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Antimicrobial Activities of 3-aryl-4-*S*-benzyl-6-phenylimino-2-hepta-*O*-acetyl-β-D-maltosylimino-2,3-dihydro-1,3,5-thiadiazines (hydrochloride)

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ABSTRACT

Several 3-aryl-4-S-benzyl-6-phenylimino-2-hepta-O-acetyl-β-D-maltosylimino- 2,3-dihydro-1,3,5-thiadiazines (hydrochloride) were synthesized by the interaction of N-hepta-O-acetyl-β-D-maltosyl isocyanodichloride with 1-aryl-5-phenyl-2-S-benzyl-2,4-isodithiobiurets. N-hepta-O-acetyl-β-D-maltosyl isocyanodichloride was prepared for the first time by the excess chlorination of hepta-O-acetyl-β-D-maltosyl isothiocyanate. The identities of these newly synthesized N-maltosides have been established on the basis of usual chemical transformations and IR, ^{1}H NMR and Mass spectral studies. The title compounds have been assayed for their antimicrobial activity against gram-positive microorganisms as well as gram-negative microorganisms.

Keywords: N-maltosides, Thiadiazines, Antibacterial, Antifungal

INTRODUCTION

The chemistry of heterocyclic compounds continues to be an explore field in the carbohydrate chemistry. One of the most common and popular methods for preparing heterocyclic compounds is the cyclization of suitable compounds. Thiadiazines and their derivatives act as antifibrinolytic (Ozcelik *et al.,* 2007), antimicrobial (Chande *et al.,* 1988) cardiotonic (Ravens *et al.,* 1997), anesthetic, cardiovascular and hypometabolic agents (Chupakhin *et al.,* 1997). Also it may be used in agriculture as insecticides (Coburn *et al.,* 1982) and fungicides (Vicentini *et al.,* 2002). Literature survey also revealed that the heterocyclic derivatives of sugar possess antimicrobial (Bhagat and Deshmukh, 2005, Mahalle *et al.,* 2008, Agrawal and Deshmukh, 2010) and antitumor activity (Shusheng *et al.,* 2008). In view of the applications of *N*-maltosides in medicinal chemistry and many other ways, it appeared interesting to synthesize some *N*-maltosylated thiadiazines (hydrochloride).

The antimicrobial activities of all the target compounds against *Escherichia coli, Proteus vulgaris, Pseudomonas aeruginosa, Bacillus subtilis, Klebsiella pneumoniae, Staphylococcus aureus, Salmonella typhimurium, Aspergillus niger* and *Candida albicans* were evaluated. The antimicrobial bioassays indicated that some title compounds exhibited noteworthy antimicrobial effects against the above strains.

MATERIAL AND METHODS

The media was prepared by dissolving weighed ingredients and was sterilized at 121°C and 15 lbs/inch^2 pressure for 15 min. After sterilization it was cooled down at about 50° C and poured into sterile Petri plates and allowed to solidify. The plates were seeded with 24 hrs. Old active nutrient broth culture of the test organism in order to obtain lawn culture. A stainless-steel cork borer of 5 mm diameter was used to bore in the agar palates.

The compounds were taken at a concentration of 1mg/ml using dimethyl sulphoxide (DMSO) as a solvent. The drug solution was allowed to diffuse for about an hour into the medium. The plates were incubated at 37°C for 24 hr. for antibacterial activity and at 30°C for 48 hr for antifungal activity. The zone of inhibition observed around the wells after respective incubation was measured and interpreted by using antibiotic zone reader. The results were cited in Table 1.

RESULTS & DISCUSSION

Co-trimazine (100 µg/ml) was used as a standard for antibacterial activity and Fluconazole (100 µg/ml) was used as a standard for antifungal activity. The compounds 3-phenyl-4-*S*-benzyl-6-phenylimino-2-hepta-*O*-acetyl-β-D-maltosylimino-2,3-dihydro-1,3,5-thiadiazine (hydrochlorides) **(4a)** and 3-*p*-tolyl-4-*S*-benzyl-6-phenylimino-2-hepta-*O*-acetyl-β-D-maltosylimino-2,3-dihydro-1,3,5-thiadiazine (hydrochlorides) **(4d)** against *B. subtilis* and the compound 3-*m*-tolyl-4-*S*-benzyl-6-phenylimino-2-hepta-*O*-acetyl-β-D-maltosylimino-2,3-dihydro-1,3,5-thiadiazine (hydrochlorides) **(4c)** against *C. albicans* exhibit promising activity. The compounds 3-*o*-tolyl-4-*S*-benzyl-6-phenylimino-2-hepta-*O*-acetyl-β-D-maltosylimino-2,3-dihydro-1,3,5-thiadiazine (hydrochlorides) **(4b)** and 3-*m*-chloro-phenyl-4-*S*-benzyl-6-phenylimino-2-hepta-*O*-acetyl-β-D-maltosylimino-2,3-dihydro-1,3,5-thiadiazine (hydrochlorides) **(4f)** showed moderate to weak activity against fungi and no activity against all bacteria.

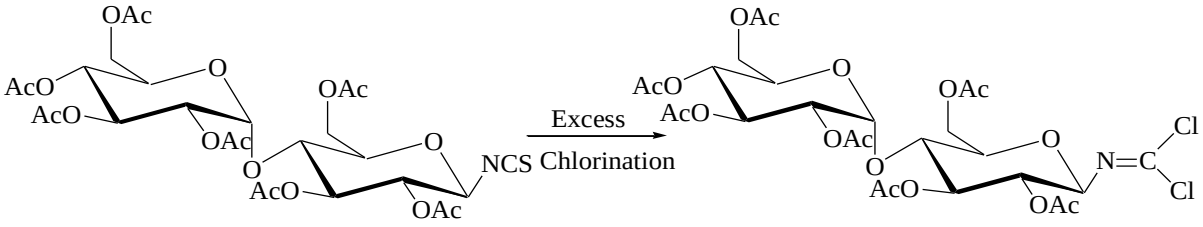
Table 1: Antimicrobial activities of some newly synthesized 3-aryl-4-*S*-benzyl-6-phenylimino-2-hepta-*O*-acetyl-β- D-maltosylimino-2,3-dihydro-1,3,5-thiadiazines (hydrochloride) (4a-g) (given in mm)

Compounds	*E. coli*	*P. vulgaris*	*Ps. aeruginosa*	*B. subtilis*	*K. pneumoniae*	*S. aureus*	*S. typhi*	*A. niger*	*C. albicans*
4a	+++	++	--	++++	+++	--	--	+++	+++
4b	--	--	--	--	--	--	--	++	+++
4c	--	--	--	--	--	--	--	--	++++
4d	++	--	--	++++	--	--	--	++	+++
4e	--	++	--	--	--	--	--	++	++
4f	--	--	--	--	--	--	--	+++	++
4g	++	--	++	+++	--	--	--	+++	+++

++++ Strong activity (above 18 mm)
+++ Moderate activity (above 14 to 18 mm)
++ Weak activity (above 8 – 14 mm)
- - Inactive (below 8 mm)
Bore size = 5 mm

Reaction Scheme

Scheme I



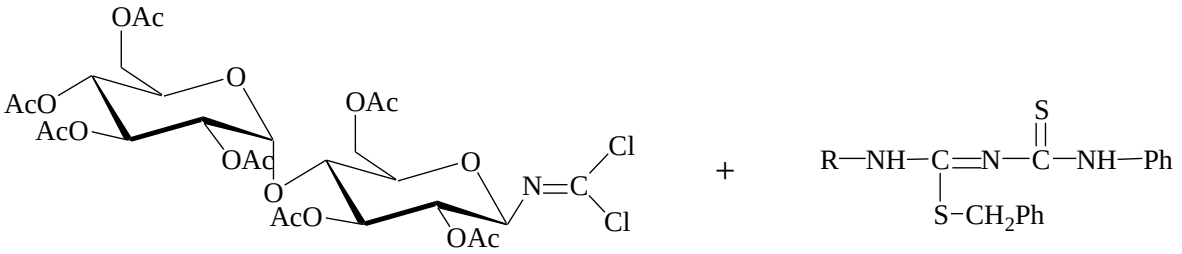
Hepta-*O*-acetyl-β–D-maltosyl isothiocyanate

(1)

N-hepta-*O*-acetyl-β–D-maltosyl isocyanodichloride

(2)

Scheme II



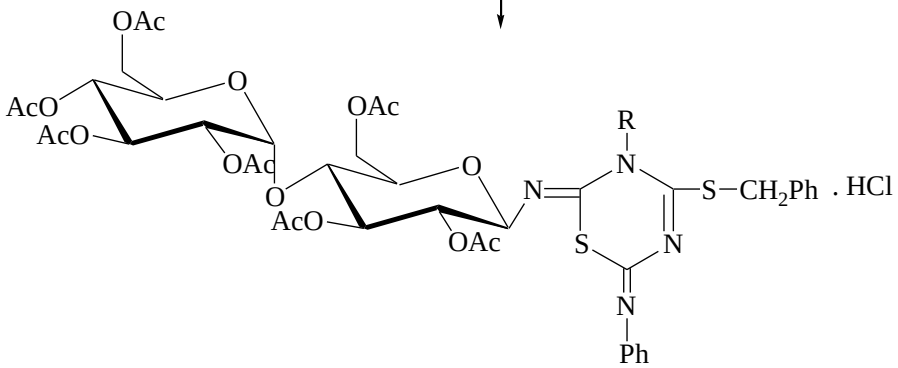
N-hepta-*O*-acetyl-β–D-maltosyl isocyanodichloride

(2)

1-aryl-5-phenyl-2-*S*-benzyl-2,4-isodithiobiurets

(3a-g)

Reflux, 2h | Chloroform



3-aryl-4-*S*-benzyl-6-phenylimino-2-hepta-*O*-acetyl-β-D-maltosylimino-2,3-dihydro-1,3,5-thiadiazines (hydrochloride) **(4a-g)**

Where, R = a) phenyl, b) *o*-tolyl, c) *m*-tolyl, d) *p*-tolyl, e) *o*-Cl-phenyl, f) *m*-Cl-phenyl, g) *p*-Cl-phenyl

CONCLUSION

From the results, it can be concluded that some of *N*-maltosylated thiadiazines (hydrochlorides) were synthesized and evaluated as antibacterial and antifungal agents. Almost many of them displayed strong to moderate activity against the tested strains of bacteria and fungi. Synthesized compounds were found to be sensitive towards *B. subtilis* and *C. albicans*.

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Conflicts of interest: The author stated that no conflicts of interest.

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