J. Serb Chem. Soc. 66(2)65–71(2001)
JSCS – 2832

UDC 547.455.643:546.814:542.9
Original scientific paper

$SnCl_4$ induced formation of C_7–C_{16}-alkyl D-glucopyranosides[1]

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(Received 12 July, revised 10 November 2000)

The $SnCl_4$ catalyzed glycosylation reaction of -peracetylated sugar derivative (glucose) with fatty alkanols is used in the synthesis of C_7–C_{16}-alkyl glucopyranosides.

Keywords: synthesis of C_7–C_{16}-alkyl D-glucopyranosides; tin(IV) chloride as Lewis acid catalyst.

INTRODUCTION

In 1970 Hughes and Lew[2] reported that alkyl polyglucosides have a wide range of physical and functional properties which make them suitable for use as biodegradable surfactants, detergents and emulsifiers. More recently, *n*-octyl -D-glucopyranoside and other similar compounds have been used as detergents to solubilize membrane proteins and to study the hydrophilic requirements of several enzymes.[3]

The synthesis of these compounds was first accomplished by Noller and Rockwell[4] using a rather complicated procedure developed by Koenigs and Knorr[5] in which sugars were first peracetylated and then converted to the acetobromo sugars. The alkyl group was introduced by reacting the desired alcohol with the brominated peracetate in the presence of silver oxide, and deacetylation was accomplished by treatment with sodium methylate. Later modifications of this procedure[6] led to simplified preparations of alkyl glycosides with increased yields.

In 1965 Boether[7] reported an alternative synthesis of alkyl glucosides involving a double alcohol interchange in the presence of an acid catalyst. Glucose was first converted to methyl glucoside, then to butyl glucoside, and finally to the desired alkyl glucoside. Later Mansfield[8] successfully prepared several alkyl glucosides and alkyl oligosaccharide mixtures directly from glucose and higher mollar mass alcohols by carefully controlling the removal of water during the reaction.

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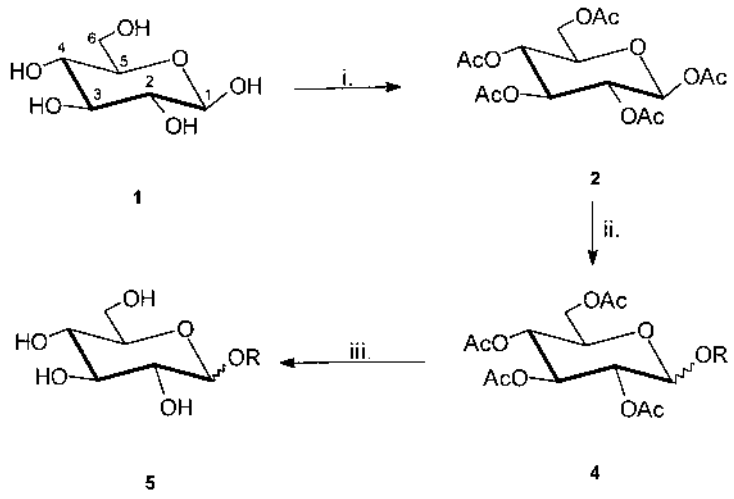


3/4/5	R	3/4/5	R	3/4/5	R
a	CH_3	e	$CH_2CH(C_2H_5)C_4H_9$	i	$C_{12}H_{25}$
b	C_4H_9	f	C_9H_{19}	j	$C_{14}H_{29}$
c	C_7H_{15}	g	$C_{10}H_{21}$	k	$C_{16}H_{33}$
d	C_8H_{17}	h	$C_{11}H_{23}$		

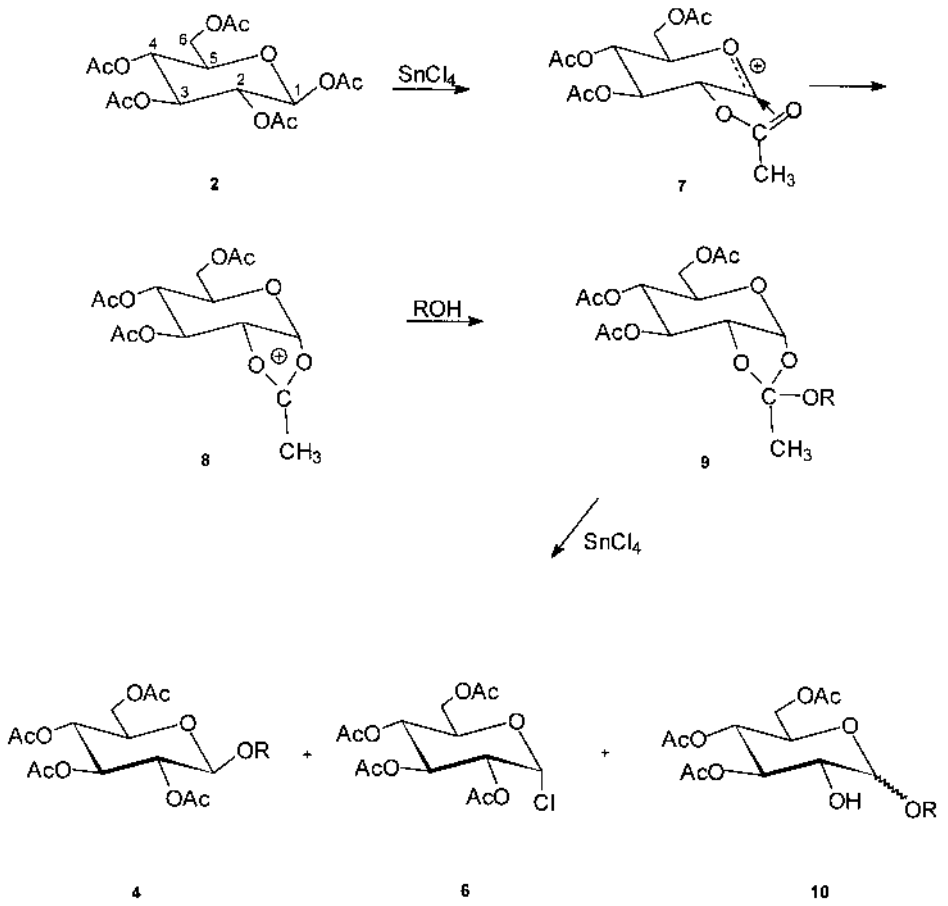
i. Ac_2O, NaOAc ii. ROH (**3**), $SnCl_4$ iii. MeOH:Et_3N:H_2O

Scheme 1.

It is known that methyl and phenyl -D-glucopyranoside may be prepared from penta-*O*-acetyl -D-glucopyranose (**2**) (Scheme 1) under Lewis acid catalysis[9] and later this procedure was modified to provide 1,2-*trans*-linked glycosides.[10–13] On the other hand, utilization of penta-*O*-acetyl -D-galactopyranose under Lewis acid catalysis[14] afforded galactopyranosides in only moderate yields, accompanied by a significant amount of by-products wihch required laborious chromatographic purification. As catalysts, $BF_3 \cdot Et_2O$ as well $SnCl_4$ were tested. With this in mind, we performed the critical glycosylation of penta-*O*-acetyl -D-glucopyranose with fatty alkanols in the presence of tin(IV) chloride as a Lewis acid catalyst.

RESULTS AND DISCUSSION

The peracetate of glucose is readily prepared in crystalline form as the -anomer by a standard procedure[15] using molten anhydrous sodium acetate and acetic anhydride. When a 1,2-*trans*-sugar per-*O*-acetate **2** (Scheme 1) is dissolved in dichloromethane containing one molar equivalent of tin(IV) chloride, 1,2-acetoxonium ion **8** (Scheme 2) formation results[12] as is the case with other Lewis acids, such as antimony pentachloride.[16] The addition of alcohol ROH (**3**) at room temperature under anhy-



Scheme 2.

drous conditions gives *trans*-linked glycoside in moderate yields. Under these conditions, room temperature for 1 h, penta-*O*-acetyl -D-glucopyranose (**2**) gave the acetylated -glucoside **4** in moderate yiedl (70 %) (Scheme 1). Reaction time extension leads to increasing proportions of -glucoside due to anomerization.

In addition to -D-glucopyranoside **4** as the major product, acetylated alcohol (ROAc) and -D-glucopyranosyl chloride (**6**, Scheme 2) are formed as side products in this reaction. With prolonged reaction times, the -D-glucopyranoside is major product and, in addition to acetylated alcohol, small amounts of 2-hydroxy -linked glucoside (**10**) are produced as side products. This latter product exhibited properties similar to 2-hydroxy glycoside isolated from Koenigs-Knorr reactions.[12]

Examination of the side products of this reaction, acetylated aglycon and glucosides **10** lacking 2-*O*-acetate, supports the conclusion that this reaction proceeds to -linked glucosides *via* 1,2-orthoacetate intermediates **9**. It is well documented that suitably oriented polyacetates in the presence of Lewis acid will gave 1,2-acetoxonium

ions.[16] Hanessian and Banoub prepared 1,2-orthoesters *via* such species under conditions similar to those used in this work.[13] Reaction of cyclic oxocarbenium ions **8** of the type presented in Scheme 2 can lead directly to 1,2-*trans*-glycosides but in light of the side products of the reaction, this probably occurs *via* a 1,2-alkyl orthoacetate intermediate **9**, which has been shown to rearrange in the presence of tin(IV) chloride catalyst. The acetylated - and -glycosides **4a-k** were analytically pure and gave ^{1}H and ^{13}C-NMR data in agreement with the assigned structure (Tables I and II). For comparison, **2** was reacted with methanol and 1-butanol.

TABLE I. ^{1}H-NMR ($CDCl_3$, 200 MHz) data of the acetylated - and -glucopyranosides (**4c** and **4c**)[a]

Proton	Compound **4c**	Compound **4c**
H-1	4.50 *d* (7.9)	5.07 *d* (3.9)
H-2	4.99 *dd* (7.9, 10.2)	4.86 *dd* (3.9, 10.2)
H-3	5.19 *dd* (9.4, 10.2)	5.49 *dd* (9.4, 10.2)
H-4	5.09 *dd* (9.4, 10.3)	5.06 *dd* (9.4, 10.3)
H-5	3.70 *ddd* (9.6, 4.8	4.02 *ddd* (10.3, 4.8,
	2.7), X part of ABX	2.3), X part of ABX
	spectra	spectra
H-6a	4.13 *dd* (2.4, 4.6	4.08 *dd* (2.4, 4.6,
	12.2), A part of ABX	12.2), A part of ABX
	spectra	spectra
H-6b	4.27 *dd* (2.4, 4.6	4.28 *dd* (2.4, 4.6,
	12.2), B part of ABX	12.2), B part of ABX
	spectra	spectra
H-1a'	3.47 *dt* (9.6, 10.	3.42 *dt* (9.6, 10.5,
	6.9), A part of ABX_2	6.9), A part of ABX_2,
	spectra	spectra
H-1b'	3.87 *dt* (9.6, 10.5	3.67 *dt* (9.6, 10.5,
	6.9), B part of ABX_2	6.9), B part of ABX_2
	spectra	spectra
$OCOCH_3$	2.01, 2.03, 2.04, 2.09	2.02, 2.04, 2.06, 2.10
	4 *s*	4 *s*
H-2'	1.56 *m*	1.60 *m*
$-(CH_2)_n-$	1.26 *m*	1.26 *m*
$-(CH_2)_nCH_3$	0.88 *t* (6.7)	0.88 *t* (6.4)

[a]Chemical shifts (in ppm) relative to TMS (= 0 ppm) as internal standard are given outside the parentheses; coupling constants *J* (in Hz) are given in the parentheses. Abbreviations: *s*, singlet; *d*, doublet; *t*, triplet; *q*, quartet; *m*, multiplet.

Following chromatographic purification, the purified peracetylated products are deesterified with the mixture methanol-triethylamine-water (2:1:1) to give alkyl -gly-

coside or alkyl -glucoside **5a-k**. The deacetylated glycosides were analytically pure and gave ^{1}H and ^{13}C-NMR data in agreement with the assigned structure (Tables I and II).

EXPERIMENTAL

General

Dry column chromatography: Merck silica gel 60 (particle size 0.046 – 0.06 mm) (toluene-ethyl acetate as eluent). *Thin layer chromatography (TLC):* Merck TLC aluminium sheets silica gel 60 F_{254} (layer thickness 0.2 mm). The sports were visualized by spraying with 10 % sulfuric acid in ethanol (carbohydrates) and 1 % anisaldehyde and 2 % sulfuric acid in glacial acitic acid (non-carbohydrate compounds) and subsequent heating. *NMR spectra*: Varian Gemini 200 (200 MHz) and Bruker AC 250 (250 MHz) in $CDCl_3$ with TMS as internal standard or DMSO-d_6 with DSS as internal standard. All solvents were purified by distillation (dichloromethane from calcium hydride).

General procedure for the preparation of alkyl glycosides

The D-glucose (10 mmol) was treated with anhydrous sodium acetate (10 mmol) and acetic anhydride (12.5 ml) at 100 ºC for 4 h and worked up as usual[15] to give the -anomer of the peracetylated saccharide.

A solution of -D-glucose pentaacetate (3.92 g, 10.0 mmol) in anhydrous dichloromethane (80 ml) was stirred for 1 – 2 h with molecular sieves 0.4 nm (4 g) under an argon atmosphere. Then the solution was treated with tin(IV) chloride (10 mmol) and immediately after the alcohol component (11 mmol) dissolved in anhydrous dichloromethane (20 ml) was added.

The preparation of -glucosides required a reaction time of about 1 hour, and that of -glucosides about 70 h. After this time, the mixture was poured into saturated sodium hydrogencarbonate solution (100 ml), the organic layer separated, the aqueous phase extracted with dichloromethane (3 40 ml), the combined organic phases washed twice with water (2 40 ml), filtered over Celite and evaporated *in vacuo*. The resulting syrup was purified by dry column chromatography (silica gel 60 (Merck), toluene/ethyl-acetate). The acetylated alcohol was isolated from the reaction mixture, together with glucosyl chloride (for -glucosides). In the preparation of -glucosides, small amoutns of glucopyranosides lacking 2-*O*-acetate were observed.

The resulting material was deacetylated by treatment of the purified sample (100–200 mg) with 2 ml of methanol:triethylamine:water (2:1:1) at room temperature for 24 h.

Yields: 30 – 60 per cent based on the starting saccharide for the three stage process, including purifications.

И З В О Д

$SnCl_4$ ИНДУКОВАНО ФОРМИРАЊЕ C_7–C_{16}-АЛКИЛ-D-ГЛУКОПИРАНОЗИДА

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$SnCl_4$ катализована реакција гликозилације -перацетилованог деривата угљеног хидрата (глукозе) са масним алканолима примењена је у синтези C_7–C_{16}-алкил-D-глукопиранозида.

(Примљено 12. јула, ревидирано 10. новембра 2000)

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TABLE II. ^{13}C-NMR ($CDCl_3$) data (chemical shifts) of the alkyl glucopyranosides **4a**–**4k** (50.0 MHz, $CDCl_3$) and **5a**–**5k** (62.9 MHz, DMSO-d_6)[a]

Compound	C-1	C-2	C-3	C-4	C-5	C-6	C-1'	$(CH_2)_n$	CH_3
4a	100.2	71.0	72.2	68.1	71.0	61.3	56.1		
4b	100.6	71.1	72.6	68.3	71.5	61.8	69.6	18.7, 31.1	13.5
4c ; **4d** ; **4f** –**4k**	100.6–100.8	71.1–71.3	72.6–72.8	68.2–68.4	71.5–71.7	61.8–61.9	70.0–70.2	22.4–31.8	13.9–14.0
4e	100.9	71.0	72.5	68.3	71.4	61.7	72.3	22.7–39.0	10.7, 13.7
4a	96.3	69.7	70.3	68.1	66.7	61.5	55.0		
4b	95.2	69.9	70.6	68.0	66.8	61.7	68.3	18.9, 30.9	13.4
4c ; **4d** ; **4f** –**4k**	95.2–95.5	69.7–70.1	70.4–70.8	68.0–68.5	66.7–67.0	61.4–61.8	68.1–68.6	22.1–31.7	13.5–13.9
4e	95.5	70.0	70.7	68.3	66.9	61.7	70.7	22.7–38.9	10.7, 13.7
5a	103.9	73.5	76.9*	70.1	76.7*	61.1	56.0		
5b	102.9	73.6	76.9	70.2	76.9	61.2	68.4	18.9, 31.5	14.0
5c ; **5d** ; **5f** –**5k**	102.9–103.0	73.5–73.6	76.8–76.9	70.1–70.2	76.7–76.9	61.1–61.2	68.6–68.8	22.1–31.5	14.0–14.1
5e	103.3, 103.4	73.7	77.0*	70.3	76.9*	61.3	71.5, 71.6	22.8–30.0	11.0, 14.2
5b	98.5	72.0	73.3	70.4	72.8	61.0	66.5	19.0, 31.3	13.9
5c [b]	101.1	74.0	75.8	71.6	74.3	62.8	70.8	25.1–31.8	16.3
5d ; **5f** –**5k**	98.5–99.2	72.0–72.6	73.3–74.1	70.3–70.8	72.7–73.0	61.0–61.6	66.8–67.8	22.2–32.1	14.0–14.4
5e	99.0	72.1	73.3	70.3	72.9	61.1	69.7	23.5–30.1	10.9, 14.1

[a]Assignments marked with asterisk are tentative and could be interchanged. [b]Data obtained in D_2O.