SYNTHETIC STUDY OF 4-PHENYL-5-ARYLIMINO-3-*S*-TETRA-*O*-ACETYL-A-D-GLUCOSYL-1,2,4-DITHIAZOLIDINES AND ITS APPLICATIONS AS ANTIBACTERIAL AGENTS

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Abstract:

Several 4-phenyl-5-arylimino-3-*S*-tetra-*O*-acetyl-α-D-glucosyl-1,2,4-dithiazolidines III (a-d) were synthesized by the interaction of *S*-tetra-*O*-acetyl-α-D-Glucosyl-1-phenyl-isodithocarbamate I with *N*-aryl-*S*-chloro isothiocarbamoyl chlorides II(a-d). The identities of these new compounds have been established on the basis of chemical transformations and spectral studies. In the present investigation the *In-vitro* bacterial assay of compounds has been evaluated by using several bacteria such as *Staphylococcus aureus*, *S. Typhi* and *Pseudomonas aeruginosa.* All compounds studied shows satisfactory antibacterial activity.

Key words: synthesis, 1,2,4-dithiazolidines, isothiocarbamoyl chlorides, isodithocarbamate, antibacterial activity.

Introduction:-

Carbohydrate derivatives have been extensively investigated, including synthesis, characterization and biological activity, partly due to facts that many naturally occurring saccharides and synthesized analogues exhibit various and potent biological activities like anti-inflammatory, analgesic, fungicidal, herbicidal and pesticide agents[1-3] and have been widely employed as agrochemicals and pharmaceuticals[5-8].

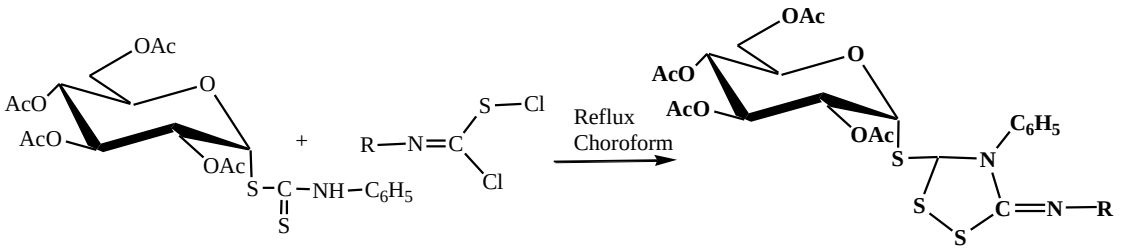
Per-*O*-acetyl and per-*O*-benzoyl derivatives of sugars are important intermediates in carbohydrates synthesis. The resulting sugar per-acetate and per-benzoates have been utilized as glycosyl donors in monosaccharide transformation and oligosaccharide synthesis.

As a result of these factors and application in various fields, synthesis of per-acetylation of sugars and derivatives of such protected sugars become valuable in common transformations and in carbohydrate synthesis.

Heterocyclic compounds and medicines are interconnected in the recent era. 1, 3, 5-thiadiazines and their derivatives have been shown to possess brightening and fibre finishing properties in textile industries[3-4]. Thiadiazines have exhibited remarkable pharmacological activities such as spasmolytic, anaesthetic, cardiovascular and hypo metabolic agents. They are also used as fungicidal[3], insecticidal[4] and as medicinal compounds.

Chemistry of *S*-Chloro-*N*-phenyl isothocarbamoyl chloride with special utility in the synthesis of nitrogen and sulfur containing heterocyclic compounds has been exhaustively investigated by number of chemists[9-11]. However, there is an increasing resistance to these drugs. Moreover, some of azole derivatives used as common antibiotics posses a toxic effect on humans as well as their antimicrobial effects.

Reaction Scheme:



S-tetra-*O*-acetyl- α –D-glucosyl-1-phenyl-isodithiocarbamate I

N-aryl-*S*-chloro isothiocarbamoyl chlorides II

4-phenyl-5-arylimino-3-*S*-tetra-***O***-acetyl -α-D-glucosyl 1,2,4-dithiazolidines III

Where, OAc = $OCOCH_3$
R= a) phenyl, b) *p*-tolyl, c) *p*- methoxy d) *p*-chloro

Experimental:-

All the melting points recorded were found to be uncorrected. The structures of newly synthesized compound were confirmed on the basis of elemental and IR spectral analysis[12-13]. IR spectra were recorded in KBr on a FTIR Perkin-Elmer (4000-450cm^{-1}) spectrophotometer and in KBr disks on SHIMADZU IR affinity-1 FTIR spectrometer. Specific rotations were measured

on Equip-Tronics EQ-801 Digital Polarimeter. Thin layer chromatography (TLC) was performed on silica gel G for TLC (Merck) and spots were visualized by iodine vapours.

General Methods:

The reagents used for the synthesis were prepared as follows-

i) Synthesis of *S*-tetra-*O*-acetyl-α-D-Glucosyl-1-phenyl-isodithocarbamate I

S-tetra-*O*-acetyl-α-D-Glucosyl-1-phenyl-isodithocarbamate I was synthesized by the interaction of tetra-*O*-acetyl-α-D-Glucosyl bromide with Ammonium phenyl dithiocarbamate in propane-2-ol.

ii) Preparation of Aryl isothiocyanates

The aryl isothiocyanates were prepared by already known method i.e. by oxidative decomposition of ammonium aryl dithiocarbamates with lead nitrate.

iii)Preparation of *S*-Chloro-*N*-aryl isothiocarbamoyl chlorides II(a-d)

It was prepared by the extension of earlier method i.e. by passing calculated quantity of gaseous chlorine into the chloroform solution of aryl isothiocyanates. *S*-chloro-*N*-phenyl isothiocarbamoyl chlorides were obtained as pale yellow oil (Chemically it is aryl-imino chloromethane sulphanyl chlorides).

iv) 4-phenyl-5-arylimino-3-*S*-tetra-*O*-acetyl-α-D-glucosyl-1,2,4-dithiazolidines III (a-d)

N-phenyl–*S*–chloro isothiocarbamoyl chloride **2** (0.001 M. 0.215 g) in 10 ml chloroform was added gradually to cold solution of *S*-tetra-*O*-acetyl-α-D-Glucosyl-1-phenyl-isodithocarbamate I (0.001M, 1.2 g) in 20 ml chloroform. The reaction was quite brisk and exothermic with the evolution of hydrogen chloride. The mixture was refluxed for 3 h. The chloroform was distilled off. The resultant solution was allowed to stand for several hours but no solid was separated out. The sticky mass thus obtained was triturated several times with petroleum ether (60-80°C). It furnished a granular solid. It was purified from ethanol-water. The spectral analysis of compounds was carried out.

Similarly when the reaction of *S*-tetra-*O*-acetyl-α-D-Glucosyl-1-phenyl-isodithocarbamate I were extended to other *N*-aryl–*S*–chloro isothiocarbamoyl chlorides IIb-d the related 1, 2, 4-dithiaazolines IIIb-d were obtained

The structures of the product were confirmed by the spectral (IR[7-13]) and elemental analysis (Table 1).

Spectral analysis:

IIIa:- **IR(KBr cm^{-1}):** 3477 (N-H), 3028 (Aromatic C-H), 2961 (Aliphatic C-H), 1751 (C=O), 1452 (C-N), 1230 (C-O), 1103, 1032 and 936 (Characteristics of glucose), 754 (C-S).

IIIb:- **IR(KBr cm^{-1}):** 3473 (N-H), 3043 (Aromatic C-H), 2961 (Aliphatic C-H), 1749 (C=O), 1452 (C-N), 1230 (C-O), 1103, 1032 and 936 (Characteristics of glucose), 754 (C-S).

IIIc:- **IR(KBr cm^{-1}):** 3404 (N-H), 3028 (Aromatic C-H), 2941 (Aliphatic C-H), 1743 (C=O), 1452 (C-N), 1228 (C-O), 1103, 1032 and 936 (Characteristics of glucose), 692 (C-S).

IIId:- **IR(KBr cm^{-1}):** 3468 (N-H), 3061 (Aromatic C-H), 2949 (Aliphatic C-H), 1757 (C=O), 1452 (C-N), 1228 (C-O), 1103, 1032 and 936 (Characteristics of glucose), 756 (C-S).

Table1:- Characterization of 4-phenyl-5-arylimino-3-*S*-tetra-*O*-acetyl-α-D-glucosyl-1,2,4-dithiazolidines III (a-d)

Compds	Mol. Formula	Yield (%)	m.p. (°C)	R_f Value	Elemental Analysis % Found (Required)		$[\alpha]_D^{31}$ (c, in $CHCl_3$]
					N	S	
IIIa	$C_{28}H_{30}O_9N_2S_2$	72	129	0.55	4.38 (4.41)	15.12 (15.14)	+90.90° (0.055 in $CHCl_3$)
IIIb	$C_{29}H_{32}O_9S_3N_2$	66	134	0.25	3.15 (3.20)	11.15 (11.18)	+188.88 (0.255 in $CHCl_3$)
IIIc	$C_{29}H_{32}O_{10}S_3N_2$	58	129	0.45	4.81 (4.19)	14.45 (14.43)	+42.86° (0.035 in $CHCl_3$)
IIId	$C_{28}H_{29}O_9S_2N_2Cl$	61	166	0.67	4.39 (4.75)	10.04 (10.02)	+25° (0.055 in $CHCl_3$)

Antibacterial activity:

All the compounds have been screened for antibacterial activities using cup plate agar diffusion method[14-15] by measuring the inhibition zone in mm. the compounds were taken at a concentration of 1 mg/mL using dimethyl sulphoxide (DMSO) as solvent. The compounds were screen for antibacterial activity against *Staphylococcus aureus, S. thypi and Pseudomonas aeruginosa* in nutrient agar medium. Amikacin (100 µg/mL) was used as standard for antibacterial activity. The results are presented in Table2.

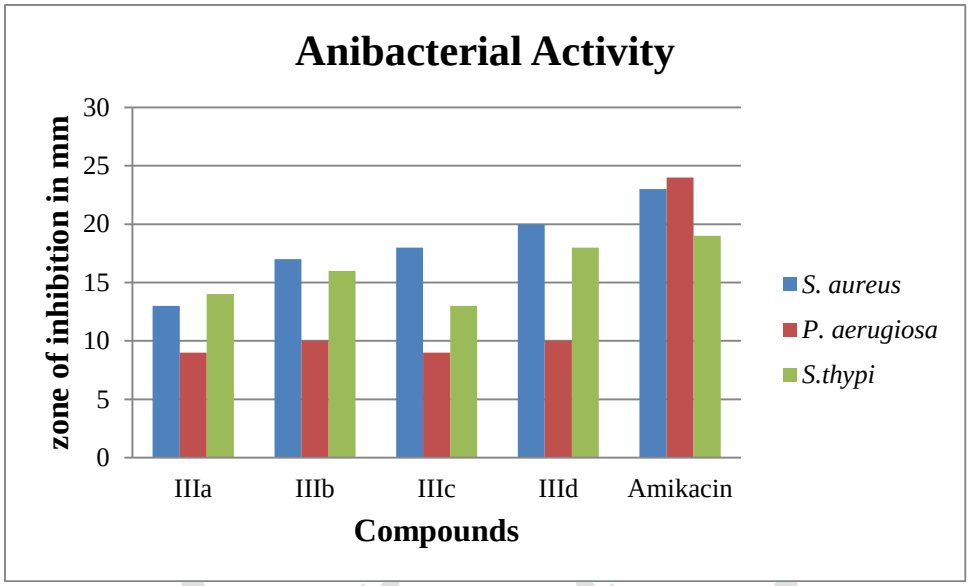
Results:

The study reveals that all compounds show antimicrobial activities. **IIIb, IIIc** and **IIId** showed more significant activities against *Staphylococcus aureus,* **IIIb** and **IIId** showed more significant activities against *Pseudomonas aeruginosa Proteus vulgaris* and **IIIb** and **IIId** showed more significant activities against *S. thypi* respectively.

Table 2: Antibacterial study of several 4-phenyl-5-arylimino-3-*S*-tetra-*O*-acetyl-α-D-glucosyl-1, 2, 4-dithiazolidines III

Compounds	*S. aureus*	*P. aerugiosa*	*S. thypi*
IIIa	13	09	14
IIIb	17	10	16
IIIc	18	09	13
IIId	20	10	18
Amikacin	23	24	19

Graphical Representation



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