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SYNTHESIS OF *S*-TETRA-*O*-ACETYL GALACTOPYRANOSYL ARYLDITHIOCARBAMATES

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ABSTRACT

The interaction of tetra-*O*-acetyl galactopyranosyl bromide with ammonium aryldithiocarbamates results in the formation of *S*-tetra-*O*-acetyl galactopyranosyl aryldithiocarbamates. The identities of these newly synthesized thiogalactosides have been established on the basis of usual chemical transformation, IR, ^{1}H NMR and mass spectral studies. The compounds were screened for their antibacterial and antifungal activities against common pathogens like *E. coli, S. aureus, P. vulgaris, S. typhi*, *C. albicans* and *A. niger*. The compounds were found sensitive to these microorganisms.

Key words: Galactopyranosyl bromide, Ammonium aryldithiocarbamates, Galactopyranosyl aryldithiocarbamates, Antibacterial, Antifungal.

INTRODUCTION

Galactopyranosyl bromide[1-3] is a versatile and important intermediate in carbohydrate chemistry. It is used as a starting material in the synthesis of thiogalactosides. Carbohydrate derivatives bearing *S*-linked functionalities at anomeric position have attracted attention because of known fungicidal, insecticidal and anticarcinogenic properties[4,5]. Acetyl derivatives of carbohydrate are interestingly becoming important in medicinal chemistry, industries and in many other ways[6-9].

The present work deals with the synthesis of several *S*-tetra-*O*-acetyl galactopyranosyl aryldithiocarbamates **(3)**. These were prepared by the interaction of tetra-*O*-acetyl galactopyranosyl bromide **(1)** and ammonium aryl dithiocarbamates **(2).**

The reaction scheme is given as -

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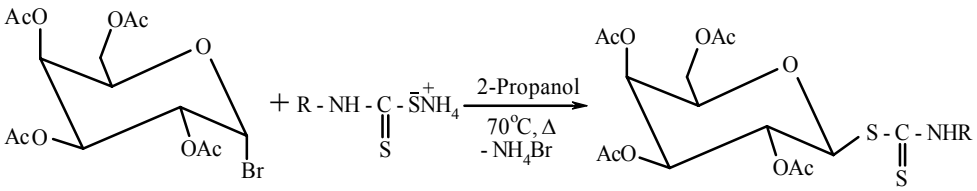

(1) **(2)** **(3)**

Where R = (a) Phenyl, (b) *o*-Cl-Phenyl, (c) *m*-Cl-Phenyl, (d) *p*-Cl-Phenyl, (e) *o*-Tolyl, (f) *m*-Tolyl, (g) *p*-Tolyl

Ac = $-COCH_3$

EXPERIMENTAL

IR spectra were recorded on FTIR Perkin-Elmer (4000-450 cm^{-1}) spectrophotometer. ^1H NMR spectra were run on Bruker DRX-300 instrument operating frequency 300 MHz using $CDCl_3$ solution with TMS as internal reference. Mass spectra were recorded on Micromass Quattro II triple quadrupole mass spectrometer. Specific rotations were recorded on Equip-Tronics digital polarimeter in $CHCl_3$ at 32°C.

General procedure

Isopropanolic (20 mL) suspension of tetra-*O*-acetyl galactopyranosyl bromide (0.01 M) and ammonium aryldithiocarbamate (0.01 M) was heated at 70°C and kept at room temperature for 18 hrs. The solid formed was filtered off and identified as NH_4Br. The reaction mixture was mixed with 100 mL distilled water. It afforded solid **(3a-g)**. The products were crystallized by ethanol-water. Purity was checked by TLC (Table 2).

RESULTS AND DISCUSSION

Isopropanolic suspension of tetra-*O*-acetyl galactopyranosyl bromide and ammonium phenyldithiocarbamate was heated at 70°C and kept at room temperature for 18 hrs. Solid thus obtained was identified as NH_4Br. Clear filtrate on dilution with distilled water afforded a solid, which was purified by ethanol-water. It gave charring and was desulphurisable with alkaline plumbite.

The IR, ^1H NMR and Mass[10-13] spectral analysis (experimental) and elemental analysis clearly indicated the product and the structure *S*-tetra-*O*-acetyl β-D-galactopyranosyl 1-phenyldithiocarbamate was assigned.

When the interaction of tetra-*O*-acetyl galactopyranosyl bromide[14] was extended to other aryl-dithiocarbamates[15], the related *S*-tetra-*O*-acetyl galactosyl-1- aryldithiocarbamates **(3a-g)** were obtained.

S-tetra-O-acetyl-β-D-galactopyranosyl-1-phenyldithiocarbamate (3a)

IR (KBr): 3449 cm^{-1} (N–H), 1751 cm^{-1} (C=O), 1446 cm^{-1} (C-N), 760 cm^{-1} (C–S), 915 cm^{-1} (β-isomer of galactose), 1154 cm^{-1} (C=S)

^{1}H NMR: δ 8.16 (1H, s, N-H), δ 7.4-7.1 (5H, m, Ar-H), δ 5.4-4.0 (7H, m, galactose unit), δ 2.3-1.8 (12H, m, 4 OAc)

Mass (m/z) : 499, 331, 229, 169, 109.

Anal. Calcd for $C_{21}H_{25}O_9NS_2$: C, 50.49; H, 5.04; N, 2.80; S, 12.84. Found : C, 50.94; H, 4.76; N, 2.71; S, 12.60 %.

S-tetra-O-acetyl β-D-galactopyranosyl-1-m-Cl-phenyldithiocarbamate (3c)

IR (KBr) : 3411 cm^{-1} (N-H), 1751 cm^{-1} (C=O), 1429 cm^{-1} (C-N) 773 cm^{-1} (C-S), 915 cm^{-1} (β-isomer of galactose) 1154 cm^{-1} (C=S).

^{1}H NMR : δ 8.2 (1H, s, N-H), δ 7.4 - 7.1 (4H, m, Ar-H) δ 6.6 - 3.9 (7H, m, galactose unit), δ 2.1 - 1.2 (12H, m, 4 OAc)

Mass (m/z) : 533, 331, 169, 229, 109.

Anal. Calcd for $C_{21}H_{24}O_9NS_2Cl$: C, 47.23; H, 4.53; N, 2.62; S, 12.01. Found C, 46.86; H, 4.89; N, 2.49; S, 11.90 %.

S-tetra - O- acetyl - β-D-galactopyranosyl-1-o-tolyl-dithiocarbamate (3e)

IR (KBr) : 3432 cm^{-1} (N-H), 1751 cm^{-1} (C=O), 1496 cm^{-1} (C-N) 759 cm^{-1} (C-S), 917 cm^{-1} (β-isomer of galactose), 1154 cm^{-1} (C=S).

^{1}H NMR : δ 7.5 (1H, s, N-H), δ 7.4 - 7.0 (4H, m, Ar-H) δ 5.4- 5.0 (7H, m, galactose unit), δ 2.3 - 1.2 (15H, m, 4 OAc + Ar -CH_3)

Mass (m/z) : 513, 331, 229, 169, 109.

Anal. Calcd for $C_{22}H_{27}O_9NS_2$: C, 51.45; H, 5.30; N, 2.73; S, 12.49. Found : C, 51.17; H, 5.53; N, 2.60; S, 12.27 %.

Antimicrobial study

The compounds were taken at a concentration of 1 mg/mL using dimethyl formamide (DMSO) as a solvent. The drug solution was allowed to diffuse for about an hour into the medium. The plates were incubated at 37°C for 24 hr. for antibacterial activity and at 30°C for 48 hr for antifungal activity.

The zone of inhibition observed around the wells after respective incubation was measured in mm by using antibiotic zone reader.

Table 1: Antimicrobial activities of some newly synthesized thiogalactosides (3a-g) (given in mm)

S. No.	Name of compound	*Ec*	*Sa*	*Pv*	*St*	*Ca*	*An*
3a	*S*-Tetra-*O*-acetyl galactosyl phenyl dithiocarbamate	7	7	8	7	13	10
3b	*S*-Tetra-*O*-acetyl galactosyl-*o*-Cl-phenyl dithiocarbamate	11	13	9	6	15	10
3c	*S*-Tetra-*O*-acetyl galactosyl-*m*-Cl-phenyl dithiocarbamate	12	19	7	11	8	12
3d	*S*-Tetra-*O*-acetyl galactosyl-*p*-Cl-phenyl dithiocarbamate	9	18	10	7	9	12
3e	*S*-Tetra-*O*-acetyl galactosyl-*o*-tolyl dithiocarbamate	--	15	9	8	15	10
3f	*S*-Tetra-*O*-acetyl galactosyl-*m*-tolyl dithiocarbamate	6	12	7	11	14	11
3g	*S*-Tetra-*O*-acetyl galactosyl-*p*-tolyl dithiocarbamate	9	13	10	7	10	11

Where Ec = *E. coli*, Sa = *S. aureus*, Pu = *P. vulgaries*, St = *S. typhi*, Ca = *C. albicans* and An = *A. niger*

Table 2: Physical data of *S*-tetra-*O*-acetyl β-D-galactopyranosyl-1-aryldithiocarbamates (3a-g)

Reactant (g)	Product	m.p. (°C)	Yield g (%)	Analysis Found/ (Required)		$[\alpha]_D^{27}$ (c, in $CHCl_3$)	R_f (3 : 1 $CHCl_3$ - EtOAc)
				N (%)	S (%)		
1a (1.8)	**3a**	150-152	1.5 (30.61)	2.71 (2.80)	12.60 (12.84)	+ 176° (c,1.00)	0.92
1b (2.2)	**3b**	146-149	2.0 (37.52)	2.50 (2.62)	11.89 (12.01)	-222° (c,1.006)	0.96
1c (2.2)	**3c**	118-120	1.6 (30.01)	2.49 (2.62)	11.91 (12.01)	-185° (c,0.993)	0.69
1d (2.2)	**3d**	176-178	1.8 (33.77)	2.45 (2.61)	11.84 (12.01)	+ 244° (c,0.966)	0.91
1e (2.0)	**3e**	180-182	2.3 (44)	2.60 (2.72)	12.27 (12.49)	+ 108° (c,0.98)	0.94
1f (2.0)	**3f**	167-168	1.8 (35.08)	2.62 (2.72)	12.25 (12.49)	- 324° (c,1.00)	0.72
1g (2.0)	**3g**	190-192	2.0 (38.98)	2.59 (2.72)	12.20 (12.49)	+ 89.02° (c,0.966)	0.70

(C and H analyses in all cases were found satisfactory)

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