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SYNTHETIC STUDY AND BIOLOGICAL EVALUATION OF 1-TETRA-*O*-BENZOYL-β-D-GLUCOPYRANOSYL-3-SUBSTITUTED THIOCARBAMIDES

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ABSTRACT

Carbohydrate play vital role in vast array of biological processes particularly there are many advantages for example carbohydrate based drug show low toxicity and immunogenicity thus it is interesting to synthesize the carbohydrate base derivatives. In the present investigation we here in report series of 1-tetra-*O*-benzoyl–β-D-glucopuranosyl-3-substituted thiocarbamides which has been synthesized by the interaction of tetra-*O*-benzoyl–β-D-glucopyranosyl isothiocyanate and various alkyl amines. The structures of the newly synthesized compounds have been established on the basis of usual chemical transformations and IR, ^{1}HNMR and Mass spectral studies. All the synthesized compounds have been evaluated for their in vitro anti-bacterial and anti-fungal activity against different bacteria and fungi by agar diffusion method.

Keywords: *N*-glucosides, alkyl amines, glucosyl isothiocyanate, thiocarbamides.

INTRODUCTION

The chemistry of thiourea of carbohydrate is extensively elaborated and well documented[1], many of these derivatives have been found to posses wide applications in industry as carbohydrate based detergent[2] and in medicine as a anti cancer agents[3] and anti fungal agents[4].

These compounds arouse interest as potential biologically active substances and versatile intermediate for preparing various derivatives. The biological activity of some polyhydroxy compounds have been reported[5-6].Glucopyranosyl isocyanate and isothiocyanate[7], likewise other glycosyl isocyanates have a significant role in synthetic carbohydrate chemistry. Many compounds have been synthesized by the use of glycosyl isothiocyanate[8-11]. On the basis of knowledge gained on the work done on *N*-glucosylated compounds, it was quite interesting to synthesize some new *N*-glucopyranosylated thioamides.

Herein, we report the synthesis of 1-tetra–*O*–benzoyl–β–D-glucopyranosyl-3-substituted thiocarbamides by the interaction of tetra–*O*-benzoyl–β–D-glucopyranosyl isothiocyanate and alkyl amines. All the products obtained have been crystallized from ethanol-water. IR spectra of the products show characteristic absorption of prominent peaks, ^{1}H NMR spectra shows characteristics peaks due to N-H, benzoyl and glucopyranosyl protons while the Mass spectra shows peak [12-14].

EXPERIMENTAL

General methods

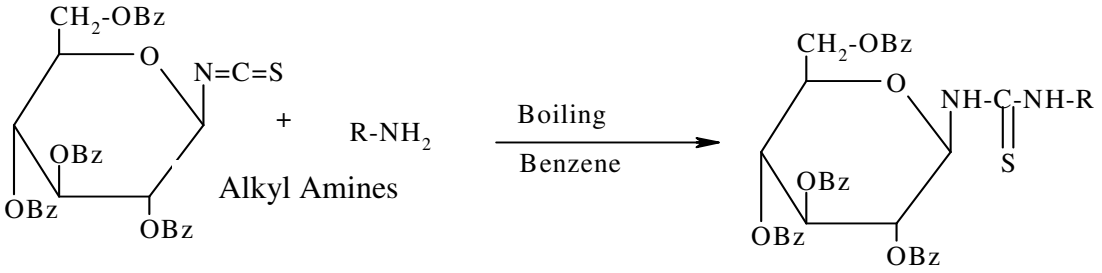
Melting points are uncorrected. Optical rotations $[\alpha]_D$ were measured on an Equip-Tronics digital polarimeter model no. EQ 800 in $CHCl_3$ at 30^0C. IR spectra were recorded on a Perkin-Elmer spectrum RXI (4000-450cm^{-1}) FTIR spectrometer. ^{1}HNMR were obtained on a Bruker DRX-300 (300 MHz FT NMR) NMR spectrometer for a sample in $CDCl_3$ solution with TMS as an internal reference. The mass spectra were recorded on a Micromass Quattro II triple quadruple mass spectrometer.

Tetra-*O*-benzoyl–β-D-glucopyranosyl isothiocyanate (2)

Tetra-*O*-benzoyl-β-glucopyranosyl isothiocyanate (**2**) was prepared by interaction of Tetra-*O*-benzoyl-α-D-glucopyranosyl bromide and lead thiocyanate in anhydrous xylene medium[15].

1-tetra–*O*–benzoyl–β–D-glucopyranosyl -3-methyl thiocarbamides

Condensation of methyl amines (0.005M, 0.95 mL) and tetra-*O*-benzoyl- β- glucopyranosyl isothiocyanate (0.005M, 2.0 g), in benzene (20mL) was carried out on boiling water bath for 4h. The reaction was monitored by TLC, after completion of the reaction, the solvent was distilled off and the resultant sticky residue was triturated with petroleum ether (60-80^0 C) to afford the solid with m.p. (100-101^{0}C). It was crystallized from water-alcohol.



Tetra-O-Benzoyl-β-D-Glucopyranosyl Isothiocyanate

1-tetra-*O*-benzoyl–β-D-glucopyranosyl-3-substituted thiocarbamides

Where, R = (a) methyl, (b) ethyl,(c) n-propyl, (d) ter-butyl, (e) n-pentyl ; Bz = - COC_6H_5.

Scheme-1

RESULTS AND DISCUSSION

Several 1-tetra–*O*–benzoyl–β–D-glucopyranosyl-3-substituted thiocarbamides (3a-e) (Scheme-1) were prepared by the condensation of alkyl amines (1a-e) and tetra-*O*-benzoyl-β-glucopyranosyl isothiocyanate (2) in benzene for 4hrs. The reaction was monitored by TLC. After complete reaction, the solvent was distilled off and the resultant sticky residue was triturated with petroleum ether (60-80^0 C) to afford the products (3a-e). All the products were crystallized from ethanol-water. Structures of all synthesized products were established on the basis of usual chemical transformations and IR, ^{1}HNMR and Mass spectral studies.

Table -1: Physical data of 1-tetra–*O*–benzoyl–β–D-glucopyranosyl-3-substituted thiocarbamides (3a-e) (Scheme-1).

S. No.	Reactant (g)	Product	m. p. (^{0}C)	Yield, (%)	$[\alpha]_D^{39}$ (c,$CHCl_3$)	R_f (3:2,CCl_4: EtOAc)	Elemental analysis found (Required)	
							N	S
1	1a (1.21)	3a	90-95	72	122.2^0 (0.9)	0.93	4.09 (4.19)	4.69 (4.79)
2	1b (1.40)	3b	100-105	74.94	-32.5^0 (0.93)	0.85	4.01 (4.10)	4.58 (4.69)
3	1c (1.40)	3c	121-125	82.21	-84.2^0 (0.95)	0.80	3.98 (4.02)	4.42 (4.59)
4	1d (1.40)	3d	115	80.50	85.1^0 (0.94)	0.79	3.82 (3.94)	4.39 (4.50)
5	1e (1.28)	3e	110	75.96	52.5^0 (0.96)	0.90	3.71 (3.86)	4.35 (4.41)

Table -2: Antimicrobial activities of synthesized compounds

Compounds	*E. coli*	*P. vulgaris*	*S. aureus*	*P. aeruginosa*	*A. niger*	*Penicillium*
3a	20	11	18	22	10	12
3b	21	13	15	20	09	14
3c	12	09	15	17	14	16
3d	15	12	13	14	11	17
3e	23	00	17	20	08	09
Amikacin	17	17	17	17	--	--
Fluconazole	--	--	--	--	35	35

Bore size = 6 mm

Antimicrobial Activities

All the compounds have been screened for both anti-bacterial and anti-fungal activities using cup plate agar diffusion method[16, 17] by measuring the inhibition zone in mm. The compounds were taken at concentration of 1μg/ml using dimethyl sulphoxide as a solvent. Amikacin was used as standard for anti-bacterial activities and Fluconazole as a standard for anti fungal activities. The compounds were screened against various pathogenic bacteria such as *Escherichia coli, Proteus vulgaris, Staphylococcus aureus, Pseudomonas aeruginosa, Aspergillus niger* and *Penicillium*. Among synthesized compounds **3a, 3b** and **3e** show strong activity against *Escherichia coli, Pseudomonas aeruginosa* and remaining compounds show good and moderate activity against *Proteus vulgaris*, *Aspergillus niger*, *Staphylococcus aureus* and *Penicillum*. Results are tabulated in Table -2.

1- tetra-*O*-benzoyl-β–D-glucopyranosyl-3-methyl thiocarbamide (3a)

IR (KBr): υ 3360 (N-H); 3061 (Ar-H); 2939 (C-H ali); 1176 (C = S) 1315 (C-N); 846(Char. D-Glucose). **^{1}HNMR ($CDCl_3$)**: δ 8.23-7.43 (m, 20H Ar-H); 6.2 (d, 1H, NH (glu.)); 5.72-5.03 (m, 7H, glucopyranosyl ring); 1.6-1.3 (s, 3H,CH_3). **ESI Mass (M/z)** : 677.4 (M^+.+1), 579, 353, 135, 121. Anal. Calcd. for: $C_{35}H_{38}O_9\ N_3S$: C, 62.13; H, 5.62; N, 6.21; S, 4.73, found, C, 56.70; H, 5.40; N, 6.75; S, 5.25, %.

1-tetra-*O*-benzoyl-β–D-glucopyranosyl-3-ethyl thiocarbamide (3b)

IR (KBr): υ 3361 (N-H); 3062 (Ar-H); 2972 (C-H ali); 1176 (C = S) 1315 (C-N); 846(Char. D-Glucose). **^{1}HNMR ($CDCl_3$)**: δ 8.23-7.43 (m, 20H Ar-H); 6.2 (d, 1H, NH (glu.)); 5.72-5.03 (m, 7H, glucopyranosyl ring); 1.6-1.3 (s, 3H,CH_3). **ESI Mass (M/z)** : 690.4 (Not located), 579, 353, 135, 121. Anal. Calcd. for: $C_{36}H_{40}O_9\ N_3S$: C, 62.03; H, 5.50; N, 6.35; S, 4.70, found, C, 59.50; H, 5.23; N, 6.75; S, 5.65, %.

1- tetra-*O*-benzoyl-β–D-glucopyranosyl-3-n-propyl thiocarbamide (3c)

IR (KBr): υ 3366 (N-H); 3056 (Ar-H); 2942 (C-H ali); 1176 (C = S) 1315 (C-N); 846(Char. D-Glucose). **^{1}HNMR ($CDCl_3$):** δ 8.23-7.43 (m, 20H Ar-H); 6.2 (d, 1H, NH (glu.)); 5.72-5.03 (m, 7H, glucopyranosyl ring); 1.6-1.3 (s, 3H,CH_3). **ESI Mass (M/z)** : 706.4 (M^+.+1), 579, 353, 135, 121. Anal. Calcd. for: $C_{37}H_{46}O_9\ N_3S$: C, 62.13; H, 5.62; N, 6.21; S, 4.73, found, C, 56.70; H, 5.40; N, 6.75; S, 5.25, %.

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