

Synthesis and Antimicrobial Activity of some Guanidino Glycosides

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Abstract:- Sugar-3-amidinothiocarbamides have been synthesized by the interaction various sugar isothiocyanates and guanidine in ethanolic medium. The identities of these newly synthesized compounds have been established on the basis of usual chemical transformation and IR, ^1H NMR and Mass spectral studies. The synthesized compounds were assayed for their antimicrobial activity against gram negative micro-organisms.

Key words: Sugar isothiocyanates, guanidine, sugar amidinothiocarbamides.

I. Introduction

Glycosides are compounds containing a carbohydrate and non-carbohydrate residue in the same molecule. The carbohydrate residue is attached by an acetal linkage at the anomeric position to a non-carbohydrate unit or aglycone. Glycosyl amines, glycosyl guanidine derivatives, glycosyl thiocarbamides have several medicinal applications such as antitumor agent¹, antileukemic agent², antibacterial properties³, antimetastatic compounds⁴ and in many other ways⁵. S- and N-glycosylated derivatives and their utilities in medicinal chemistry have been extensively studied⁶⁻¹⁷.

In this communication several sugar-3-amidinothiocarbamides (IIIa-f) have been reported and were prepared by the interaction of sugar isothiocyanates (Ia-f) and guanidine (II).

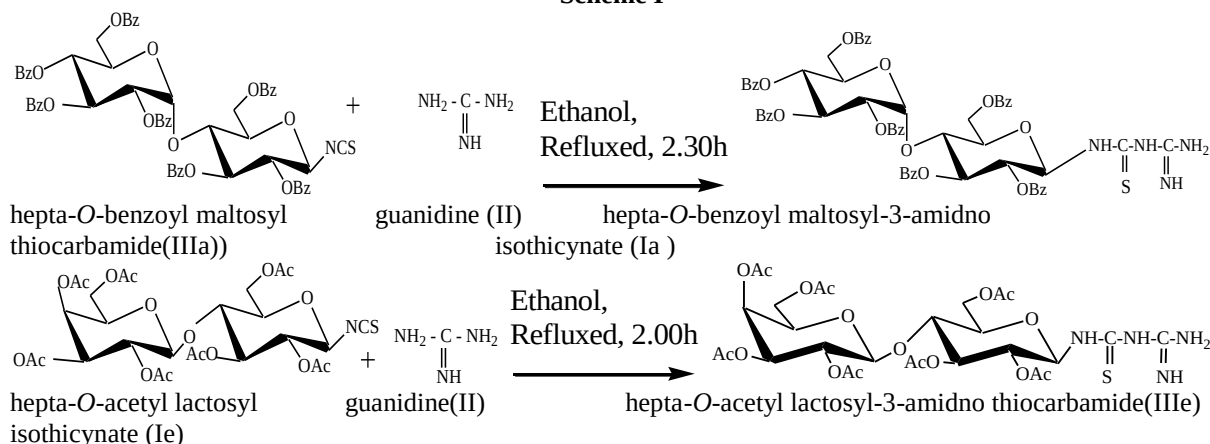
II. Results and Discussion

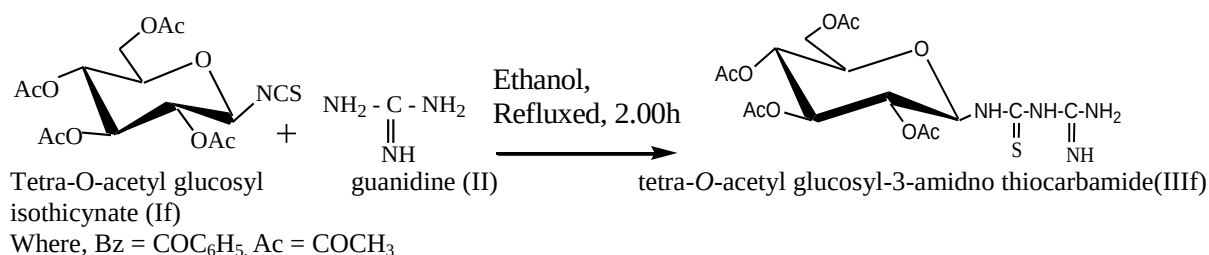
Hepta-O-benzoyl maltosyl isothiocyanate (0.001 M, 1.1 g in 20 ml) was mixed with guanidine in ethanolic medium (0.001 M, 0.12 g in 20 ml). This mixture was refluxed for 2.30 h. in water bath. After that it is kept for solvent evaporation which affords a sticky mass which is isolated by ethanol-water system. It was purified by ethanol-water (Yield- 1.07g). It gives charring test and was desulphurisable with alkaline plumbite solution. Its specific rotation¹⁸ was found $[\alpha]_{\text{D}}^{31} -184.30^\circ$ (c, 0.5 g in CHCl_3) having melting point 127°C .

The IR, ^1H NMR and Mass¹⁹⁻²² spectral analysis and elemental analysis (Table 1) indicate the product and design the structure as Hepta-O-benzoyl maltosyl-3-amidinothiocarbamide (IIIa).

Similarly, when the hepta-O-benzoyl lactosyl isothiocyanate (Ib), tetra-O-benzoyl glucosyl isothiocyanate (Ic), hepta-O-acetyl maltosyl isothiocyanate (Id), hepta-O-acetyl lactosyl isothiocyanate (Ie) and tetra-O-acetyl glucosyl isothiocyanate (If) interacts with guanidine (II) the related Sugar-3-amidino thiocarbamides (IIIb-f) were obtained.

Scheme I





III. 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 spectral analysis. IR spectra were recorded in KBr on a FTIR Perkin-Elmer (4000-450 cm⁻¹) spectrophotometer. ¹H NMR spectra are run on Bruker DRX-300 instrument operating at 300 MHz using CDCl₃ solution with TMS at internal standard and Mass spectra on JEOL-AccuTof JMS-T100LC Mass spectrometer. Specific rotations were measured on Equip-Tronics EQ-800 Digital Polarimeter. Thin layer chromatography (TLC) was performed on silica gel G for TLC (Merck) and spot were visualized by iodine vapour.

IIIa:- IR(KBr cm⁻¹): 3510 (N-H), 3062 (Aromatic C-H), 2920 (Aliphatic C-H), 1730 (C=O), 1452 (C=N), 1068 (C=S), 1269 (C-O), 1177 and 1026 (Characteristics of maltose), 709.80 (Monosubstituted benzene);

¹H NMR (CDCl₃, ppm): δ 5.912-5.399 (5H, s, 5N-H), 8.054-7.260 (39H, m, Aromatic proton), 4.871-3.894 (14H, m, maltosyl proton)

IIIc:- IR(KBr cm⁻¹): 3298 (N-H str.), 2980, 2941 (Aliphatic C-H str.), 1745 (C=O str.), 1514 (C=N str.), 1059 (C=S str.), 1371 (C-O str.), 1223 and 952 (Characteristics of lactose);

¹H NMR (CDCl₃, ppm): δ 2.013-1.374 (5H, s, 5 aliphatic N-H), (39H, m, Aromatic proton), 5.648-3.9 (14H, m, lactosyl proton).

IIIIf:- IR(KBr cm⁻¹): 3317 (N-H str.), 2964 (Aliphatic C-H str.), 1745 (C=O str.), 1519 (C=N str.), 1037 (C=S str.), 1371 (C-O str.), 1136 and 947 (Characteristics of glucose);

¹H NMR (CDCl₃, ppm): δ 1.574 (2H, s, 2 aliphatic N-H), 1.574 (2H, s, aliphatic NH₂), 2.184-2.020 (12H, m, aliphatic) 5.588-3.861 (7H, m, glucosyl ring), 6.34-6.329 (1H, s, aliphatic N-H); **Mass (m/z):** 458 (M⁺-1), 398 (M⁺-CH₃N₃,H₂O), 169 (M⁺-CH₃N₃,H₂O,CHNS,2AcOH,CH₂CO), 109 (M⁺-CH₃N₃,H₂O,CHNS,2AcOH,CH₂CO,H₂O).

IV. Antibacterial activity

Amikasin (100 µg/ml) was used as standard for antibacterial activity. The compounds were screen for antibacterial activity against *Escherichia coli*, *Staphylococcus aureus*, *Proteus vulgaris* and *Pseudomonas aeruginosa* in nutrient agar medium. Amikasin (100 µg/ml) was used as standard for antibacterial activity. The results are presented in Table 2.

It has been observed that some of these compounds exhibited interesting microbial activities. IIIa, IIIc, IIId and IIIe exhibited most significant activity against *S. aureus*. All the other compounds exhibited low to moderate activity. (Table2).

Antifungal activity:-

The compounds were screen for antifungal activity against *Aspergillus niger* and *Candida albicans* in potato dextrose agar medium fluconazole (100 µg/ml) as standard for antifungal activity.

The results of antifungal activities are also tabulated in Table2. IIIa, IIId and IIIf are effective towards *Candida albicans*. IIId, IIIc, IIIe and IIIf inhibited *Aspergillus niger*. While other compounds inhibited moderate to low activity.

Table 1:- Sugar-3-amidinothiobamides (IIIa-f) (Scheme 1). Reactants - i) Sugar isothiocyanates (Ia-f). ii) guanidine (II).

Sr. No.	Product	m.p. (°C)	Yield (%)	Analysis(%) found(required)		Rf Value	[α] _D ³¹ (c, in CHCl ₃)
				N	S		
1.	IIIa	127	93	4.48 (4.85)	2.76 (2.77)	0.60	-184.30° (0.5 in CHCl ₃)
2.	IIIb	123	89	4.57 (4.85)	2.75 (2.77)	0.59	-109.37 (0.5 in CHCl ₃)

3.	IIIc	110	60	8.0 (8.04)	4.47 (4.59)	0.54	-136.36° (0.5 in CHCl ₃)
4.	IIId	130	81	7.56 (7.77)	4.38 (4.44)	0.79	-92.30° (0.5 in CHCl ₃)
5.	IIIe	143	84	7.66 (7.77)	4.40 (4.44)	0.62	-78.12° (0.5 in CHCl ₃)
6.	IIIf	118	73	10.87 (10.95)	6.18 (6.26)	0.59	-169.23° (0.5 in CHCl ₃)

C and H analysis were found satisfactory in all cases.

Table2: Antimicrobial activities of novel thiocarbamides

Compounds	Antibacterial**				Antifungal**	
	<i>E. coli</i>	<i>S. aureus</i>	<i>P. vulgaris</i>	<i>Ps. aeruginosa</i>	<i>C. albicans</i>	<i>A. niger</i>
IIIa	13	13	13	17	18	14
IIIb	14	16	12	14	15	16
IIIc	17	14	12	14	15	16
IIId	12	16	20	13	17	14
IIIe	18	17	12	15	15	16
IIIf	13	15	15	18	16	18
Amikacin	19	23	22	24	-	-
Fluconazole	-	-	-	-	25	26

**zone of inhibition in mm (15 or less) resistance, (16-20mm) moderate and (more than 20mm) sensitive. *Escherichia coli* (*E. coli*), *Staphylococcus aureus* (*S. aureus*), *Proteus vulgaris* (*P. vulgaris*), *Pseudomonas aeruginosa* (*Ps. aeruginosa*), *Candida albicans* (*C. albicans*) and *Aspergillus niger* (*A. niger*).

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