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Synthesis of 5-Glucosyl-2,4-Isodithiobiurets and Their Antimicrobial Study

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1-Aryl/(H)-5-tetra-O-benzoyl β-D-glucopyranosyl-2-S-benzyl 2,4-isodithio-biurets (3) have been prepared by the interaction of 1-aryl/H-2-S-benzyl-isothiocarbamides (1) with tetra-O-benzyol-β-D-glucopyranosyl isothiocyanate (2). Antibacterial and antifungal activities of these compounds were carried out on *E. coli, S. aureus, P. vulgaris, Pseudomonas, Bacillus, Salmonella, A. niger* and *Fusarium*. These compounds show sufficient activity towards these micro-organisms.

Key words: Synthesis, 5-glucosyl-2,4-isodithiobiurets, antimicrobial study

INTRODUCTION

Recently, we have reported several N-glucosyl thiocarbamides[1] and N-glucopyranosyl benzothiazolyl thiocarbamides[2]. In the present communication the synthesis of a few 1-aryl/(H)-5-tetra-O-benzoyl-β-D-glucopyranosyl-2-S-benzyl-2,4-isodithiobiurets **(3)** have been reported, having antibaterial and antifungal activities. The identities of these new 5-glucosyl-2,4-isodithiobiurets have been established on the basis of usual chemical transformations IR, NMR and mass spectral studies.

RESULTS AND DISCUSSION

The reaction of 1-*m*-Cl-phenyl-2-S-benzyl isothiocarbamide **(1d)** and tetra-O-benzoyl-(β-D-glucopyranosyl isothiocyanate **(2)** in boiling dry benzene afforded a clear solution. On removing benzene a syrupy mass was left which on repeated trituration with petroleum ether (b.p. 60–80°C) followed by treatment with ethanol gave white granular solid **(3d)**. On crystallisation with ethanol pure **(3d)** was obtained (m.p. 175°C). The specific rotation was found to be $\alpha_D^{28} = +79.54°C$ (C, 0.880 in $CHCl_3$).

Its IR spectrum clearly indicated the presence of ν(NH) (3327cm^{-1}), ν(C=C) (1726 cm^{-1}), ν(C=N) (1573 cm^{-1}), ν(C=S) (1093 cm^{-1}) and band at 854 cm^{-1} due to β-D-glucopyranosyl ring deformation[3–5.] Its NMR spectrum displayed signals due to NH (δ 8.2 ppm), aromatic protons at (δ 7.2–7.3 ppm) and signals in the form of multiplets characteristic of the pyranosyl ring proton[7] were also located at (δ 4.3–5.7 ppm). In its mass spectrum the molecular ion peak at m/z 914 was located along with other fragment peaks. Probable fragmentation patterns along with their masses (m/z) are shown in Scheme-1. On the basis of all the above facts, the product with m.p. 175°C was assigned the structure 1-*m*-Cl-phenyl-5-tetra-O-benzoyl-β-D-glucopyranosyl-2-S-benzyl-2,4-isodithio biurets **(3d)**.

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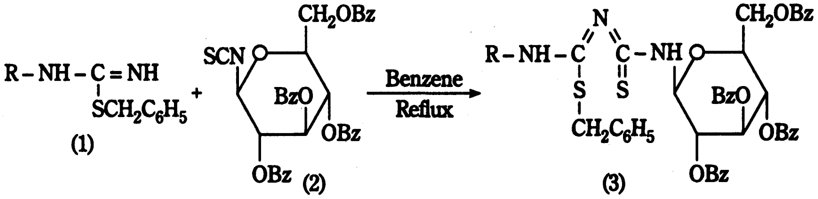
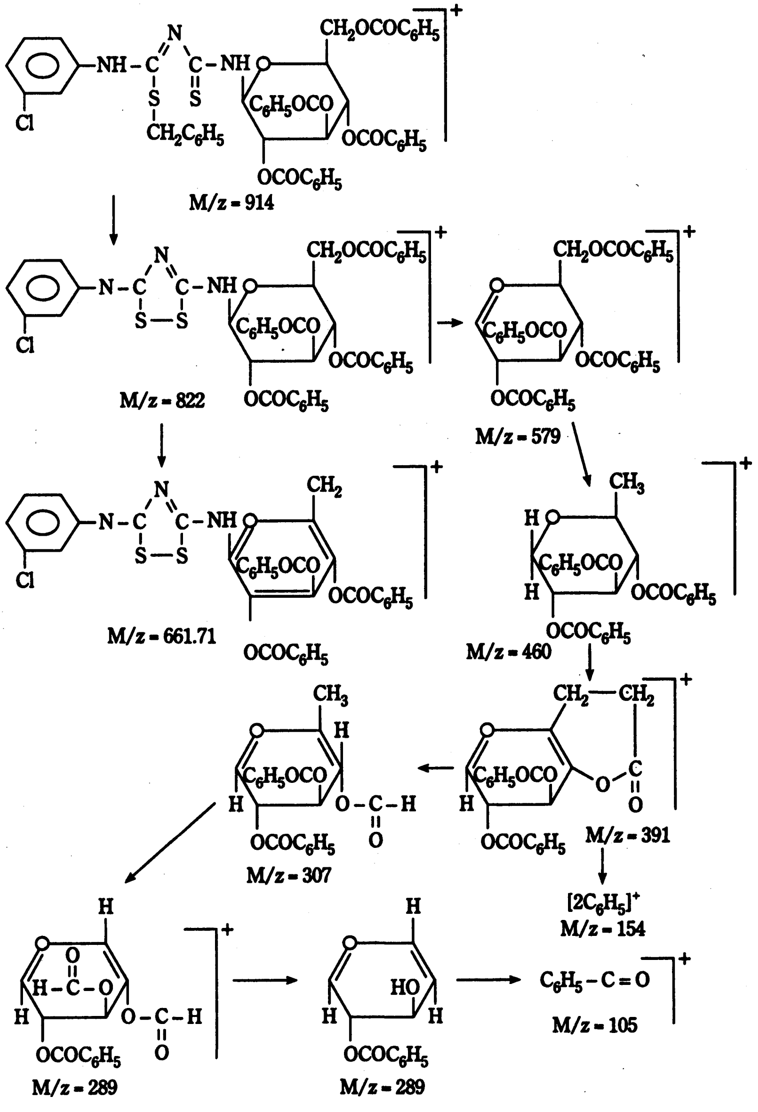


where R = (a) phenyl, (b) 4-methyl, (c) 4-Cl, (d) 5-Cl, (e) 6-Cl, (f) H (Bz = —COC_6H_5).

SCHEME-1

Probable fragmentation pattern of 1-*m*-Cl-phenyl-5-tetra-O-benzoyl-β-D-glucopyranosyl-2-S-benzyl-2,4- isodithiobiurets (**3d**)



The reaction of tetra-O-benzoyl-β-D-glucopyranosyl isothiocyanate was also extended to several other S-benzyl-isothiocarbamides and the corresponding products **(3a–f)** were isolated (Table–1).

TABLE-1
1-ARYL/(H)-5-TETRA-O-BENZOYL-β-D-GLUCOPYRANOSYL-2-S-BENZYL-2,4-ISODITHIOBIURETS **(3)**

Reactant: Tetra-O-benzoyl-β-D-glucopyranosyl isothiocyanate used (0.01 M, 6.3 g) **(2)**

1-aryl/(H)-2-S-benzyl isothiocarbamide	1-Aryl/(H)-5-tetra-O-benzoyl-β-D-glucopranosyl-2-S-benzyl-2,4-isodithiobiurets	Yield(%)	m.p. (°C)	α_D^{28} in chloroform	Analysis (%) found	reqd.
1-Phenyl-2-S .... **(1a)** 2.4 g	1-Phenyl .... **(3a)**	93.52	95	–118.57	N, 4.69 S, 7.21	4.77 7.28
1-*o*-Tolyl-2-S .... **(1b)** 2.5 g	1-*o*-Tolyl .... **(3b)**	64.23	139	–45.04	N, 4.63 S, 7.09	4.70 7.16
1-*o*-Cl-Phenyl-2-S ...... **(1c)** 2.7 g	1-*o*-Cl-Tolyl .... **(3c)**	67.26	128	+94.53	N, 4.53 S, 6.93	4.59 7.00
1-*m*-Cl-Phenyl-2-S ..... **(1d)** 2.7 g	1-*m*-Cl-Phenyl ...... **(3d)**	69.81	175	+79.54	N, 4.50 S, 6.91	4.59 7.00
1-*p*-Cl-Phenyl-2-S ...... **(1e)** 2.7 g	1-*p*-Cl-Phenyl .... **(3e)**	87.83	189	–60.67	N, 4.54 S, 6.96	4.59 7.00
1-H-2-S .... **(1f)** 1.6 g	1-Hydrogen .... **(3f)**	55.43	124	–58.15	N, 5.19 S, 7.85	5.23 7.97

Satisfactory C and H analysis found in all cases.

Antibacterial Activity: The compounds were screened for their antibacterial activity against various pathogenic bacteria, such as *S. aureus. E. coli, P. vulgaris, Pseudomonas, Bacillus* and *Salmonella* by cup-plate method[8] at a concentration 100 μg mL^{-1} in DMF by using the standard Co-trimazine (25 μg mL^{-1}) for bacteria. Amongst the compounds tested for the antibacterial activity, the antibacterial activity of compound **3a, 3b, 3c** and **3d** were found higher and other compounds showed moderate activity.

Antifungal Activity: All the compounds were also screened for their antifungal activities by cup-plate method at concentration 100 μg mL^{-1} in DMF by using the standard Griseofulvin (10 μg m^{-1}), against *Aspergillus niger* and *Fusarium*. Compounds **3d** and **3f** showed higher activity against the fungi, while the other compounds remained resistant against the fungi.

EXPERIMENTAL

The required 1-aryl-2-S-benzyl isothiocarbamides were prepared by the method described earlier[9].

(a) *Tetra-O-benzoyl-β-D-glucopyranosyl isothiocyanate:* The required tetra-

O-benzoyl-β-D-glucopyranosyl bromide was prepared by the already known method[10].

A solution of 1-tetra-O-benzoyl-β-D-glucopyranosyl bromide (5 g) in sodium dried xylene (30 mL) was treated with lead thiocyanate (4 g). The mixture was refluxed gently for 3 h. The solution was allowed to cool and was filtered from lead salt and then treated with 70 mL petroleum ether (60–80°C) with stirring. Tetra-O-benzoyl-β-D-glucopyranosyl isothiocyanate was precipitated. (yield 3.2 g). The crude isothocyanate was crystallised from ethanol water (m.p. 125°C). (Found: C, 64.96; H, 4.09; N, 2.12; S, 4.98%. $C_{35}H_{27}NO_9S$ requires C, 65.86; H, 4.23 ; N, 2.19; S, 5.015%).

(b) *1-m-Cl-phenyl-5-tetra-O-benzoyl-β-D-glucopyranosyl-2-S-benzyl-2,4-iso-dithiobiuret* **(3d)**: The benzene solution of tetra-O-benzoyl-β-D-glucopyranosyl isothiocyanate (0.001 m, 6.3g in 40 mL) was mixed with a suspension of 1-*m*-Cl-phenyl-2-S-benzyl isothiocarbamide **(1d)** (0.01 m, 2.7 g in 20 mL) and the reaction mixture was refluxed over a water bath for 6 h. Benzene was then removed by distillation and the resultant syrupy mass triturated several times with petroleum ether followed by ethanol to yield a white solid **(3d)** which was crystallized from ethanol to yield pure **(3d)** (m.p. 175°C). [Found: N, 4.50; S, 6.91%. $C_{49}H_{40}N_3O_9S_2Cl$ requires N, 4.9; S, 7.00 %]

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