

# SYNTHESIS OF 2-HEPTA-*O*-BENZOYL- $\beta$ -D-LACTOSYLIMINO-3-ARYL-4-S-BENZYL-6-PHENYLIMINO-2, 3-DIHYDRO-1, 3, 5-THIADIAZINE (HYDROCHLORIDES)

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## ABSTRACT

A new series of 2-hepta-*O*-benzoyl- $\beta$ -D-lactosylimino-3-aryl-4-S-benzyl-6-phenylimino-2, 3-dihydro-1, 3, 5-thiadiazines (Hydrochlorides) have been prepared by the interaction of 1-aryl-5-phenyl-2-S-benzyl-2, 4-isodithiobiurets and hepta-*O*-benzoyl- $\beta$ -D-lactosyl isocynodichloride. The structures of this new N-lactosylated -1, 3, 5-thiadiazines have been established on the basis of usual chemical transformations and IR, <sup>1</sup>HNMR and Mass spectral analysis.

**Keyword:** 2, 4-isodithiobiurets, hepta-*O*-benzoyl- $\beta$ -D-lactosyl-isocynodichloride, 1, 3, 5-thiadiazines.

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## INTRODUCTION

Very few compounds containing thioamide group and having lactosyl substituent on nitrogen are known which have been studied for their biological activity such N-lactosylated derivatives exhibit a wide range of medicinal activities, such as antiviral, antidiabetic, analgesic, antitumor and some other activities<sup>1,2</sup>. Likewise sugar with heterocyclic nucleus are known for having variety of biological<sup>3-6</sup>, pharmacological<sup>7-8</sup> properties and many of them function as therapeutic agents<sup>9-10</sup>. A simple method for the synthesis of 1, 3, 5 thiadiazines has been reported. This was essentially based on the reaction of hepta-*O*-benzoyl- $\beta$ -D-lactosyl isocynodichloride with thioamide group containing compounds<sup>11-12</sup>. Here is reported the synthesis of several N- lactosylated- 1, 3, 5-thiadiazine (hydrochlorides) prepared by the reaction of 1-aryl-5-phenyl-2-S-benzyl-2, 4-isodithiobiurets with hepta-*O*-benzoyl- $\beta$ -D-lactosyl isocynodichloride. The required 1-aryl-5-phenyl-2-S-benzyl-2, 4 isodithiobiurets were obtained by the reaction of 1-aryl-S-benzyl isothiocarbamides with phenyl isothiocyanates.

## EXPERIMENTAL

All chemicals were research grade. Melting points were taken in open capillary tubes and are uncorrected. IR spectra were recorded in Nujol, KBr on a FT-IR Perkin-Elmer RXI (4000-450cm<sup>-1</sup>) spectrophotometer. <sup>1</sup>H NMR measurement were performed on a Bruker DRX-300 (300 MHz FT NMR) NMR spectrometer in CDCl<sub>3</sub> solution with TMS as an internal reference. The Mass spectra were recorded on a THERMO Finnigan LCQ Advantage max ion trap Mass spectrometer. Optical rotation [ $\alpha$ ]<sub>D</sub><sup>31</sup> measured on a Equip-Tronics Digital Polarimeter EQ-800 at 31<sup>0</sup> c in CHCl<sub>3</sub>. Thin layer chromatography (TLC) was performed on silica gel G for TLC (Merck) and spots were visualized by iodine vapour. The compounds described in this paper were first time synthesized by the multistep reaction protocol.

### Synthesis of hepta-*O*-benzoyl- $\beta$ -D-lactosyl isocynodichloride(1)

The hepta-*O*-benzoyl- $\beta$ -D-lactosyl isocynodichloride was prepared by the interaction of hepta-*O*-benzoyl- $\beta$ -D-lactosyl isothiocyanate and excess of chlorine in chloroform medium.

### Synthesis of 1-aryl-5-phenyl-2-S-benzyl-2, 4-isodithiobiurets(2a-f)

Several 1-aryl-5-phenyl-2-S-benzyl-2, 4-isodithiobiurets have been prepared by the interaction of 1 aryl-2-S-benzyl-thiocarbamide and phenyl isothiocyanate in benzene medium.

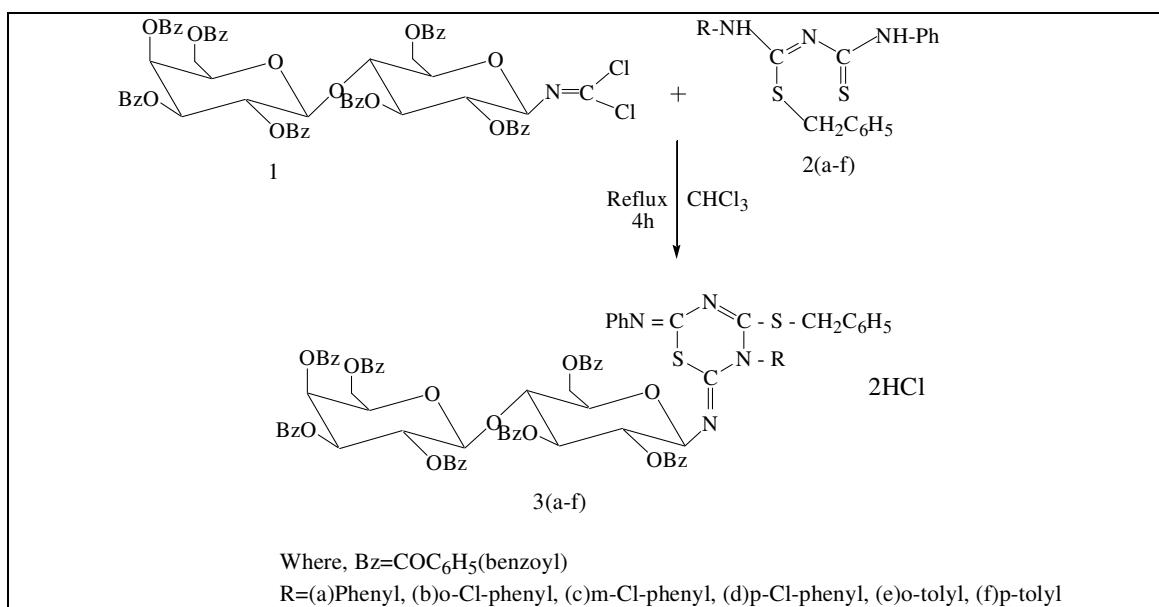
### Synthesis of 2-hepta-*O*-benzoyl- $\beta$ -D-lactosylimino-3-aryl-4-*S*-benzyl-6-phenylimino-2, 3-dihydro-1, 3, 5-thiadiazines (hydrochloride) (3a-f)

A solution of hepta-*O*-benzoyl- $\beta$ -D-lactosyl isocynodichloride(1) [0.005M, in 15 ml  $\text{CHCl}_3$ ] was added to a solution of 1-phenyl-5-phenyl-2-*S*-benzyl- 2, 4 isodithiobiurets [0.005M, 15 ml  $\text{CHCl}_3$ ] (2a) and the reaction mixture was reflux for 4h. Afterwards the solvent was distilled off to obtain a sticky residue. This residue was triturated with petroleum ether (60-80<sup>0</sup> c) to afford a pale yellow solid (3a). The product was purified by chloroform – petroleum ether.

On extending the reaction of 1 hepta-*O*-benzoyl- $\beta$ -D-lactosyl isocynodichloride (1) with 1-aryl-5-phenyl-2-*S*-benzyl-2, 4 –isodithiobiurets(2b-f) several 2-hepta-*O*-benzoyl- $\beta$ -D-lactosylimino-3-aryl-4-*S*-benzyl-6-phenylimino-2, 3-dihydro-1, 3, 5-thiadiazines (hydrochloride)(3b-f) have been isolated. IR, <sup>1</sup>HNMR and Mass spectra of the compound were also recorded.

(3a) Yield-2.7g(90.0%); m.p.-140-144<sup>0</sup>c;  $[\alpha]_D^{31} +31.8$  (c,0.1gm in  $\text{CHCl}_3$ );  $R_f$ -0.69(petroleum ether:EtoAc 1:1); IR- $\nu$ 3065.3(Ar-H); 2955.1(ali C-H);1728.5(C=O); 1603.6(C=N); 1267.8(C-O); 1097.0(charecteristic of lactose); 709(C-S); <sup>1</sup>HNMR ( $\delta$  in ppm,  $\text{CDCl}_3$ )  $\delta$ 8.19-7.12(50H, m, 7C<sub>6</sub>H<sub>5</sub>CO, 3C<sub>6</sub>H<sub>5</sub>);  $\delta$ 6.01-3.52 (16H, m, lactosyl ring protons, S-CH<sub>2</sub>), Mass(m/z): 1527(M<sup>+</sup>), 1487(M-N<sub>2</sub>S),1053(HBL<sup>+</sup>), 932(HBL-C<sub>7</sub>H<sub>5</sub>O<sub>2</sub>),579(TBG<sup>+</sup>),377(TBG-C<sub>6</sub>H<sub>5</sub>O, C<sub>6</sub>H<sub>5</sub>O<sub>2</sub>) 232(HBL-TBG, 2C<sub>7</sub>H<sub>5</sub>O<sub>2</sub>) (Found:C,65.30; H, 4.38; N, 3.18; S,4.20 calculated for C<sub>83</sub>H<sub>66</sub>O<sub>17</sub>N<sub>4</sub>S<sub>2</sub>.2HCl requires C, 65.25; H, 4.32; N,3.14; S4.19%)

(3b) Yield 1.5g(76.53%); m.p.-137-140<sup>0</sup>c;  $[\alpha]_D^{31} -20$  (c,0.1 in  $\text{CHCl}_3$ );  $R_f$  0.73 (petroleum ether :EtOAc 1:1) (Found: C,63.79; H, 4.18; N,3.56; S,4.15 calculated for for C<sub>83</sub>H<sub>65</sub>O<sub>17</sub>N<sub>4</sub>S<sub>2</sub>Cl.2HCl requires C,63.84; H,4.16; N,3.58; S,4.10%)



(3c) Yield-2.7g (90.69%); m.p.-139-141<sup>0</sup>c;  $[\alpha]_D^{31} +53.8$  (c,0.1gm in  $\text{CHCl}_3$ );  $R_f$ -0.60(petroleum ether:EtoAc 1:1); IR-  $\nu$  3065.8(Ar-H); 2955.8(ali C-H);1728.4(C=O); 1481.4(C=N); 1599.6(S-C=N),1268.9(C-N),1175 (C-O); 1097.0(charecteristic of lactose);756.1(C-S-C) 709(Benzene ring);507.8(C-Cl) ; <sup>1</sup>HNMR ( $\delta$  in ppm,  $\text{CDCl}_3$ )  $\delta$ 8.3-6.9(49H, m, 7C<sub>6</sub>H<sub>5</sub>CO, 2C<sub>6</sub>H<sub>5</sub>,C<sub>6</sub>H<sub>4</sub>);  $\delta$ 6.01-3.51 (16H, m, lactosyl ring protons, S-CH<sub>2</sub>), Mass(m/z): 1560(M<sup>+</sup>),1488(M-2HCl),1053(HBL<sup>+</sup>),579(TBG<sup>+</sup>),444(TBG-C<sub>8</sub>H<sub>7</sub>O<sub>2</sub>), 232(HBL-TBG, 2C<sub>7</sub>H<sub>5</sub>O<sub>2</sub>) (Found:C,63.76; H, 4.13; N, 3.60; S,4.12 calculated for C<sub>83</sub>H<sub>65</sub>O<sub>17</sub>N<sub>4</sub>S<sub>2</sub>Cl.2HCl requires C, 63.84; H, 4.16; N,3.58; S4.10%)

(3d) Yield 2.8g (94.18%); m.p.-152-153<sup>0</sup>c;  $[\alpha]_D^{31} +80$ (c,0.1 in  $\text{CHCl}_3$ );  $R_f$  0.55 (petroleum ether :EtOAc 1:1) (Found: C,63.80; H, 4.20; N,3.52; S,4.14 calculated for for C<sub>83</sub>H<sub>65</sub>O<sub>17</sub>N<sub>4</sub>S<sub>2</sub>Cl.2HCl requires C,63.84; H,4.16; N,3.58; S,4.10%).

(3e) Yield 2.7g (91.66%); m.p.-131-133<sup>0</sup>c;  $[\alpha]_D^{31} +93.8$ (c,0.1 in CHCl<sub>3</sub>); R<sub>f</sub> 0.62 (petroleum ether :EtOAc 1:1) (Found: C,65.40; H, 4.40; N,3.65; S,4.19 calculated for for C<sub>84</sub>H<sub>68</sub>O<sub>17</sub>N<sub>4</sub>S<sub>2</sub>.2HCl requires C,65.45; H,4.41; N,3.63; S,4.15%)

(3f) Yield-2.6g (86.49%); m.p.161-163<sup>0</sup>c;  $[\alpha]_D^{31} +130$  (c,0.1gm in CHCl<sub>3</sub>);R<sub>f</sub>-0.72(petroleum ether:EtoAc 1:1); IR(KBr)-  $\nu$  3065.2(Ar-H); 2957.9(ali C-H);1728.7(C=O); 1602.2(C=N); 1562.1(-S-C=N-) 1269.1(C-N),1176.2 (C-O); 1098(characteristic of lactose);756.5(C-S-C), 709.9(Benzene ring);cm<sup>-1</sup>; <sup>1</sup>HNMR ( $\delta$  in ppm, CDCl<sub>3</sub>)  $\delta$ 8.25-6.92(49H, m, 7C<sub>6</sub>H<sub>5</sub>CO, 2C<sub>6</sub>H<sub>5</sub>,C<sub>6</sub>H<sub>4</sub>);  $\delta$ 5.53-3.52 (16H, m, lactosyl ring protons, S-CH<sub>2</sub>),  $\delta$  2.4 (3H,S,Ar-CH<sub>3</sub>)Mass(m/z): 1540(M<sup>+</sup>),1468(M-2HCl),1053(HBL<sup>+</sup>),579(TBG<sup>+</sup>), 232(HBL-TBG, 2C<sub>7</sub>H<sub>5</sub>O<sub>2</sub>) (Found:C,65.42; H, 4.38; N, 3.61; S,4.20 calculated for C<sub>84</sub>H<sub>68</sub>O<sub>17</sub>N<sub>4</sub>S<sub>2</sub>.2HCl requires C, 65.45; H, 4.41; N,3.63; S4.15%)

## RESULTS AND DISCUSSION

2-hepta-O-benzoyl- $\beta$ -D-lactosylimino-3-aryl-4-S-benzyl-6-phenylimino-2, 3-dihydro-1, 3, 5-thiadiazines (hydrochlorides)(3a-f) were prepared by the condensation of hepta-O-benzoyl- $\beta$ -D-lactosyl isocynodichloride(1) with 1-aryl-5-phenyl-2-S-benzyl-2, 4-isodithiobiurets (2a-f) in CHCl<sub>3</sub>. After condensation, the solvent was distilled off to obtain sticky residue. This residue was triturated several times with petroleum ether (60-80<sup>0</sup>) to afford a pale yellow solid (3a-f).The products were found to be non desulphurised when boiled with alkaline lead acetate. The specific rotation were measured in chloroform. The results were summarized in Table 1. In spectral analysis <sup>15-17</sup> IR spectrum of product shows bands due to Ar-H, ali C-H, C=O, C=N, C-N, C-O, C-S stretching and <sup>1</sup>HNMR spectrum of product distinctly displayed signals due to aromatic protons and lactose ring protons. The Mass spectrum of product was also observed. The reaction was monitored by T L C. All the products were purified by chloroform – petroleum ether.

Table-1: Physical data characterisation of compounds (3a-f)  
Reactant (1) hepta-O-benzoyl- $\beta$ -D-lactosyl isocynodichloride (2) 1-aryl-5-phenyl-2-S-benzyl-2, 4-isodithiobiurets(2a-f)

| 1-Aryl-5-phenyl-2,4-isodithiobiurets (1[a-g]) | g    | Product (g) | Yield % | m.p. <sup>0</sup> C | Rf value (Pet.Ether:EtOAc) 6:4 | $[\alpha]_D^{31}$ CHCl <sub>3</sub> | Analysis Found (Required) |             |
|-----------------------------------------------|------|-------------|---------|---------------------|--------------------------------|-------------------------------------|---------------------------|-------------|
|                                               |      |             |         |                     |                                |                                     | S                         | N           |
| -Phenyl-                                      | 0.75 | 2.7(3a)     | 90      | 140-144             | 0.69                           | +31.8                               | 4.20 (4.19)               | 3.18 (3.14) |
| o-Cl-Phenyl-                                  | 0.82 | 1.5(3b)     | 76.53   | 137-140             | 0.73                           | -20                                 | 4.15 (4.10)               | 3.56 (3.58) |
| m-Cl-Phenyl-                                  | 0.82 | 2.7(3c)     | 90.69   | 139-141             | 0.60                           | +53.8                               | 4.12 (4.10)               | 3.60 (3.58) |
| p-Cl-Phenyl-                                  | 0.82 | 2.8(3d)     | 94.18   | 152-153             | 0.55                           | +80                                 | 4.14 (4.10)               | 3.52 (3.58) |
| o-Tolyl-                                      | 0.78 | 2.7(3e)     | 91.66   | 131-133             | 0.62                           | +93.8                               | 4.19 (4.15)               | 3.65 (3.63) |
| p-Tolyl-                                      | 0.78 | 2.6(3f)     | 86.49   | 161-163             | 0.72                           | +130                                | 4.18 (4.15)               | 3.61 (3.63) |

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