



Synthesis and Antimicrobial Studies of Some Bis-Glycosyl Isodithiobiurets

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Received 22 October 2009; Accepted 15 December 2009

Abstract: Certain 2-*S*-tetra-*O*-benzoyl-*D*-glucopyranosyl-1-aryl-5-tetra-*O*-acetyl- β -*D*-galactopyranosyl-2, 4- isodithiobiurets have been synthesized by the interaction of tetra-*O*-acetyl- β -*D*-galactopyranosyl isothiocyanate and various *S*- tetra-*O*-benzoyl-*D*- glucopyranosyl-1-aryl isothiocarbamides. The newly synthesized compounds were screened for their antimicrobial activities.

Keywords: Synthesis, Antimicrobial studies, Bis-glycosyl isodithiobiurets

Introduction

Aryl/alkyl isothiocarbamides, due to their basic nature are found to interact with isothiocyanate to form corresponding isodithiobiurets. Several non-glycosidic isodithiobiurets are known for their anticonvulsant and hypnotic activities¹, several *S*-glucosides have been described in the literature to possess antimicrobial activities². Glycopyranosyl isothiocyanates are attractive synthons in organic chemistry due to their availability and their tendency to undergo nucleophilic additions and cycloadditions. Several *N*-glycosides have been found several applications in industries as carbohydrate based detergents³ and in medicine as antitumour⁴ and antitubercular⁵ activities.

In view of applications of all the compounds described above and our interest in the synthesis of bis glycosyl isodithiobiurets, we report the synthesis of 2-*S*-tetra-*O*-benzoyl-*D*-glucopyranosyl-1-aryl-5- tetra-*O*-acetyl- β -*D*-galactopyranosyl-2, 4-isodithiobiurets by the interaction of tetra- *O*- acetyl- β -*D*- galactopyranosyl isothiocyanate and various *S*- tetra-*O*-benzoyl -*D*- glucopyranosyl - 1-aryl isothiocarbamides.

Experimental

Melting points are uncorrected. Optical rotations $[\alpha]_D$ were measured on a Equip-Tronics digital polarimeter model no. EQ 800 in CHCl_3 at 39 °C. IR spectra were recorded on a Perkin-Elmer spectrum RXI (4000-450 cm^{-1}) FTIR spectrometer. ¹HNMR were obtained on

a Bruker DRX-300 (300 MHz FT NMR) NMR spectrometer for a sample in CDCl₃ solution with TMS as an internal reference. The mass spectra were recorded on a Joel - SX 102 FAB Mass spectrometer.

Tetra-O-acetyl-β-D-galactopyranosyl isothiocyanate (1)

Tetra-O-acetyl-β-galactopyranosyl isothiocyanate (**2**) was prepared from tetra-O-acetyl-α-galactopyranosyl bromide using lead thiocyanate in xylene medium¹⁰.

S-tetra-O-benzoyl-D-glucopyranosyl 1-aryl isothiocarbamides (2a-g)

S-Tetra-O-benzoyl-D-glucopyranosyl 1-aryl isothiocarbamides have been prepared by the methods described earlier which involves interaction of tetra-O-benzoyl-D-glucopyranosyl bromide with various aryl isothiocarbamides¹¹.

2-S-tetra-O-benzoyl-D-glucopyranosyl-5-tetra-O-acetyl-β-D-galactopyranosyl-1-aryl-2,4-isodithiobiurets (3a-g)

2-S-tetra-O-benzoyl-D-glucopyranosyl-5-tetra-O-acetyl-β-D-galactopyranosyl-1-aryl 2,4-isodithiobiurets (**3a-g**) were prepared by the condensation of S-tetra-O-benzoyl-D-glucopyranosyl 1-aryl isothiocarbamides (**2a-g**, 0.005 M) and tetra-O-acetyl-β-D-galactopyranosyl isothiocyanate (**1**, 0.005 M) in benzene for 4 h. After the reaction was completed the solvent was distilled off and the sticky residue was triturated with petroleum ether to give the solids. The characterization data of the synthesized products is given in the Table 1.

Table 1. Characterization data of the synthesized products (**3a-g**).

Reagent: Tetra-O-acetyl-β-D-galactopyranosyl isothiocyanate; S-tetra-O-benzoyl-D-glucopyranosyl-1-aryl-isothiocarbamides (**2a-g**).

S. No.	Product	% Yield	m. p. °C	[α] _D ³⁹ (CHCl ₃)	Analysis		R _f (CCl ₄ : EtOAc)
					Found %	Required %	
1	3a	55	115	75.25° (c, 0.94)	N, 3.62 S, 5.85	N, 3.62 S, 5.85	0.77 (3:2)
2	3b	57	132	48.86° (c, 1.00)	N, 3.58 S, 5.61	N, 3.64 S, 5.54	0.79 (3:2)
3	3c	64	142	39.71° (c, 1.03)	N, 3.60 S, 5.49	N, 3.64 S, 5.54	0.81 (3:2)
4	3d	55	135	39.73° (c, 1.00)	N, 3.77 S, 5.48	N, 3.64 S, 5.54	0.83 (3:2)
5	3e	56	152	91.22° (c, 0.98)	N, 3.77 S, 5.55	N, 3.70 S, 5.64	0.66 (3:2)
6	3f	59	129	69.54° (c, 1.00)	N, 3.63 S, 5.71	N, 3.70 S, 5.64	0.79 (3:2)
7	3g	65	166	49.01° (c, 1.02)	N, 3.63 S, 5.56	N, 3.70 S, 5.64	0.75 (3:2)

Satisfactory C and H analysis are found in all cases.

3a: IR (KBr):- ν 3468 (N-H); 2974 (Ar-H); 1730 (C=O); 1602 (C=N) 1373 (C-N); 1271 (C-O); 1095 (C=S). ¹HNMR (CDCl₃):- δ 8.65-7.26 (m, N-H and Ar-H); 5.44 – 3.97 (m, glucopyranosyl + galactopyranosyl protons); 2.17-1.08 (m, 4COCH₃). Mass (FAB):- 331, 169, 105.

3c: IR (KBr):- ν 3419 (N-H); 2973 (Ar-H); 1729 (C=O); 1602 (C = N) 1373 (C-N); 1270 (C-O); 1096 (C=S). $^1\text{H NMR}$ (CDCl_3): δ 8.3-7.25 (m, N-H and Ar-H); 5.77 – 3.95 (m, glucopyranosyl + galactopyranosyl protons); 2.22-1.06 (m, 4COCH₃). Mass (FAB):- 331, 169, 105.

3f: IR (KBr):- ν 3451 (N-H); 2972 (Ar-H); 1730 (C=O); 1602 (C = N) 1372 (C-N); 1271 (C-O); 1094 (C=S). $^1\text{H NMR}$ (CDCl_3): δ 8.65-7.26 (m, N-H and Ar-H); 5.44 – 3.97 (m, glucopyranosyl + galactopyranosyl protons); 2.17-1.08 (m, 4COCH₃). Mass (FAB):- 331, 169, 105.

Antimicrobial activity

All the compounds were screened for their antibacterial activity against pathogenic bacteria such as *E. coli*, *S. aureus*, *P. vulgaris* and *P. aregenosa* by cup plate agar diffusion method^{12,13}, at a concentration 100 $\mu\text{g/mL}$ in DMSO by using the standard Amikacin at the same concentration. All compounds were also screened for their antifungal activity against *A. niger* and *C. albicans* by cup plate method at a concentration of 100 $\mu\text{g/mL}$ in DMSO by using the standard Fluconazole at the same concentration. The zone of inhibition was measured in mm and is average of three readings. The readings are shown in Table 2.

Table 2. Antimicrobial activities of compounds (**3a-g**).

Compounds	Antibacterial activity				Antifungal activity	
	<i>E. coli</i>	<i>S. aureus</i>	<i>P. Vulgaris</i>	<i>P. aregenosa</i>	<i>C. albicans</i>	<i>A. niger</i>
3a	17	-	15	-	09	14
3b	-	11	13	-	08	15
3c	21	19	-	21	-	14
3d	-	11	13	-	-	-
3e	14	17	18	19	11	14
3f	-	11	-	15	-	19
3g	09	09	-	08	-	-
Amikacin	25	23	23	25	-	-
Fluconazole	-	-	-	-	15	21

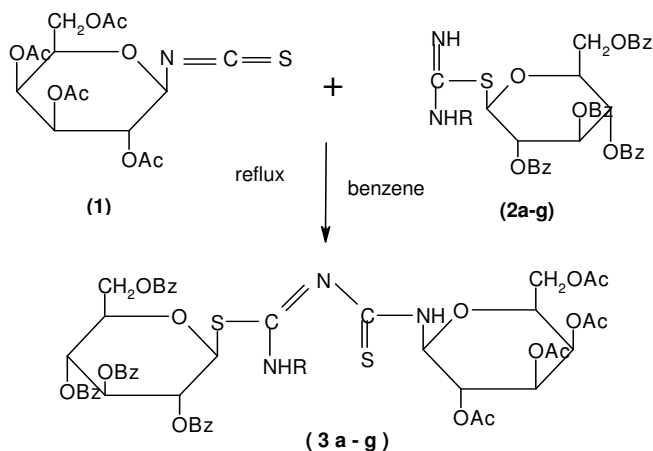
Including well diameter of 5 mm.

From the above observations, it is clear that compounds **3c** and **3e** are active against *E.coli*, *S. aureus* and *P. aregenosa* as compared to standard, while **3b**, **3d**, **3f** and **3g** show low or moderate activity against the bacteria.

In antifungal activity, compounds **3a**, **3b** and **3e** show good activity against *C. albicans* while other are inactive and compounds **3a**, **3b**, **3c**, **3e** and **3f** show good activity, while others show low activity against *A. niger*.

Results and Discussion

Several 2-*S*-tetra-*O*-benzoyl-*D*-glucopyranosyl 1-aryl-5-tetra-*O*-acetyl- β -*D*-galactopyranosyl-2, 4- isodithiobiurets (**3a-g**) have been synthesized by the interaction of tetra-*O*-acetyl- β -*D*-galactopyranosyl isothiocyanate (**1**) and various *S*-tetra-*O*-benzoyl-*D*-glucopyranosyl-1-aryl isothiocarbamides (**2a-g**). All the products were recrystallised from ethanol. The structures of all the synthesized products were developed on the basis of usual chemical transformation and IR, NMR and Mass Spectral analysis⁶⁻⁹. The newly synthesized compounds were screened for their antibacterial and antifungal activities.



Scheme 1

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, Bz = COC₆H₅, Ac = COCH₃.

Acknowledgment

Authors are thankful to RSIC, CDRI Lucknow for providing the spectra and also to Dr. S. G. Bhadange, Principal, Shri Shivaji College, Akola for providing necessary facilities.

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