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SYNTHESIS OF SOME NOVEL PER-ACETYLATED GLUCOSYL N–CARBAMIDES, BENZOTHIAZOLYL CARBAMIDES AND CARBAMATES

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ABSTRACT

Several 1- tetra-O-acetyl -β-D- glucosyl -3-aryl carbamides **(II_{a-g})**, tetra-O-acetyl-β-D-glucosyl (3)-2 substituted benzothiazolyl carbamides **(III_{a-g})** and tetra-O-acetyl-β-D-glucosyl-O- alkyl carbamates **(IV_{a-e})** have been prepared by the interaction of tetra-O-acetyl-β-D-glucosyl isocyanate **(I)** and various amines, substituted benzothiazoles and various alcohols. The identities of these newly synthesized compounds were established on the basis of elemental analysis, I.R., NMR and mass spectral analyses.

Key words: Glucosyl isocyanate, Aryl amines, Substituted benzothiazoles carbamides, Carbamates.

INTRODUCTION

Per-acetylated derivatative of sugar isocyanate are important class of organic compounds in the field of carbohydrate chemistry. In last few years, hundreds of compounds have been synthesized from glucosyl isocyanate. Glucosyl isocyanate is one of the versatile reagent in the field of carbohydrate chemistry.

N-Glucosylated compounds have wide applications in industry, medicinal chemistry and in many other ways[1]. Carbamides and their derivatative shows strong anti-bacterial activity[2]. Many of these derivatative have been found to posses wide applications in industry like paper[3], textile[3-5] and food industry[6]. Benzothiazoles are bicyclic ring system with multiple applications. They have diverse chemical reactivity and broad spectrum of biological activity[7]. 2-Aminobenzothiazole show anti-tumor[8] and anti- malarial activity. Bis substituted benzothiazole acts as the potential anti- HIV agent[9]. Also Schiff base of benzothiazole posses anti-cancer, anti-pyretics and sterase inhibitory activity[10,11]. Hence, it is quite interesting to synthesize carbamides having benzothiazole substitutent.

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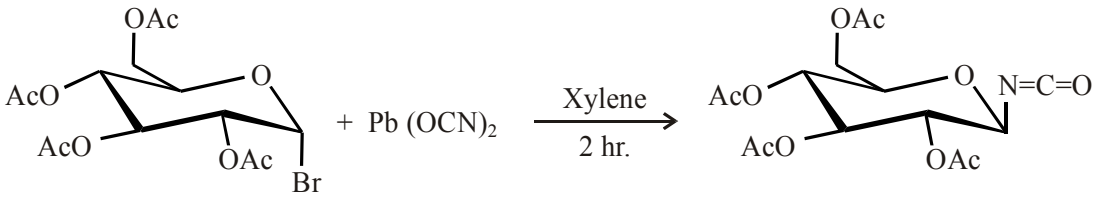
In view of interest in synthesis of N-glucosylated amido group contaning compounds, a synthetic method has been evolved for synthesis of 1, 3-disubstituted carbamides and carbamates.

Here, the synthesis of several tetra-O-acetyl-β-D-glucosyl-3-aryl carbamides **(II_{a-g})**, tetra-O-acetyl-β-D-glucosyl (3)-2-substituted benzothiazolyl carbamides **(III_{a-g})** and tetra-O-acetyl-β-D-glucosyl–O–alkyl carbamates **(IV_{a-e})** has been reported for the first time using tetra-O-acetyl-β-D-glucosyl isocyanate **(I)**. The required tetra-O-acetyl-β-D-glucosyl isocyanate was prepared by the interaction of tetra-O-acetyl-α-D-glucosyl bromide and lead cyanate in place of silver cyanate in boiling xylene medium.

EXPERIMENTAL

Optical rotations $[\alpha]^{31}_{D}$ were measured on Equip-Tronics EQ 800 Digital Polarimeter at 31 ^{0}C in $CHCl_3$. I.R. spectrum were recorded on Perkin- Elmer RXI-FTIR spectrometer. ^{1}H NMR were obtained on a Bruker DRX–300 NMR spectrometer. The sample were prepared in $CDCl_3$ with TMS as an internal reference.



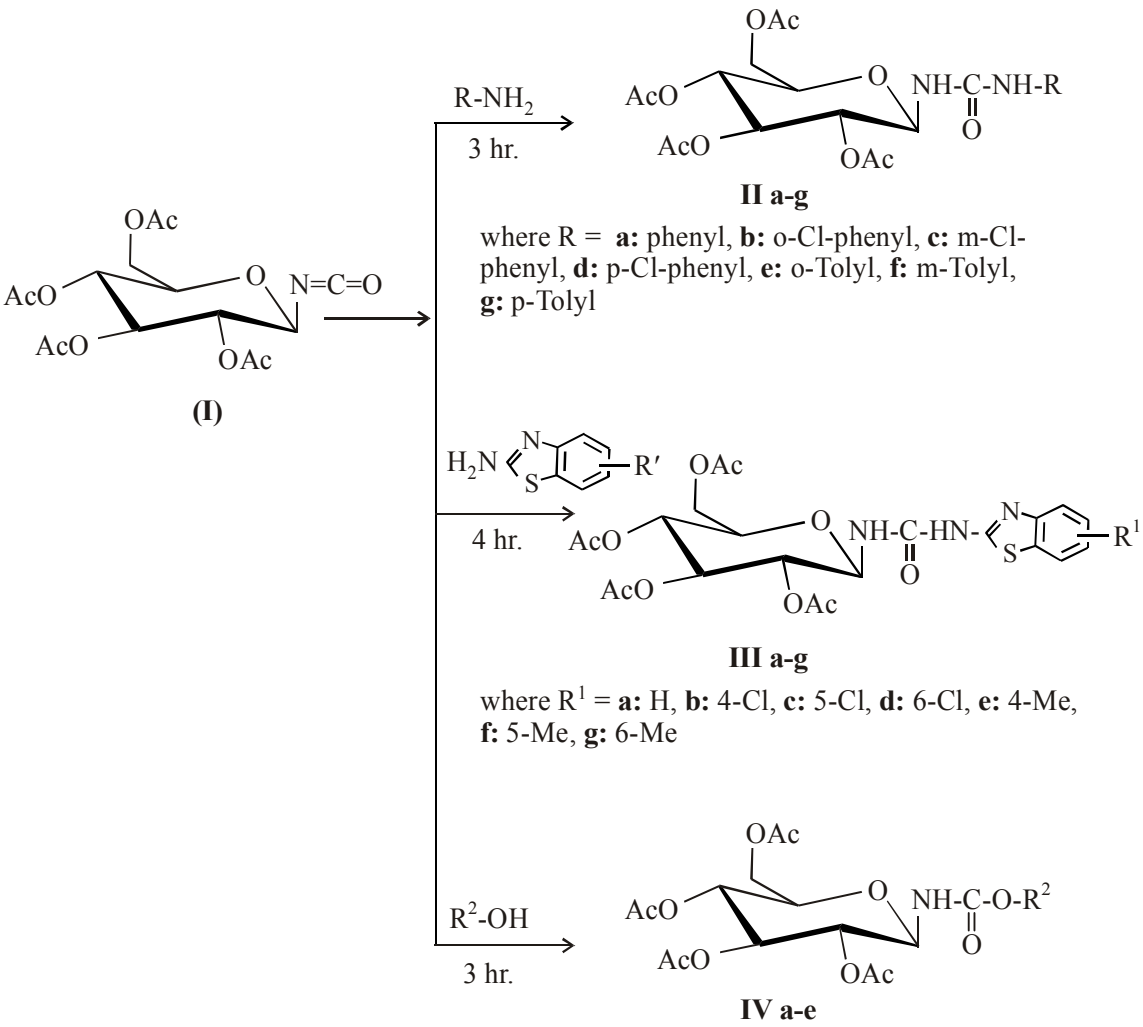
Tetra-O-acetyl-α-D -glucosyl bromide

Lead cyanate

Tetra-O-acetyl-β-D -glucosyl isocyanate **(I)**

Scheme 1

Tetra-O-acetyl-β-D-glucosyl isocyanate **(I)** was prepared for the first time by the condensation of tetra-O-acetyl-α-D-glucosyl bromide (0.005M, 2.2 g) and lead cyanate (0.005 M, 1.5 g) in boiling xylene medium (30 mL) for 2 hr. with frequent shaking. After the removel of lead bromide, the xylene filtrate was titutrated with petroleum ether (60-80 ^{0}C), where tetra-O-acetyl-β-D-glucosyl isocyanate was precipitate out. It was purified by dissolving it in a minimum quantity of chloroform and re-precipitating with petroleum ether (60-80 ^{0}C) to affored a pale yellow solid. The homogeneity of the product was checked by TLC.



Scheme 2

General procedure

Tetra-O-acetyl-β-D-glucosyl isocyanate (I)

Yield 75.50%, M.P. 115-120^{0}C, $[\alpha]_D^{31}$ = - 280^0 (c, 0.93 mol, chloroform), I.R. (KBr): ν 2924 (ali. C-H), 2121 (N=C=O), 1741 (C=O), 1428 (C-N), 1226 (C-O) and 846cm^{-1} (D-glucose ring deformation[12-15]) ^{1}H NMR ($CDCl_3$) : δ 5.1-6.0 (m, 7H pyranosyl ring)[15] 2.1-1.9

(m, 12H, 4 $COCH_3$); Mass : m/z 373 (M^+) 331, 169, 109, Anal. Calcd. for $C_{15}H_{19}NO_{10}$ C, 46.27; H,4.88; N, 3.59; Found C, 46.17; H 4.80; N, 3.44%

Tetra-O-acetyl-β-D-glucosyl-3- aryl carbamides (IIa-g)

A 0.005M of aryl amines in 5 mL of benzene was added to a 0.005M solution of tetra-O-acetyl-β-D-glucosyl isocyanate **(I)** in 15 mL of benzene. The reaction mixture was refluxed over boiling water bath for 3 hr. After refluxing, the solvent was distilled off and the sticky residue obtained was titutrated with petroleum ether (60-80^{0}C) to afford white solid **(II a-g)**. The product was purified by recrystalization from ethanol –water system (3 : 1). The homogeneity of the product was checked by TLC. The percent yield, M.P., optical rotation and elemental analysis are shown in Table 1.

Table 1: Reactant - i) Tetra-*O*-acetyl-β-D-glucosyl isocyanate **(I)** (0.005 M, 2 g)
ii) Aryl amines **(3a-g)** (0.005 M)

Sr. No.	Products (IIa-h)	Amine (g)	Yield (%)	m.p. (^{o}C)	$[\alpha]_D^{32}$ ($CHCl_3$)	Analysis		R_f (CCl_4 : EtOAc)
						Found (%)	Required (%)	
1	**IIa**	Aniline (0.45)	65.58	95	+133.94^o (c, 0.373)	N, 5.80	N, 6.03,	0.69 (3:2)
2	**IIb**	o-Cl-Aniline (0.64)	71.69	130	+117.64^o (c, 0.340)	N, 5.42	N, 5.62	0.73 (3:2.2)
3	**IIc**	m-Cl-Aniline (0.64)	62.26	105	+91.85^o (c, 0.326)	N, 5.37	N, 5.62	0.79 (3:2.2)
4	**IId**	p-Cl-Aniline (0.64)	69.81	145	+155.19^o (c, 0.386)	N, 5.49	N, 5.62	0.86 (3:2.1)
5	**IIe**	o-Toluidine (0.54)	54.90	155	+205.88^o (c, 0.340)	N, 5.74	N, 5.83,	0.89 (3:2.1)
6	**IIf**	m-Toluidine (0.54)	66.66	140	+242.42^o (c, 0.333)	N, 5.58	N, 5.83,	0.71 (3:2.1)
7	**IIg**	p-Toluidine (0.54)	68.23	122	+187.50^o (c, 0.320)	N, 5.65	N, 5.83,	0.77 (3:2.3)

(IIa) IR (KBr) ν 3461 (N-H), 2966 (Ar-H), 1742 (C=O) , 1430 (C-N) , 1237 (C-O), 845 cm^{-1} (D-glucose ring deformation); ^1H NMR; ($CDCl_3$) δ 7.49-7.19 (m, 5H, Ar-H), 6.6-6.0 (s, 2H, N-H), 5.1-5.9 (m, 7H pyranosyl ring), 2.1-1.9 (m, 12H, 4 $COCH_3$); Mass; m/z 464 (M^+), 331, 221, 169, 109; Anal. Calcd. for $C_{21}H_{26}N_2O_{10}$; C, 52.28; H, 5.39; N, 5.80; found C, 52.33; H, 5.46; N, 6.03%

(IIb) IR (KBr): ν 3361 (N-H), 2967 (Ar-H), 1742 (C=O), 1430 (C-N), 1237 (C-O) and 845 cm^{-1} (D-glucose ring deformation); ^1H NMR ($CDCl_3$) δ 7.55-7.38 (m, 4H, Ar-H), 6.7-6.0 (s, 2H , N-H), 5.1-5.9 (m, 7H , Pyranosyl ring), 2.1-1.9 (m, 12H, 4 $COCH_3$); Mass; m/z (M^+ Not predictable) 331, 169, 109; Anal. Calcd. for $C_{21}H_{25}N_2O_{10}Cl$, C, 48.83; H, 4.84; N, 5.42, Found C, 48.76; H, 4.88; N, 5.62%

(IIe) IR (KBr): ν 3461 (N-H), 2966 (Ar-H), 1742 (C=O), 1430 (C-N), 1238 (C-O) and 845 cm^{-1} (D-glucose ring deformation); ^1H NMR: $CDCl_3$) δ 8.05 (s, 1H, N-H), 7.27-7.21 (d, 2H, Ar-H), 7.08-7.06 (d, 2H, Ar-H), 5.05-585 (t, 1H, H_2), 2.3 (s, 3H Ar-CH_3), 2.1-1.9 (m, 12H, 4$COCH_3$), 5.1-5.5 (m, 7H, pyranosyl ring); Mass: m/z 480 (M^+) 331, 211, 109, Anal. Calcd. for $C_{22}H_{28}N_2O_{10}$ C, 53.22; H, 5.64; N, 5.74 Found C, 53.18; H, 5.61; N, 5.83%

Tetra-O-acetyl-β-D-glucosyl-(3)-2-substituted benzothiazolylcarbamides (IIIa-g)

A 0.005M solution of 2-amino benzothiazole / substituted benzothiazole in 5 mL benzene was added to a 0.005M solution of tetra-O-acetyl-β-D-glucosyl isocyanate **(I)** in 15 mL benzene and the reaction mixture were refluxed for 4 hr. After refluxing, the solvent was distilled off and sticky residue was obtained, which was titutrated with petroleum ether (60-80^{0}C). The products were purified by recrystallization with ethanol-water system (1 : 3). The homogeneity of the product was checked by TLC. The percent of yield, M.P., optical rotation and elemental analysis are shown in Table 2.

(IIIa) IR (KBr) : ν 3374 (N-H), 2969 (Ar-H) 1743 (C=O), 1588 (C=N), 1382 (C-N), 1239 (C-O) and 753 cm^{-1} (C-S); ^1H NMR ($CDCl_3$) : δ 7.57-7.20 (m, 5H Ar-H), 6.3-6.2 (s 1H N-H), 5.1-5.5 (m, 7H Glucopyranosyl ring), 2.1-1.9 (m, 12 H, 4$COCH_3$); Mass : m/z 508 (M^+), 331, 169, 109, Anal. Calcd. for $C_{22}H_{25}N_3O_9S$; C, 48.97; H, 4.63; N, 8.24; S, 6.31; found C, 48.84; H, 4.59; N, 8.45; S 6.51%

(IIIb) IR (KBr) : ν 3340 (N-H), 2966 (Ar-H), 1745 (C=O), 1615 (C=N), 1378 (C-N), 1231 (C-O) and 753 cm^{-1} (C-S) ; ^1H NMR ($CDCl_3$) : δ 7.7-7.6 (m, 1H, N-H), 7.4 - 7.1 (m, 4H, Ar-H), 5.1-4.7 (m, 7H, glucopyranosyl ring), 2.2-1.9 (m, 12H, 4 $COCH_3$); Mass : m/z 544 (M^+), 331, 169, 109; Anal. Calcd., $C_{22}H_{24}N_3O_9S$-Cl, C, 46.07; H, 4.18; N, 7.72; S, 5.88 Found C, 46.13; H, 4.23; N, 7.21; S, 5.98%

(IIIe) IR (KBr) : ν 3468 (N-H), 2997 (Ar-H), 1743 (C=O), 1610 (C=N), 1383 (C-N), 1238 (C-O) and 845 cm^{-1} (Glucopyranosyl ring); ^1H NMR ($CDCl_3$) : δ 7.4-7.0 (m, 4H, Ar-H), 5.15 (s, 1H , N-H), 2.3 (m, 3H, Ar-CH_3) 5.4-5.5 (m, 7H, Glucopyranosyl ring), 2.2-1.8 (m, 12H, 4$COCH_3$) Mass: m/z (Not predictable) 331, 109; Anal. Calcd. for $C_{23}H_{27}N_3O_9S$; C, 49.90; H, 4.33; N, 8.04; S, 6.13; Found C, 4997; H, 4.26; N8.22; S , 6.21%.

Table 2: Reactant - i) Tetra-*O*-acetyl-β-D-glucosyl isocyanate **(I)** (0.005 M)
ii) 2-Aminobenzothiazole/substituted benzothiazoles **(a-g)** (0.005M)

Sr. No.	Product (IIIa-g)	Benzothiazole (g)	% Yield	m.p. (^oC)	$[\alpha]_D^{29}$ ($CHCl_3$)	Analysis		R_f (CCl_4: EtOAc)
						Found (%)	Requires (%)	
1	**IIIa**	2-amino (0.75)	54	135-142	+74.46^0 (c,0.94)	N,8.45 S,6.51	N,824 S,631	0.57 (3:2.1)
2	**IIIb**	4-Chloro- (0.92)	68	112-120	+49.67^0 (c,1.00)	N, 7.21 S, 5.98	N, 7.72 S, 5.88	0.60 (3:2)
3	**IIIc**	5-Chloro- (0.92)	51	162-170	-38.71^0 (c,1.03)	N, 7.21 S, 5.98	N, 7.72 S, 5.88	0.66 (3:2)
4	**IIId**	6-Chloro- (0.92)	61	155-160	-39.73^0 (c,1.00)	N, 7.21 S, 5.98	N, 7.72 S, 5.88	0.62 (3:2.2)
5	**IIIe**	4-Methyl- (0.82)	74	152-155	+91.22^0 (c,0.98)	N, 8.82 S, 6.21	N, 8.04 S, 6.13	0.71 (3:2)
6	**IIIf**	5-Methyl- (0.82)	77	115-125	+69.54^0 (c,1.00)	N, 8.82 S, 6.21	N, 8.04 S, 6.13	0.76 (3:2)
7	**IIIg**	6-Methyl- (0.82)	74	165-170	+49.01^0 (c,1.02)	N, 8.82 S, 6.21	N, 8.04 S, 6.13	0.80 (3:2)

Tetra-O-acetyl-β-D-glucosyl-O-alkyl carbamates (IV a-e) scheme 2

A 0.005M solution of tetra-O-acetyl-β-D-glucosyl isocyanate **(I)** in 15 mL of alcohol was added to various alcohols (20 mL) and reaction mixture was refluxed for 3 hr. After refluxing, it was allowed to cool and poured in water with vigorous stirring. A white granular solid seprated out, which was purified by recrystallization from aqueous ethanol.

The homogeneity of the product was checked by TLC. The percent yield, M. P., optical rotation and elemental analysis are shown in Table 3.

(IVa) IR (KBr) : ν 3368 (N-H), 2926 (ali. C-H), 1751 (C=O), 1372 (C-N) and 1222 cm^{-1} (C-O), ^1H NMR ($CDCl_3$) : δ 6.87-6.84 (d, 1H N-H), 5.57 (s, 1H, H_1), 4.5-4.4 (m, 2H CH_2), 2.2-1.6 (m, 12H, 4 $COCH_3$), 1.3-1.2 (m, 3H, CH_3); Mass : m/z 420 (M^+) 331, 169, 109; Anal. Calcd. for C_{17} H_{25} N O_{11}, C, 44.33; H, 5.41; N, 6.89; Found C, 44.28; H, 5.49; N, 6.75.

(IVe) IR, (KBr) : ν 3362 (Ar-H), 2984 (ali. C-H), 1750 (C=O), 1371 (C-N), 1225 cm^{-1} (C-O), ^1H NMR, ($CDCl_3$) : δ 6.74-6.71 (d, 1H, N-H), 5.6-5.4 (m, 3H, CH_2), 2.2-1.9 (m, 12H, 4 $COCH_3$), 5.4-5.5 (m, 7H, Glucopyranosyl ring); Mass : m/z 435 (M^+), 331, 169, 109; Anal. Calcd. for C_{18} H_{27} N O_{11} C, 48.10; H, 6.01; N, 3.21; found C, 48.17; H, 6.09; N, 3.05.

Table 3: Reactants - i) Tetra-*O*-acetyl-β-D-glucosyl isocyanate **(II)** (0.005 M)
ii) Alcohols (5a-e, 20mL)

Sr. No.	Products (IVa-e)	Alcohols	Yield (%)	m.p. (^oC)	$[\alpha]_D^{35}$ ($CHCl_3$)	R_f (CCl_4: EtOAc)	Analysis	
							Found (%)	Required (%)
1	**IVa**	Ethyl	68	146	-136^0 (c, 0.74)	0.62 (3:2.1)	N, 6.75	N, 6.89
2	**IVb**	*n*-Propyl	65	122	-87.5^0 (c, 0.8)	0.76 (3:2)	N, 3.15	N, 3.33
3	**IVc**	isoPropyl	52	142	-25.3^0 (c, 0.79)	0.70 (3:2)	N, 2.95	N, 3.03
4	**IVd**	IsoAmyl	61	115 -120	87^0 (c, 0.74)	0.86 (3:2.2)	N, 3.00	N, 2.93
5	**IVe**	n-Butyl	46	190 (d)	52.6^0 (c, 0.76)	0.82 (3:2)	N, 3.05	N, 3.21

RESULTS AND DISCUSSION

Tetra-O-acetyl-β-D-glucosyl-3- aryl carbamides **(II a-g)** and tetra-O-acetyl-β-D-

glucosyl-3(-2)- substituted benzothiazolyl carbamides **(IIIa-g)** were prepared by the reaction of tetra-O-acetyl-β-D-glucosyl isocyanate **(I)** and various amines and 2-amino benzothiazole/ substituted benzothiazoles, in a benzene medium for 3 hr. and 4 hr., respectively. After condensation, the solvent was distilled off and sticky residue was obtained, which was titutrated with petroleum ether (60-80^{0}C) to afford white solid. It was purified by water ethanol system (1 : 3).

Tetra-O-acetyl-β-D-glucosyl–O–alkyl carbamates **(IVa-e)** were prepared by the reaction of tetra-O-acetyl-β-D-glucosyl isocyanate and various alcohols by refluxing for 3 hr. After condensation, the reaction mixture was poured in water with vigorous stirring, where white granular solid seprated out. It was purified by aqueous ethanol. The required 2-amino benzothiazole /substituted benzothiazole were prepared by the oxidatative cyclization of 1-aryl thiocarbamides with the help of molecular bromine, 1-Aryl thiocarbamides have been prepared by the interaction of ammonium thiocyanate with aryl amines hydrochlorides.

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