Synthetic Communications: An International Journal for Rapid Communication of Synthetic Organic Chemistry
Publication details, including instructions for authors and subscription information:
http://www.tandfonline.com/loi/lsyc20

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Version of record first published: 23 Sep 2006.

To cite this article: Zhan-Jiang Li , Li-Ning Cai & Meng-Shen Cai (1992): Studies on Glycosides. X. An Alternate Method For Highly Stereoselective Synthesis of Alkyl-β-D-glucopyranosides, Synthetic Communications: An International Journal for Rapid Communication of Synthetic Organic Chemistry, 22:14, 2121-2124

To link to this article: http://dx.doi.org/10.1080/00397919208021347

SYNTHETIC COMMUNICATIONS, 22(14), 2121-2124 (1992)

STUDIES ON GLYCOSIDES.X.AN ALTERNATE METHOD FOR HIGHLY STEREOSELECTIVE SYNTHESIS OF ALKYL-β-D-GLUCOPYRANOSIDES

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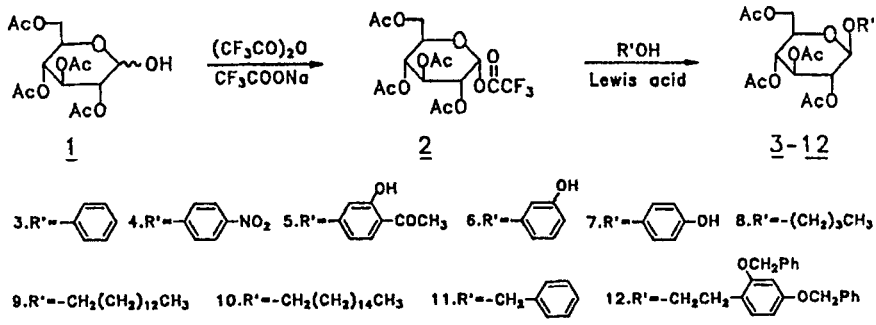
ABSTRACT: An alternate method for the synthesis of alkyl-β-D-glucopyranosides using 2,3,4,6-terta-O-acetyl-1-0-trifluoroacetyl-α-D-glucopyranose with alcohols or phenols in the presence of Lewis acid at low temperature was reported. β-anomers were the sole product or predominated.

In the preceeding paper[1], we reported the reaction of 2,3,4,6-tetra-O-acetyl-1-O-trifluoroacetyl-α-D-glucopyanose with some carboxylic acids afforded the corresponding 1-O-acyl-2,3,4,6-tetra-O-acetyl-β-D-glucopyranoses. Now we reported here using the same intermediate(2) for the synthesis of alkyl -β-D-glucopyranosides.



Part IX. Chem. J. Chinese Univ., 1990, 11, 1376.

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Table 1 Synthesis of 1–O–aryl–2,3,4,6–tetra–O–acetyl–β–D–glucosides

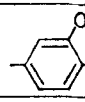
Product	R′	Lewis Acid	Reaction Conditions	Yield (%)	m.p.(℃) [Ref.]
3		$BF_3 \cdot Et_2O$ $CF_3SO_3SiMe_3$	−15℃,60min −15℃,60min	91.6 90.0	87–89 87–89
4		$BF_3 \cdot Et_2O$ $CF_3SO_3SiMe_3$	−20℃,50min −20℃,50min	62.1 80.0	119–121 119–121
5		$BF_3 \cdot Et_2O$	−20℃,50min	53.2	132–134
6		$BF_3 \cdot Et_2O$	−20℃,50min	85.6	125–127 [124–126][6] [136]7
7		$BF_3 \cdot Et_2O$	−20℃,50min	87.6	86–88 [84–86][6]

Table 2 Synthesis of 1–O–alkyl–2,3,4,6–tetra–O–acetyl–β–D–glucosides

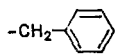
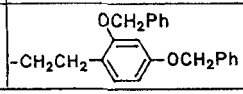
Product	R′	Lewis Acid	Reaction Conditions	Yield (%)	m.p. (℃)
8	$-(CH_2)_3CH_3$	$BF_3 \cdot Et_2O$	−25℃,50min	83.0	78–80
9	$-CH_2(CH_2)_{12}CH_3$	$BF_3 \cdot Et_2O$	−25℃,50min	73.2	82–84
10	$-CH_2(CH_2)_{14}CH_3$	$CF_3SO_3SiMe_3$	−20℃,45min	81.0	90–92
11		$BF_3 \cdot Et_2O$	−20℃,50min	69.0	131–132
12		$BF_3 \cdot Et_2O$	−20℃,55min	67.0	140–142

Table 3 Data of ^1H NMR and ^{13}C NMR spectra of glucosyl ring

Product	^1H NMR ppm J (C_1–H) (Hz)	^{13}C NMR (δppm, $CDCl_3$) C1	C2	C3	C4	C5	C6	Ratio (α:β)
3	5.41 7.3	100.1	72.3	67.4	55.4	71.2	62.0	0:1
4	5.59 7.6	99.3	72.4	68.0	61.9	71.0	65.3	0:1
5	5.28 7.4	100.4	72.2	67.0	60.9	71.8	63.5	0:1
6	5.27 8.0	99.8	72.3	66.9	61.0	71.3	63.4	0:1
7	5.39 7.1	101.3	72.9	67.1	59.8	70.5	63.0	0:1
8	5.30 7.4	99.7	72.3	68.2	60.5	71.0	63.8	0.1
9	5.35 7.8	100.5	72.2	70.0	61.3	71.8	67.5	0:1
10	5.45 7.0	101.2	72.0	67.3	61.7	69.7	64.0	0:1
11	5.39 7.2	102.1	72.5	67.6	61.3	70.1	64.8	0:1
12	5.93 3.4	97.1	72.8	67.7	61.4	70.2	63.9	1:4
	5.40 7.1	100.4	73.0	68.1	61.5	71.2	64.0	

2,3,4,6–Tetra–O–acetyl–α–D–glucopyranose(1) was treated with trifluoroacetic anhydride to give 2,3,4,6–tetra–O–acetyl–1–O–trifluoroacetyl–α–D–glucopyranose (2). When (2) was reacted with alcohols or phenols, the alkyl–β–D–glucopyranosides (3–12) were obtained with inversion of configuration at the anomeric center. The reaction was performed at −15℃ to −25℃ in the presence of BF_3Et_2O or $CF_3SO_3SiMe_3$ to give good yields of products. This is a simple and highly stereoselective method for the synthesis of alkyl–β–D–glucopyranosides.

The following is the general procedure for the preparation of alkyl–β–D–glucopyranosides: To a mixture of compound[2–5] (2) (0.6g, 1.40mmol), alcohol or phenol(2.80mmol) in CH_2Cl_2(5ml) was added with BF_3Et_2O or $CF_3SO_3SiMe_3$ (2 drops). The mixture was stirred at low temperature (−15℃ to −25℃) for the suitable minutes (see Table 1 and 2). when TLC(cyclohexane:ethyl acetate=6:4) showed the absence of 2,3,4,6–tetra–O–acetyl–1–O–trifluoroacetyl–α–D–glucopyranose(2) and the presence of one new major spot. The solvents were evaporated off. The reaction mixture was subjected to preparative TLC (silic gel) using the same eluant (cyclohexane:ethyl acetate=6:4) to afford alkyl–β–D–glucopyranosides (3–12).

The configuration of these alkyl-2,3,4,6-tetra-O-acetyl-D-glucopyranosides was assigned by ^{1}H NMR and ^{13}C NMR spectra[8] (see Table 3). ^{1}H NMR and ^{13}C NMR showed that the products (3-11) are β-anomers, while product 12 is a mixture of α- and β-anomers, in which β-anomers prodominated. We supposed that neighboring-group (2-acetyl) participation are favorable to 1,2-trans glucopyranosides, i.e., the reaction went on through the attack of the nucleophilic reagent from equatorial side(SN_2 mechanism).So β-anomers of glucopyranosides would be the main products.

The yields and physical data for products (3-12) are given in Table 1 and Table 2. Table 3 lists the main data of ^{1}H NMR and ^{13}C NMR spectra of products.

ACKNOWLEDGEMENT: The project supported by the National Natural Science Foundation of China.

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(Accepted in USA 1 April, 1992)