

# Synthesis of D-Glycopyranosyl Azides from 1,2-Anhydrosugars Using Lithium Azidohydridodiisobutylaluminumate

Goo Soo Lee, Hye Kyung Min, and Bong Young Chung\*

Department of Chemistry, Korea University, Seoul 136-701, Korea

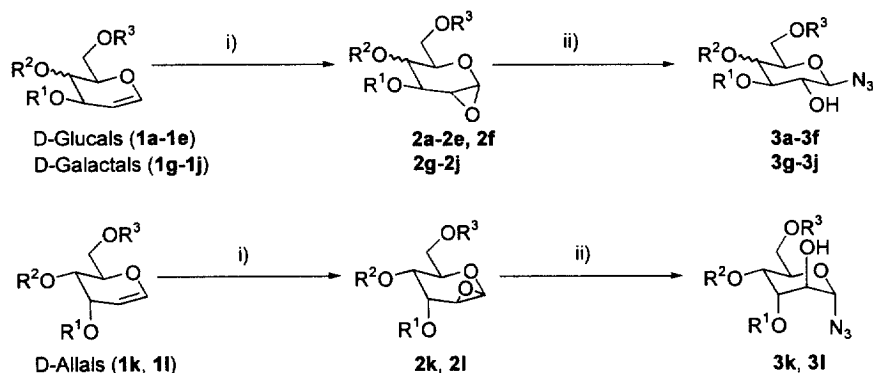
Received 22 September 1998; revised 9 November 1998; accepted 11 November 1998

## Abstract

1,2-Anhydrosugars were transformed regio- and stereoselectively into the corresponding D-glycopyranosyl azides in high yield by treatment with lithium azidohydridodiisobutylaluminumate in THF. © 1998 Elsevier Science Ltd. All rights reserved.

*Keywords:* Aluminum and compounds; Azides; Glycosides; Stereoselection

We have recently reported lithium azidohydridodiisobutylaluminumate (DIBAH-LiN<sub>3</sub>) [1] and lithium *B*-azido-*B*-hydrido-9-BBN [2] transfer an azido group to the epoxides regioselectively to produce *vic*-azidoalcohols. In connection with these results, we have also applied lithium azidohydridodiisobutylaluminumate to 1,2-anhydrosugars to synthesize D-glycopyranosyl azides, the precursors for the glycoconjugate synthesis.



i) DMDO (2eq), CH<sub>2</sub>Cl<sub>2</sub>-CH<sub>2</sub>COCH<sub>3</sub>, 0 °C, 1 h ii) DIBAH-LiN<sub>3</sub> (2eq), THF, 0 °C, 1 h

1,2-Anhydrosugars were prepared stereospecifically and quantitatively through direct epoxidation of the corresponding D-glycals with 3,3-dimethyldioxirane (DMDO) [3,4,5]. D-Glucals (**1a-1e**) and D-galactals (**1g-1j**) afforded the corresponding 1 $\alpha$ ,2 $\alpha$ -anhydrosugars (**2a-2e**, **2g-2j**) whereas D-allals (**1k,1l**) gave 1 $\beta$ ,2 $\beta$ -anhydrosugars (**2k**, **2l**) stereoselectively [6]. This stereochemical outcome is probably due to the configuration of the 3-OH protected with relatively bulky groups. 1 $\alpha$ ,2 $\alpha$ -Anhydro-3,4,6-tri-*O*-acetyl-D-glucopyranose (**2f**) was also prepared from D-glucose in 4 steps [7].

Treatment of these 1,2-anhydrosugars with lithium azidohydridodiisobutylaluminatate (DIBAH-LiN<sub>3</sub>) (2eq) in THF afforded D-glycopyranosyl azides in 64–92% yield even though the reaction condition was not optimized. Nucleophilic attack of the azido group to the more positive anomeric carbon gave rise to the regio- and stereoselectivity of this epoxide-opening reaction. A typical reaction procedure is as follows: DIBAH (0.2 ml of 1M solution in THF, 0.2 mmol) was added to a stirred suspension of lithium azide (9.8 mg, 0.2 mmol) in THF (1 ml) under argon atmosphere at rt. The mixture was stirred for 30 min and the resulting clear solution was cooled to 0 °C. A solution of 1 $\alpha$ ,2 $\alpha$ -anhydro-3,4,6-tri-*O*-benzyl-D-glucopyranose (**2a**, 44 mg, 0.1 mmol) in THF (1 ml) was added and the solution was stirred at 0 °C for 1 h. The mixture was poured into the saturated aqueous sodium bicarbonate solution (3 ml) and extracted with chloroform (3 x 5 ml). The organic extracts were dried over anhydrous MgSO<sub>4</sub>, filtered and concentrated. Silica gel column chromatography afforded 3,4,6-tri-*O*-benzyl- $\beta$ -D-glucopyranosyl azide (**3a**) in 73% yield. The results are summarized in the Table.

**Table.** Reaction of 1,2-Anhydrosugars with DIBAH-LiN<sub>3</sub>

Anhydro-sugars	Protective Groups	Products	Isolated Yield(%)	Anhydro-sugars	Protective Groups	Products	Isolated Yield(%)
<b>2a</b>	R <sup>1</sup> = R <sup>2</sup> = R <sup>3</sup> = Bn	<b>3a</b>	73	<b>2g</b>	R <sup>1</sup> = R <sup>2</sup> = R <sup>3</sup> = Bn	<b>3g</b>	78
<b>2b</b>	R <sup>1</sup> = R <sup>2</sup> = R <sup>3</sup> = TBS	<b>3b</b>	64	<b>2h</b>	R <sup>1</sup> , R <sup>2</sup> = >CO, R <sup>3</sup> = TBDPS	<b>3h</b>	65
<b>2c</b>	R <sup>1</sup> = Bn, R <sup>2</sup> , R <sup>3</sup> = >C(CH <sub>3</sub> ) <sub>2</sub>	<b>3c</b>	75	<b>2i</b>	R <sup>1</sup> = Bn, R <sup>2</sup> , R <sup>3</sup> = >CHPh	<b>3i</b>	70
<b>2d</b>	R <sup>1</sup> = Bn, R <sup>2</sup> , R <sup>3</sup> = >CHPh	<b>3d</b>	80	<b>2j</b>	R <sup>1</sup> = TBS, R <sup>2</sup> , R <sup>3</sup> = >CHPh	<b>3j</b>	72
<b>2e</b>	R <sup>1</sup> = TBS, R <sup>2</sup> , R <sup>3</sup> = >CHPh	<b>3e</b>	92	<b>2k</b>	R <sup>1</sup> = Bn, R <sup>2</sup> , R <sup>3</sup> = >CHPh	<b>3k</b>	76
<b>2f</b>	R <sup>1</sup> = R <sup>2</sup> = R <sup>3</sup> = Ac	<b>3f</b>	71	<b>2l</b>	R <sup>1</sup> = TBS, R <sup>2</sup> , R <sup>3</sup> = >CHPh	<b>3l</b>	80

In conclusion, a mild and facile method for the preparation of D-glycopyranosyl azides from 1,2-anhydrosugars has been established by using lithium azidohydridodiisobutylaluminatate in THF [8].

**Acknowledgment:** Financial support from OCRC-KOSEF and BSRI Program of Ministry of Education is gratefully acknowledged.

#### References and notes

- [1] Youn YS, Cho IS, Chung BY. *Tetrahedron Lett.* 1998;39:4337-4338.
- [2] Lee HW, Kim YJ, Chung BY. *Bull. Korean Chem. Soc.* 1997;18:1144-1145.
- [3] Murray RW, Jeyaraman R. *J. Org. Chem.* 1985;50:2847-2853.
- [4] Halcomb RL, Danishefsky SJ. *J. Am. Chem. Soc.* 1989;111:6661-6666.
- [5] Gordon DM, Danishefsky SJ. *Carbohydr. Res.* 1990;206:361-366.
- [6] A typical epoxidation procedure is as follows: 3,4,6-Tri-*O*-benzyl-D-glucal (**1a**, 0.1 mmol) was dissolved in CH<sub>2</sub>Cl<sub>2</sub> (10 ml) and the resulting solution was cooled to 0 °C. A solution of dimethyldioxirane in acetone (0.2 mmol, 0.05-0.1M) was added dropwise and the reaction mixture was stirred at 0 °C for 1 h. Solvent removal with a stream of dry nitrogen and vacuum drying afforded 1 $\alpha$ ,2 $\alpha$ -anhydro-3,4,6-tri-*O*-benzyl-D-glucopyranose (**2a**) in quantitative yield.
- [7] Lemieux RU, Howard J. 1,2-Anhydro- $\alpha$ -D-glucopyranose triacetate. In: Whistler RL, Wolfrom ML, editors. *Methods in carbohydrate chemistry*, Vol. II. New York: Academic Press, 1963:400-402.
- [8] 1,2-Anhydrosugars and D-glycopyranosyl azides were identified through <sup>1</sup>H-NMR, IR, and [ $\alpha$ ]<sub>D</sub> values.