

## Synthesis of 2-S-Tetra-O-Benzoyl-D-Glucopyranosyl-1-Aryl-5-Phenyl-2-Isothiobiurets and Their Antibacterial and Antifungal Studies

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Certain 2-S-tetra-O-benzoyl-D-glucopyranosyl-1-aryl-5-phenyl-2-isothiobiurets have been prepared by the interaction of S-tetra-O-benzoyl-D-glucopyranosyl aryl isothiocarbamides and phenyl isocyanate. The identities of these new compounds have been established on the basis of usual chemical transformations and IR, NMR and mass spectral studies. The compounds were screened for their antibacterial and antifungal activity against various pathogenic bacteria and fungi such as *S. aureus*, *P. vulgaris*, *Pseudomonas*, *Bacillus*, *E. coli*, *Salmonella*, *Fusarium* and *A. niger*. These compounds showed good to moderate activity against above micro-organisms. The polarimetric studies of these compounds has also been carried out.

**Key Words:** Synthesis, 2-S-tetra-O-benzoyl-D-glucopyranosyl-1-aryl-5-phenyl-2-isothiobiurets, Antibacterial, Antifungal.

### INTRODUCTION

In our laboratory we have prepared several S-tetra-O-benzoyl-D-glucopyranosyl aryl isothiocarbamides<sup>1</sup> by the interaction of tetra-O-benzoyl-D-glucopyranosyl bromide and aryl thiocarbamides. The aryl isothiocarbamides, because of their basic nature, are known to react with alkyl/aryl isocyanates and produce corresponding 2-isothiobiurets<sup>2,3</sup>. It was interesting to study the chemistry of these glucosyl aryl isothiocarbamides with special reference to their reactions with phenyl isocyanate.

### RESULTS AND DISCUSSION

In the present work, seven 2-S-tetra-O-benzoyl-D-glucopyranosyl-1-aryl-5-phenyl-2-isothiobiurets have been reported. These were prepared by the interaction of S-tetra-O-benzoyl-D-glucopyranosyl aryl isothiocarbamides (I) and phenyl isocyanate.

The benzene solution of S-tetra-O-benzoyl-D-glucopyranosyl-*o*-tolyl isothiocarbamide was mixed with phenyl isocyanate and the mixture was shaken (the reaction was exothermic). The clear solution formed was kept at room temperature for 24 h. The excess of benzene was distilled off and a sticky mass was obtained which on trituration several times with petroleum ether afforded a

white solid which was crystallized from ethanol, m.p. 162°C (d). The elemental analysis of this new product indicated the molecular formula  $C_{49}H_{41}N_3O_{10}S$ .

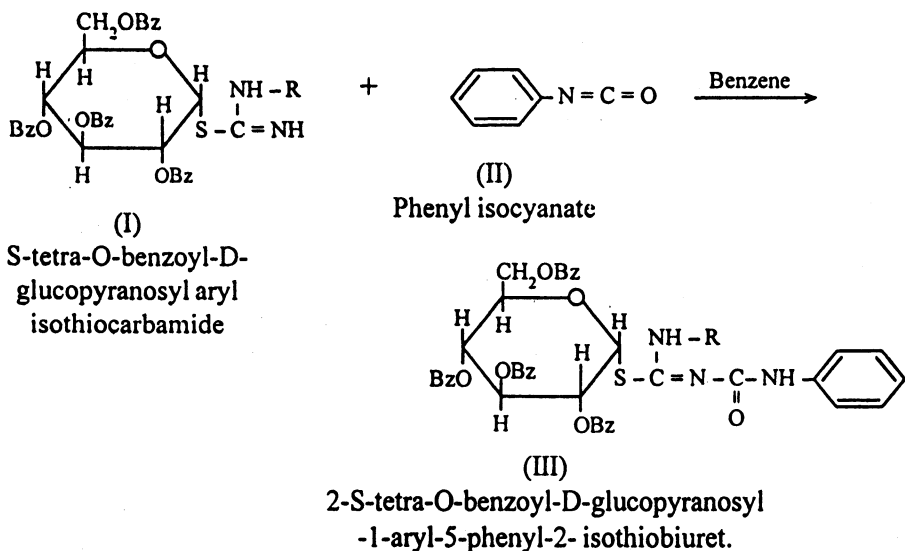
The product was soluble in acetone, benzene, chloroform, carbon tetrachloride and acetic acid while insoluble in water and petroleum ether. It becomes charred when boiled with conc. sulphuric acid. It is optically active and its specific rotation  $[\alpha]_D^{29}$  was found to be  $-181^\circ$  ( $c = 0.220$ , chloroform). It is non-desulphurisable when boiled with alkaline plumbite solution. On thermal decomposition in dry test tube, the odour of phenyl isocyanate was quite perceptible.

The IR spectrum clearly indicates the presence of bands due to  $\nu(N-H)$  ( $3328\text{ cm}^{-1}$ )<sup>4-8</sup>,  $\nu(C-H)$  (Ar) ( $3064\text{ cm}^{-1}$ )<sup>9</sup>,  $\nu(C=O)$  ( $1730\text{ cm}^{-1}$ )<sup>5,7</sup>,  $\nu(C=N)$  ( $1600\text{ cm}^{-1}$ )<sup>5</sup>,  $\nu(C-N)$  ( $1268\text{ cm}^{-1}$ )<sup>6</sup>, glucopyranosyl  $\nu(C-H)$  deformation at ( $853\text{ cm}^{-1}$ )<sup>8</sup> and  $\nu(C-S)$  ( $709\text{ cm}^{-1}$ )<sup>5b</sup>. The NMR spectrum distinctly displayed the signals due to N—H proton at  $\delta$  5.7–4.4 ppm<sup>4,6,7</sup>, aromatic protons at  $\delta$  8.06–6.25 ppm<sup>6,7,10</sup>, methyl protons at  $\delta$  2.33–1.23 ppm<sup>6</sup> and protons of pyranosyl ring at  $\delta$  5.74–4.5 ppm<sup>7,10,11</sup>. The mass spectrum<sup>12,13</sup> did not display the molecular ion peak at  $m/z$  863. ( $M^+$  protonated at  $m/z$  864 was present). The probable fragmentation patterns of the molecular ion are shown in Scheme-1.

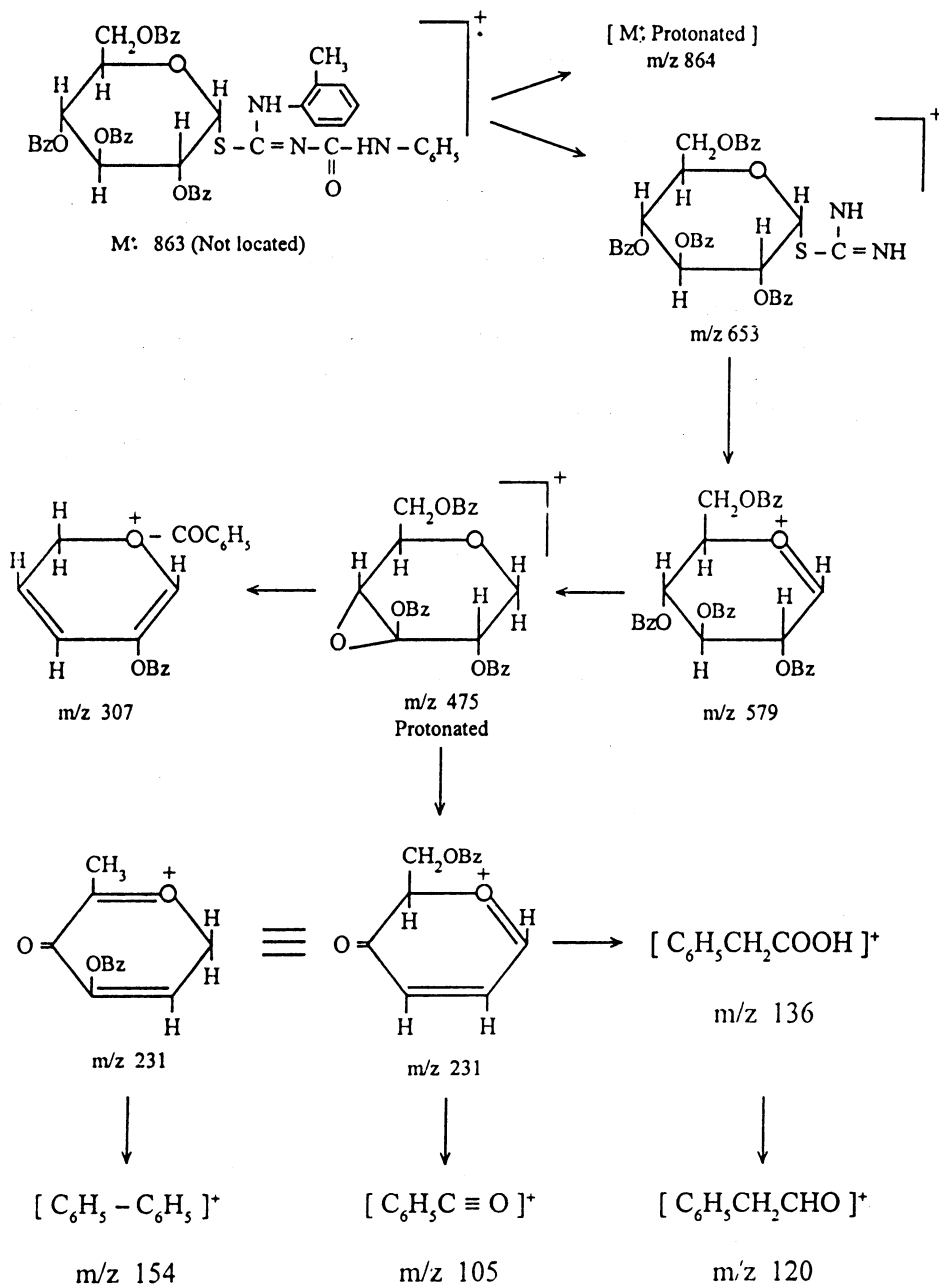
On the basis of all the above facts the product with m.p. 162°C (d) was assigned a structure as 2-S-tetra-O-benzoyl-D-glucopyranosyl-1-*o*-tolyl-5-phenyl-2-isothiobiuret (IIIa).

When the interaction of other S-tetra-O-benzoyl-D-glucopyranosyl aryl isothiocarbamides and phenyl isocyanate was carried out, the related 2-S-tetra-O-benzoyl-D-glucopyranosyl-1-aryl-5-phenyl-2-isothiobiurets (IIIb–IIIg) were isolated. All products are listed in Table-1.

Reaction scheme is as given below:



where Bz = Benzoyl ( $-\text{COC}_6\text{H}_5$ ), R = (a) *o*-tolyl, (b) phenyl, (c) *m*-tolyl, (d) *p*-tolyl, (e) *o*-Cl-phenyl, (f) *m*-Cl-phenyl, (g) *p*-Cl-phenyl.



Where, Bz = Benzoyl ( -COC<sub>6</sub>H<sub>5</sub> )

**Scheme-1**

Probable fragmentation pattern of 2-S-tetra-O-benzoyl-D-glucopyranosyl-1-*o*-tolyl-5-tolyl-2-isothiobiuret (IIIa)

TABLE-I  
 INTERACTION OF S-TETRA-O-BENZOYL-D-GLUCOPYRANOSYL D-GLUCOPYRANOSYL ARYL ISOTHIOCARBAMIDES (I) (0.005 M) AND PHENYL ISOCYANATE (II) (0.005 M, 0.6 G)

S. No.	S-Tetra-O-benzoyl-D-glucopyranosyl aryl isothiocarbamides	Yield (g)	m.p. (°C)	2-S-tetra-O-benzoyl-D-glucopyranosyl-1-aryl-5-phenyl-2-isothiobiurets	Yield (g)	Yield (%)	Analysis		[ $\alpha$ ] <sub>D</sub> <sup>25</sup> in CHCl <sub>3</sub>	
							Found	Reqd.		
1.	<i>o</i> -tolyl isothiocarbamide	(3.7)	162 (d)	1- <i>o</i> -tolyl-5-phenyl-2-isothiobiuret (IIIa)	(3.8)	88.63	N, 4.70 S, 3.52	N, 4.86 S, 3.70	-181.00° (c = 0.220)	
2.	phenyl isothiocarbamide	(3.6)	98 (d)	1,5-di-phenyl-2-isothiobiuret (IIIb)	(3.7)	87.26	N, 4.72 S, 3.49	N, 4.94 S, 3.76	-43.85° (c = 0.228)	
3.	<i>m</i> -tolyl isothiocarbamide	(3.7)	108-109 (d)	1- <i>m</i> -tolyl-5-phenyl-2-isothiobiuret (IIIc)	(3.3)	76.56	N, 4.59 S, 3.61	N, 4.86 S, 3.70	-133.92° (c = 0.224)	
4.	<i>p</i> -tolyl isothiocarbamide	(3.7)	122-123 (d)	1- <i>p</i> -tolyl-5-phenyl-2-isothiobiuret (IIId)	(3.8)	88.16	N, 4.90 S, 4.48	N, 4.86 S, 3.70	+172.00° (c = 0.232)	
5.	<i>o</i> -chloro phenyl isothiocarbamide	(3.8)	107 (d)	1- <i>o</i> -chloro phenyl-5-phenyl-2-isothiobiuret	(IIIe)	(3.0)	68.02	N, 4.62 S, 3.42	N, 4.75 S, 3.62	-65.78° (c = 0.304)
6.	<i>m</i> -chloro phenyl isothiocarbamide	(3.8)	103 (d)	1- <i>m</i> -chloro phenyl-5-phenyl-2-isothiobiuret	(IIIf)	(2.8)	63.49	N, 4.48 S, 3.40	N, 4.75 S, 3.62	-54.34° (c = 0.368)
7.	<i>p</i> -chloro phenyl isothiocarbamide	(3.8)	127	1- <i>p</i> -chloro phenyl-5-phenyl-2-isothiobiuret	(IIIg)	(2.9)	65.75	N, 4.61 S, 3.38	N, 4.75 S, 3.62	-100° (c = 0.300)

Antibacterial and antifungal activity of 2-S-tetra-O-benzoyl-D-glucopyranosyl-1-aryl-5-phenyl-2-isothiobiurets (**III**) were carried out by using cup-plate agar diffusion method<sup>14-16</sup> at a concentration of 100  $\mu\text{g mL}^{-1}$  in DMF, using standard Co-trimazine (25  $\mu\text{g mL}^{-1}$ ) for Gram positive and Gram negative bacteria and griseofulvin for fungi. The tested microorganisms were *S. aureus*, *Bacillus*, *E. coli*, *P. vulgaris*, *Pseudomonas*, *Salmonella*, *Fusarium* and *A. niger*.

**Antibacterial study:** Inhibition zone record of the compounds clearly indicates that **IIIa**, **IIIf** and **IIIg** were moderately active against Gram positive *S. aureus*. Almost all compounds showed much more activity against *Bacillus*. All compounds showed enhanced activity against Gram negative *E. coli* and *Pseudomonas* whereas on *Salmonella* showed low to moderate activity.

**Antifungal activity:** As compared to the bacteria, compounds **IIIe** and **IIIf** were moderately active against *A. niger* whereas other compounds showed low to moderate activity against *A. niger*. Against *Fusarium* all compounds showed low antifungal activity.

## EXPERIMENTAL

The reagents required for the reactions carried out in this chapter were prepared as follows:

**I. Preparation of glucopyranose pentabenzoate<sup>17</sup>:** The glucopyranose pentabenzoate was prepared by already known procedure, *i.e.*, by the interaction of D-glucose and benzoylating reagent.

**II. Preparation of tetra-O-benzoyl-D-glucopyranosyl bromide<sup>1</sup>:** Required tetra-O-benzoyl-D-glucopyranosyl bromide was prepared by already developed procedure, *i.e.*, by the interaction of glucopyranose pentabenzoate and brominating reagent<sup>18</sup>.

**III. Preparation of aryl thiocarbamides<sup>19</sup>:** Required aryl thiocarbamides were prepared by the interaction of amines, hydrochloric acid and ammonium thiocyanate.

**IV. Preparation of S-tetra-O-benzoyl-D-glucopyranosyl aryl isothiocarbamides<sup>1</sup>:** Required S-tetra-O-benzoyl-D-glucopyranosyl aryl isothiocarbamides were prepared by already developed procedure, *i.e.*, by the interaction of tetra-O-benzoyl-D-glucopyranosyl bromide and aryl thiocarbamides.

**V. Phenyl isocyanate:** The phenyl isocyanate used was of commercial grade.

**VI. Synthesis of 2-S-tetra-O-benzoyl-D-glucopyranosyl-1-aryl-5-phenyl-2-isothiobiuret:** The benzene solution of S-tetra-O-benzoyl-D-glucopyranosyl-*o*-tolyl isothiocarbamide (0.005 M, 3.7 g in 25 mL) was mixed with phenyl isocyanate (0.005 M, 0.6 g) and the mixture was shaken. A clear solution formed was kept at room temperature for 24 h. The excess of benzene was distilled off and the sticky mass obtained which on trituration several times with petroleum ether (60–80°C) afforded a white solid, (3.8 g) (**IIIa**). Crystallised from ethanol, m.p. 162°C (**d**). [Found: C, 67.86, H, 4.48, N, 4.70, S, 3.52.  $\text{C}_{40}\text{H}_{41}\text{O}_{10}\text{N}_3\text{S}$  requires: C, 68.13, H, 4.75, N, 4.86, S, 3.70%].

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