydroxy 3',5'-dichloroacetophenone :

2'-Hydroxy-5-chloroacetophenone (3g) was dissolved in acetic acid (5 ml), and mixed with sodium acetate (3g). To this reaction mixture chlorine in acetic acid reagent (40 ml; 7.5 w/v) was added dropwise with stirring. The temperature of the reaction mixture was maintained below 20°C. The mixture was allowed to stand for 30 minutes and then poured into water. A pale yellow solid thus obtained was filtered, dried and crystallized from ethanol to yield the compound.

Preparation of 2'-hydroxy-3,5-dichlorophenyl-4-(4"-nitrophenyl)-chalcone (a) :

2'-Hydroxy-3',5'-dichloroacetophenone (0.1 mol) was dissolved in ethanol (50 ml) and p-nitrobenzaldehyde (0.1 mol) was added gradually to the solution and the mixture was heated to boiling. Then aquous sodium hydroxide solution [40%; 40 ml] was added dropwise with constant stirring. The mixture was stirred mechanically at room temperature for about half an hour and kept for overnight. It was then acidified by hydrochloric acid (10%) solution . The solid product thus separated, was filtered, and washed with sodium bicarbonate (10%) followed by water. Finally it was crystallized from ethanol acetic acid mixture to get the compound (a).

Preparation of 4-(2'-hydroxy-3',5'-dichlorophenyl)-6-(4"-nitrophenyl)-2- iminophenyl-3,6-dihydro-1,3-thiazine (B) :

2'-Hydroxy-3,5-dichlorophenyl-4-(4"-nitrophenyl)-chalcone (a) (0.01 mol) and phenyl thiourea (0.02 mol) were dissolved in ethanol (30 ml). To this aquous solution of KOH (0.02 mol) was added. The reaction

mixture was refluxed for three hours cooled, diluted with water and acidified with 1:1 HCl. The product thus separated was filtered and crystallized from ethanol to get the compound (B).

The newly synthesized compounds were characterised on the basis of elemental analysis, molecular determination, UV, IR, NMR. spectral data.

The UV, IR, and NMR spectral data :-

Compound (B) :

UV : Spectrum No. 1

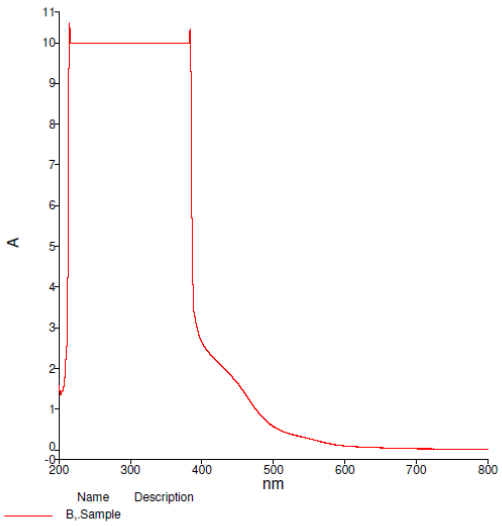
The UV-Vis spectrum of the compound B reported in dioxane showed λ_{max} value 395 nm corresponding to $n \rightarrow \pi^*$ transition.

IR KBr : Spectrum No. 2

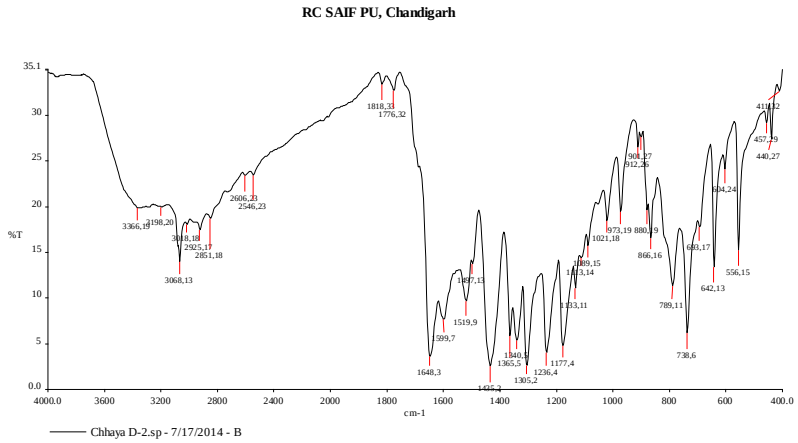
3366.19 cm^{-1} (O-H phenolic) , 2925.17 cm^{-1} (aliphatic -C-H stretching) , 3018.18 cm^{-1} (aromatic C-H stretching) , 3198.28 cm^{-1} (-NH stretching) , 1648.3 cm^{-1} (-C=N-stretching) , 1340.5 cm^{-1} [(C-N=) ($C-NO_2$) stretching] , 738.6 cm^{-1} [C-Cl stretching in aliphatic) , 1177.4 cm^{-1} [C-Cl stretching in aromatic].

PMR : Spectrum No. 3

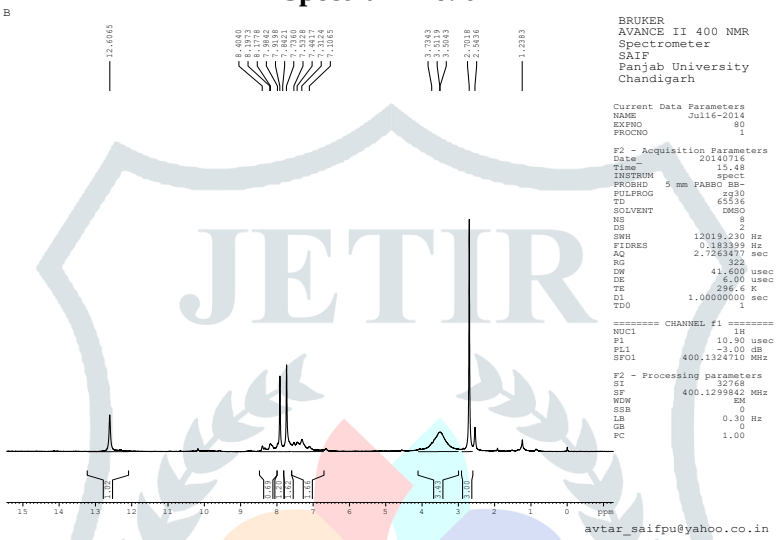
∂ 2.6 (d, 1H, -C=C-C-**H**) ; ∂ 3.5 (hump 1H, -N**H**) ; ∂ 3.7 (d, 1H, -C=C- **H**) ; ∂ 7.1 to 8.4 (m, 11H, Ar-**H**) ; ∂ 12.6 (s, 1H, O-**H**).



Spectrum No.01

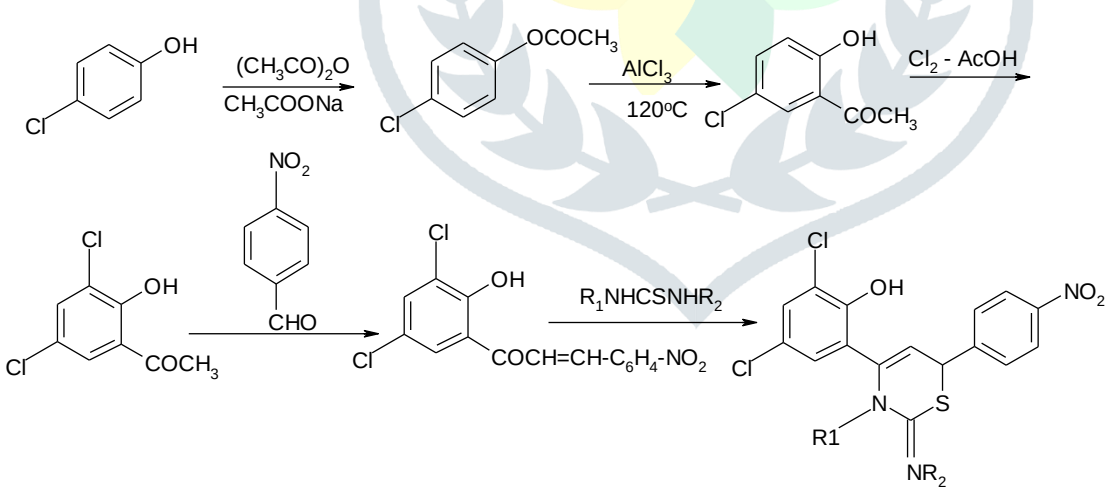


Spectrum No. 02



Spectrum No. 03

Scheme :



Where :

1) R_1 = -H
2) R_2 = $-C_6H_5$

All the newly synthesised compound (B) an its nanoparticles were screened for their antibacterial activity against some *Gram positive* pathogens viz. *Staphylococcus aureus* and *Streptococcus sp.* and some *Gram negative* pathogens viz. *Pseudomonas sp.* and *Solmonella Typhi.* at conc.of 1000 µm

gentamycine as a standard. DMF was used as solvent control using agar plate techniques. The zones of inhibition formed were measured in mm and are shown in table -2.

TABLE-2

ANTIBACTERIAL ACTIVITIES OF SYNTHESISED NEW COMPOUNDS :

Zones of inhibition (mm)

Compounds	Staphylococcus aureus	Streptococcus sp.	Pseudomonas sp.	Solmonella typhi
B	14	12	14	14
Nanoparticles of B	14	14	15	15

RESULT AND DISCUSSION :

The newly synthesized compound (B) and its nanoparticles were found to be active against test pathogens. However a further detailed study in the light of Medical sciences is advised.

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