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Note

Synthesis of 2-phenylimino-3-aryl-4-S-benzyl-6-hepta-O-acetyl-β–lactosylimino-2,3-dihydro-1,3,5-thiadiazine hydrochlorides

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2-Phenylimino-3-aryl-4-S-benzyl-6-hepta-O-acetyl-β-lactosyl-imino-2,3-dihydro-1,3,5-thiadiazine hydrochlorides have been prepared by the interaction of 1-aryl-5-hepta-O-acetyl-β-D-lactosyl-2-S-benzyl-2,4-isodithiobiurets and phenyl isocyano-dichloride. The structures of these new N-lactosylated-1,3,5-thiadiazines have been established on the basis of usual chemical transformations and IR, NMR and mass spectral studies.

Keywords: 1-Aryl-5-hepta-O-acetyl-β-D-lactosyl-2-S-benzyl-2,4-isodithiobiurets, phenyl isocyanodichloride, β-lactosylimino-1,3,5-thiadiazine

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Very few compounds containing thioamido group and having lactosyl substituent on nitrogen are known which have been studied for their biological activity[1,2]. A simple method for the synthesis of 1,3,5-thiadiazines has been reported. This was essentially based on the reaction of phenylisocyanodichloride with thioamido group containing compounds[3,4]. Thiadiazines containing β-D-lactosyl substituent on nitrogen have not been prepared earlier. Herein is reported the synthesis of several N-lactosylated-1,3,5-thiadiazine hydrochlorides prepared by the reaction of 1-aryl-5-hepta-O-acetyl-β-D-lactosyl-2-S-benzyl-2,4-isodithiobiurets with phenylisocyanodichloride. The required 1-aryl-5-hepta-O-acetyl-β-D-lactosyl-2-S-benzyl-2,4-isodithiobiurets were obtained by the reaction of 1-aryl-S-benzyl isothiocarbamides[5] with hepta-O-acetyl-β-D-lactosyl isothiocyanate[6].

Results and Discussion

2-Phenylimino-3-aryl-4-S-benzyl-6-hepta-O-acetyl-β-lactosylimino-2,3-dihydro-1,3,5-thiadiazine hydrochloride **3a-g** (**Scheme I**) was prepared by the condensation of 1-aryl-5-hepta-O-acetyl-β-D-lactosyl-2-S-benzyl-2,4-isodithiobiuret **1a-g** with phenyl-isocyanodichloride **2** in $CHCl_3$. After condensation, the solvent was distilled off to obtain a sticky residue. This residue was triturated with petroleum ether (60-80°C, 60 mL) to afford a pale yellow solid **3a-g**. The product was found to be non-desulphurised when boiled with alkaline lead acetate. IR spectrum of the product shows characteristic absorption of lactose unit in the range of 900-910, 1000-1100 and 1200-1300 cm^{-1} (ref. 7, 8). The coupling constant of the anomeric proton ranged between 9-10 Hz which indicated the β-configuration of glycosidic bond[9,10]. Mass spectrum showed the characteristics of lactose unit[11].

Experimental Section

Optical rotations $[\alpha]_D^{31}$ were measured on an EQUIP-TRONICS EQ-800 Digital Polarimeter at 31°C in $CHCl_3$. IR spectra were recorded on a Perkin-Elmer Spectrum RXI FTIR spectrophotometer. ^1H NMR were obtained on a Bruker DRX-300 NMR spectrometer. Samples were prepared in $CDCl_3$ with TMS as an internal reference. The Mass spectra were recorded on a Jeol SX-102 mass spectrometer.

General procedure for the synthesis of 2-phenyl-imino-3-aryl-4-S-benzyl-6-hepta -O-acetyl-β-lacto-sylimino-2,3-dihydro-1,3,5-thiadiazine hydrochlo-rides 3a-g. A solution of phenylisocyanodichloride **2** (0.003 *M* in 5 mL $CHCl_3$) was added to a solution of 1-aryl-5-hepta-O-acetyl-β-D-lactosyl-2-S-benzyl-2,4-isodithiobiuret **1a-g** (0.003 *M* in 15 mL $CHCl_3$) and the reaction mixture was refluxed for 3hr. Afterwards the solvent was distilled off to obtain a sticky residue. This residue was triturated with petroleum ether (60-80°C, 60 mL) to afford a pale yellow solid (**3a-g**). The product was purified by recrystallisation from ethanol-water. The homogeneity of the product was checked by TLC using $CHCl_3$-ethyl acetate as the mobile phase. Yield, m.p., optical rotation, elemental analysis and R_f values are shown in **Table I**.

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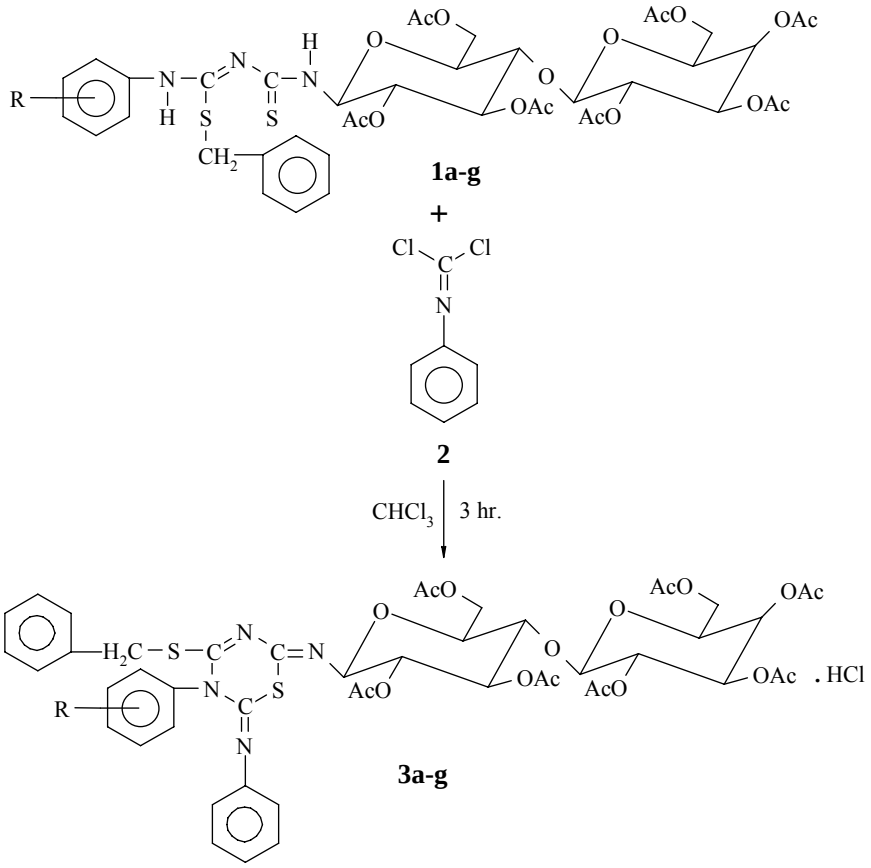

R = **a**: H **d**: *p*-tolyl **g**: *p*-Cl-phenyl
b: *o*-tolyl **e**: *o*-Cl-phenyl
c: *m*-tolyl **f**: *m*-Cl-phenyl

Scheme I

Table I – Characterisation data of 2-phenylimino-3-aryl-4-S-benzyl-6-hepta-O-acetyl-β-lactosylimino -2,3-dihydro-1, 3, 5-thiadiazine hydrochlorides (**3a-g**)

Compd	Yield %	m.p. °C	$[\alpha]_D^{31}$* (°)	Found N	(Calcd)% S	R_f Value	^{1}H NMR δ, ppm	MS (m/z)
3a	75.07	143	+64.10 (c=1.092)	5.10 (5.12	5.75 5.85)	0.79	1.84-2.04 (21H, m, 7-$COCH_3$,), 2.14-2.25, (2H,m,lactose unit), 3.76-3.88 (3H,m,2H,CH_2-S, 1H, lactose unit), 4.02 -4.15 (4H,m,2CH_2-O), 4.48-5.10 (5H,m, lactose unit), 5.32-5.36 (2H,t,1H, anomeric J=9.9 Hz., 1H, lactose unit), 7.14-7.54 (15H,m,Ar-H)	1094 $(M+1)^+$, 1052, 992, 618, 558, 331, 169(Base peak), 109
3b	69.27	138	+50.20 (c=0.996)	5.01 (5.05	5.69 5.78)	0.89	--	--
3c	72.28	167	+79.68 (c=1.004)	4.97 (5.05	5.71 5.78)	0.40	1.84-2.15 (21H, m, 7-$COCH_3$), 2.34-2.40 (3H,s,Ar-CH_3), 3.67-4.36 (7H,m, 2H,CH_2-S, 4H,2CH_2-O, 1H,lactose unit), 4.48-5.10 (7H,m,lactose unit), 5.26-5.35 (2H, t, 1H, anomeric J=9.0 Hz., 1H,lactose unit), 6.82-7.54 (14H,m,Ar-H)	1108 $(M+1)^+$, 931, 643, 331, 169 (Base peak), 109
3d	75.30	151	+128.08 (c=1.068)	5.03 (5.05	5.64 5.78)	0.69	--	--

— Contd

Table I — aracterisation data of 2-phenylimino-3-aryl-4-S-benzyl-6-hepta-O-acetyl-β-lactosylimino -2,3-dihydro-1, 3, 5-thiadiazine hydrochlorides (**3a-g**) — *Contd*

Compd	Yield %	m.p. °C	$[\alpha]_D^{31}$* (°)	Found N	(Calcd)% S	R_f Value	^{1}H NMR δ ppm	MS (m/z)
3e	64.32	147	-27.57 (c=1.088)	4.96 (4.96	5.58 5.67)	0.78	--	--
3f	55.55	148	+23.92 (c=0.836)	4.90 (4.96	5.54 5.67)	0.75	--	--
3g	64.32	172	+57.47 (c=1.044)	4.89 (4.96	5.61 5.67)	0.68	1.82-2.11 (21H,m,7-$COCH_3$), 2.16-2.19 (2H,m,lactose unit), 3.76-4.19 (6H,m, 2H,CH_2-S, 4H,2CH_2-O), 4.43-5.11 (6H,m,lactose unit), 5.29-5.35 (2H,t, 1H,anomeric J=9.0 Hz., 1H,lactose unit), 7.14-7.54 (14H,m, Ar-H)	1128 $(M+1)^+$, 951, 619, 559, 331, 169 (Base peak), 109

***** All $[\alpha]_D^{31}$ values were measured in $CHCl_3$.

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