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ANTIMICROBIAL ACTIVITTIES OF SOME ARYLIMINO N-GALACTOPYRANOSYL DITHIAZOLIDINES

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ABSTRACT

The target compounds 5 - arylimino - 4 - phenyl - 3 - tetra - O - acetyl - β -D-galactopyranosylimino-1,2,4-dithiazolidines(hydrochlorides) have been synthesized by the interaction of N-tetra-O-acetyl-β-D-galactopyranosyl-S-Chloro isothiocarbamoyl chloride and 1-phenyl-3-aryl thiocarbamides. The characterization of the newly synthesized dithiazolidines has been established on the basis of usual chemical and IR, ^{1}HNMR and Mass spectral analysis. The products were also screened for their potential antimicrobial activities.

Keywords: Dithiazolidine, thiocarbamide, dithiazolidine, Mass spectral analysis, antimicrobial activity.

INTRODUCTION

Dithiazolidines constitutes a pivotal role in the synthesis of various heterocycles. They act as dynamic precursors in synthetic heterocyclic chemistry. Some glucopyranosyl dithiazolidines have been reported in the literature showing antimicrobial properties[1-5]. Also, the synthetic applications of N-aryl-S- Chloro isothiocarbamoyl chloride have been investigated by the earlier workers[6,7]. In reference to above synthetic applications of isothiocarbamoyl chloride, it appeared quite interesting to prepare N - tetra - O - acetyl - β - D - galactopyranosyl - S - Chloro isothiocarbamoyl chloride and to use this reagent as intermediate in the synthesis of N and S containing heterocyclic compounds. Thus, N-tetra-O-acetyl-β-D-galactopyranosyl-S-Chloro isothiocarbamoyl chloride was prepared and its reaction with 1, 3 disubstituted thiocarbamides has been carried out and new products have been synthesized[8]. The present paper describes antimicrobial activities of these products.

EXPERIMENTAL

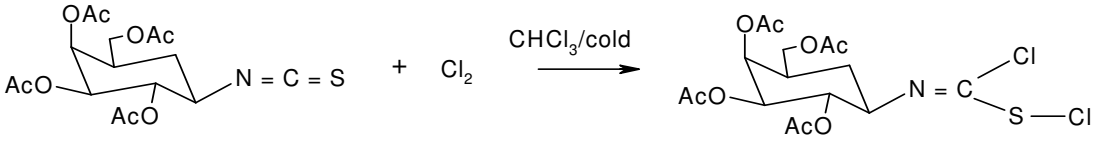
Melting points are found to be uncorrected. The IR spectra were recorded on a Perkin - Elmer spectrum RXI (4000-450 cm^{-1}) FT IR spectrometer[9]. ^{1}H NMR were obtained on a Bruker DRX-300 (300MHz FT NMR) NMR spectrometer for a sample in $CDCl_3$ solution with TMS as an internal reference[10,11]. The mass spectra were recorded on Joel SX-102 mass spectrometer[12,13]. Optical rotations $[\alpha]_D$ were measure on an Equiptronics digital polarimeter Model No. EQ 800 in $CHCl_3$ at 39^{o}C.

N - tetra - O - acetyl - β - D - galactopyranosyl - S - Chloro isothiocarbamoyl Chloride (1)

Through a chloformic solution of Tetra- O - acetyl - β - D- galactopyranosyl isothiocyanate[14] , (2g,0.005M) chlorine gas (0.005M) was bubbled maintaining the temperature between 0-5 °C . After the addition of chlorine is completed. The yellow reaction mixture was diluted with petroleum ether. The ether was removed by distillation under vacuum. The whole operation was repeated several times with petroleum ether. A pale yellow liquid (1) was obtained (Scheme-1).

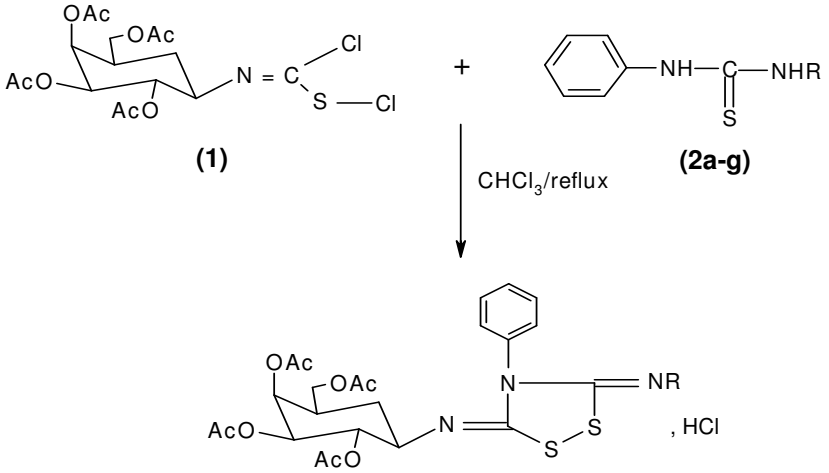
1 - Phenyl - 3 - aryl thiocarbamides (2a-g)

The required1 - phenyl - 3 - aryl thiocarbamides (2a-g), were prepared by the interaction of phenyl isothiocyanate and appropriate aryl amines in benzene medium as described in the literature[15].



Where, Ac = acetyl (CH_3CO) **(1)**

Scheme - 1



(3a-g)

Where R= phenyl, o-Cl-phenyl, m-Cl-phenyl, p-Cl-phenyl, o-tolyl, m-tolyl, p-tolyl

Scheme - 2

RESULTS AND DISCUSSION

5-arylimino - 4- phenyl -3-tetra- O- acetyl- β - D- galactopyranosylimino-1,2,4- dithiazolidines (Hydrochlorides) (3a-g) Scheme-2

N-tetra - O- acetyl - β - D- galactopyranosyl - S- chloro isothiocarbamoyl chloride (1, 0.005M) was refluxed with 1 - phenyl - 3 - aryl thiocarbamides (2a-g, 0.005M) in chloroform for 3hrs. Afterwards the solvent was distilled off and the sticky residue was triturated with petroleum ether to obtain the products (3a-g). These were recrystallised for chloroform- petroleum ether mixture. The products were characterized by their IR, NMR and mass spectra as given below. The general characterization is given in Table -1.

(3a): 5 - phenylimino - 4 - phenyl - 3 - tetra - O - acetyl - β - D- galactopyranosylimino -1,2,4- dithiazolidine(Hydrochloride)

IR (KBr, cm^{-1}):1752(C=O); 1539(C=N); 1372(C-N), 1225(C-O); 1074, 934 (β - D- galactopyranosyl ring deformation[16]); 758(C-S). ^{1}H NMR ($CDCl_3$): δ 8.01-7.22 (10H, m, Ar-H); δ5.50-4.08 (7H, m, galactopyranosyl protons); δ 2.2-2.00 (12H, m, $COCH_3$).

Mass (m/z): 687, 616, 421, 331, 227, 169,109.

(3b):5-o - Cl - phenylimino - 4- phenyl -3-tetra- O- acetyl- β - D- galactopyranosylimino-1,2,4- dithiazolidine(Hydrochloride)

IR (KBr, cm^{-1}):1753(C=O); 1541(C=N); 1372(C-N), 1225(C-O); 1074, 935 (β- D- galactopyranosyl ring deformation); 761(C-S).^{1}H NMR ($CDCl_3$): δ 7.61-7.00 (9H, m, Ar-H); δ5.50-4.08 (7H, m, galactopyranosyl protons); δ 2.20-1.97 (12H, m, $COCH_3$). Mass (m/z): 721, 650, 421, 331, 227, 169,109.

(3c): 5-m- Cl -phenylimino - 4- phenyl -3-tetra- O- acetyl- β - D- galactopyranosylimino-1,2,4-dithiazolidine(Hydrochloride)
IR (KBr, cm^{-1}):1751(C=O); 1542(C=N); 1375(C-N), 1228(C-O); 1070, 938 (β- D- galactopyranosyl ring deformation); 760(C-S). ^{1}H NMR ($CDCl_3$): δ 7.84-7.22 (9H, m, Ar-H); δ5.55-4.08 (7H, m, galactopyranosyl protons); δ 2.2-1.87 (12H, m, $COCH_3$).

(3d): 5-p- Cl-phenylimino - 4- phenyl -3-tetra- O- acetyl- β - D- galactopyranosylimino-1, 2,4-dithiazolidine (Hydrochloride)
IR (KBr, cm^{-1}): 1750(C=O); 1545(C=N); 1378(C-N), 1230(C-O); 1074, 932 (β- D- galactopyranosyl ring deformation); 762(C-S). ^{1}H NMR ($CDCl_3$): δ 7.94-7.12 (9H, m, Ar-H); δ5.65-4.18(7H, m, galactopyranosyl protons); δ 2.22-1.97 (12H, m, $COCH_3$).

(3e):5-o- tolylimino - 4- phenyl -3-tetra- O- acetyl- β - D- galactopyranosylimino-1,2,4-dithiazolidine (Hydrochloride)
IR (KBr, cm^{-1}):1751(C=O); 1535(C=N); 1374(C-N), 1225(C-O); 1074, 938(β- D- galactopyranosyl ring deformation); 758(C-S). ^{1}H NMR ($CDCl_3$): δ 7.74-7.02 (9H, m, Ar-H); δ5.55-4.08 (7H, m, galactopyranosyl protons); δ 2.38 (3H, m, Ar-CH_3); δ 2.12-1.97 (12H, m, $COCH_3$).

(3f):5-m-tolylimino - 4- phenyl -3-tetra- O- acetyl- β - D- galactopyranosylimino-1, 2,4-dithiazolidine (Hydrochloride)
IR (KBr, cm^{-1}): 1752(C=O); 1537(C=N); 1371(C-N), 1222(C-O); 1072, 934(β- D- galactopyranosyl ring deformation); 755(C-S). ^{1}H NMR ($CDCl_3$): δ 7.61-7.05 (9H, m, Ar-H); δ5.50-4.08 (7H, m, galactopyranosyl protons); δ 2.44 (3H, m, Ar-CH_3); δ 2.16-2.00 (12H, m, $COCH_3$).Mass (m/z): 701, 630, 331, 227, 169,109.

(3g):5-p-tolylimino - 4- phenyl -3-tetra- O- acetyl- β - D- galactopyranosylimino-1, 2,4-dithiazolidine (Hydrochloride)
IR (KBr, cm^{-1}): 1754(C=O); 1535(C=N); 1375(C-N), 1225(C-O); 1074, 935(β- D- galactopyranosyl ring deformation); 752(C-S).^{1}H NMR ($CDCl_3$) : δ 7.84-7.15 (9H, m, Ar-H); δ5.56-4.10(7H, m, galactopyranosyl protons); δ 2.42 (3H, m, Ar-CH_3); δ 2.14-1.98 (12H, m, $COCH_3$).

Table-1: Characterization data of the synthesized compounds (3a-g):

Product	m.p. (°C)	Yield (%)	$[\alpha]_D$ (c, $CHCl_3$)	R_f (n-hexane: EtOAc: EtOH) (3:1:1)	Analysis Found (Calcd.)	
					% N	% S
3 a	112	63	-44.22°(0.43)	0.82	6.19(6.11)	9.22(9.31)
3 b	114	74	-52.22° (0.52)	0.88	5.76(5.82)	8.80(8.87)
3 c	118	68	-47.88° (0.61)	0.85	5.89(5.82)	8.94(8.87)
3 d	121	66	-66.66° (0.61)	0.79	5.74(5.82)	8.79(8.87)
3 e	119	63	-60.26° (0.58)	0.91	6.06(5.99)	9.19(9.12)
3 f	124	56	-39.46° (0.54)	0.88	5.90(5.99)	9.02(9.12)
3 g	134	69	-58.62° (0.62)	0.91	6.05(5.99)	9.17(9.12)

Antimicrobial activity[17,18]

All the compounds 3a-3g has been screened for antimicrobial activity against various pathogenic bacteria and fungi by cup-plate agar diffusion method. Amikacin was used as a standard for antibacterial activity and fluconazole was used as standard for antifungal activity at a concentration of 25 µg/ml.
The solutions of compounds were prepared at the conc. of 50 µg/ml in DMSO. The compounds were incubated for 24 hrs. for antibacterial activity and 48 hr. for antifungal activity. The zone of inhibition was measured in mm using antibiotic zone reader. The observations were taken as an average of three

readings these are tabulated in Table-2. Bacteria like *P.aregenosa, S. aureus* and *P.Vulgaris* were used to study antibacterial activity and *C. albicans* and *A. Niger* were employed for antifungal activity respectively.

Table-2: Antimicrobial activities of Compounds 3a-3g.

Compound	Antibacterial Activity			Antifungal Activity	
	S. aureus	P. aregenosa	P. vulgaris	C. albicans	A. niger
3a	12	-	12	-	-
3b	10	-	-	09	10
3c	11	9	20	-	
3d	13	10	12	08	09
3e	15	9	15	08	08
3f	16	-	12	-	-
3g	13	-	12	10	10
Amikacin	20	20	20	-	-
Fluconazole	-	-	-	13	13

* Including well diameter of 5mm.

It was observed that Compounds 3a-3g show moderate activity against S. aureus and P. vulgaris while. Compounds 3c, 3d, 3e show low activity against P. aregenosa as compared to the standard.

Compounds 3b, 3d, 3g show good to moderate activity against the fungi C. albicans and A. Niger while others are inactive against the fungi.

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