SYNTHESIS, CHARACTERIZATION AND BACTERIAL ASSAY OF 4-PHENYL-5-ARYLIMINO-3-*S*-TETRA-*O*-ACETYL GLUCOSYL-1,2,4 DITHIAZOLIDINES

K. N. Puri[1] and G. V. Korpe[2]
1. Department of Chemistry, Shri Shivaji Science and Arts College, Chikhali 443201 (M.S.) India,
2. Department of Chemistry, Shri Shivaji College, Akola-444001, (M.S.), India
E-mail: knpuri2008@rediffmail.com

Abstract:
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. In recent years, there has been increasing interest in the synthesis of heterocyclic compounds by cyclization of appropriate linear compounds. In view of applications of these compounds in various fields, the current study was related to investigate the following reactions. 4-phenyl-5-arylimino-3-*S*-tetra-*O*-acetyl glucosyl-1, 2, 4- dithiazolidines have been synthesized by the interaction of *S*-tetra-*O*-acetyl Glucosyl-1-phenyl-isodithocarbamate with various *N*-aryl-*S*-chloro isothiocarbamoyl chlorides. The identities of these new compounds have been established on the basis of chemical transformation and spectral studies. In the present investigation the *In-vitro* bacterial assay of compounds has been evaluated by using several bacteria such as *Escherichia coli, Staphylococcus aureus* and *Pseudomonas aeruginosa.* All compounds studied shows satisfactory bacterial assay.

Key words: 1, 2, 4- dithiazolidines, Isodithocarbamate, *N*-aryl-*S*-chloro isothiocarbamoyl chlorides, bacterial assay.

Introduction:

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. Thiadiazines have exhibited remarkable pharmacological activities such as spasmolytic, anaesthetic, cardiovascular and hypo metabolic agents. They are also used as fungicidal, insecticidal and as medicinal compounds. Heterocyclic compounds are found to exhibit anti-inflammatory, anti-parasitic, anti-tubercular, antidiabetic activity[1-3].

Organosulfur compounds play an important role in modern organic synthesis. In laboratory there are various reports on sugar heterocyclic possessing antimicrobial and antifungal activities[4-10]. In view of applications of these compounds in various fields, the current study was related to investigate the following reactions. 4-phenyl-5-arylimino-3-*S*-tetra-*O*-acetyl glucosyl-1, 2, 4- dithiazolidines 3(a-f) have been synthesized by the interaction of *S*-tetra-*O*-acetyl Glucosyl-1-phenyl-isodithocarbamate 1 with various *N*-aryl-*S*-chloro isothiocarbamoyl chlorides 2(a-f) .

Results and Discussion:-

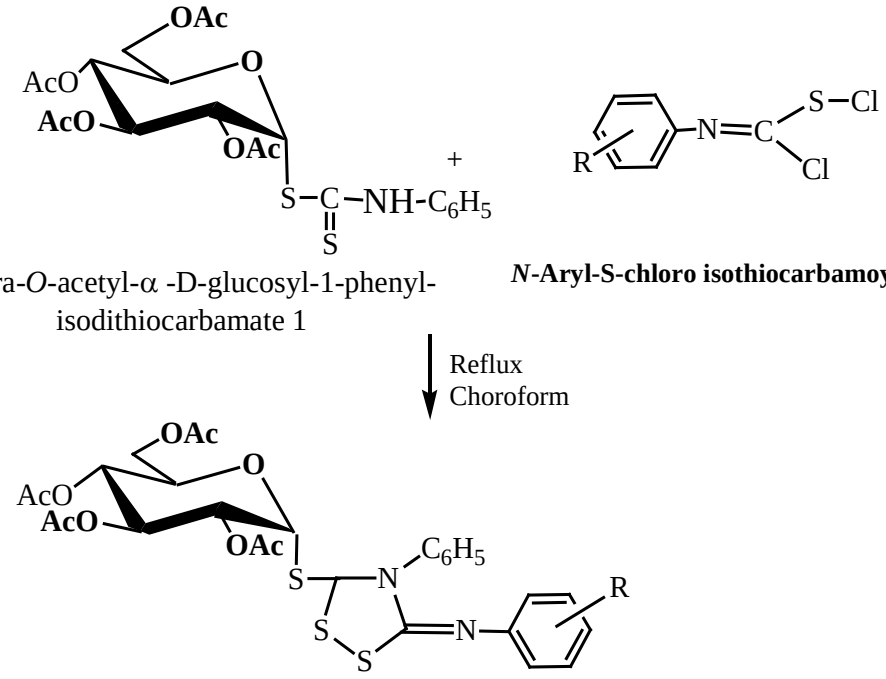
N- phenyl-*S*-chloro isothiocarbamoyl chloride 2a (0.005 M, 1.025 gm) in 10 ml chloroform was added gradually to cold solution of *S*-tetra-*O*-acetyl-α-D-glucosyl-1-phenyl-isodithiocarbamate 1 (0.005M, 2.49gm) in 25 ml chloroform. The reaction was quite brisk and exothermic with the evolution of hydrogen chloride. The mixture was refluxed for 3 hr. 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 IR, ^{1}H NMR and mass spectral analysis (Experimental) and elemental analysis (Table 1) clearly indicated the product and assign the structure as 4-phenyl-5-phenylimino-

3-*S*-tetra-*O*-acetyl glucosyl-1, 2, 4-dithiazolidine **3a.**

When the interaction of *S*-tetra-*O*-acetyl-α-D-glucosyl-1-phenyl-isodithiocarbamate 1 was extended to other *N*-Aryl-*S*-chloro isothiocarbamoyl chlorides 2 **(b-f)** the related 4-phenyl-5-arylimino-3-*S*-tetra-*O*-acetyl glucosyl-1, 2, 4- dithiazolidines 3(b-f) were obtained.

Scheme:



S-Tetra-*O*-acetyl-α -D-glucosyl-1-phenyl-isodithiocarbamate 1

***N*-Aryl-S-chloro isothiocarbamoyl chlorides 2(a-f)**

4-Phenyl-5-arylimino-3-*S*-tetra-*O*-acetyl-α-D-glucosyl-1,2,4dithiazolidines 3(a-f)

Where, OAc- OCO- CH_3,

R- a) H, b) *o*-Methyl, c) *p*-Methyl, d) *o*-methoxy, e) *p*-methoxy, f) *p*-Chloro, c)

Material and Method

The reagents required for the given synthesis are obtained as follows-

i) Synthesis of S-tetra-O-acetyl-α-D-glucosyl-1-phenyl-isodithiocarbamates 1:-

Isopropanolic suspension of tetra-O-acetyl-α-D-glucosyl bromide and ammonium phenyl dithiocarbamate was heated on water bath at about 70°C until the suspension gets cleared. The clear solution was kept at room temperature for 20 hours. It was mixed with 100 ml distilled water. This aqueous solution was acidic and non-desulphurisable when boiled with alkaline plumbite solution. The aqueous solution was basified with ammonium hydroxide afforded a sticky mass which was not solidified on standing for several hours. It was purified by ethanol-water.

ii) Synthesis of N-aryl-S-chloro isothiocarbomoyl chlorides2(a-f):-

N-Aryl-*S*-chloro isothiocarbomoyl chlorides obtained from intraction of aryl isothiocyanates with Cl_2 gas.

Experimental Section:-

The melting point of compounds were determined with the help of Thermonic melting point apparatus and were found uncorrected. The structures of newly synthesized compounds were confirmed on the basis of elemental and spectral analysis. IR Spectra were recorded on KBr disks on SHIMADZU IR affinity-1 FTIR spectrometer. ^{1}H NMR was obtained on Bruker DRX-300 NMR Spectrometer. Samples were prepared in $CDCl_3$ with TMS as an internal reference. The mass spectra were obtained on JEOL-AccuTof JMS-T100LC and Thermo Fennigan LCQ Advantage max ion trap mass spectrometer. Thin layer chromatography (TLC) was performed on silica gel G for TLC (Merck) and spot were visualized by iodine vapour.

Spectral and Elemental analysis[11-15]:-

4-phenyl-5-phenylimino-3-*S*-tetra-*O*-acetyl-α-D-glucosyl-1, 2, 4- dithiazolidine 3a:

IR(KBr cm^{-1}): 3477 (N-H str.), 3028 (Aromatic C-H str.), 2978 (Aliphatic C-H str.), 1751 (C=O str..), 1527 (C=C str.), 1159 (C-N

str.), 1230 (C-O str.), 1056 (Characteristics of glucose), 754 (C-S str.); **^{1}H NMR ($CDCl_3$, ppm):** δ 8.17-7.138 (10H, m, Aromatic protons), 4.242-4.205 (7H, m, glucosyl protons), 2.74-2.35 (12H, m, acetyl protons) **Mass (m/z):** 634 (M^+), 331, 211, 169, 109 (100%).

4-phenyl-5-*o*-tolylimino-3-*S*-tetra-*O*-acetyl-α-D-glucosyl-1, 2, 4- dithiazolidine 3b:

IR(KBr cm^{-1}): 3472 (N-H str.), 3022 (Aromatic C-H str.), 2971 (Aliphatic C-H str.), 1752 (C=O str..), 1530 (C=C str.), 1157 (C-N str.), 1230 (C-O str.), 1056 (Characteristics of glucose), 754 (C-S str.).

4-phenyl-5-*p*-tolylimino-3-*S*-tetra-*O*-acetyl-α-D-glucosyl-1, 2, 4- dithiazolidine 3c:

IR(KBr cm^{-1}): 3473 (N-H str.), 3043 (Aromatic C-H str.), 2972 (Aliphatic C-H str.), 1749 (C=O str..), 1521 (C=C str.), 1160 (C-N str.), 1230 (C-O str.), 1050 (Characteristics of glucose), 754 (C-S str.); **^{1}H NMR ($CDCl_3$, ppm):** δ 8.28-7.38 (10H, m, Aromatic protons), 4.248-4.25 (7H, m, glucosyl protons), 2.54-2.39 (12H, m, acetyl protons), 1.85 (3H, s, methyl Protons); **Mass (m/z):** 648 (M^+), 331, 211, 169, 109 (100%).

4-phenyl-5-*o*-methoxy phenylimino-3-*S*-tetra-*O*-acetyl-α-D-glucosyl-1, 2, 4-dithiazolidine 3d:

IR(KBr cm^{-1}): 3477 (N-H str.), 3028 (Aromatic C-H str.), 2978 (Aliphatic C-H str.), 1751 (C=O str..), 1527 (C=C str.), 1159 (C-N str.), 1230 (C-O str.), 1056 (Characteristics of glucose), 754 (C-S str.).

4-phenyl-5-*p*-methoxy phenylimino-3-*S*-tetra-*O*-acetyl-α-D-glucosyl-1, 2, 4-dithiazolidine 3e:

IR(KBr cm^{-1}): 3404 (N-H str.), 3068 (Aromatic C-H str.), 2941 (Aliphatic C-H str.), 1743 (C=O str..), 1527 (C=C str.), 1159 (C-N str.), 1228 (C-O str.), 1050 (Characteristics of glucose), 792 (C-S str.); **^{1}H NMR ($CDCl_3$, ppm):** δ 8.25-7.31 (10H, m, Aromatic protons), 4.240-4.05 (7H, m, glucosyl protons), 2.50-2.32 (12H, m, acetyl protons), 1.98 (3H, s, methoxy Protons); **Mass (m/z):** 664 (M^+), 331, 211, 169, 109 (100%).

4-phenyl-5-*p*-Chloro phenylimino-3-*S*-tetra-*O*-acetyl-α-D-glucosyl-1, 2, 4- dithiazolidine 3f:

IR(KBr cm^{-1}): 3468 (N-H str.), 3061 (Aromatic C-H str.), 2949 (Aliphatic C-H str.), 1757 (C=O str..), 1527 (C=C str.), 1224 (C-N str.), 1228 (C-O str.), 1066 (Characteristics of glucose), 756 (C-S str.).

Table 1:-

Characterization of 4-phenyl-5-arylimino-3-*S*-tetra-*O*-acetyl glucosyl-1, 2, 4- dithiazolidines 3(a-f)

Sr. No.	Product	Yield (%)	Rf Value	m. p. (^{o}C)	Analysis (%): Found(Required)	
					N	S
1.	3a	62	0.69	129	4.38 (4.41)	15.12 (15.14)
2.	3b	71	0.72	162	4.29 (4.32)	14.75 (14.81)
3.	3c	69	0.79	166	4.30 (4.32)	14.72 (14.81)
4.	3d	56	0.75	132	4.17 (4.21)	14.42 (14.45)
5.	3e	72	0.82	129	4.15 (4.21)	14.41 (14.45)
6.	3f	77	0.88	171	4.12 (4.18)	14.31 (14.34)

C and H analysis were found satisfactory in all cases.

Bacterial assay:

The bacterial assay[16-17] of compounds was studied against *Escherichia coli, Staphylococcus aureus and Pseudomonas aeruginosa* in nutrient agar medium. Amikacin (100 μg/ml) was used as standard for antibacterial activity. The results are presented in Table2.

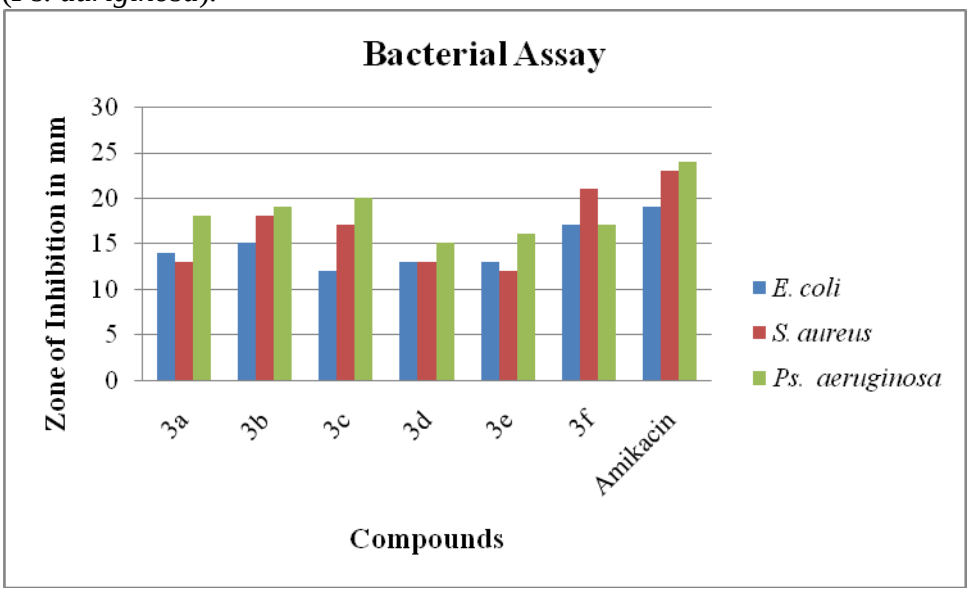
It has been observed that some of these compound exhibited interesting microbial activities. IIIa, Vc and Vd exhibited most significant activity against *Escherichia coli*, IIIa and Vb exhibited most significant activity against *Staphylococcus aureus*, IIIb and Vb exhibited most significant activity against *S. Typhi* and IIIa and Vd exhibited most significant activity against *Pseudomonas aeruginosa* respectively. All the other compounds exhibited low to moderate activity. (Table-2).

Table2:

Bacterial assay of 4-phenyl-5-arylimino-3-*S*-tetra-*O*-acetyl glucosyl-1, 2, 4- dithiazolidines III(a-f)**.**

Compounds	**Antibacterial****		
	E. coli	*S. aureus*	*Ps. Aeruginosa*
3a	14	13	18
3b	15	18	19
3c	12	17	20
3d	13	13	15
3e	13	12	16
3f	17	21	17
Amikacin	19	23	24

**zone of inhibition in mm (15 or less) resistance, (16-20mm) moderate and (more than 20mm) sensitive. *Escherichia coli* (*E*. coli), *Staphalococcus aureus* (*S*. aureus) and *Psudomonas auriginosa* (*Ps. auriginosa*).



Acknowledgement:-

Authors are thankful to SAIF/CIL, Panjab University, Chandigarh, Central Instrumental Cell, Shri Shivaji College, Akola for providing spectral data and also thankful to Dr. R. M. Bhise, Principal, Shri Shivaji College, Akola and Principal, Shri Shivaji Science and Arts College, Chikhali for providing necessary facilities.

References:

1. Achgill RK, Call LW, Erdelen C, EP 1989, 339964.
2. L. Heuer M, Paulus KW, Lorentzen J and Dehne HW, Erdelen C, EP 1993, 571857.
3. Rao TS, Revankar GR, Vinayak RS, Robins RK, J. Heterocycl. Chem., 1991, 28, 1779.
4. Dhonde MG and Deshmukh SP, J. Carbohydr. Chem., 2004, 23(4), 305.

5. Paranjpe MG and Mahajan_AS, Indian J. Chem., 1972, 10, 1138.
6. Paranjpe MG and Mahajan AS, J. Indian Chem. Soc., 1972, 49, 585.
7. Mahajan AS, Kamble VS and Paranjpe MG, J. Indian Chem. Soc., 1974, 51, 714.
8. Nimdeokar NM and Paranjpe MG, Indian J. Chem., 1977, 15B, 1068.
9. Nimdeokar NM, 1979, Chemistry of Nitrogen, Sulphur and Oxygen Containg Organic Compounds : Dithiazolines, Triazines and Related Compounds", Ph. D. Thesis, Nagpur University.
10. Bhagat SK and Deshmukh SP, J. Indian Chem. Soc., 2005, 82, 1022-1024.
11. Silverstein RM, Bassler GC, and Morrill TC, 1991, "Specrometric Identification of organic compounds", *5th ed, Wiley, New York.*
12. Colthup NB, Daly LH and Weberley SE, 1964 "Introduction of Infrared and Raman Spectroscopy", *Academic, Press New York.*
13. Biemann, Dejongh DC and Schnoes HK, 1963, J Amm Chem Soc, 85, 1763.
14. Buclzikiewicz H, Djerassi C and Williams DH, 1964, "Structural Elucidation of natural product by mass spectrometry", *II Holden Day*, 207.
15. Jacobsen NE, 2007, NMR Spectroscopy Explained, Wiley, 15.
16. Kawangh F, 1963, Analytical Microbiology, Academic press, New York.
17. British pharmacopaeia- II, Biological assay and Tests, The Stationary Office Ltd., London, A-205, 1998.