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SYNTHESIS OF NEW *N*-LACTOSYLATED THIOCARBAMIDES

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ABSTRACT

A series of new 1-hepta-*O*-benzoyl-β-D-lactosyl-3-substituted benzothiazolyl thiocarbamides have been synthesized by the interaction of hepta-*O*-benzoyl-β-D-lactosyl isothiocyanate with 2-aminobenzothiazole/substituted benzothiazoles. The identities of these new *N*-lactosides have been established on the basis of usual chemical transformations and IR, NMR and Mass spectral studies.

Key words: Lactosyl isothiocyanate, Benzothiazolyl thiocarbamides.

INTRODUCTION

Benzothiazoles are bicyclic ring system with multiple applications. Although they have been known from long ago to be biologically active[1-4], their varied biological features are still of great scientific interest. Some derivatives of benzothiazoles possess antituberculosis, anticancer, antitumor, antipyretic activites[5,6].

In view of applications of benzothiazoles and its derivatives in medicinal chemistry and in many other ways, we herein report the synthesis of several 1-hepta-*O*-benzoyl-β-D-lactosyl-3-[2- substituted benzothiazolyl] thiocarbamides **(4a-f)** by the condensation of hepta-*O* –benzoyl - β-D-lactosyl isothiocyanate **(2)** with 2-aminobenzothiazole/ substituted benzothiazloles **(3a-f).** The required lactosyl isothiocyanate was prepared by the reaction of hepta- *O* –benzoyl - α-D-lactosyl bromide **(1)** with lead thiocyanate[7] **(Scheme 1)**. Required 2-aminobenzothiazoles / substituted benzothiazoles were prepared by the already known method of oxidative cyclization of 1-aryl thiocarbamides with the help of molecular bromine[8,9] and 1-aryl thiocarbamides was prepared by reaction of aryl amine hydrochlorides with ammonium thiocyanate[10].

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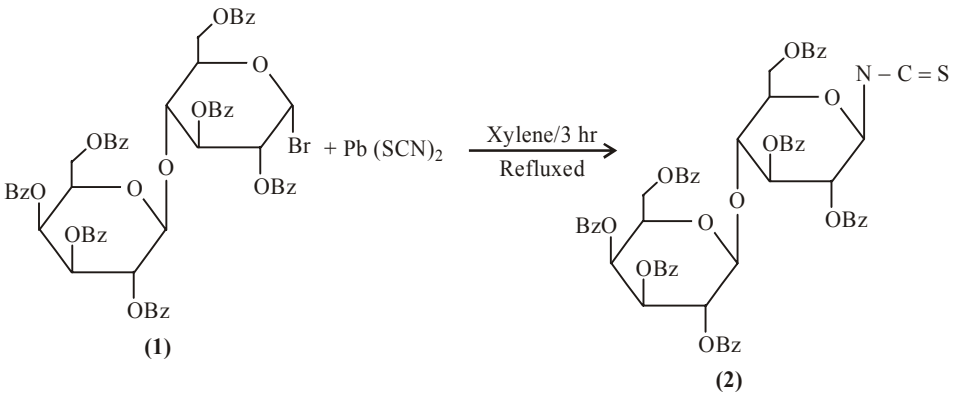
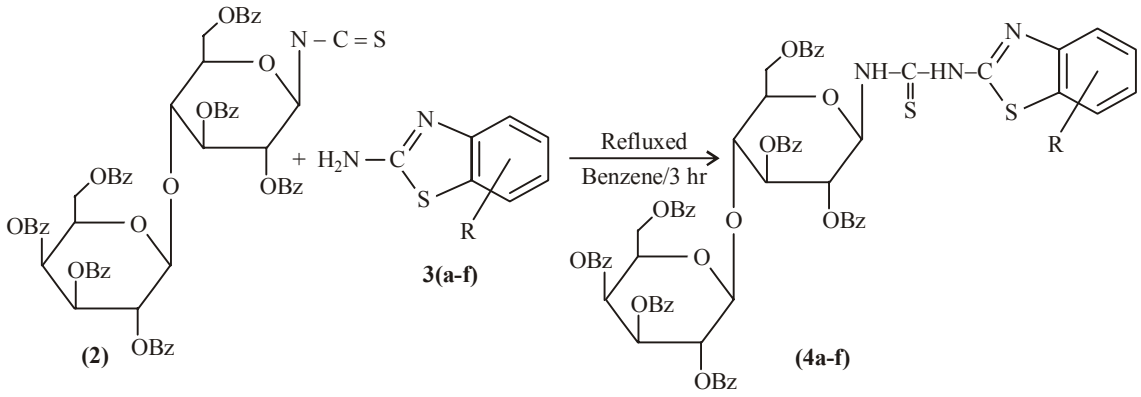


Scheme 1



Scheme 2

Where,

R = (a) Phenyl, (b) 4-Cl, (c) 6-Cl, (d) 6-Methyl, (e) 4- Methyl and (f) 5- Methyl.

EXPERIMENTAL

Specific rotations were measured on Equip-Tronics digital polarimeter at 28^0C in $CHCl_3$. IR spectra were recorded on Perkin-Elmer spectrum RXI FTIR spectrophotometer (4000-450 cm^{-1}). ^1H NMR was recorded in $CDCl_3$ on Bruker DRX-300 spectrometer operating at 300 MHz. The mass spectra were recorded on Jeol-SX-102 (FAB) instrument.

Synthesis of 1-hepta-*O*-benzoyl-β-D-lactosyl-3-[2-substituted benzothiazolyl] thiocarbamides (4a-f) (Scheme 2)

A mixture of 1- hepta -*O*-benzoyl-β-D- lactosyl isothiocyanate **(2) (**0.005 M, 5.5 g in

35 mL) and (0.005 M, 0.8 g) 2-aminobenzothiazole/substituted benzothiazoles **(3a-f)** in 30 mL of benzene was refluxed for 3 h and monitored by TLC. After completion of the reaction, the solvent was triturated with petroleum ether (60-80^{0}C) to afford a white solid (**4a-f)**. The products were purified from acetone- petroleum ether.

(4a) m.p. 155-160^{0}C; yield 70%, $[\alpha]^{28}_D$ +190^0 (c, 1.11 in $CHCl_3$); **IR(KBr):** 3331 cm^{-1} (N-H) 1758 cm^{-1} (C=O), 1527 cm^{-1} (C-N), 1237 cm^{-1} (C-O), 1049 cm^{-1} (C=S), 609 cm^{-1} (C-S); **^{1}H NMR (ppm):** δ8.01-7.18 (39H, m, aromatic protons), 5.93-3.79 (16H, m, 14 lactosyl protons, 2 NH protons); **Mass (m/z):** 1252 (M^+), 1145 (M-CH_3COOH), 1100 (M-CH_3COOH CH_2CO), 1052 (HBL^+), 579 (TBG^+), 391 (TBG^+ -$C_{12}H_{12}O_2$), 335 (TBG-$C_{14}H_{12}O_4$), 105 ($C_6H_5CO^+$); Anal. calcd for $C_{69}H_{55}O_{17}N_3S_2$: C, 67.77; H, 4.65; N, 3.33; S, 5.09% ; Found: C, 67.71; H, 4.62; N, 3.31; S, 5.07%.

(4b) m.p. 162^{0}C; yield 80%, $[\alpha]^{28}_D$ +170^0 (c, 1.11 in $CHCl_3$); **IR (KBr):** 3331 cm^{-1} (N-H), 1758 cm^{-1} (C=O), 1527 cm^{-1} (C-N), 1237 cm^{-1} (C-O), 1049 cm^{-1} (C=S), 609 cm^{-1} (C-S).; **^{1}H NMR (ppm):** δ 8.02-7.19 (38H, m, aromatic protons), 5.91-3.79 (16H, m, 14 lactosyl protons, 2 NH protons); **Mass (m/z):** 1280 (M^+), 1145 (M-CH_3COOH), 1100 (M-CH_3COOH CH_2CO), 1052 (HBL^+), 579 (TBG^+), 391(TBG^+ -$C_{12}H_{12}O_2$), 335(TBG-$C_{14}H_{12}O_4$), 105 ($C_6H_5CO^+$); Anal. calcd for $C_{69}H_{54}O_{17}N_3S_2Cl$: C, 67.77; H, 4.65; N, 3.24; S, 4.93% ; Found: C, 67.78; H,4.62; N, 3.21; S, 4.90%.

(4e) m.p. 160-170^{0}C; yield 72%, $[\alpha]^{28}_D$ +250^0 (c, 1.11 in $CHCl_3$); **IR(KBr):** 3331 cm^{-1} (N-H), 1758 cm^{-1}(C=O), 1527 cm^{-1}(C-N), 1237 cm^{-1}(C-O), 1049 cm^{-1}(C=S), 609 cm^{-1}(C-S).; **^{1}H NMR (ppm):** δ 8.02-7.15 (38H, m, aromatic protons), 5.91-3.79 (16H, m, 14 lactosyl protons, 2 NH protons); 2.29 (3H, s, -CH_3); **Mass (m/z):** 1259 (M^+), 1145 (M-CH_3COOH), 1100 (M-CH_3COOH CH_2CO), 1052 (HBL^+), 579 (TBG^+), 391 (TBG^+ -$C_{12}H_{12}O_2$), 335 (TBG-$C_{14}H_{12}O_4$), 105 ($C_6H_5CO^+$); Anal.calcd for $C_{70}H_{57}O_{17}N_3S_2$: C,67.77; H,4.65; N, 3.29; S, 5.01% ; Found: C, 67.73; H, 4.65; N, 3.26; S, 4.99%.

RESULTS AND DISCUSSION

1-Hepta-*O*-benzoyl-β-D- lactosyl-3-[2- substituted benzothiazolyl] thiocarbamides **(4a-f)** were prepared by the condensation of 1-hepta-*O*-benzoyl-β-D-lactosyl isothiocyanate **(2)** with 2-aminobenzothiazole/ substituted benzothiazoles **(3a-f)** in benzene medium for 5 h. Then, the solvent was distilled off and sticky residue obtained was triturated with petroleum ether (60-80 ^{0}C) to afford a white solid (**4a-f)**. The structure of the products were confirmed on the basis of IR[11], NMR[12] and mass[13] spectral analysis. The specific rotation of the products were also recorded[14].

Table 1: 1-Hepta-*O*-benzoyl–β–D-lactosyl-3-substituted benzothiazolyl thiocarbamide (4a-f)

Reactants: (a) 1-Hepta-*O*-benzoyl-β-D-lactosyl-isothiocyanate (0.005M) **(2)**
(b) Substituted benzothiazolyl thiocarbamides **(3a-f)**

Product	Melting point (^oC)	Yield (%)	Analysis found (requires)		$[\alpha]^{28}$ (c, 0.15)
			N (%)	S (%)	
4a	155-160	70	3.31 (3.33)	5.01 (5.09)	190^0 (c,0.156)
4b	160-170	72	3.21 (3.24)	4.90 (4.93)	250^0 (c,0.156)
4c	165-170	68	3.22 (3.24)	4.99 (4.93)	140^0 (c,0.156)
4d	162-168	78	3.28 (3.29)	5.01 (5.01)	180^0 (c,0.157)
4e	162	80	3.26 (3.29)	4.99 (5.01)	170^0 (c,0.157)
4f	170-174	85	3.26 (3.29)	4.99 (5.01)	140^0 (c,0.157)

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