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Synthesis of S-Tetra-O-Benzoyl-D-Glucopyranosyl Aryl Isothiocarbamides

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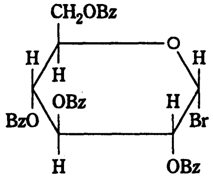
The pharmacological and biochemical aspects of alkyl/aryl ureides, thioureides and guanidines have been extensively investigated and many compounds of this series have been described in the literature. They have been found to possess marked biological activities and are used as bacteriostatic agents and diuretic, analgesic, antithyroid drugs. Several S-tetra-O-benzoyl-D-glucopyranosyl aryl isothiocarbamides have been prepared by the interaction of aryl thiocarbamides and tetra-O-benzoyl-D-glucopyranosyl bromide. The identities of these new compounds have been established on the basis of usual chemical transformations and IR, NMR and mass spectral studies.

Key words: Synthesis, S-tetra-O-benzoyl-D-glucopyranosyl aryl isothiocarbamides.

INTRODUCTION

Comparatively few thioglucosides of thiocarbamides are reported earlier[1, 2]. In the present communication six S-tetra-O-benzoyl-D-glucopyranosyl aryl isothiocarbamides have been reported. These were prepared by the interaction of aryl isothiocarbamides **(II)** and tetra-O-benzoyl-D-glucopyranosyl bromide **(I)**.



(I)

Tetra-O-benzoyl-D-glucopyranosyl bromide (TBG-Br), where Bz = benzoyl (—COC_6H_5)

RESULTS AND DISCUSSION

Isopropanolic solution of tetra-O-benzoyl-D-glucopyranosyl bromide and phenyl thiocarbamide was refluxed for 3 h over a hot water bath. The clear solution was then kept at room temperature for about 20 h. It was mixed with water when a small quantity of semi-solid mass was obtained. The aqueous layer was separated. This aqueous solution was acidic and non-desulphurizable when boiled with alkaline plumbite solution. When treated with aqueous picric acid, it afforded a picrate, m.p. 192°C (d). All these clearly indicate the presence of S-tetra-O-benzoyl-D-glucopyranosyl isothiocarbamide hydrobromide in aqueous solution.

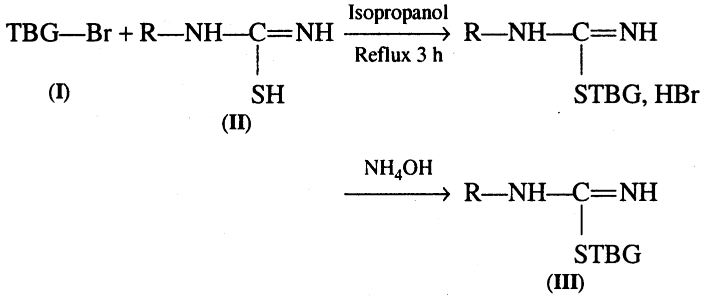
The aqueous solution, when made basic with NH_4OH, aforded a sticky mass which solidified on standing for several hours and the crude product was crystallized from ethanol-water, m.p. 84°C. It gave Molisch test and was non-desulphurizable when boiled with alkaline plumbite solution. It gave a picrate, m.p. 192°C (d), when warm ethanolic solution of it was treated with ethanolic picric acid. Its specific rotation was found $[\alpha]^{32} + 87.10°$ ($c = 1.184$ in $CHCl_3$). The IR spectrum clearly indicated the presence of ν(NH) 3427 cm^{-1}, ν(C=O) 1728 cm^{-1}, ν(C=N) 1598 cm^{-1} and ν(C=S) 709 cm^{-1} bands[3, 4].

The NMR spectrum of the product distinctly displayed signals due to NH (δ 8.25 ppm) and aromatic protons (δ 7.2–8.0 ppm). It also showed the signals due to the protons of β-D-glucopyranosyl ring at (δ 4.25–6.25 ppm)[5].

All these clearly indicated the product as S-tetra-O-benzoyl-D-glucopyranosyl phenyl isothiocarbamide **(IIIa).**

When the interaction of tetra-O-benzoyl-D-glucopyranosyl bromide was extended to other aryl thiocarbamides, the related S-tetra-O-benzoyl-D-glucopyranosyl aryl isothiocarbamides **(IIIb–IIIf)** were isolated. All these products and the afforded picrates have been listed in Table-1.

Reaction scheme is as given below:



$$\underset{\textbf{(I)}}{\mathrm{TBG{-}Br}} + \underset{\textbf{(II)}}{\mathrm{R{-}NH{-}}\underset{\mathrm{SH}}{\underset{|}{\mathrm{C}}}\mathrm{{=}NH}} \xrightarrow[\text{Reflux 3 h}]{\text{Isopropanol}} \mathrm{R{-}NH{-}}\underset{\mathrm{STBG,\ HBr}}{\underset{|}{\mathrm{C}}}\mathrm{{=}NH} \xrightarrow{NH_4OH} \underset{\textbf{(III)}}{\mathrm{R{-}NH{-}}\underset{\mathrm{STBG}}{\underset{|}{\mathrm{C}}}\mathrm{{=}NH}}$$

where R = (a) phenyl, (b) *o*-tolyl, (c) *p*-tolyl, (d) *o*-Cl-phenyl, (e) *m*-Cl-phenyl, (f) *p*-Cl-phenyl, TBG = tetra-O-benzoyl-D-glucopyranosyl.

EXPERIMENTAL

The reagents used for the reactions were prepared as follows:

Preparation of 1-aryl thiocarbamides: The required 1-aryl thiocarbamides were prepared by the already known procedure, *i.e.*, by the interaction of the appropriate amine monochloride and ammonium thiocyanate[6].

Preparation of brominating reagent: Glacial acetic acid (30 mL) was taken in a conical flask and to it was added red phosphorus (4.0 g). To this mixture molecular bromine (2.0 mL) was added gradually with constant shaking and cooling. The resultant mixture was allowed to stand at ice-cold temperature for about 30 min.

Preparation of tetra-O-benzoyl-D-glucopyranosyl bromide: Finely powdered D-glucopyranose pentabenzoate (0.02 M, 14.0 g) was added gradually to the brominating reagent. After the addition, the content of the flask was refluxed on low flame for 1.30 h. Then it was kept overnight at room temperature. The

TABLE-1
INTERACTION OF TETRA-O-BENZOYL-D-GLUCOPYRANOSYL BROMIDE (0.001 M, 6.59 g) AND ARYL THIOCARBAMIDE (0.01 M) IN ISOPROPANOL

Aryl thiocarbamide (g)	S-tetra-O-benzoyl-D-glucopyranosyl aryl isothiocarbamides, m.p., (°C) (yield, g)	Yield (%)	Analysis		$[\alpha]_D^{32}$ in $CHCl_3$	Picrates		
						m.p. (°C)	Analysis	
			Found	Reqd.			Found	Reqd.
-Phenyl (1.52)	-Phenyl **(IIIa),** 84 (1.5)	61.60	N, 3.85 S, 3.77	N, 3.83 S, 4.38	+87.10 (c = 1.148)	192 (d)	N, 7.60 S, 3.16	N, 7.41 S, 3.39
-*o*-tolyl (1.66)	-*o*-tolyl **(IIIb),** 81 (4.6)	62.90	N, 3.48 S, 4.01	N, 3.76 S, 4.30	+64.65 (c = 0.928)	180	N, 7.62 S, 3.09	N, 7.31 S, 3.34
-*p*-tolyl (1.66)	-*p*-tolyl **(IIIc),** 82 (4.26)	52.20	N, 3.58 S, 4.52	N, 3.76 S, 4.30	+92.21 (c = 1.952)	145 (d)	N, 7.74 S, 3.18	N, 7.31 S, 3.34
o-Cl-phenyl (1.85)	*o*-Cl-phenyl **(IIId),** 88 (5.2)	67.97	N, 3.72 S, 4.07	N, 3.66 S, 4.18	+53.47 (c = 1.496)	240 (d)	N, 7.27 S, 3.09	N, 7.15 S, 3.27
m-Cl-phenyl (1.85)	*m*-Cl-phenyl **(IIIe),** 98 (3.5)	45.75	N, 3.39 S, 3.94	N, 3.66 S, 4.18	+52.66 (c = 3.608)	242 (d)	N, 7.36 S, 3.42	N, 7.15 S, 3.27
p-Cl-phenyl (1.85)	*p*-Cl-phenyl **(IIIf)**, 86 (2.8)	42.48	N, 3.82 S, 4.08	N, 3.66 S, 4.18	+39.18 (c = 1.788)	222 (d)	N, 7.42 S, 3.03	N, 7.15 S, 3.27

Satisfactory C, H analyses were obtained for all the compounds.

reaction mixture was then mixed with carbon tetrachloride (30 mL) and then the mixture was shaken vigorously for about 15 min. The resultant mixture was poured into ice-cold water. The carbon tetrachloride layer was then separated. It was washed several times with aqueous sodium bicarbonate to remove excess of acetic acid followed by sodium metabisulphite to remove excess of bromine and finally 2–3 times with water. The carbon tetrachloride layer on addition of petroleum ether afforded a white solid (10.2 g). This solid was the expected tetra-O-benzoyl-D-glucopyranosyl bromide. It was crystallized from ethanol, m.p. 125–129°C (Lit., m.p. 129–130°C)[7].

Synthesis of S-tetra-O-benzoyl-D-glucopyranosyl isothiocarbamide: Isopropanolic solution of tetra-O-benzoyl-D-glucopyranosyl bromide (0.01 M, 6.5 g in 25 mL) was mixed with a suspension of phenyl thiocarbamide (0.01 M, 1.5 g in 25 mL isopropanol) and the mixture after shaking for about 10 min was refluxed over hot water bath at 70°C for about 3 h. The clear solution was kept for 20 h. It was mixed with water when a small quantity of semi-solid was obtained. The aqueous layer was separated. This aqueous solution was acidic and non-desulphurizable when boiled with alkaline plumbic solution.

The aqueous solution when rendered basic with NH_4OH afforded a sticky mass which solidified on standing for several hours and a crude product was crystallized from ethanol-water (4.5 g), m.p. 84°C **(IIIa)** (found: N, 3.85; S, 3.77%; $C_{41}H_{34}N_2O_9S$ requires N, 3.83; S, 4.38%). When warm ethanolic solution of **IIIa** was treated with ethanolic picric acid, it aforded a picrate, m.p. 192°C **(IIId)** (found: N, 7.60; S, 3.16%; requires N, 7.41; S, 3.39%). All these clearly indicate the product as S-tetra-O-benzoyl-D-glucopyranosylphenyl isothiocarbamide **(IIIa)**.

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