Int. J. Chem. Sci.: 10(2), 2012, 889-894
ISSN 0972-768X
www.sadgurupublications.com

ISOTHIOBIURETS AS AN ANTIBACTERIAL AND ANTIFUNGAL COMPOUNDS

P. T. AGRAWAL[*] and S. P. DESHMUKH[a]

P.G. Department of Chemistry, Shri R. L. T. College of Science, AKOLA – 444001 (M.S.) INDIA
[a]P.G. Department of Chemistry, Shri Shivaji College, AKOLA – 444001 (M.S.) INDIA

ABSTRACT

Isothiobiurets and its derivative are found to be having physiological and potential chemotherapeutic properties. In view of this certain 1-hepta-O-benzoyl-β-D-lactosyl-5-substituted-2-S-benzyl-2-isothiobiurets have been synthesized for the first time by the interaction of 1-hepta-O-benzoyl-β-D-lactosyl-2-*S*-benzyl isothio-carbamide with various isocyanates. The structures of these new 2-isothiobiurets have been established on the basis of usual chemical transformations and IR, NMR and Mass spectral analysis. The polarimetric study of title compounds has been carried out. All the compounds are screened for their antibacterial and antifungal activity.

Key word: Iosothiocarbamide, Isocyantes, Isothiobiurets.

INTRODUCTION

In recent years the chemistry of thiobiurets and related compounds has attracted increasing attention. Physiological and potential chemotherapeutic[1] properties of numerous derivatives have been studied, and possible technical applications, particularly in the field of plastic and resins are embedded in an intensive patent literature. Carbohydrate compounds also shows antibacterial and antifungal activity[2,3].

Isothiobiurets and its alkylated derivatives act as antipyretics when administered subcutaneously (to rabbits). Lethal doses cause decreased blood pressure, lung edema and general collapse[4].

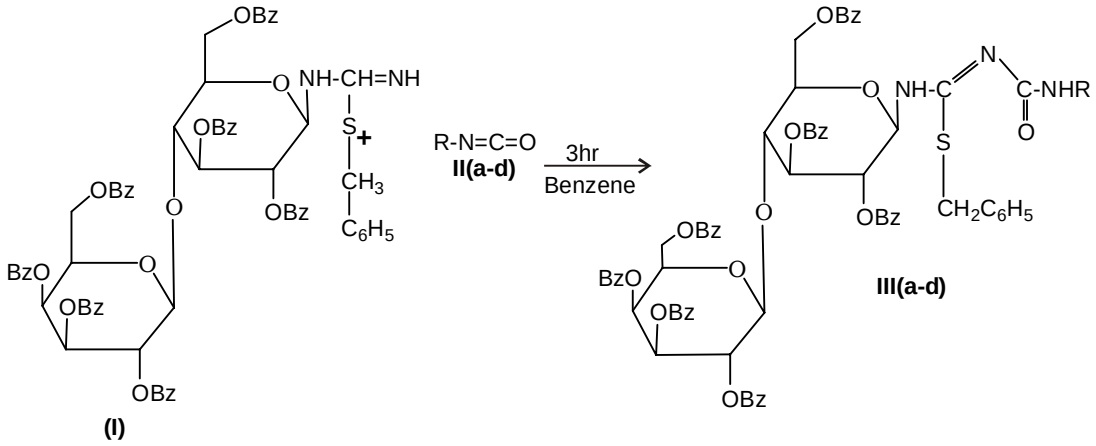
In our laboratory, we have prepared several S-hepta-O-acetyl-lactosyl-1-aryl-5-phenyl-2-isothiobiurets and tested for their biological activity[5,6]. So in view of our interest in the synthesis of new ever type of N-lactosylated isothiobiurets, here we have reported the

[*]Author for correspondence; E-mail: poonamagrawal2575@rediffmail.com

simple method for the synthesis of isothiobiurets having lactosyl substituent by the interaction of hepta-O-benzoyl-β-D-lactosyl-2-*S*-benzyl isothiocarbamide with various isocyanates.

EXPERIMENTAL

Condensation of 1-hepta-O-benzoyl-β-D-lactosyl-2-*S*-benzyl isothiocarbamide (I) has been carried out with 1-hepta-O-acetyl-β-D-lactosyl isocyanate (II a-d) in benzene medium for 3 hr. has been carried out to give 1-hepta-O-benzoyl β-D-lactosyl-5-substituted-2-S-benzyl-2-monothiobiurtes (III a-d). The structure of the products were confirmed by spectral analysis (IR[7], NMR[8]and Mass[9]). The specific rotations of the products were also recorded[10].



1-hepta-O-benzoyl-β-D-lactosyl-2-S benzyl isothiocarbamide

1-hepta-O-benzoyl-β-D-lactosyl-5-substituted-2-S-benzyl-2 monothiobiurtes

Scheme 1

Where, R = Where,

R = a) Hepta-O-acetyl-β-D-lactosyl,

b) Hepta-O-*acetyl*-β-D-maltosyl,

c) Tetra-O-acetyl-β-D-glucosyl,

d) Tetra-O-acetyl-β-D-galactosyl.

RESULTS AND DISCUSSION

Melting points were taken in open capillary tubes and are uncorrected. Specific rotations were measured on Equip-Tronics Digital Polarimeter at 28^{o}C in $CHCl_3$. IR spectra

were recorded on Perkin-Elmer spectrum RXI FTIR spectrophotometer (4000-450 cm^{-1}). ^1H NMR were recorded in $CDCl_3$ on Bruker DRX-300 spectrometer operating at 300 MHz. The Mass spectra were recorded on Jeol-SX-102 (FAB) instrument.

Preparation of 1-hepta-O-benzoyl-β-D-lactosyl-2-*S*-benzyl isothiocarbamide (I)

The required 1-hepta-O-benzoyl-β-D-lactosyl-S-benzyl-isodithiocarbamide was prepared by already known method. Details of a typical preparation are as follows:

To an ethanolic suspension of thiocarbamide (0.005M, 6 g in 30 mL) was added benzyl chloride (0.005 M, 3.4 g) and the reaction mixture was refluxed for 90 min. Afterwards, it was cooled and rendered basic with dilute ice cold ammonium hydroxide a sticky residue was obtained which on standing for 1 or 2 hr. solidified (5 g). It was filtered, washed with petroleum ether.

Preparation of sugar isocyanate

To a suspension of hepta-O-acetyl-α-D-lactosyl-bromide (0.03 M, 21 g) in sodium dried xylene (80 mL) was added lead cyanate (0.03 M, 9 g). The reaction mixture was refluxed gently for 3 hr. with frequent shaking. This solution was then cooled and the liberated lead bromide was removed by filtration. The xylene filtrate was then treated with petroleum ether (60-80^oC) with stirring, a pale yellow solid. The products were purified by chloroform – petroleum ether.

Synthesis of 1-hepta-O-benzoyl-β-D-lactosyl-substituted-2-*S*-benzyl-2-isothiobiurets (III a-d)

To a benzene solution of 1-hepta-O-benzoyl-β-D-lactosyl-2-S-benzyl isothiocarbamide (I) (0.005 M, 3.6 g in 40 mL) was added benzene solution of 1-hepta-O-acetyl-β-D-lactosyl isocyanate (II a-d) (0.005 M, 1.9 g, 20 mL) and reaction mixture was refluxed over boiling water bath for 3 hr. After heating solvent benzene was distilled off and the sticky mass obtained as residue was triturated several times with petroleum ether to afford a solid (III a-d) (Table 1). The products were purified by chloroform – petroleum ether.

Spectral data

3a. **IR(KBr):** 3065.4 cm^{-1} (Ar-H stretching),1729 cm^{-1} (C = O), 1600 cm^{-1} (C = N), 850.5 cm^{-1} (lactosyl C-H deformation), 708.9 cm^{-1} (C-H aromatic); **^{1}H NMR (ppm) :** δ7.12-7.07 (10H, m, Ar-H), 8.08-7.89 (2H, S, N-H) 7.14-5.73 (20H, m, lactosylprotons), 4.57-4.21 (5H, d, $-OCH_2$), 5.91-5.73 (35H, m, 7-COC_6H_5); 4.57-4.21 (21H, S,7-$COCH_3$) **Mass (m/z):** 1879 (M^+),1880, 1052, 579, 391, 335, 105 .

3c. IR(KBr): 3065.4 cm^{-1} (Ar-H stretching), 1747cm^{-1} (C = O), 1600 cm^{-1} (C = N), 850.5 cm^{-1} (lactosyl C-H deformation), 708.9 cm^{-1} (C-H aromatic); **^{1}H NMR (ppm):** δ 7.12-7.07 (10H, m, Ar-H), 8.08-7.89 (2H, S, N-H) 7.14-5.73 (20H, m, lactosylprotons), 4.57-4.21 (5H, d, -OCH_2), 5.91-5.73 (35H, m, 7-COC_6H_5); 4.57-4.21 (12H, S, 4-$COCH_3$) **Mass (m/z):** 1594 (M^+), 1595, 1053, 579, 391, 335, 105.

Table 1: Synthesis of 1-hepta-O-benzoyl-β-D-lactosyl-5-Substituted-2-S-benzyl-2-isothiobiurets (III a-d)

Reactants-

I. 1-hepta-O-benzoyl-β-D-lactosyl-2-S-benzyl isothiocarbamide (I):

II. Sugar isocyanate (II a-d):

Product	Melting point (^{o}C)	Yield (%)	Analysis found (requires)		$[\alpha]^D_{28}$ (c,0.156, $CHCl_3$)
			N (%)	S (%)	
3a	160^{o}C	80	2.21 (2.23)	1.62 (1.70)	+113^o
3b	110-112^{o}C	82	2.19 (2.23)	1.52 (1.70)	+95^o
3c	120-122^{o}C	86	2.51 (2.63)	1.89 (2.00)	+98^o
3d	115^{o}C	85	2.41 (2.63)	1.89 (2.00)	+138^o

Antimicrobial activities

All the compounds have been screened for both antibacterial and antifungal activity using cup plate agar diffusion method[11] by measuring the inhibition zone in mm. The compounds were taken at a concentration of 1 mg/mL using dimethyl sulphoxide as solvent. Amikacin (100 ůg/mL) was used as a standard for antibacterial and *fluconazole* (100 ůg/mL) as a standard for antifungal activity. The compounds were screened for antibacterial activity against *Escherichia coli, Staphylococcus aureus, Proteus vulgaris, and Salmonella typhi* in nutrient agar medium and for antifungal activity against *Candida guilliermondii* and *Microsporum* in potato dextrose agar medium.

From the Table 2, it has been observed that these compounds exhibited interesting microbial activities. **IIIc** and **IIId** exhibited most significant activity against *Salmonella* and *E. coli* while **IIIa** inhibited *S. aureus* and *P. vulgaris*. All other compounds exhibited low to moderate activity.

Table 2: Antimicrobial activity of compounds (III a-d)

Compd. No.	Antibacterial**				Antifungal**	
	E. coli	*S. aureus*	*P. vulgaris*	*S. typhi*	*C. Guillier mondii*	*A. Niger*
III a	17	22	23	16	18	17
III b	18	18	17	16	21	20
III c	23	19	18	21	20	22
III d	23	19	17	22	20	22
Amikacin	18	21	23	24	-	-
Fluconazole	-	-	-	-	24	25

*including the well diameter of 8 mm.

**zone of inhibition in mm (15 or less) resistance,
(16-20 mm) moderate and (more than 20 mm) sensitive

Amongst the compounds tested for antifungal activity,compounds **III b**, **III c** and **III d** are active against *A. niger* and C. *guilliermondii*. All other compouns show low to moderate activity.

ACKNOWLEDGEMENT

Authors are thankful to RSIC, CDRI Lucknow for providing the spectra and also to Dr. S.G. Bhadange, Principal, Shri Shivaji College, Akola for providing necessary facilities.

REFERENCES

1. O. Mellet and F. Gareia, Sulphur Reports, **19**, 61 (1996).
2. P. T. Agrawal and S. P. Deshmukh, J. Indian. Chem. Soc., **86**, 645-648 (2009)**.**
3. P. T. Agrawal and S. P. Deshmukh, Int. J. Chem. Sci., **7(2)**, 775-784 (2009).
4. E. Hesse and C. Taubmann, Arch. Exptl. Pathol Pharmakol., **113**, 2511 (1929).
5. D. V. Mangte and S. P. Deshmukh, Ind. J. Chem., **45B**, 1285-1287 (2006).
6. M. Lacova, J. Chovancova , O. Hyblova and S. Varkonda, Chem. Pap., **44**, 131 (1990).
7. R. M. Silverstein and G. C. Bassler, T. C. Morril, Spectrometric Identification of Organic Compounds, 5th Ed., John Wiley and Sons, INC, New York (2003) pp. 108-123.

8. N. B. Colthup, L. H. Daly and S. E. Wiberley, Introduction to Infrared and Raman Spectroscopy, Academic Press, New York (2003) pp. 279.

9. D. H. Williams and I. Flemming, Spectroscopic Methods in Organic Chemistry, 4th Ed., Tata McGraw-Hill Publication, New Delhi (2003) pp. 40-53.

10. Arnold Weissberger, Physical Methods of Organic Chemistry, Part II, 2nd Ed., Interscience Publisher, INC, New York (2005).

11. F. Kavangh, Analytica Microbiology, Academic Press, New York (1963).

Revised : 19.01.2012 *Accepted : 20.01.2012*