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SYNTHESIS OF 4H, 4–THIO–2–(TETRA–O–BENZOYL–β–D–GLUCOPYRANOSYLIMINO)–3–PHENYL–2,3–DIHYDRO–(1,3,5)–TRIAZINO–(2,1b)6,7 OR 8–ARYL BENZOTHIAZOLES DIHYDROCHLORIDES

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ABSTRACT

Synthesis of 4H, 4–thio–2–(tetra–O–benzoyl–β–D–glucopyranosylimino)–3–phenyl–2,3–dihydro–(1,3,5)–triazino–(2,1b)6,7 or 8–aryl benzothiazoles have been prepared by the interaction of 1–tetra–O–benzoyl–β–D–glucopyranosyl–3–aryl benzo–thiazolyl thiocarbamides and N–phenyl isocyanodichloride. These compounds were screened for their antibacterial activities against *Escherichia coli*, *Staphylococcus aureus*, *Protrus mirabilis*, and *Salmonella typhi*. The identities of these new N–glucosides have been established on the basis of usual chemical transformations and also IR, and NMR spectral analysis.

Key words : Arylbenzothiazoles, β–D–Glucopyranosylimino

INTRODUCTION

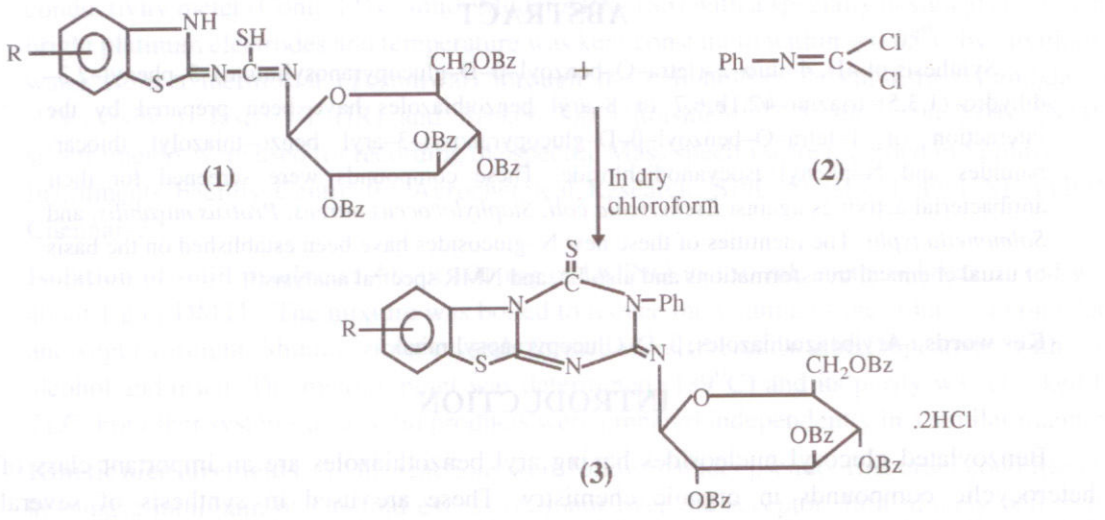
Benzoylated glucosyl nucleosides having aryl benzothiazoles are an important class of heterocyclic compounds in organic chemistry. These are used in synthesis of several heterocyclic derivatives. Recently in our laboratory, 1–tetra–O–benzoyl–β–D–glucopyranosyl–3–aryl benzothiazolyl thiocarbamides have been prepared for the first time by the interaction of tetra–O–benzoyl–β–D–glucopyranosyl isothiocyanate with 2–amino aryl benzothiazoles. In view of our interest in N–glucosylated heterocyclic compounds, we now report the synthesis of 4H, 4–thio–2–(tetra–O–benzoyl–β–D–glucopyranosylimino)–3–phenyl–2,3–dihydro–(1,3,5)–triazino–(2,lb) 6,7 or 8–aryl benzothiazoles dihydrochlorides.

Seven 4H,4–thio–2–(tetra–O–benzoyl–β–D–glucopyranosylimino)–3–phenyl–2,3–dihydro–(1,3,5)–triazino–(2,lb) 6, 7 or 8–aryl benzothiazoles (**3**) have been prepared by the interaction of l–tetra–O–benzoyl–β–D–glucopyranosyl–3–aryl benzothiazolyl thiocarbamides (**1**) and N–phenyl isocyanodichloride (**2**) (Scheme 1). The identities of these new N–glucosides have been established on the basis of usual chemical transformations and also IR, and NMR spectral analysis. Recently, seven l–tetra–O–benzoyl–β–D–glucopyranosyl–3–aryl ben-

zothiazolyl thiocarbamides have been prepared for the first time by the interaction of tetra–O–benzoyl–β–D–glucopyranosyl isothiocyanate with 2–amino aryl benzothiazoles[1].

RESULTS AND DISCUSSION

The reaction of l–tetra–O–benzoyl–β–D–glucopyranosyl–3–aryl benzothiazolyl thiocarbamides (**1a–g**) and N–phenyl isocyanodichloride (**2**) were carried out in cold dry chloroform over 24 h. The solvent was distilled off and resulting sticky residues were then triturated several times with petroleum ether to give a granular yellow solids (**3a–g**) (**scheme–1**) and recrystallized from ethanol. The products were found to be non–desulphurised upon boiling with alkaline lead acetate solution. The specific rotations[2] are shown in Table–1. The purity of products was checked by TLC and the recorded R_f values[3] are given in Table–1.



Where, Bz = Benzoyl (C_6H_5CO),
R = (a) phenyl, (b) o-tolyl, (c) m-tolyl, (d) p-tolyl, (e) o - Cl - phenyl, (f) m - Cl - phenyl, (g) p - Cl - phenyl

Scheme 1

Microbial Activity (Antibacterial activity)

The compounds were screened for their antibacterial activities against various pathogenic bacteria such as *Escherichia coli*, *Staphylococcus aureus*, *Proteus mirabili* and *Salmonella typhi* by disc method[4] at a concentration 10 μg mL^{-1} in DMF. Amongst the compounds tested for the antibacterial activity, the compounds **3b–g** showed higher activity against *Salmonella typhi* while compounds **3a–g** showed moderate activity against *Escherichia coli*, *Staphylsococcus aureus* and *Proteus mirabilis*.

Table 1. Reactant : N–Phenyl isocyanodichloride (2) (0.005 mol, 0.87 g)

1–Tetra–O–benzoyl–β–D–glucopyranosylimino–3–aryl–benzothiazolyl thiocarbamides Aryl			4H,4–Thio–2–(Tetra–O–benzoyl–β–D–gluopyranosylimino)–3–phenyl–2–3–dihydro–(1,3,5)–triazino–(2, lh) 6,7 or 8–aryl benzothiazoles Aryl			Yield (%)	m.p. (°C)	$[\alpha]_D$41 in $CHCl_3$	R_f	Elementel analysis (%)	
	(g)	(1)		(g)	(3)					Found	Calcd.
3–Phenyl	3.93	(a)	....phenyl....	3.0	(a)	66.66	151	+ 42.10 (c, 0.0019)	0.87	N,5.83; S, 6.40; Cl, 7.01	N, 5.75; S, 6.57; Cl, 7.29
3–o–Tolyl	3.99	(b)	....o–tolyl...	3.0	(b)	65.64	142	+ 23.07 (c, 0.0012)	0.49	N, 5.12; S, 6.01; Cl, 6.97	N, 5.67; S, 6.48; Cl, 7.19
3–m–Tolyl	3.99	(c)	...m–tolyl...	2.4	(c)	52.51	165	– 23.07 (c, 0.0013)	0.65	N, 5.01; S, 6.05; Cl, 7.00	N, 5.67; S, 6.48; Cl, 7.19
3–p–Tolyl	3.99	(d)	..–p–tolyl...	2.2	(d)	48.14	170	– 41.17 (c, 0.0017)	0.79	N, 5.71; S, 6.14; Cl, 6.99	N, 5.67; S, 6.48; Cl, 7.19
3–o–Choloro–phenyl.....	4.10	(e)	...–o–Cl–phenyl...	2.2	(e)	47.10	149	+ 0.09 (c, 0.0011)	0.88	N, 5.30; S, 5.95; Cl, 10.11	N, 5.56; S, 6.35; Cl, 10.42
3–m–Chloro–phenyl.....	4.10	(f)	... –m–Cl–phenyl...	2.0	(f)	42.82	142	+ 15.38 (c, 0.0013)	0.52	N, 5.02; S, 6.12; Cl, 9.97	N, 5.56; S, 6.35; Cl, 10.42
3–p–Chloro–phenyl.....	4.10	(g)	... –p–Cl–phenyl–	3.3	(g)	70.66	169	+ 57.14 (c, 0.0014)	0.59	N, 5.21; S, 6.03; Cl, 10.00	N, 5.56; S, 6.35; Cl, 10.42

C and H analysis was found satisfactory in all cases.

Experimental

General Methods

Melting points are uncorrected. Optical rotations were measured $[\alpha]_D 41$ in $CHCl_3$ at 41°C. IR spectra[5–8] were recorded in the range 4000–200 cm^{-1}. NMR H spectra[6, 9–10] were obtained at 300 MHz for solution in $CDCl_3$ (reference – TMS). Thin layer chromatography was conducted on E. Merck TLC aluminum sheet Silica gel 60 F_{254}.

The required l–tetra–O–benzoyl–β–D–glucopyranosyl–3–aryl benzothiazolyl thiocarbamides (**1a–g**) and N–phenyl isocyanodichloride[11] (**2**) were prepared by the methods described earlier.

4H,4–Thio–2–(tetra–O–benzoyl–β–D–glucopyranosylimino)– 3 – phenyl –2, 3 – dihydro–(1,3,5) – triazino –(2,1b) 6,7 or 8–phenyl benzothiazole (3a).

The reaction of l–tetra–O–benzoyl–β–D–glucopyranosyl–3–phenyl benzothiazolyl thiocarbamide (**1a**), 3.93 g, 0.005 mol) and N–phenyl isocyanodichloride (**2**), (0.87 g, 0.005 mol) was carried out in cold dry chloroform for 24 h. The chloroform was then evaporated to leave an sticky syrup, triturated with petroleum ether to a yellow solid (**3a**) (3.0 g, 66.66%), recrystallised from ethanol; mp 151°C; $[\alpha]_D 41$ + 42.10° (c, 0.0019 in $CHCl_3$). The purity of product was checked by TLC; R_f , 0.87; IR (KBr) cm^{-1} : ν 3062.7 (Ar–H), 2889.2(C–H), $–CH_2–$), 1728.1 (C=O), 1535.0 (N–C(=S)–N), 1269.1 (C–O), 1091.6(C=S), 852.5(β–D–glucopyranosyl ring deformation), 756.0(1,2–disubstituted ring), 709.8 (monosubstituted ring), 680.0 (C–S–C). NMR ^1H data ($CDCl_3$): δ 8.0–7.0 (m, 29H, Ar–H), 5.3–4.2 (m, 5H, β–D–glucopyranosyl ring), 4.5–4.0 (d, 2H, CH_2–O). (Table–1) Anal. Calcd. for $C_{50}H_{36}O_9 N_4S_2$ 2HCl; C, 61.66; H, 3.90; N, 5.75; S, 6.57; Cl, 7.29 found : C, 61.05; H, 3.70; N, 5.83; S, 6.40; Cl, 7.01.

On the basis of all the above facts, the product was assigned the structure 4H,4–Thio–2–(tetra–O–benzoyl –β–D–glucopyranosylimino)–3–phenyl–2,3–dihydro–(1,3,5)–triazino–(2,1b)6,7 or 8–phenyl benzothiazole (**3a**).

4H,4 – Thio–2 – (tetra – O – benzoyl – β – D – glucopyranosylimino)–3–phenyl–2,3–dihydro–(1,3,5)–triazino–(2,1b)6,7 or 8–o–tolyl benzothiazole (3b).

m.p. 142°C; $[\alpha]_D^{41}$ + 23.07° (c, 0.0012 in $CHCl_3$), R_f 0.49; IR (KBr)cm^{-1} : ν 3062.7 and 3035.7 (Ar–H), 2950.9 (C–H, CH_3), 2889.2 (C–H, $–CH_2$), 1732.0(C=O), 1531.4 (N–C(=S–N), 1269.1 (C–O), 1091.6(C=S), 975.9(1,2,3–trisubstituted ring), 852.5 (β–D–glucopyranosyl ring deformation), 802.3 (1,3–disubstituted ring), 687.3(C–S–C). NMR ^1H data ($CDCl_3$): δ 8.0 – 7.2 (m, 28H, Ar–H), 5.4 – 4.2 (m, 5H, β–D–glucopyranosyl ring), 4.5–4.0(d, 2H, CH_2O), 2.4–1.7 (s, 3H, Ar–CH_3). (Table–1) Anal. Calcd. for $C_{51}H_{38}O_9 N_4S_2$ 2HCl; C, 62.00; H, 4.05; N, 5.67; S, 6.48; Cl, 7.19 found : C, 62.05; H, 3.91; N, 5.12; S, 6.01; Cl, 6.97.

On the basis of all the above facts, the product was assigned the structure 4H, 4– Thio – 2 – (tetra – O – benzoyl – β – D – glucopyranosylimino)–3–phenyl–2,3–dihydro–(1,3,5)–triazino–(2,1b)6, 7 or 8–o–tolyl benzothiazole (**3b**).

4H,4 – Thio – 2 – (tetra – O – benzoyl–β–D–glucopyranosylimino)–3–phenyl–2,3–dihydro–(1,3,5)–triazino–(2,1b)6,7or8–o–chloro–benzothiazole (3e).

m.p. 149°C; $[\alpha]_D^{41}$ + 9.09°(c, 0.0011 in $CHCl_3$), R_f 0.88; IR (KBr)cm^{-1}: ν 3062.7 (C–H, Ar–H), 2896.9 (C–H, $–CH_2$), 1728.1 (C=O), 1535.2 (N–C(=S)–N), 1269.1(C–O), 1091.6(C=S), 975.9(1,2,3–trisubstituted ring), 852.5 (β–D–glucopyranosyl ring deformation), 802.3 (1,3–disubstituted ring), 709.8 (monosobstituted ring), 617.2(C–S–C), 574.7(C–Cl). NMR ^1H data ($CDCl_3$): δ 8.0–7.5 (m, 28H, Ar–H), 5.3–4.0 (m, 5H, β–D–glucopyranosyl ring). 4.5–4.0(d, 2H, CH_2O). (Table–1) Anal. Calcd. for $C_{50}H_{35}O_9N_4S_2Cl$ 2HCl; C, 59.58; H, 3.47; N, 5.56; S, 6.35; Cl, 10.42 found : C, 59.18; H, 3.37; N, 5.30; S, 5.95; Cl, 10.11.

On the basis of all the above facts, the product was assigned the structure 4H, 4– Thio – 2 – (tetra – O – benzoyl – β – D –glucopyranosylimino)–3–phenyl–2,3–dihydro–(1,3,5)–triazino–(2,1b)6,7 or 8–o–chloro benzothiazole (**3e**).

The reaction of N–phenyl isocyanodichloride was extended to several other l–tetra–O–benzoyl–β–D–glucopyranosyl–3–aryl benzothiazolyl thiocarbamides and corresponding products (**3c–3g**) were prepared.

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REFERENCES

1. G. V. Korpe, S. P. Deshmukh and A. K. Fokmare, Indian, J. Heterocyclic Chem., **10**, 287 (2001).
2. Arnold Weissberger, "Physical Methods of Organic Chemistry", Part II, 2nd Ed., Interscience Publisher, INC, New York (1949).
3. B. Fried and S. H. Sherama, "Thin–Layer Chromatography", 2nd Ed., Chromatographic Science Series, New York, Dekker, (1986), p. 35.
4. J. G. Colley, J. P. Duguid, A. G. Fraser, B. P. Marmion, Mackie and Mc Carty, Practical Microbiology, Churchill Livingstone (1989).
5. J. Fuentes, W. Moreda, C. Ortiz, I. Robina and C. Welsh, Tetrahedran, **48**, 6413 (1992).
6. R. Babino, C., Jose and F. Mota, Carbohy. Res, **154**, 280 (1986).

7. J. Fuentes, M., Jose M. Garcia, F., Carmen, O. Mellet, M. Angeles and P. Adrian, Carbohy. Res., **188**, 35 (1989).

8. H. Spedding, "Advances in Carbohydrate Chemistry", Academic Press, INC, New York, (1964), p. 19, 31.

9. S. A. Baker, J. Homer, M. C. Keith and L. F. Thomas, J. Chem. Soc., 1538 (1963).

10. B. D. Norma Inge Accorsa and M. E. Thiel, Carbohy. Res., **124**, 177 (1983).

11. G. M. Dyson and T. Haringto, J. Chem. Soc., 191 (1940).

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