SYNTHESIS, STRUCTURAL STUDY AND ANTIMICROBIAL EVALUATION OF BIOLOGICALLY IMPORTANT 1-TETRA-O-BENZOYL-B-D-GLOCOSYL-3-ARYL-2-PHENYL THIOCARBAMIDE 2-S-BENZYL-ISOTHIOCARBAMIDE

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Abstract

Carbohydrates are a major class of organic compounds occurring in nature. They include such familiar substances as sugar, glucose, starch, cellulose etc., which are all very important for the maintenance of life in plants and animals. Heterocyclic compounds are widely distributed in nature and are essential to life in various ways. Isothiocyanates are important intermediates belonging to the family of compounds known as heterocumulenes. Isothiocyanates are versatile synthetic intermediates in organic chemistry due to their availability and their tendency to undergo nucleophilic addition and cycloadditions[1-3]

Serial of novel 1-Tetra-O-Benzoyl-β-D-Glocosyl-3-aryl-2-phenyl thiocarbamide 2-*S*-benzyl-isothiocarbamide was prepared by the interaction of the of 1-Tetra-O-Benzoyl- β -D Glocosyl-3-aryl-2-*S*-benzyl-isothiocarbamide and Phenyl thiocarbamide in benzene medium. The Reaction was refluxed for 3hr in benzene medium. After completion of the reaction, the reaction mixture was brought to room temperature and the solvent removed under reduced pressure to obtain residue. This residue was triturated several times with petroleum ether (60-80^{o}C) to afford a pale yellow solid. Product was purified from chloroform-petroleum ether. These compounds were screened for their antibacterial activities against–*Escherichia coli*, *Staphylococcus aurous*. These compounds show appreciable activity towards these microorganisms.

Keyword: Phenyl Thiocarbamide substituted S-Benzyl isothiocarbamide, Phenyl isothiocyanate, and Biological studies.

1. Introduction:

Sugar isothiocyanate and their thiourea and thiocarbamide derivatives exhibits wide range of pharmacological activities[4-7] like antimicrobial, antiviral and antitumor. Isothiocyanates are important intermediates belonging to the family of compounds known as heterocumulenes. Isothiocyanates are versatile synthetic intermediates in organic chemistry due to their availability and their tendency to undergo nucleophilic addition and cycloadditions. Thiourea and its derivatives are a group of compounds possessing a wide spectrum of biological activities such as anticonvulsant, herbicidal and it is versatile reagent in organic synthesis. Also thiomaltosides are an important constitute of carbohydrate chemistry.

2. Experimental

2.1 Material and Methods

All chemicals were research grade. Melting points determined are uncorrected. IR spectrawere recorded in KBr on a FT-IR Perkin-Elmer RXI (4000-450cm^{-1}) spectrophotometer. ^{1}H NMR measurements were performed on a Bruker DRX-300 (300 MHz FT NMR) NMR spectrometer in $CDCl_3$ solution with TMS as internal reference. The Mass spectra were recorded on a THERMO Finnigan LCQ Advantage max ion trap Mass spectrometer. Thin layer chromatography (TLC) was performed on silica Gel G and spots were visualized by iodine vapour. The compounds describe in this paper were first time synthesized by the multistep reaction protocol.

2.2 Preparation of 1- tetra-*O*-benzoyl-β-D-glucosyl -3 aryl-2-*S*-benzyl-isothiocarbamide

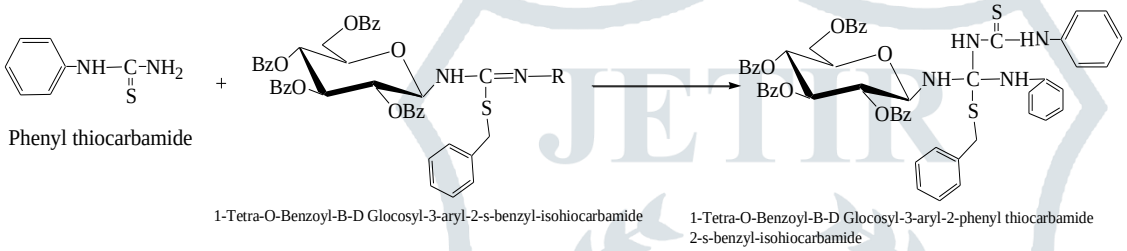
To the ethanolic suspension of 1-tetra-*O*-benzoyl- **β** –D-glucosyl-3-aryl-thiocarbamide was added benzyl chloride and the reaction mixture was reflux for 90 min. Afterward the reaction mixture was cooled and rendered basic with dil. ice cold NH_4OH and a sticky residue was obtained which on standing for 1 to 2 hrs. Solidifies. It was filtered and washes with petroleum ether, gives or affords a white solid. It was recrystallised wih ethanol.

2.3 Preparation of Phenyl Thiocarbamide

Concerntrated solution of Ammonia was added to the benzene solution of phenyl thiocyanate (7.7g in 40 ml benzene) and reaction mixture was refluxed over boiling water bath for 30 mins. Afterwards it was cooled and titurate with pet ether (60-80^{o}C). A white solid was seperate out as phenyl thiocarbamide.

2.4 Preparation 1-Tetra-*O*-Benzoyl- β -D Glocosyl-3-aryl-2-phenyl thiocarbamides, 2-*S*-benzyl-isohiocarbamide

1-Tetra-*O*-Benzoyl-β-D Glocosyl-3-aryl-2-phenyl thiocarbamides, 2-*S*-benzyl-isothiocarbamide was prepared by the interaction of the 1- tetra-*O*-benzoyl-β-D-glucosyl -3 aryl-2-*S*-benzyl-isothiocarbamide and Phenyl thiocarbamide in benzene medium. The Reaction was refluxed for 3hr in benzene and then the benzene was evaporated. The formed product is washed and recrystallised by the pertroleum ether (60-80^{0}C).



Where, R= (a) Phenyl, (b) o-chloro-aniline, (c) m-chloro-aniline, (d) p-chloro-aniline,

Results and discussion

Herein, we report the synthesis of various 1-Tetra-*O*-Benzoyl- β -D Glocosyl-3-aryl-2-phenyl thiocarbamides, 2-*S*-benzyl-isohiocarbamide (**1-4)** by interaction of Phenyl Thiocarbamide **(1)** and 1-tetra-*O*-benzoyl-β-D-glucosyl-3-aryl-2-*S*-benzyl-isothiocarbamide **(1-4)** in benzene medium. All products were crystallized from ethanol before recording the physical data (Table-1). The purity of compounds was checked by TLC. The spectral analysis[8-10] IR, 1H NMR and Mass spectra of the product were observed.

1: IR (KBr):υ 3050 (Ar-H), 2779 (Ali C-H), 1728 (C=O), 1449 (C=N), 1250(C=S), 1100 (Charactristic of glucose), 652 (C-S), ^{1}H NMR (δ in ppm, $CDCl_3$): δ 7.4-6.4 (m, aromatic protons), δ 6.2 (s, N-H), δ 5.2-3.6 (m, glucosyl protons), δ 2.12-1.38 (Methyl protons) Mass (m/z): 994 (M^+), 579, 420, 105; Anal. Calcd for $C_{56}H_{51}N_4S_2O_9$: C, 65.44; H, 4.82; N, 5.87; S, 6.71; Found: C, 65.40; H, 4.86; N, 5.80; S, 6.75.

On the basis of all above facts the product with m. p. 140^{o}C was assigned the structure 1-tetra-O-Benzoyl- β -D Glocosyl-3-phenyl-2-phenyl-thiocarbamide, 2-S-benzyl-isothiocarbamide . When the reaction of phenyl thiocarbamide was extended to several other 1-tetra-O-benzoyl-β-D-glucosyl-3-aryl-2-S-benzyl-isothiocarbamide corresponding 1-tetra-O-Benzoyl- β -D Glocosyl-3-aryl-2-phenyl-thiocarbamide, 2-S-benzyl-isohiocarbamide has been synthesized.

2: IR (KBr):υ 3069 (Ar-H), 2975 (Ali C-H), 1728 (C=O), 1459 (C=N), 1229 (C-O), 1199 (C=S), 905 (Charactristic of glucose), 690 (C-S), ^{1}H NMR (δ in ppm, $CDCl_3$): δ 7.4-6.4 (m, aromatic protons), δ 6.2 (s, N-H), δ 5.2-3.6 (m, glucosyl protons), δ 2.12-1.38 (Methyl protons) Mass (m/z): 994 (M^+), 579, 420, 105; Anal. Calcd for $C_{56}H_{50}N_4S_2O_9Cl$: C, 65.78; H, 4.89; N, 5.48; S, 6.26; Found: C, 65.82; H, 4.92; N, 5.55; S, 6.30.

On the basis of all above facts the product with m. p. 142^{o}C was assigned the structure 1-tetra-O-Benzoyl- β -D Glocosyl-3-o-Cl-phenyl-2-phenyl-thiocarbamide, 2-S-benzyl-isothiocarbamide .

Table -1: Physical data for characterization of compounds (1-4)

Compd	Yield %	R_f	M.P. ^{0}C	Analysis (%): Found (calcd)	
				N	S
1	72.00	0.46	140	5.80(5.87)	6.75(6.71)
2	62.00	0.52	142	5.55 (5.48)	6.30(6.26)
3	70.00	0.50	162	5.42 (5.48)	6.32(6.26)
4	69.00	0.61	159	5.45 (5.48)	6.23(6.26)

C and H analysis was found satisfactory in all cases.

Antimicrobial activity[11]:

All the compounds have been screened for both; antimicrobial and antifungal activity by using disc diffusion assay. For this, sterile filter paper disc (6 mm) impregnated with fixed doses of compounds was placed on pre-innoculated surface. The disc bearing plates were incubated at 37ºC for 24 hr. After incubation, zone diameters were measured. The compounds were taken at a concentration or 1 mg/mL using dimethyl sulphoxide as a solvent. Amikacin (100 µg/mL) was used as standard for antibacterial activity (100µg/mL). The compound was screened for antibacterial activity against *Eschrichia coli*, *Staphylococcus aureus*, *Salmonella typhi*, in nutrient agar medium. It has been observed that all the compounds showed good activity against bacteria.

Compound	*E. coli*	*S. aureus*	*S. typhi*
1(3a)	17	16	18
2(3b)	10	15	20
3(3c)	18	14	15
4(3d)	14	19	19
Amikacin	18	21	20

Zone of inhibition in mm. (15 or less) resistance, (16-20 mm) moderate and more than

Conclusion

Derivatives were synthesized and characterized for their structure elucidation. As outline in synthesis process, important novel substituted 2-*S*-benzyl-isothiocarbamide has been synthesized. All the structure of the above compounds was in good agreement with Spectral and Analytical data. Various chemical and spectral data supported the structures. Some of the compounds synthesized showed promising antimicrobial activities. The newly synthesized thiocarbamides exhibits comparable antibacterial activities against the organisms tested. The method adopted in this investigation is simple, efficient and inexpensive and is useful in synthesizing pharmacologically important molecules.

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