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SYNTHESIS AND CHARACTERIZATION OF METHYL 4, 6-*O*-ENZYLIDENE-α-D-GLUCOPYRANOSIDE DERIVATIVES

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Abstract

Regioselective benzoylation of methyl 4,6-*O*-benzylidene-α-**D**-glucopyranoside (**1**) using direct acylation method furnished the methyl 4,6-*O*-benzylidene-2-*O*-(4-t-butylbenzoyl)-α-**D**-glucopyranoside (**2**) in an excellent yield. In order to obtain newer products for antimicrobial screening studies, the 2-*O*-4-t-butylbenzoyl derivative was further transformed to a series of 3-*O*-acyl derivatives (**2-12**) containing a wide variety of functionalities in a single molecular framework.

Introduction

Carbohydrates play an essential role in our daily life. Carbohydrate chemists consider selective acylation as one of the most important and fundamental methods for protection of the hydroxyl groups. A number of methods for selective acylation of carbohydrates have so far been developed and successfully employed[1-4]. Of these, the direct method is considered as one of the most effective[4] for selective acylation of carbohydrates. Of the carbohydrates isolated from natural sources, acyl glycoses and acyl glycosides have immense importance and some of them have effective biological activity[5]. It was found from the literature survey that N, S and X-containing heterocyclic compounds showed marked antimicrobial activities[6]. When heterocyclic compounds attached to a carbohydrate compound[7], their efficiency to inhibit bacteria or fungal strains increased sharply. A large number of biologically active compounds also possess aromatic, heteroaromatic and acyl substituents[7]. It also known that if an active nucleus is linked to another active nucleus, the resulting molecule may possess greater potential for biological activity[7].

As a continuation of a project on antimicrobial screening of monosaccharide derivatives and guided by some interesting results obtained so far[8-13], we synthesized a number of derivatives Methyl 4,6-*O*-benzylidene-α-**D**-glucopyranoside (**1**), deliberately incorporating a wide variety of functionalities in a single molecular framework. Biological evaluation of these derivatives were studied employing various bacterial and fungal strains. The synthetic part is reported here while the antimicrobial part is currently under preparation for communication.

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Experimental

All reagents used were commercially available (Aldrich) and were used as received, unless otherwise specified. Melting points were determined on an electro-thermal melting point apparatus (England) and are uncorrected. Evaporations were carried out under reduced pressure using VV-1 type vacuum rotary evaporator (Germany) with a bath temperature below 40°C. ^{1}H-NMR spectra (300 MHz) were recorded for solutions in deuteriochloroform ($CDCl_3$) (internal Me_4Si) with a Bruker DPX-40C spectrometer. Thin layer chromatography (t.l.c) was performed on Kieselgel GF_{254} and spots were detected by spraying the plates with 1% H_2SO_4 and heating at 150-200°C until coloration took place. Column chromatography was performed with silica gel G_{60}. Solvent system employed for t.l.c analyses was ethyl acetate-hexane in different proportions.

Methyl 4,6-O-benzylidene-α-D-glucopyranoside, **1**

A solution of methyl-α-**D**-glucopyranoside (5 gm, 25.74 mmol) in dry DMF (30 ml) was treated with benzaldehydedimethylacetal (5 ml, 33.5 mmol) and camphor-10-sulphonic acid (100 mg) and the mixture was heated at 50ºC for 6 hours. After cooling to room temperature, the mixture was neutralized with Et_3N, diluted with EtOAc, washed with saturated $NaHCO_3$ and brine and dried over Na_2SO_4. The progress of the reaction was monitored by t.l.c. (ethyl acetate-hexane, 3:1) and the solvent was then removed. The residue was purified by passing through a silica gel column with ethyl acetate-hexane (3:1) as an eluant to afford methyl 4,6-*O*-benzylidene-α-**D**-glucopyranoside **1** (5.5 gm, yield 76%) as a white crystalline solid according to the literature[14].

Methyl 4,6-O-benzylidene-2-O-(4-t-butylbenzoyl)-α-D-glucopyranoside, **2**

A solution of methyl 4,6-*O*-benzylidene-α-**D**-glucopyranoside (**1**) (2 gm, 7.09 mmol) in dry pyridine (6 ml) was cooled to 0ºC whereupon 4-t-butylbenzoyl chloride (1.4 ml, 7.8 mmol) was added to it. The mixture was stirred at the same temperature for 5 hours and then allowed to stand overnight at room temperature. The progress of the reaction was monitored by t.l.c. (ethyl acetate-hexane1:3), which indicated the formation of a major product. A few pieces of ice was added to the flask and then extraction of the product mixture with chloroform (3×10 ml). The combined chloroform layer was washed successively with dilute hydrochloric acid (10%), saturated aqueous sodium hydrogen carbonate ($NaHCO_3$) solution and distilled water. The chloroform layer was then dried over $MgSO_4$, filtered and the filtrate was concentrated under reduced pressure to leave a syrup. The syrup mass was passed through a silica gel column and eluted with ethyl acetate-hexane (1:3), to furnish the 4-t-butylbenzoyl derivative, **2** as a white crystalline solid. Recrystallisation from ethyl acetate-hexane gave the analytically pure sample as needles.

Yield 52%; R_f = 0.51) as a white crystalline solid; m.p. 156-157ºC; **^{1}H-NMR ($CDCl_3$):** δ_H 8.00 (2H, m, Ar-H), 7.48 (2H, m, Ar-H), 7.37 (5H, m, Ar-H), 5.57 (1H, s, PhC*H*-), 5.04 (1H, dd, J = 3.7 Hz, and 9.8 Hz, H-2), 5.00 (1H, d, J = 3.8 Hz, H-1), 4.32 (2H, m, H-3 and

H-6a), 3.92 (1H, m, H-5), 3.81 (1H, t, J = 10.2 Hz, H-6b), 3.63 (1H, t, J = 9.8 Hz, H-4), 3.39 (3H, s, 1-OCH_3), 1.38 {9H, s, (CH_3)$_3$C-}.

Methyl 3-O-acetyl-4,6-O-benzylidene-2-O-(4-t-butylbenzoyl)-α-D-glucopyranoside, **3**

A cooled (0ºC) and stirred solution of methyl 4,6-*O*-benzylidene-2-*O*-(4-t-butylbenzoyl)-α-**D**-glucopyranoside (**2**) (93.4 mg, 0.21 mmol) in dry pyridine (3 ml) was treated with acetic anhydride (0.1 ml). The low temperature was maintained by ice and common salt for eight hours and then allowed to stand at room temperature overnight. The progress of the reaction was monitored by t.l.c. (ethyl acetate-hexane, 1:7), which indicated completion of the reaction and formation of a faster-moving product. Few pieces of ice were added to the flask and the product mixture was extracted with chloroform (3×10 ml). The combined chloroform layer was washed successively with dilute hydrochloric acid (10%), saturated aqueous sodium hydrogen carbonate ($NaHCO_3$) solution and distilled water. The chloroform layer was then dried over $MgSO_4$, filtered and the filtrate was concentrated under reduced pressure to leave syrupy mass. The syrup residue was passed through a silica gel column and eluted with ethyl acetate-hexane (1:7), to furnish the 4-t-butylbenzoyl derivative, **3**. Similar reaction and purification procedure was applied to prepare; compounds **4** -**12**.

Yield 90%; R_f = 0.51) as pasty mass; **^{1}H-NMR ($CDCl_3$):** δ_H 7.96 (2H, d, J = 8.5 Hz, Ar-H), 7.46 (5H, m, Ar-H), 7.34 (2H, d, J = 8.5 Hz, Ar-H), 5.78 (1H, t, J =9.8 Hz, H-3), 5.53 (1H, s, PhC*H*-), 5.10 (1H, d, J = 3.6 Hz, H-1), 5.03 (1H, dd, J = 3.6 Hz and 9.8 Hz, H-2), 4.32 (1H, dd, J = 4.7 and 10.1 Hz, H-6a), 3.98 (1H, ddd, J = 4.8, 9.8 and 14.2 Hz, H-5), 3.84 (1H, t, J = 10.2 Hz, H-6b), 3.72 (1H, t, J = 9.8 Hz, H-4), 3.44 (3H, s,1-OCH_3), 1.98 (3H, s, CH_3CO-), 1.28 {9H, s, (CH_3)$_3$C-}.

Methyl 4,6-O-benzylidene-2-O-(4-t-butylbenzoyl)-3-O-pentanoyl-α-D-glucopyranoside, **4**

Yield 78%; (R_f = 0.51) as a colorless pasty mass; **^{1}H-NMR ($CDCl_3$):** δ_H 7.95 (2H, d, J = 8.4 Hz, Ar-H), 7.45 (5H, m, Ar-H), 7.35 (2H, d, J = 8.4 Hz, Ar-H), 5.79 (1H, t, J = 9.8 Hz, H-3), 5.54 (1H, s, PhC*H*-), 5.09 (1H, d, J = 3.6 Hz, H-1), 5.04 (1H, dd, J = 3.6 Hz, and 9.8 Hz, H-2), 4.30 (1H, dd, J = 4.7 and 10.2 Hz, H-6a), 3.98 (1H, ddd, J = 4.7, 9.8 and 14.2 Hz, H-5), 3.82 (1H, t, J = 10.2 Hz, H-6b), 3.73 (1H, t, J = 9.8 Hz, H-4), 3.45 (3H, s,1-OCH_3), 2.25 {2H, m, $CH_3(CH_2)_2CH_2CO$-}, 1.46 {2H, m, $CH_3CH_2CH_2CH_2CO$- }, 1.28 {9H, s, (CH_3)$_3$C-}, 1.22 {2H, m, CH_3CH_2 $(CH_2)_2CO$-}, 0.88 {3H, t, J = 7.3 Hz, $CH_3(CH_2)_3$ CO-}

Methyl 4,6-O-benzylidene-2-O-(4-t-butylbenzoyl)-3-O-decanoyl-α-D-glucopyranoside, **5**

Yield 96%; (R_f = 0.52) as a colorless thick syrup; **^{1}H-NMR ($CDCl_3$):** δ_H 7.96 (2H, d, J = 8.4 Hz, Ar-H), 7.45 (5H, m, Ar-H), 7.33 (2H, d, J = 8.4 Hz, Ar-H), 5.79 (1H, t, J = 9.7 Hz, H-3), 5.53 (1H, s, PhC<u>H</u>-), 5.10 (1H, d, J = 3.5 Hz, H-1), 5.06 (1H, dd, J = 3.5 Hz, and 9.8 Hz, H-2), 4.33 (1H, dd, J = 4.7 and 10.1 Hz, H-6a), 3.99 (1H, m, H-5), 3.80 (1H, t, J = 10.1 Hz, H-6b), 3.71 (1H, t, J = 9.8 Hz, H-4), 3.38 (3H, s,1-OC<u>H</u>$_3$), 2.23 {2H, m,

$CH_3(CH_2)_7CH_2CO$-}, 1.46 {2H, m, $CH_3(CH_2)_6CH_2CH_2CO$-}, 1.32 {2H, m, $CH_3(CH_2)_5CH_2(CH_2)_2CO$-}, 1.25 {9H, s, $(CH_3)_3C$-}, 1.22 {4H, m, $CH_3(CH_2)_3(CH_2)_2(CH_2)_3CO$-}, 1.13 {6H, m, $CH_3(CH_2)_3(CH_2)_5CO$-}, 0.84 {3H, t, J = 6.9 Hz, $CH_3(CH_2)_8CO$-}.

Methyl 4,6-O-benzylidene-2-O-(4-t-butylbenzoyl)-3-O-lauroyl-α-D-glucopyranoside, **6**

Yield 92%; (R_f = 0.51) as a syrup; **^{1}H-NMR ($CDCl_3$):** δ_H 7.96 (2H, m, Ar-H), 7.45 (4H, m, Ar-H), 7.34 (3H, m, Ar-H), 5.79 (1H, t, J = 9.7 Hz, H-3), 5.53 (1H, s, PhC*H*-), 5.07 (1H, dd, J = 3.7 and 9.7 Hz, H-2), 5.04 (1H, d, J = 3.7 Hz, H-1), 4.32 (1H, dd, J = 4.7 and 10.1 Hz, H-6a), 3.98 (1H, m, H-5), 3.79 (1H, t, J = 10.1 Hz, H-6b), 3.70 (1H, t, J = 9.7 Hz, H-4), 3.38 (3H, s,1-OCH_3), 2.23 {2H, m, $CH_3(CH_2)_9CH_2CO$-}, 1.44 {2H, m, $CH_3(CH_2)_8CH_2CH_2CO$-}, 1.34 {2H, m, $CH_3(CH_2)_7CH_2(CH_2)_2CO$-}, 1.32 {9H, s, $(CH_3)_3C$-}, 1.25 {10H, m, $CH_3(CH_2)_2(CH_2)_5(CH_2)_3CO$-}, 1.17 {4H, m, $CH_3(CH_2)_2(CH_2)_8CO$-}, 0.86 {3H, t, J = 5.3 Hz, $CH_3(CH_2)_{10}CO$-}.

Methyl 4,6-O-benzylidene-2-O-(4-t-butylbenzoyl)-3-O-(3-chlorobenzoyl)-α-D-glucopyranoside, **7**

Yield 92%; (R_f = 0.51) as a syrup; **^{1}H-NMR ($CDCl_3$):** δ_H 7.85 (5H, m, Ar-H), 7.42 (4H, m, Ar-H), 7.30 (4H, m, Ar-H), 6.03 (1H, t, J = 9.8 Hz, H-3), 5.55 (1H, s, PhC*H*-), 5.21 (1H, dd, J = 3.6 and 9.8 Hz, H-2), 5.15 (1H, d, J = 3.7 Hz, H-1), 4.37 (1H, dd, J = 4.8 and 10.2 Hz, H-6a), 4.07 (1H, m, H-5), 3.91 (1H, t, J = 10.2 Hz, H-6b), 3.85 (1H, t, J = 9.8 Hz, H-4), 3.42 (3H, s, 1-OCH_3), 1.29 {9H, s, $(CH_3)_3C$-}.

Methyl 4,6-O-benzylidene-2-O-(4-t-butylbenzoyl)-3-O-(4-chlorobenzoyl)-α-D-glucopyranoside, **8**

Yield 61%; (R_f = 0.51) as a pasty mass; **^{1}H-NMR ($CDCl_3$):** δ_H 7.90 (4H, d, J = 8.3 Hz, Ar-H), 7.39 (4H, m, Ar-H), 7.31 (5H, m, Ar-H), 6.01 (1H, t, J = 9.8 Hz, H-3), 5.55 (1H, s, PhC*H*-), 5.23 (1H, dd, J = 3.6 and 9.9 Hz, H-2), 5.14 (1H, d, J = 3.6 Hz, H-1), 4.36 (1H, dd, J = 4.7 and 10.2 Hz, H-6a), 4.05 (1H, ddd, J = 4.7, 9.8 and 14.5 Hz, H-5), 3.87 (1H, t, J = 9.5 Hz, H-4), 3.84 (1H, t, J = 10.2 Hz, H-6b), 3.42 (3H, s, 1-OCH_3), 1.29 {9H, s, $(CH_3)_3C$-}.

Methyl 4,6-O-benzylidene-2-O-(4-t-butylbenzoyl)-3-O-(4-nitrobenzoyl)-α-D-glucopyranoside, **9**

Yield 87%; (R_f = 0.50) as a colorless syrup; **^{1}H-NMR ($CDCl_3$):** δ_H 8.14 (4H, m, Ar-H), 7.90 (2H, d, J = 8.5 Hz, Ar-H), 7.40 (5H, m, Ar-H), 7.31 (2H, d, J = 8.5 Hz, Ar-H), 6.03 (1H, t, J = 9.8 Hz, H-3), 5.55 (1H, s, PhCH-), 5.27 (1H, dd, J = 3.7 and 9.9 Hz, H-2), 5.14 (1H, d, J = 3.6, H-1), 5.37 (1H, dd, J = 4.7 and 10.2 Hz, H-6a), 4.08 (1H, m, H-5), 3.90 (1H, t, J = 10.2 Hz, H-6b), 3.85 (1H, t, J = 9.8 Hz, H-4) 3.44 (3H, s, 1-OCH_3), 1.29 {9H, s, $(CH_3)_3C$-}.

Methyl 4,6-O-benzylidene-2-O-(4-t-butylbenzoyl)-3-O-(3,5-dinitrobenzoyl)-α-D-glucopyranoside, **10**

Yield 51%; (R_f = 0.50) as a syrup; **^{1}H-NMR ($CDCl_3$):** δ_H 9.12 (1H, s, Ar-H), 9.06 (2H, s, Ar-H), 7.90 (2H, d, J = 8.5 Hz, Ar-H), 7.41 (5H, m, Ar-H), 7.32 (2H, d, J = 8.5 Hz, Ar-H), 6.07 (1H, t, J = 9.7 Hz, H-3) 5.58 (1H, s, PhC*H*-), 5.30 (1H, dd, J = 3.7 and 9.8 Hz, H-2), 5.17 (1H, d, J = 3.7 Hz, H-1), 4.38 (1H, dd, J = 4.6 and 10.2 Hz, H-6a), 4.10 (1H, m, H-5), 4.01 (1H, t, J = 10.2 Hz, H-6b), 3.91 (1H, t, J = 9.8 Hz, H-4) 3.46 (3H, s, 1-OCH_3), 1.28 {9H, s, (CH_3)$_3$C-}.

Methyl 4,6-O-benzylidene-2-O-(4-t-butylbenzoyl)-3-O-(2,6-dichlorobenzoyl)-α-D-glucopyranoside, **11**

Yield 85%; (R_f = 0.52) as a syrupy mass; **^{1}H-NMR ($CDCl_3$):** δ_H 7.50 (2H, m, Ar-H), 7.44 (2H, m, Ar-H), 7.35 (5H, m, Ar-H), 7.31 (3H, m, Ar-H), 6.07 (1H, t, J = 9.7 Hz, H-3), 5.57 (1H, s, PhC*H*-), 5.20 (1H, dd, J = 3.7 and 9.7 Hz, H-2), 5.14 (1H, d, J = 3.7 Hz, H-1), 4.37 (1H, dd, J = 4.7 and 10.2 Hz, H-6a), 4.06 (1H, m, H-5), 3.84 (2H, m, H-4 and H-6b), 3.41 (3H, s, 1-OCH_3) 1.33 {9H, s, (CH_3)$_3$C-}.

Methyl 4,6-O-benzylidene-2-O-(4-t-butylbenzoyl)-3-O-pivaloyl-α-D-glucopyranoside,**12**

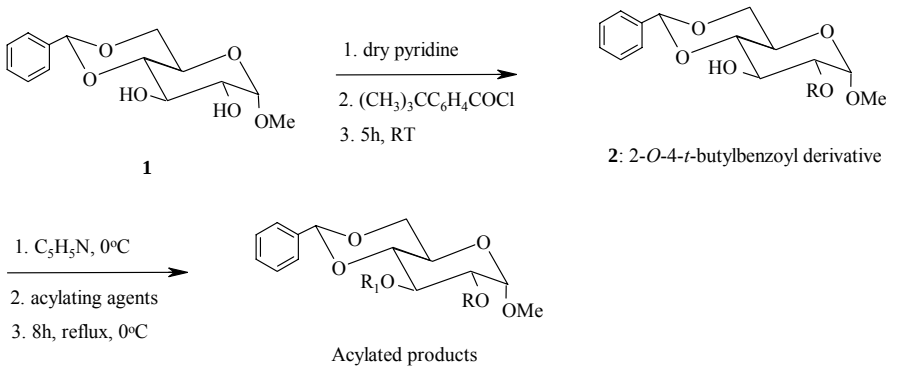
Yield 90%; (R_f = 0.52) as a thick colorless syrup; **^{1}H-NMR ($CDCl_3$):** δ_H 7.93 (2H, d, J = 8.5 Hz, Ar-H), 7.45 (5H, m, Ar-H), 7.33 (2H, d, J = 8.5 Hz, Ar-H), 5.77 (1H, t, J = 9.5 Hz, H-3), 5.55 (1H, s, PhC*H*-), 5.11 (2H, m, H-1 and H-2), 4.34 (1H, dd, J = 4.7 and 10.1 Hz, H-6a), 3.98 (1H, m, H-5), 3.80 (1H, t, J = 10.1 Hz, H-6b), 3.74 (1H, t, J = 9.8 Hz, H-4), 3.39 (3H, s, 1-OCH_3), 1.33{9H, s, (CH_3)$_3$C-}, 1.07 {9H, s, (CH_3)$_3$CCO-}.

Results and Discussion

The aim of the research work reported here was to carry out regioselective 4-t-butylbenzoylation of methyl 4,6-*O*-benzylidene-α-**D**-glucopyranoside (**1**) and transformation of the synthesized 2-*O*-4-t-butylbenzoyl (**2**) into a number of substituted derivatives. The 2-*O*-4-t-butylbenzoyl **2** and its 3-*O*-acyl derivatives (**3-12**) were employed as test chemicals for antibacterial and antifungal screening studies against a number of human pathogenic bacteria and plant pathogenic fungi and the results will be reported later.

Our initial effort was to prepare the starting 4,6-*O*-benzylidene derivative (**1**). Thus, reaction of methyl-α-**D**-glucopyranoside with benzaldehydedimethylacetal and camphor-10-sulphonic acid in dry DMF provided the benzylidene derivative (**1)** in 76% yield. The structure of this compound was ascertained by analyzing its ^{1}H-NMR spectra[14]. With the starting benzylidene derivative (**1**) in hand, we then allowed it to react with a unimolecular amount of 4-t-butylbenzoyl chloride using the direct acylation method, followed by usual workup and purification procedures, gave compound **2** in 52% yield as needles, m.p. 150-157ºC (ethyl acetate-hexane). The ^{1}H-NMR spectrum of compound **2** displayed the following characteristic peaks at δ 7.96 (2H, d, J = 8.5 Hz), δ 7.34 (2H, d, J

= 8.5 Hz) and δ 1.28 (9H, s) corresponded to the presence of one 4-t-butylbenzoyl group in the molecule. The introduction of this group to position 2 was shown by deshielding of the C-2 proton to δ 5.04 (as dd, J = 3.7 and 9.8 Hz) from its value in the precursor diol (**1**). Complete analysis of the ^{1}H-NMR spectrum led us to establish its structure as methyl 4,6-*O*-benzylidene-2-*O*-(4-t-butylbenzoyl)-α -**D**-glucopyranoside (**2**).



Compounds	R	R_1	Compounds	R	R_1
3	t-Bu—C$_6$H$_4$—CO-	$(CH_3CO)O$-	**8**	t-Bu—C$_6$H$_4$—CO-	-OC—C$_6$H$_4$—Cl
4	t-Bu—C$_6$H$_4$—CO-	$CH_3(CH_2)_3CO$-	**9**	t-Bu—C$_6$H$_4$—CO-	-OC—C$_6$H$_4$—NO_2
5	t-Bu—C$_6$H$_4$—CO-	$CH_3(CH_2)_8CO$-	**10**	t-Bu—C$_6$H$_4$—CO-	-OC—C$_6$H$_3$(NO_2)$_2$
6	t-Bu—C$_6$H$_4$—CO-	$CH_3(CH_2)_{10}CO$-	**11**	t-Bu—C$_6$H$_4$—CO-	-OC—C$_6$H$_3$Cl$_2$
7	t-Bu—C$_6$H$_4$—CO-	-OC—C$_6$H$_4$—Cl	**12**	t-Bu—C$_6$H$_4$—CO-	$(CH_3)_3CCO$-

Fig.-1: The structure of compounds **1-12**

The structure of the 2-*O*-(4-t-butylbenzoyl) derivative (**2**) was further supported by its conversion to and identification of the acetyl derivative (**3**). Thus, reaction of compound **2** with an excess of acetic anhydride in pyridine, followed by usual work-up procedure, provided the acetyl derivative (**3**). The attachment of one acetyl group in the molecule was demonstrated by the appearance of a three-proton singlet at δ 1.98 in its ^{1}H-NMR spectrum. Also the C-3 proton resonated downfield to δ 5.78 (as t, J = 9.8 Hz) as compared to the precursor compound **2** (δ 4.33, t, J = 9.8 Hz), thereby suggesting the

introduction of the acetyl group at position 2. By complete analysis of the ^{1}H-NMR spectrum, the structure of this compound was assigned as methyl 3-*O*-acetyl-4,6-*O*-benzylidene-2-*O*-(4-t-butylbenzoyl)-α-**D**-glucopyranoside (**3**).

The 4-t-butylbenzoyl derivative (**2**) was then converted to a number of fatty acyl derivatives using pentanoyl chloride, decanoyl chloride and lauroyl chloride in order to get further support to its structure and also prepare newer products. Thus, pentanoylation of compound **2** in pyridine using the usual work-up procedure provided the pentanoyl derivative (**4**) in 78% yield. In its ^{1}H-NMR spectrum, the resonance peaks at δ 2.25 (2H, m), δ 1.46 (2H, m), δ 1.22 (2H, m) and δ 0.88 (3H, t, J = 7.3 Hz) showed the presence of one pentanoyl group in the molecule. The downfield shift H-3 to δ 5.79 (as t, J = 9.8 Hz) from its value in the precursor compound **2** (δ 4.33, t, J = 9.8 Hz), indicated the introduction of the pentanoyl group at position 3. Thus, by complete analysis of the ^{1}H-NMR spectrum, a structure of this compound as methyl 4,6-*O*-benzylidene-2-*O*-(4-t-butylbenzoyl)-3-*O*-pentanoyl-α-**D**-glucopyranoside (**4**).

Compound **2** was then converted to the decanoyl derivative (**5**) in high yield. In its ^{1}H-NMR spectrum, the presence of three two-proton multiplets at δ 2.23, δ 1.46, δ 1.32, a four-proton multiplet at δ 1.22, a six-proton multiplet at δ 1.13 and a three-proton triplet at δ 0.84 (J= 6.9 Hz) suggested the attachment of one decanoyl group in the molecule. The C-3 proton deshielded considerably to δ 5.79 (as t, J = 9.7 Hz) from its value in the precursor compound **2** (δ 4.33, t, J = 9.8 Hz), thereby suggesting the introduction of the decanoyl group at position 3. Compound **2** was then subjected to lauroylation by reaction with lauroyl chloride in anhydrous pyridine using the direct acylation method and isolated the lauroyl derivative (**6**). The structure of this compound was confidently assigned as methyl 4,6-*O*-benzylidene-2-*O*-(4-t-butylbenzoyl)-3-*O*-lauroyl-α-**D**-glucopyranoside (**6**) by complete analyzing its ^{1}H-NMR spectrum.

3-Chlorobenzoylation of compound **2** was carried out by reacting with 3-chlorobenzoyl chloride, followed by usual work-up procedure. In its ^{1}H-NMR spectrum, all the protons resonated in their anticipated positions thereby ascertaining its structure as methyl 4,6-*O*-benzylidene-2-*O*-(4-t-butylbenzoyl)-3-*O*-(3-chlorobenzoyl)-α-**D**-glucopyranoside (**7**). The 4-t-butylbenzoyl derivative (**2**) was then allowed to react with 4-chlorobenzoyl chloride in pyridine. Work-up procedure as used in direct acylation method and chromatographic purification, furnished the 4-chlorobenzoyl derivative (**8**). In its ^{1}H-NMR spectrum, the aromatic protons resonated in the expected positions. The C-3 proton resonated at δ 6.01 (as t, J = 9.8 Hz) and shifted downfield as compared to the precursor compound **2**, thus showing the attachment of the 4-chlorobenzoyl group at C-3.

Reaction of compound **2** with 4-nitrobenzoyl chloride in dry pyridine provided compound **9** in good yield. The ^{1}H-NMR spectrum of this compound displayed two lowfield two-proton doublets at δ 8.14 and δ 7.90 corresponding to the presence of one 4-nitrobenzoyl group in the molecule. Also, C-3 proton deshielded considerably to δ 6.03 (as t, J = 9.8 Hz) as compared to its precursor compound **2** (δ 4.33, t, J 9.8 Hz), thus suggesting that

the 4-nitrobenzoyl group was introduced at position 3. We then performed 3,5-dinitrobenzoylation of the 4-t-butylbenzoyl derivative (**2**) using similar reaction procedures and isolated compound **10** in 51% yield. The appearance of the very low field one-proton singlet at δ 9.12 and the two-proton singlet at δ 9.06 were due to the aromatic protons of one 3,5-dinitrobenzoyl group. Complete analysis of the ^{1}H-NMR spectrum of this compound led us to propose as methyl 4,6-*O*-benzylidene-2-*O*-(4-t-butylbenzoyl)-3-*O*-(3,5-dinitrobenzoyl)-α-**D**-glucopyranoside (**10**).

2,6-Dichlorobenzoylation of compound **2** with 2,6-dichlorobenzoyl chloride in pyridine using conventional work-up and purification procedures provided compound **11**. By complete analysis of its ^{1}H-NMR spectrum, the structure of this compound was ascertained as methyl 4,6-*O*-benzylidene-2-*O*-(4-t-butylbenzoyl)-3-*O*-(2,6-dichlorobenzoyl)-α-**D**-glucopyranoside (**11**).

Finally, we employed pivaloyl chloride for derivatizing compound **2**. By using conventional reaction, work-up and purification procedures, we isolated the pivaloyl derivative (**12**) in 90%. In its ^{1}H-NMR spectrum, the presence of one characteristic nine-proton singlet at δ 1.07 was due to one pivaloyl group. Also, H-3 shifted considerably downfield to δ 5.77 (as t, J = 9.5 Hz) as compared to precursor compound **2** (δ 4.33, t, J = 9.8 Hz), ascertaining the introduction of the pivaloyl group at C-3.

Thus, a series of acylated **D**-glucose derivatives were prepared by direct acylation method employing a wide variety of differently substituted acylating agents. These acylating agents were chosen so as to contain probable biologically active **D**-glucose derivatives. All these substitution products were subjected to antimicrobial evaluation studies against a number of human and phytopathogens and the results will be reported in a forthcoming paper.

Conclusion

A novel series of methyl 4,6-*O*-benzylidene-α-D-glucopyranoside derivatives were synthesized successfully by the direct acylation method. The structure and purity of all the compounds were shown by their spectral and physical data. These acylations were found to be very promising since in all the reactions a single monosubstitution product was isolated in reasonably high yields. The simplicity of the present procedure makes it an interesting alternative to other approaches.

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