Int. J. Chem. Sci.: 11(1), 2013, 419-424
ISSN 0972-768X
www.sadgurupublications.com

SYNTHESIS, CHARACTERIZATION AND ANTIMICROBIAL STUDY OF NEW *S*-MALTOSYLATED 1,2,4-THIADIAZOLINES

U. W. KARHE and S. P. DESHMUKH*

P. G. Department of Chemistry, Shri Shivaji College, AKOLA – 444001 (M.S.) INDIA

ABSTRACT

A series of 2-aryl-5-phenylimino-3-*S*-hepta-*O*-benzoyl maltosyl-1, 2, 4-thiadiazolines **2** have been synthesized by the oxidative cyclization of *S*-hepta-*O*-benzoyl maltosyl-1-aryl-5-phenyl-2, 4-isodithiobiurets **1** by using bromine in chloroform as oxidizing agents. The identities of these new compounds have been established on the basis of chemical transformations and IR, ^{1}H NMR and Mass spectral studies. The antimicrobial study of these *S*-maltosides have been evaluated by using *Escherichia coli*, *Staphylococcus aureus*, *Proteus vulgaris*, *Pseudomonas aeruginosa*, *Candida albicance* and *Aspergillus niger*. The study reveals that most of the compounds show satisfactory antimicrobial activities.

Key words: Synthesis, Oxidative cyclization, 2, 4-isodithiobiurets, 1, 2, 4-thiadiazolines, Antimicrobial study.

INTRODUCTION

In organic chemistry, a series of heterocyclic compounds containing an unsaturated five member ring, which contains two carbons, two nitrogens and one sulphur atom are termed as thiadiazolines. Derivatives of thiadiazolines played a crucial role in history of heterocyclic compounds because of their wide variety of important biological properties such as antimicrobial, antioxidant, radio protective, and anti-leishmanial[1-3]. The synthesis and pharmacological evaluation of variety of glycosyl thiadiazolines have been reported[4-5].

In view of applications of these compounds, we report the synthesis of 2-aryl-5-phenylimino-3-*S*-hepta-*O*-benzoyl maltosyl-1, 2, 4-thiadiazolines **2** by the oxidative cyclization of *S*-hepta-*O*-benzoyl maltosyl-1-aryl-5-phenyl-2, 4-isodithiobiurets **1**.

*Author for correspondence; E-mail: karhe4787@gmail.com

EXPERIMENTAL

Melting points of all synthesized compounds were determined using open capillary tube on Mac digital melting point apparatus and were uncorrected. The IR spectrum was recorded in KBr Disks on Shimadzu IR affinity-1-FTIR spectrometer. The NMR spectrum was recorded in Brucker DRX-300 instruments operating at 300 mHz using $CDCl_3$ solution with TMS as internal standard. The mass spectrum was recorded on a THERMO Finnigan LCO Advantage max ion trop Mass Spectrometer. Specific rotations were measured on Equip-Tronics EQ-801 Digital Polarimeter. Thin layer chromatography (TLC) was performed on silica gel G for TLC (Merck) and spot were visualized by iodine vapours.

General procedure

Synthesis of S-hepta-O-benzoyl maltosyl-1-arylisothiocarbamides: *S*-hepta-*O*-benzoyl maltosyl-1-arylisothiocarbamides have been synthesized by the interaction of hepta-*O*-benzoyl maltosyl bromide with aryl thiocarbamides.

Synthesis of S-hepta-O-benzoyl maltosyl-1,5-diaryl-2,4-isodithiobiurets 1: *S*-hepta-*O*-benzoyl maltosyl-1, 5-diaryl-2, 4-isodithiobiurets have been synthesized by the interaction of *S*-hepta-*O*-benzoyl maltosyl-1-arylisothiocarbamides with phenyl isothiocyanate.

2-aryl-5-phenylimino-3-S-hepta-O-benzoyl maltosyl-1,2,4-thiadiazolines 2: 2-aryl-5-phenylimino-3-*S*-hepta-*O*-benzoyl maltosyl-1,2,4-thiadiazolines **2** has been synthesized by the oxidative cyclization of *S*-hepta-*O*-benzoyl maltosyl-1-aryl-5-phenyl-2,4-isodithiobiurets **1** by using bromine in chloroform as oxidizing agent.

RESULTS AND DISCUSSION

S-hepta-*O*-benzoyl maltosyl-1, 5-diphenyl-2, 4-isodithiobiuret **1a** (0.001 M, 1.34 g) was made into a paste with chloroform and to it was added bromine in chloroform (20% bromine solution in chloroform, v/v) drop by drop with stirring. The bromine in chloroform was added till an orange red sticky mass was obtained. It was then allowed to stand for 5-6 h. The sticky mass was washed several times with petroleum ether to removed excess of bromine and then dissolved it in ethanol and was basified by using NH_4OH the product was isolated as free base.

The IR, ^1H NMR and mass spectral analysis (Experimental) and elemental analysis (Table 1) clearly indicated the product and assign the structure as 2-phenyl-5-phenylimino-3-*S*-hepta-*O*-benzoyl maltosyl-1, 2, 4-thiadiazolines **2a.**

Table 1: Characterization of 2-aryl-5-phenylimino-3-*S*-hepta-*O*-benzoyl maltosyl-1, 2, 4-thiadiazolines 2

S. No.	Product	Yield (%)	R_f Value	M.P. (^oC)	$[\alpha]_D^{31}$ (*c* in $CHCl_3$)	Analysis (%): Found (Required)	
						N	S
1	**2a**	69	0.75	110	$+191.66^o$ (c,0.06)	3.17 (3.37)	4.39 (4.49)
2	**2b**	70	0.78	116	-75^o (c, 0.06)	3.21 (3.29)	4.31 (4.39)
3	**2c**	72	0.68	112	-105.14^o (c, 0.07)	3.22 (3.29)	4.29 (4.39)
4	**2d**	68	0.62	121	$+57.14^o$ (c, 0.07)	3.19 (3.29)	4.25 (4.39)
5	**2e**	62	0.92	136	-41.17^o (c, 0.085)	3.24 (3.34)	4.41 (4.45)
6	**2f**	71	0.88	118	$+46.15^o$ (c, 0.065)	3.28 (3.34)	4.38 (4.45)

C and H analysis were found satisfactory in all cases.

Similarly, when the reaction was extended to other isodithiobiurets **1b-f** the corresponding 1, 2, 4-thiadiazolines **2b-f** has been isolated.

Spectral analysis[6-9]

2a. IR (KBr) : ν 3061 (Aromatic C-H), 2962 (Aliphatic C-H), 1730 (C=O), 1492 (C=N), 1454 (C-N), 1269 (C-O), 1093, 1026 and 937 (characteristic of maltose) and 709 (C-S); ^{1}H NMR ($CDCl_3$): δ 8.047- 7.262 (45 H, m, Aromatic protons), 6.212-3.72 (14 H, m, maltosyl protons); MS (*m/z*): 1337 (M^+), 1235, 1100, 1089, 1025, 984, 845, 579, 475.

2b. IR (KBr) : ν 3061 (Aromatic C-H), 2962 (Aliphatic C-H), 1730 (C=O), 1492 (C=N), 1452 (C-N), 1269 (C-O), 1095, 1026 and 937 (characteristic of maltose) and 711 (C-S); ^{1}H NMR ($CDCl_3$): δ 8.102- 7.213 (44 H, m, Aromatic protons), 6.13-3.911 (14 H, m, maltosyl protons); MS (*m/z*): 1371 (M^+), 1129, 1088, 1089, 1026, 984, 579.

2e. IR (KBr) : ν 3061 (Aromatic C-H), 2958 (Aliphatic C-H), 1730 (C=O), 1492 (C=N), 1454 (C-N), 1269 (C-O), 1093, 1026 and 937 (characteristic of maltose) and 709 (C-S); ^{1}H NMR ($CDCl_3$): δ 8.101-7.262 (44 H, m, Aromatic protons), 6.211-3.176 (14 H, m,

maltosyl protons), 1.947 (3H, m, CH_3); MS (*m/z*): 1351 (M^+), 1093, 1129, 1088, 1026, 984, 758, 579.

Antimicrobial study

All the compounds have been screened for both antibacterial and antifungal activity using cup plate agar diffusion method[10-11] by measuring the inhibition zone in mm. the compounds were taken at a concentration of 1 mg/mL using dimethyl sulphoxide (DMSO) as solvent. The compounds were screen for antibacterial activity against *Escherichia coli, Staphylococcus aureus, Proteus vulgaris and Pseudomonas aeruginosa* in nutrient agar medium. Amikasin (100 µg/mL) was used as standard for antibacterial activity. The compounds were screen for antifungal activity against *Aspergillus niger* and *Candida albicance* in potato dextrose agar medium. fluconazole (100 µg/mL) as standard for antifungal activity. The results are presented in Table 2.

Table 2: Antimicrobial activities of 2-aryl-5-phenylimino-3-*S*-hepta-*O*-benzoyl maltosyl-1, 2, 4-thiadiazolines 2

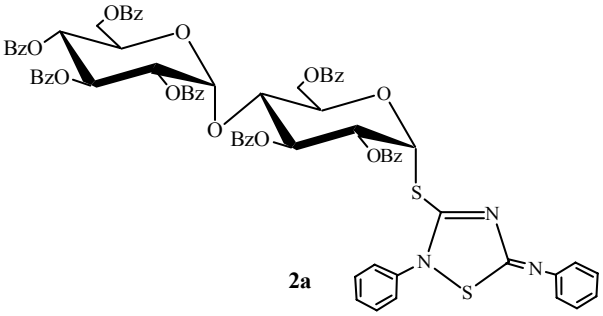
Compds.	Antibacterial**				Antifungal**	
	E. coli	***S. aureus***	***P. vulgaris***	***Ps. aeruginosa***	***C. albicance***	***A. niger***
2a	16	13	14	16	14	16
2b	17	18	16	16	14	16
2c	18	17	18	15	16	15
2d	20	16	15	15	15	17
2e	16	16	22	14	15	16
2f	16	13	16	15	16	17
Amikacin	19	23	22	24	-	-
Fluconazole	-	-	-	-	25	26

**zone of inhibition in mm (15 or less) resistance, (16-20 mm) moderate and (more than 20 mm) sensitive. *Escherichia coli* (*E. coli*), *Staphalococcus aureus* (*S. aureus*), *Proteus vulgaris* (*P. vulgaris*), *Psudomonas auriginosa* (*Ps. auriginosa*), *Candida albicancs* (*C. albicancs*) and *Aspergillus niger* (*A. niger*)

It has been observed that some of these compounds exhibited interesting microbial activities. **2c** and **2d** exhibited most significant activity against *E. coli*, **2b** and **2c** exhibited most significant activity against *S. aureus*, **2c** and **2e** exhibited most significant activity

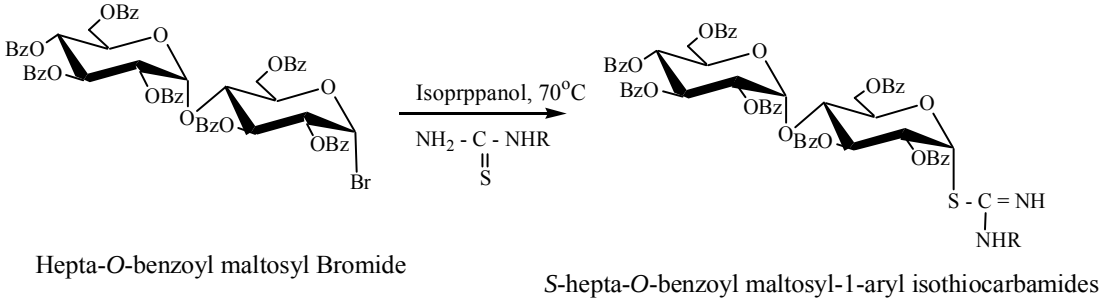
against *P. Vulgaris,* **2a** and **2b** exhibited most significant activity against *P. aeruginosa* respectively. All the other compounds exhibited low to moderate activity.

Structure



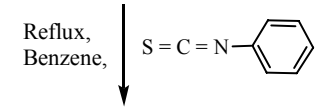
2a

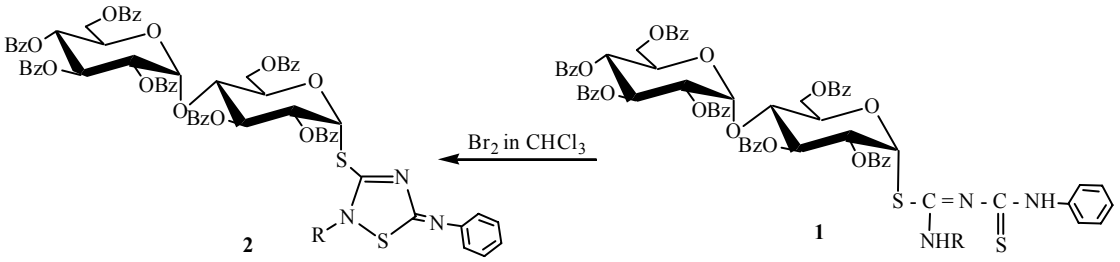
2-phenyl-5-phenylimino-3-*S*-hepta-*O*-benzoyl maltosyl-1, 2, 4-thiadiazolines



Hepta-*O*-benzoyl maltosyl Bromide

S-hepta-*O*-benzoyl maltosyl-1-aryl isothiocarbamides





2 **1**

2-aryl-5-phenylimino-3-*S*-hepta-*O*-benzoyl maltosyl-1, 2, 4-thiadiazolines

S-hepta-*O*-benzoyl maltosyl-1-aryl-5-phenyl-2, 4-isodithiobiurets

Scheme

Where, Bz = COC_6H_5

R = a) Phenyl, b) *o*-Cl Phenyl, c) *m*-Cl Phenyl, d) *p*-Cl Phenyl, e) *o*-tolyl, f) *p*-tolyl.

The results of antifungal activities are also tabulated in Table 2. **2c** and **2f** are effective towards *C. albicance,* **2d** and **2f** inhibited *A. niger*. While other compounds inhibited moderate to low activity.

ACKNOWLEDGEMENT

Authors are thankful to SAIF, C. D. R. I., Lucknow for providing spectral data and also Dr. S. G. Bhadange, Principal, Shri Shivaji College, Akola for providing necessary facilities.

REFERENCES

1. P. Manna, R. Singh, K. Naranga, S. K. Manna, Indian J. Chem., **9(44B)**, 1880 (2005).
2. N. Siddiquia, P. Ahujaa, W. Ahsana, S. N. Pandeyab and M. Shamsher Alama, J. Chem. Pharm. Res., **1(1)**, 19 (2009).
3. A. Gupta, P. Mishra, S. K. Kashaw, V. Jatav and J. P. Stables, Eur. J. Med. Chem.**, 43(4)**, 749 (2008).
4. S. K. Bhagat and S. P. Deshmukh, J. Indian Chem. Soc., **82**, 1022 (2005).
5. D. V. Mangate and S. P. Deshmukh, Heteroatom Chemistry, **18(2)**, 390 (2007).
6. R. M. Silverstein, G. C. Bassler and T. C. Morill, Spectrometric Identification of Organic Compound, 5th Ed., Sons, Inc, New York (2001) p. 100, 127.
7. D. H. Williams and I. Fleming, Spectroscopic Methods in Organic Chemistry, IV, Tata Mc Graw Hill (1991) p. 42.
8. S. Cao, F. D. Tropper and R. Roy, Chem. Inform., **26(42)**, 17 (1995).
9. R. Varma, S. Y. Kulkarni, C. I. Jose and V. S. Pansare, Carbohydr. Res., **25**, 133 (1984).
10. F. Kawangh, Analytical Microbiology, Academic Press, New York (1963).
11. British Pharmacopaeia-II, Biological Assay and Tests, The Stationary Office Ltd., London (1998) A-205.

Accepted : 18.12.2012