This article was downloaded by: [University of Chicago]

On: 12 March 2013, At: 07:45 Publisher: Taylor & Francis

Informa Ltd Registered in England and Wales Registered Number: 1072954 Registered office: Mortimer House, 37-41 Mortimer Street, London W1T 3JH,

UK



## Synthetic Communications: An International Journal for Rapid Communication of Synthetic Organic Chemistry

Publication details, including instructions for authors and subscription information: <a href="http://www.tandfonline.com/loi/lsyc20">http://www.tandfonline.com/loi/lsyc20</a>

Studies on Glycosides. X. An Alternate Method For Highly Stereoselective Synthesis of Alkyl-β-D-glucopyranosides

Zhan-Jiang Li <sup>a</sup>, Li-Ning Cai <sup>a</sup> & Meng-Shen Cai <sup>a</sup> School of Pharmaceutical Sciences, Beijing Medical University, Beijing, 100083, P.R.China 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: <a href="http://dx.doi.org/10.1080/00397919208021347">http://dx.doi.org/10.1080/00397919208021347</a>

## PLEASE SCROLL DOWN FOR ARTICLE

Full terms and conditions of use: <a href="http://www.tandfonline.com/page/terms-and-conditions">http://www.tandfonline.com/page/terms-and-conditions</a>

This article may be used for research, teaching, and private study purposes. Any substantial or systematic reproduction, redistribution, reselling, loan, sub-licensing, systematic supply, or distribution in any form to anyone is expressly forbidden.

The publisher does not give any warranty express or implied or make any representation that the contents will be complete or accurate or up to date. The accuracy of any instructions, formulae, and drug doses should be independently verified with primary sources. The publisher shall not be liable for any loss, actions, claims, proceedings, demand, or costs or damages whatsoever or howsoever caused arising directly or indirectly in connection with or arising out of the use of this material.

## STUDIES ON GLYCOSIDES.X.AN ALTERNATE METHOD FOR HIGHLY STEREOSELECTIVE SYNTHESIS OF ALKYL- $\beta$ -D-GLUCOPYRANOSIDES

Zhan-Jiang Li, Li-Ning Cai, Meng-Shen Cai\*

School of Pharmaceutical Sciences, Beijing Medical University Beijing 100083, P.R.China

ABSTRACT: An alternate method for the synthesis of alkyl- $\beta$ -D-gluco-pyranosides using 2,3,4,6-terta-O-acetyl-1-0-trifluoroacetyl- $\alpha$ -D-glu-copyranose with alcohols or phenols in the presence of Lewis acid at low temperature was reported.  $\beta$ -anomers were the sole product or predominated.

In the preceding paper<sup>1</sup>, we reported the reaction of 2,3,4,6-te-tra-O-acetyl-1-O-trifluoroacetyl- $\alpha$ -D-glucopyanose with some carboxylic acids afforded the corresponding 1-O-acyl-2,3,4,6-tetra-O-acetyl- $\beta$ -D-glucopyranoses. Now we reported here using the same intermediate(2) for the synthesis of alkyl  $-\beta$ -D-glucopyranosides.

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

\* To whom correspondence should be addressed.

Table 1 Synthesis of 1–O-aryl-2,3,4,6-tetra-O-acetyl- $\beta$ -D-glucosides

				-	
Product	R′	Lewis Acid	Reaction Conditions	Yield (%)	m.p.(°C) [Ref.]
3	-	BF <sub>3</sub> · Et <sub>2</sub> O CF <sub>3</sub> SO <sub>3</sub> SiMe <sub>3</sub>	-15°C,60min -15°C,60min	91.6 90.0	87–89 87–89
4	-NO <sub>2</sub>	BF <sub>3</sub> · Et <sub>2</sub> O CF <sub>3</sub> SO <sub>3</sub> SiMe <sub>3</sub>	-20℃,50min -20℃,50min	62.1 80.0	119-121 119-121
5	он -<	BF₃ • Et₂O	~20℃,50min	53.2	132-134
6	ОН	BF, • Et <sub>2</sub> O	~20°C ,50min	85.6	125-127 [124-126] <sup>6</sup> [136]7
7	-{>>-ОН	BF <sub>3</sub> · Et <sub>2</sub> O	−20℃,50min	87.6	86-88 [84-86] <sup>6</sup>

Table 2 Synthesis of 1–O-alkyl-2,3,4,6-tetra-O-acetyl- $\beta$ -D-glucosides

Product	R′	Lewis Acid	Reaction Conditions	Yield (%)	m.p. (℃)
8	−(CH <sub>2</sub> )₃CH₃	BF <sub>3</sub> • Et <sub>2</sub> O	-25°C,50min	83.0	78-80
9	-CH <sub>2</sub> (CH <sub>2</sub> ) <sub>12</sub> CH <sub>3</sub>	BF <sub>3</sub> • Et <sub>2</sub> O	-25°C,50min	73.2	82-84
10	-CH <sub>2</sub> (CH <sub>2</sub> ) <sub>14</sub> CH <sub>3</sub>	CF <sub>3</sub> SO <sub>3</sub> SiMe <sub>3</sub>	-20°C ,45min	81.0	90-92
11	-CH <sub>2</sub> —	BF <sub>3</sub> • Et <sub>2</sub> O	−20℃,50min	69.0	131-132
12	OCH <sub>2</sub> Ph -CH <sub>2</sub> CH <sub>2</sub> —————————OCH <sub>2</sub> Ph	BF <sub>3</sub> · Et <sub>2</sub> O	−20℃,55min	67.0	140-142

Product	'H NMR ppm J (C <sub>1</sub> -H) (Hz)	<sup>13</sup> C NMR (δppm, CDCl <sub>3</sub> ) 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	

Table 3 Data of <sup>1</sup>H NMR and <sup>13</sup>C NMR spectra of glucosyl ring

2,3,4,6-Tetra-O-acetyl- $\alpha$ -D-glucopyranose(1) was treated with trifluoroacetic anhydride to give 2,3,4,6-tetra-O-acetyl-1-O-trifluoroacetyl- $\alpha$ -D-glucopyranose (2). When (2) was reacted with alcohols or phenols, the alkyl- $\beta$ -D-glucopyranosides (3-12) were obtained with inversion of configuration at the anomeric center. The reaction was performed at -15°C to -25°C in the presence of BF<sub>3</sub>Et<sub>2</sub>O or CF<sub>3</sub>SO<sub>3</sub>SiMe<sub>3</sub> to give good yields of products. This is a simple and highly stereoselective method for the synthesis of alkyl- $\beta$ -D-glucopyranosides.

The following is the general procedure for the preparation of al-kyl- $\beta$ -D-glucopyranosides: To a mixture of compound<sup>2-5</sup> (2) (0.6g, 1.40m mol), alcohol or phenol(2.80mmol) in CH<sub>2</sub>Cl<sub>2</sub>(5ml) was added with BF<sub>3</sub>Et<sub>2</sub>O or CF<sub>3</sub>SO<sub>3</sub>SiMe<sub>3</sub> (2 drops). The mixture was stirred at low temperature (-15°C to -25°C ) 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- $\alpha$ -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- $\beta$ -D-glucopyranosides (3-12).

2124 LI, CAI, AND CAI

The configuration of these alkyl-2,3,4,6-tetra-O-acetyl-D-glucopy-ranosides was assigned by <sup>1</sup>H NMR and <sup>13</sup>C NMR spectra<sup>8</sup> (see Table 3). <sup>1</sup>H NMR and <sup>13</sup>C NMR showed that the products (3-11) are  $\beta$ -anomers, while product 12 is a mixture of  $\alpha$ - and  $\beta$ -anomers, in which  $\beta$ -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<sub>2</sub> mechanism). So  $\beta$ -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 <sup>1</sup>H NMR and <sup>13</sup>C NMR spectra of products.

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

## REFERENCES AND NOTES:

- 1. C.-F. Yu, Z.-J. Li, M.-S. Cai, Synth. Commun., 1990, 20, 943.
- 2. M.-S. Cai, D.-X. Qiu, Carbohydr. Res., 1989, 191, 125.
- 3. M. Kobayashi, T. Shimadate, Chem. Pharm. Bull., 1986, 34, 4069.
- 4. Z.-J. Li, et al. Chem. J. Chinese Universities, 1990, 11, 1376.
- 5. M.-S. Cai, D.-X. Qiu, Chinese Sci. Bull., 1990, 35, 615.
- 6. S.-Q. Peng, L.-P. Li, et al. Acta Chim. Sinica, 1989, 47, 512.
- 7. K. Tatsuo, T. Mitsuo, T. Kiyokazu, J. Pharm. Soc. Japan, 1952,72,13.
- 8. K. Bock and C. Pedersen, Chem. Soc. Perkin Trans, 1974, 2, 293.

(Accepted in USA 1 April, 1992)