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Synthesis & screening for antimicrobial activity of N-Glucosylated aryl substituted s-benzyl isothiocarbamide

Kavita. M. Heda *
*Department of Chemistry,Shri R. L. T. College of Science,Akola – 444001(M.S.) India
E-mail: kavitaheda25@gmail.com

Abstract

Carbohydrates, "The building blocks of life" comprises the most abundant group of natural product. They are prime biological substances, which are metabolized as monosaccharides, oligo-saccharides and polysaccharides. They are indispensable for living organism, serving as skeletal structure in plants and also in insects. They also occur as food reserves in the storage organs of plants and in the liver and muscles of animals. In addition, they are an important source of energy required for the various metabolic source of energy required for the various metabolic activities of the living organism. The energy being derived as a result of their oxidation. They also serve to lubricate skeletal joint, to provide adhesion between cells and they confer biological specificity on the surface of animal cell.

Series of new 1-Tetra-O-Benzoyl-β-D-Glocosyl-3-aryl (nitro substituted aniline)-2-phenyl thiocarbamide 2-*S*-benzyl-isothiocarbamide was prepared by the interaction of the of 1-Tetra-O-Benzoyl- β -D Glocosyl-3-aryl (nitro substituted aniline)-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. The newly synthesized compounds have been characterized by analytical and IR, ^{1}HNMR and Mass spectral studies. 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:

Carbohydrate derivatives have been extensively investigated including synthesis, characterization and biological activity. Partly due to the facts that many natural occurring saccharides and synthesized analogues exhibit various and potent biological activities and they have been widely employed as agrochemicals and pharmaceuticals[1-5].

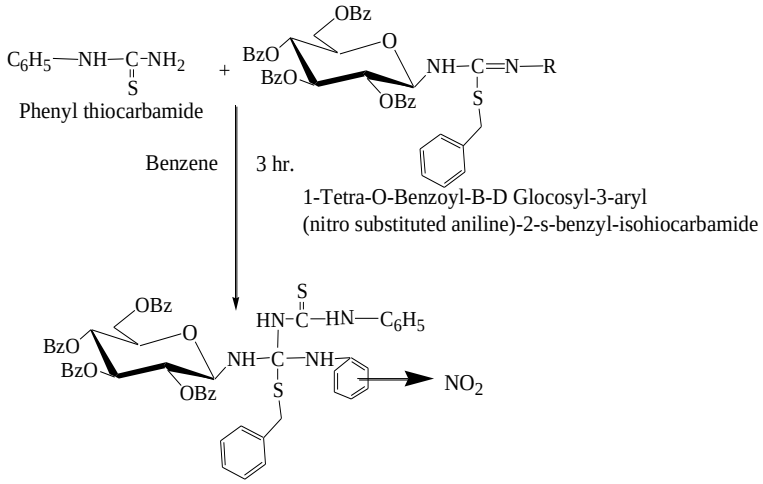
Sugar isothiocyanate and their thiourea and thiocarbamide derivatives exhibits wide range of pharmacological activities[6-9] like antimicrobial, antiviral and antitumor. Isothiocyanates are important intermediates belonging to the family of compounds known as heterocumulenes. Isothiocyanates are versatile 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

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.

Preparation 1-Tetra-*O*-Benzoyl- β -D Glocosyl-3-aryl (nitro substituted aniline)-2-phenyl thiocarbamides, 2-*S*-benzyl-isohiocarbamide

1-Tetra-*O*-Benzoyl-β-D Glocosyl-3-aryl (nitro substituted aniline)-2-phenyl thiocarbamides, 2-*S*-benzyl-isothiocarbamide was prepared by the interaction of the 1- tetra-*O*-benzoyl-β-D-glucosyl -3 aryl (nitro substituted aniline)-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-Nitro-aniline, (c) m- Nitro -aniline, (d) p- Nitro -aniline,

Results and discussion

Herein, we report the synthesis of various 1-Tetra-*O*-Benzoyl- β -D Glocosyl-3-aryl (nitro substituted aniline)-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 (nitro substituted aniline)-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[10-12] 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, 68.08; H, 5.16; N, 5.67; S, 6.48; Found: C, 68.12; H, 5.28; N, 5.72; S, 6.50.

On the basis of all above facts the product with m. p. 140ºC 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 30789 (Ar-H), 2875 (Ali C-H), 1728 (C=O), 1449 (C=N), 1229 (C-O), 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): 1028 (M^+), 579, 420, 150; Anal. Calcd for $C_{56}H_{50}N_5S_2O_{11}$: C, 65.11; H, 4.84; N, 6.78; S, 6.20; Found: C, 65.22; H, 4.92; N, 6.70; S, 6.18.

On the basis of all above facts the product with m. p. 145ºC was assigned the structure 1-tetra-O-Benzoyl- β -D Glocosyl-3-o-nitro-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
a	70%	0.69	140^0 C	5.72(5.67)	6.50(6.48)
b	85%	0.65	145^0 C	6.70 (6.78)	6.18(6.20)
c	68%	0.59	152^0 C	6.75 (6.78)	6.25(6.20)
d	83.6%	0.75	160^0 C	6.82 (6.78)	6.15 (6.20)

C and H analysis was found satisfactory in all cases.

Antimicrobial activity[13]:

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*, in nutrient agar medium. It has been observed that all the compounds showed good activity against bacteria.

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

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

Conclusion

In this research work, the characterizations of newly synthesized products were established on the basis of IR, ^{1}H NMR, & Mass spectral studies. Various various 1-Tetra-*O*-Benzoyl- β -D Glocosyl-3-aryl (nitro substituted aniline)-2-phenyl thiocarbamides, 2-*S*-benzyl-isohiocarbamide were synthesized and yield of product ranged from 68-83%.

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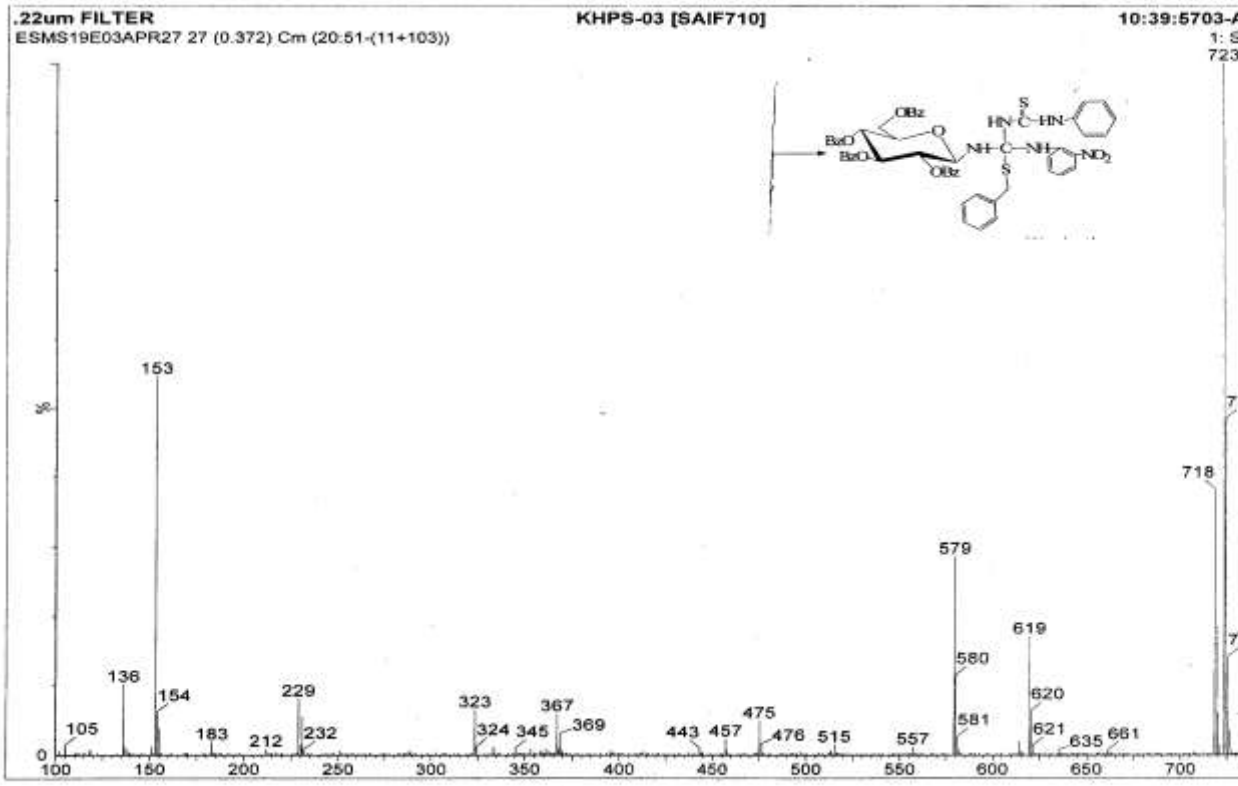

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SAIF

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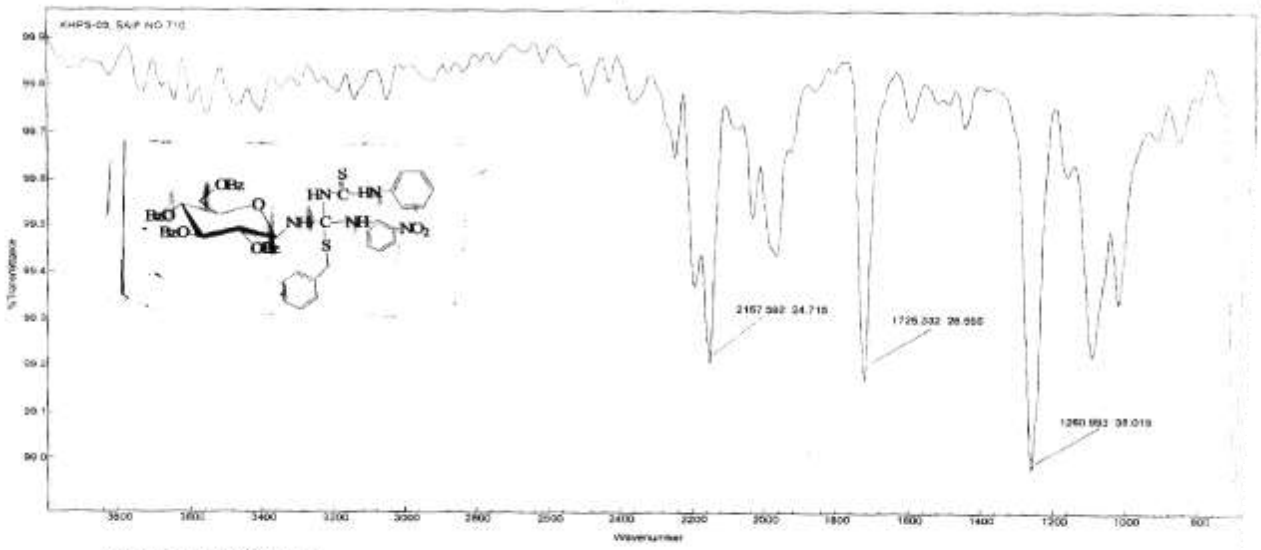

Analysed By :- Dr A.K.Mandwal

Seal and Signature :-