Available online at www.derpharmachemica.com

ISSN 0975-413X
CODEN (USA): PCHHAX

Der Pharma Chemica, 2017, 9(10):120-122
(http://www.derpharmachemica.com/archive.html)

Antimicrobial Activities of 2-phenylimino-3-aryl-4-S-benzyl-6-tetra-O-acetyl-β-D-galactosylimino-2,3-dihydro-1,3,5-thiadiazine (hydrochlorides)

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ABSTRACT

2-phenylimino-3-aryl-4-S-benzyl-6-tetra-O-acetyl-β-D-galactosylimino-2, 30-dihydro-1,3,5-thiadiazine (hydrochlorides) have been prepared by the interaction of 1-aryl-5-tetra-O-acetyl-β-D-galactosyl-2-S-benzyl-2,4-isodithiobiurets and phenyl isocyanodichloride. The identities of new products formed have been established on the basis of usual chemical transformations and Infra-red (IR), Proton Nuclear Magnetic Resonance (^{1}H-NMR) and mass spectral studies. The present paper describes antimicrobial activities of the synthesized compounds.

Keywords: Thiadiazine, Heterocyclic, Galactosyl, Antimicrobial activities

INTRODUCTION

Thiadiazines and its derivatives are important biologically active precursors in the field of heterocyclic chemistry. Some amino derivatives of thiadiazine show antiviral, anesthetic, cardiovascular and hypo metabolic activities [1,2]. Some disubstituted 1,2,4-triazolo-1,3,4 thiadiazine are found to possess antifungal, anti-inflammatory and analgesic activities [3].

Some halogen containing 1,2,4 triazolo-1,3,4 thiadiazine exhibits antibacterial and anticancer (lung, breast and CNS) activities [4]. Simple thiadiazine show antifungal activity [5], while pyrazole derivatives of thiadiazine show potential anti-HIV activities [6]. Some 2-amino-6-hydroxy derivatives of thiadiazine show anticonvulsant activity [7], while 3,5-disubstituted thiadiazine thiones exhibit potential antitubercular activity [8].

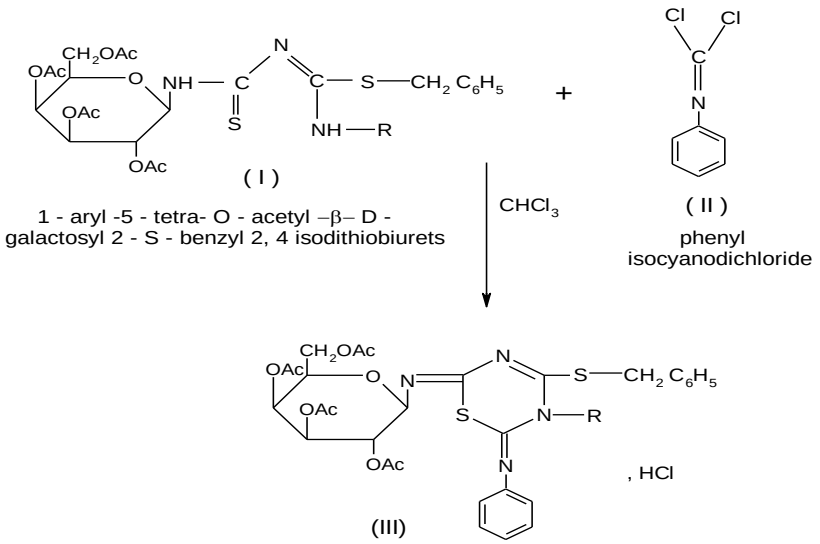
Variety of 1,3,5-thiadiazines and 1,3,5-triazines have been reported by the interaction of phenyl isocyanodichloride and several thioamido group containing compounds [9-11]. In view of pharmacological properties of these derivatives of thiadiazine in the field of heterocyclic chemistry, it appeared sufficiently interesting to develop a new route in the synthesis of thiadiazine having a N-galactosyl substitutent in its structural frame work. Thus, 2-phenylimino-3-aryl-4-S-benzyl-6-tetra-O-acetyl-β-D-galactosylimino-2,30-dihydro-1,3,5-thiadiazine (hydrochlorides) were prepared [12] involving the interaction of 1-aryl-5-tetra-O-acetyl-β-D-galactosyl-2-S-benzyl-2,4-isodithiobiuret (I) with phenyl isocyanodichloride (II).

MATERIALS AND METHODS

Melting points are found to be uncorrected. The IR spectra were recorded on a Perkin-Elmer spectrum RXI (4000-450 cm^{-1}) FTIR spectrometer. ^{1}H-NMR were obtained on a Bruker DRX-300 (300 MHz FT NMR) NMR spectrometer for a sample in Deuterated Chloroform ($CDCl_3$) solution with Tetramethylsilane (TMS) as an internal reference. The mass spectra were recorded on Joel SX-102 mass spectrometer. Optical rotations [α] D were measure on an Equiptronics digital polarimeter Model No. EQ 800 in $CHCl_3$ at 39°C.

RESULTS AND DISCUSSION

Synthesis of the target compounds has been carried out by the following method. Reaction of 1-phenyl-5-tetra-O-acetyl-β -D-galactosyl-2-S-benzyl-2,4-isodithiobiuret (Ia) and phenyl isocyanodichloride (II) in boiling chloroform medium for 3 h, evolution of hydrogen chloride was clearly noticed. After heating, solvent was removed by distillation and a syrupy mass was left behind. It was triturated with petroleum ether to give a solid. It was crystallized from aqueous ethanol, m.p. 112°C. The elemental analysis of this product indicated its molecular formula as $C_{36}H_{38}O_9N_4S_2Cl_2$. This reaction of phenyl isocyanodichloride was capable of extension to other 1-aryl-5-tetra-O-acetyl-β-D-galactosyl-2-S-benzyl-2,4-isodithiobiuret (Ib-Ig) and the corresponding 2-phenylimino-3-aryl-4-S-benzyl-6-tetra-O-acetyl-β-D-galactosylimino-2,3-dihydro-1,3,5-thiadiazines (hydrochlorides) (IIIb-IIIg) have been isolated (Table 1). The formation of III can be represented as follow:



Where, R=(a) Phenyl, (b) o-Cl-phenyl, (c) m-Cl-phenyl, (d) p-Cl-phenyl, (e) o-tolyl, (f) m-tolyl, (g) p-tolyl, Ac=$COCH_3$

Table 1: 2-Phenylimino-3-aryl-4-S-benzyl-6-tetra-O-acetyl-β-D galactosylimino-2,3-dihydro-1,3,5 thiadiazine (hydrochlorides) (III)

S. No.	1-Aryl-5-tetra-O-acetyl-β -D-galactosyl 2-S-benzyl-2,4 isodithiobiurets (I)	2-Phenylimino-3-aryl-4-S-benzyl-6-tetra-O-acetyl-β -D-galactosylimino-2,3-dihydro-1,3,5-thidiazine (Hydrochlorides) (III)	Yield (%)	m.p. (°C)
1	1-phenyl….(Ia)	--3-phenyl---(IIIa)	66.66	112
2	1-o-Cl-phenyl...(Ib)	--3-o-Cl-phenyl--(IIIb)	68.71	118
3	1-m-Cl-phenyl… (Ic)	--3-m-Cl-phenyl--(IIIc)	69.90	122
4	1-p-Cl-phenyl… (Id)	--3-p-Cl-phenyl--(IIId)	62.20	142
5	1-o-tolyl….(Ie)	--3-o-tolyl--(IIIe)	71.22	156
6	1-m-tolyl….(If)	--3-m-tolyl--(IIIf)	70.11	138
7	1-p-tolyl…..(Ig)	--3-p-tolyl--(IIIg)	77.75	140

Antimicrobial activity

All the compounds IIIa-IIIg were screened for their antimicrobial activity [13,14] against various pathogenic bacteria and fungi by cup-plate agar diffusion method. Amikacin was used as standard for antibacterial activity at a concentration of 50 µg/ml and fluconazole was used as standard for antifungal activity at the same concentration. The compounds were dissolved in Dimethyl Sulfoxide (DMSO) at 100 µg/ml concentration. The zone of inhibition was measured in mm and is represented as an average of three readings. The observations of the activity of the compounds IIIa-IIIg against the bacteria *Staphylococcus aureus*, *Escherichia coli*, *Pseudomonas aeruginosa*, *Proteus vulgaris* and fungi like *Aspergillus niger* and *Candida albicans* are quoted in following Table 2.

Table 2: Antimicrobial activity of compound IIIa-IIIg

Compound	Antibacterial activity				Antifungal activity	
	S. aureus	*E. coli*	*P. aeruginosa*	*P. vulgaris*	*C. albicans*	*A. niger*
IIIa	12	-	-	12	-	-
IIIb	10	-	-	-	08	11
IIIc	11	-	9	20	09	09
IIId	13	-	10	12	-	-
IIIe	15	-	9	15	-	-
IIIf	16	-	-	12	09	08
IIIg	13	-	-	12	-	-
Amikacin	20	20	20	20	-	-
Fluconazole	-	-	-	-	15	15

*Including well diameter of 5 mm

CONCLUSION

It was observed that the target compounds IIIa-IIIg except IIIb show low to moderate activity against bacteria like *S. aureus* and *P. vulgaris*. Compounds IIIc, IIId and IIIe show low activity against *P. aeruginosa*. All compounds are inactive against *E. coli*. Compounds IIIa, IIId, IIIe, IIIg does not show any activity against the fungi, *C. albicans* and *A. niger*, while others show low to moderate activity.

ACKNOWLEDGEMENTS

Author is thankful Dr. S.G. Bhadange, Principal Shri Shivaji College, Akola & Dr. S.P. Deshmukh, Research supervisor for encouragement and providing necessary facilities.

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