ANTIMICROBIAL ACTIVITIES OF SOME N-GALACTOPYRANOSYL THIOCARBAMATES

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Abstract:
N – tetra – O – acetyl - β- D – galactosyl – O – alkyl thiocarbamates have been prepared by the interaction of tetra-O-acetyl-β -D-galactosyl isothiocyanate with various alcohols respectively. The identities of these new N-galactosides have been established on basis of usual chemical transformation and IR, ^{1}HNMR and Mass spectral analysis. The synthesized compounds were screened for their antimicrobial properties against various pathogenic bacteria such as E. coli, S. aureus, P. vulgaris and P. aregenosa and fungi like C. albicans, A. niger by cup plate agar diffusion method.

Key words: N- Galactosides, isothiocyanate, alcohols, thiocarbamates, antimicrobial activites.

Introduction

Sugar thioureas containing an N-azolyl substitutent, such as thiazole, thiazoline or benzoxazole rings, have been the subject of attention in connection with the interest in azole nucleoside analogs as antineoplastic[1] and antiviral[2] compounds. During past few years, N-glucosylated[3] benzothiazolyl thiocarbamides having potential antimicrobial activity and N-lactosylated[4] benzothiazolyl thiocarbamides have been reported.

Also, the addition of alcohols to carbohydrate isothiocyanates is a general method for the preparation of linear N-sugar, O-alkyl thiocarbamates. This reaction is frequently used as a tool for structure determination. During past few years, N-glucosylated having potential antimicrobial activity and N- lactosylated & N-Galactosylated[5] Compounds have been reported.

The literature survey revealed that N-galactosylated thiocarbamates were not been prepared earlier, so due to applications of the different compounds mentioned above, it was of sufficient interest to synthesize new N-galactosylated thiocarbamates. And we have reported for the first time synthesis of N-Galactopyranosyl thiocarbamates in the year 2008. The antimicrobial activites of the synthesized thiocarbamates have been reported in the present paper.

Materials and Method:

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. ^{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. The mass spectra were recorded on Joel SX-102 mass spectrometer. Alcohols used were of commercial grade and were purified by conventional methods.

Preparation of Tetra-O-Acetyl- β -D-galactosyl isothiocyanate:

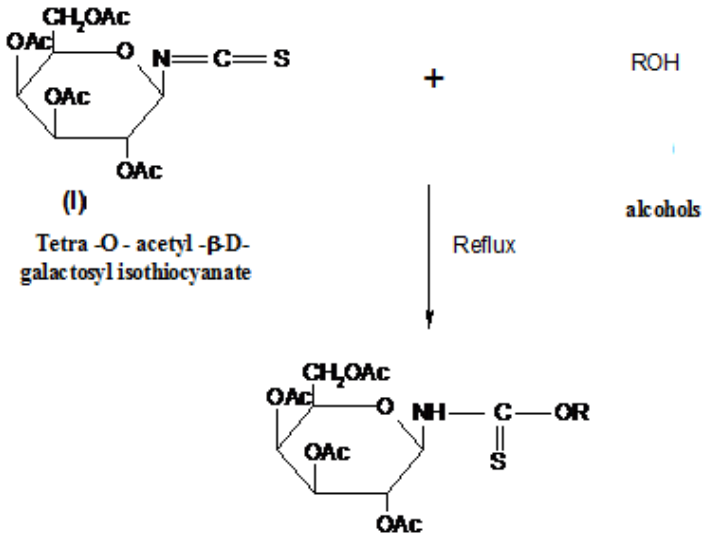
Tetra-O-Acetyl- β -D-galactosyl isothiocyanate [6] was prepared from Tetra –O – acetyl – α - D- galactosyl bromide according to procedure described earlier.

Preparation of N- tetra-O-acetyl - β -D-galactosyl-O-alkyl thiocarbamates:

For a typical reaction Tetra-O-acetyl- β -D-galactosyl isothiocyanate was refluxed with absolute ethanol for 3hr. On cooling and mixing with ice cold water, a white granular solid was obtained. It was crystallized from ethanol-water, m. p. 136^{0}C. This reaction of tetra-O-acetyl- β -D- galactosyl isothiocyanate was extended to four more alcohols and corresponding N-tetra-O-

acetyl- β -D- galactosyl-O-alkyl thiocarbamates have been isolated (Table-1).

The reaction can be represented as follows:



N - tetra - O - acetyl - β – D – galactosyl – O - alkyl thiocarbamates.
Where, R = a) ethyl, b) isopropyl, c) n-propyl, d) isoamyl, e) n-butyl.
Ac = - $COCH_3$.

Table -1: N- tetra - O – acetyl - β – D - galactosyl – O - alkyl thiocarbamates:

Sr. No.	Alcohols	N-tetra-O-acetyl- β -D-galactosyl -O-alkyl thiocarbamates	Yield (%)	m. p. (^{0}C)
1	Ethyl	N-tetra-O-acetyl- β -D-galactosyl -O-ethyl thiocarbamate	68.18	136
2	Isopropyl	N-tetra-O-acetyl- β -D-galactosyl -O-isopropyl thiocarbamate	52.17	128
3	n-propyl	N-tetra-O-acetyl- β -D-galactosyl -O-n-propyl thiocarbamate	65.21	158
4	Isoamyl	N-tetra-O-acetyl- β -D-galactosyl -O-isoamyl thiocarbamate	61.22	114-115
5	n-butyl	N-tetra-O-acetyl- β -D-galactosyl -O-n-butyl thiocarbamate	46.20	210(d)

Antimicrobial Activity[7, 8] :
All the newly synthesized compounds were screened for their antimicrobial activity against various pathogenic bacteria such as *E. Coli, S. aureus, P. vulgaris and P. aregenosa* and fungi like *C. albicans, A. niger* by cup plate agar diffusion method at a concentration of 100ug/ml in DMSO against the standards Amikacin (100µg/ml) for antibacterial activity and

fluconazole for antifungal activity at the same concentration.

The zone of inhibition was measured in mm and is reported as an average of three readings. The results are tabulated in the Table -2 given below:

Table -2: Antimicrobial activity of products :

Sr. No	Product	Antibacterial activity				Antifungal Activity	
		S. aureus	*E. coli*	*P. aregenosa*	*P. Vulgaris*	*A. niger*	*C. albicans*
1	N-tetra-O-acetyl- β -D-galactosyl -O-ethyl thiocarbamate	7	07	-	18	07	09
2	N-tetra-O-acetyl- β -D-galactosyl -O- isopropyl thiocarbamate	-	14	-	9	10	12
3	N-tetra-O-acetyl- β -D-galactosyl -O-n-propyl thiocarbamate	-	-	-	21	09	09
4	N-tetra-O-acetyl- β -D-galactosyl -O-isoamyl thiocarbamate	9	-	-	17	09	08
5	N-tetra-O-acetyl- β -D-galactosyl -O-n-butyl thiocarbamate	9	07	-	13	07	09
6	Amikacin	23	23	19	24	-	-
7	Fluconazole	-	-	-	-	15	15

- Including Well diameter of 5 mm.

From the above table it is clear that, newly synthesized compounds show low to moderate activity against *S. aureus, E. coli, P. Vulgaris, A. niger and C. albicans*. While all compounds were inactive against *P. aregenosa.*

Conclusion:

Thus it is evident from the above discussion that the synthesized thiocarbamates play an important role in the field of carbohydrate chemistry and play an active role in biological activities.

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