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SYNTHESIS OF NEW *N*-LACTOSYLATED THIOCARBAMATES

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ABSTRACT

A series of new 1-hepta-*O*-benzoyl -β-D- lactosyl-3-alkyl thiocarbamates have been synthesized by the interaction of hepta-*O*-benzoyl-β-D-lactosyl isothiocyanate with various alcohols. The identities of these new *N*-lactosides have been established on the basis of usual chemical transformations, IR, NMR and Mass spectral studies.

Key words: Lactosyl isothiocyanate, Thiocarbamates.

INTRODUCTION

Thiocarbamates and their derivatives show strong antimicrobial activity and are also a versatile reagent in organic synthesis[1]. Although they have been known from long ago to be biologically active[2-4], their varied biological features are still of great scientific interest. Some derivatives of these possess antituberculosis, anticancer, antitumor, antipyretic activites[5,6].

In view of applications of thiocarbamates 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-*O*-alkyl thiocarbamates (**4a-f**) by the condensation of hepta-*O* –benzoyl - β-D-lactosyl isothiocyanate **(2)** with various alcohols **(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**).

EXPERIMENTAL

Specific rotations were measured on Equip-Tronics Digital Polarimeter at 28^{o}C in

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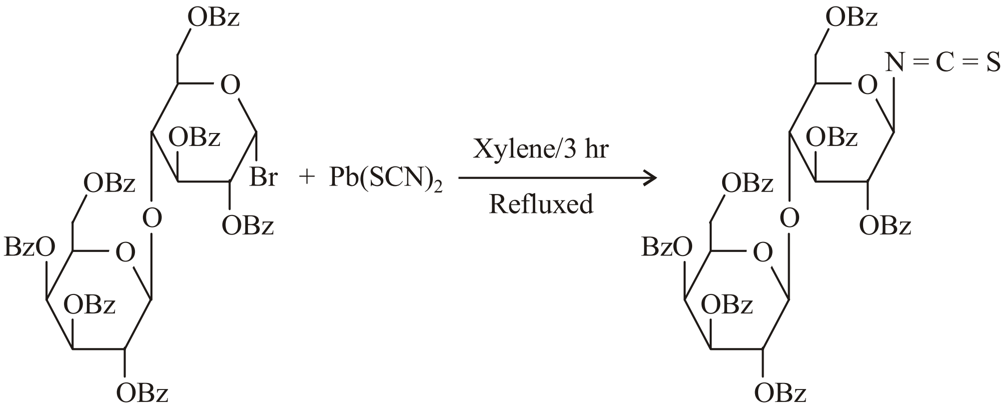
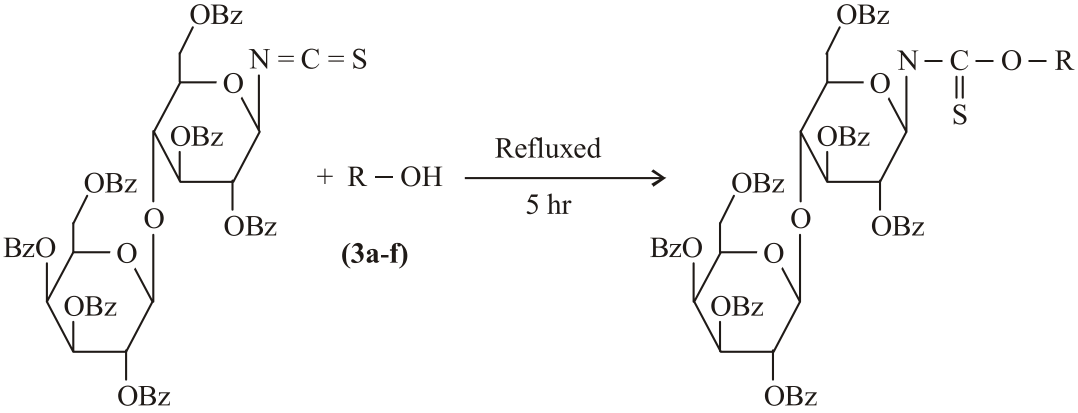
$CHCl_3$. IR spectra were recorded on Perkin-Elmer spectrum RXI FTIR spectrophotometer (4000-450 cm $^{-1}$). ^1H NMR was recorded in $CDCl_3$ on Bruker DRX-300 spectrometer operating at 300 MHz. The mass spectra were recorded on Jeol-SX-102(FAB) instrument.



(1) **(2)**

Scheme 1



(3a-f)

(2) **(4a-f)**

Scheme 2

Where,

R = **(a)** Ethyl, **(b)** Methyl, **(c)** n-Propyl, **(d)** iso-Propyl, **(e)** n-Butyl and **(f)** t-Butyl.

Table 1: 1-Hepta-*O*-benzoyl-β-D-lactosyl -*O*-alkyl thiocarbamates (4a-f)

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

Product	Melting point (°C)	% Yield	Analysis found (required)		$[\alpha]^{28}_D$ (c, 0.15)
			N (%)	S (%)	
4a	153-155	78	1.20 (1.21)	2.71 (2.76)	+ 85^0
4b	146-148	73	1.19 (1.20)	2.72 (2.79)	+ 90^0
4c	143-145	70	1.17 (1.19)	2.72 (2.73)	+ 88^0
4d	142-144	75	1.18 (1.19)	2.71 (2.73)	+ 82^0
4e	158-160	65	1.17 (1.18)	2.68 (2.70)	+ 118^0
4f	166-170	69	1.17 (1.18)	2.69 (2.70)	+ 79^0

Synthesis of 1-hepta-*O*-benzoyl-β-D-lactosyl-*O*-alkyl thiocarbamates (4a-f) (Scheme 1) (Table 1)

1-Hepta-*O*-benzoyl-β-D-lactosyl isothiocyanate **(2)** (0.005M, 3.5 g) was taken in 30 mL of alcohols **(3a-f)** and the reaction was carried out over boiling water bath for 5 h . Then the reaction mixture was poured into ice cold water, when 1-hepta-*O*-benzoyl-β-D-lactosyl – *O*-alkyl thiocarbamates **(4a-f)** separated out .

(4a). m.p. 153-155^{0}C; yield 78%, $[\alpha]^{28}_D$ +85^0 (c,1.11 in $CHCl_3$); **IR(KBr):** 3427 cm^{-1} (N-H),1730 cm^{-1} (C=O), 1272 cm^{-1} (C-N), 1237 cm^{-1} (C-O), 1028 cm^{-1} (C=S), 709 cm^{-1} (C-S); **^{1}H NMR (ppm):** δ 7.99-7.18 (35 H, m, aromatic protons), 5.93-3.76 (15H, m, 14 lactosyl protons, 1 NH protons), 2.99-1.60 (5H, m,-CH_2-CH_3); **Mass (m/z):** 1157 (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_6H5CO$^+$); Anal. Calcd for $C_{64}H_{55}O_{18}NS$: C,66.37; H,4.75; N, 1.21; S, 2.76% ; Found: C,66.31; H, 4.71; N, 1.20; S, 2.71%.

(4d). m.p. 142-144^{0}C; yield 75%, $[\alpha]^{28}_D$ +82^0 (c, 1.11 in $CHCl_3$); **IR(KBr):** 3445 cm^{-1} (N-H), 1729.8 cm^{-1}(C=O), 1527 cm^{-1} (C-N), 1175 cm^{-1} (C-O), 1097 cm^{-1} (C=S), 609 cm^{-1} (C-S).; **^{1}H NMR (ppm):** ^{1}H NMR (ppm) : δ 7.99-6.99 (35H, m, aromatic protons), 5.91-3.72 (15H, m, 14 lactosyl protons, 1 NH protons), 2.29-1.39 (7H, m, -$CH(CH_3)_2$); **Mass (m/z):** 1172 (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 $C_{65}H_{57}O_{18}NS$: C, 66.60; H, 4.86; N, 1.19; S, 2.73% ; Found: C, 66.57; H, 4.82; N, 1.18; S, 2.71%.

(4f). m.p. 166-170°C; yield 69%, $[\alpha]^{28}_{D}$ +79^0 (c, 1.11 in $CHCl_3$); **IR (KBr):** 3458 (N-H), 1729.6 cm^{-1} (C=O), 1527 cm^{-1} (C-N), 1097 cm^{-1} (C=S), 609 cm^{-1} (C-S).; **^{1}H NMR (ppm):** δ 8.05-7.18 (35H, m, aromatic protons), 5.91-3.79 (15H, m, 14 lactosyl protons, 1NH protons), 2.99-1.20 (9H, m, -$C(CH_3)_3$); **Mass (m/z):** 1186 (M^+ + 1), 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 $C_{66}H_{59}O_{18}NS$: C,66.83; H, 4.97; N, 1.18; S, 2.70% ; Found: C, 66.69; H, 4.77; N, 1.15; S, 2.60%.

RESULTS AND DISCUSSION

1-Hepta- *O* -benzoyl-β-D- lactosyl-*O*-alkyl thiocarbamates **(3a-f)** were prepared by the condensation of 1-hepta-*O*-benzoyl-β-D-lactosyl isothiocyanate **(2)** with various alcohols **(3a-f)** 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[8], NMR[9] and Mass[10] spectral analysis. The specific rotation of the products were also recorded[11].

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