PERKIN 1
COMMUNICATION

exo-Glycals from glycosyl cyanides. First generation of *C*-glycosylmethylene carbenes from 2,5- and 2,6-anhydroaldose tosylhydrazones

Marietta Tóth and László Somsák *

Department of Organic Chemistry, University of Debrecen, POB 20, H-4010, Debrecen, Hungary. E-mail: somsak@tigris.klte.hu; Fax: +36-52-435-836; Tel.: +36-52-512-900/2348

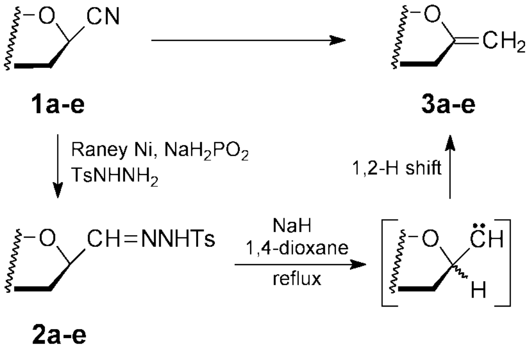
Received (in Cambridge, UK) 3rd January 2001, Accepted 2nd April 2001
First published as an Advance Article on the web 18th April 2001

In a one-pot reaction acylated glycosyl cyanides were transformed with Raney nickel–sodium hypophosphite into 2,5- and 2,6-anhydroaldose tosylhydrazones, which gave *exo*-glycals under Bamford–Stevens conditions.

exo-Glycals (2,5- or 2,6-anhydro-1-deoxy-hex- or -hept-1-enitols) are useful carbohydrate derivatives exemplified by their applications *e.g.* in syntheses[1] and biological investigations.[2]

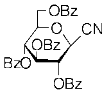
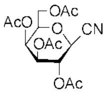
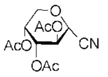
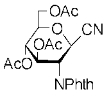
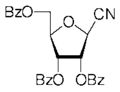
Several synthetic protocols are known for the preparation of such compounds: olefination of sugar lactones by using the Tebbe reagent,[3] dimethyltitanocene,[1a] or the Wittig methodology;[4] hydrogen halide eliminations from *C*-glycosyl-iodomethanes;[5] other methods using glycosyl carbanions as intermediates have been reviewed recently.[6]

Here we report a novel method for the preparation of *exo*-glycals based on the generation of *C*-glycosylmethylene carbenes by application of the aprotic Bamford–Stevens reaction[7] to tosylhydrazones of 2,5- and 2,6-anhydroaldose derivatives followed by their spontaneous rearrangement (Scheme 1). The reaction of acylated glycosyl cyanides[8] (**1**) with Raney nickel–sodium hypophosphite in the presence of 1.2–1.7 eq. of tosylhydrazine[9] in acetic acid–water–pyridine solvent mixture proved to provide easy access to the previously unknown 2,5- and 2,6-anhydroaldose tosylhydrazones **2** (Table 1). With the exception of **2e**, one isomer was formed in



Scheme 1

Table 1 Synthesis and selected data of 2,5- and 2,6-anhydroaldose tosylhydrazones **2** and *exo*-glycals **3**

		2					**3**			
				NMR[a]					NMR[a]	
	1	Yield (%)	$[\alpha]_D$[b] (*c*)	H-1 ($J_{1,2}$) *C-1*	H-2 ($J_{2,3}$)	NH	Yield (%)	$[\alpha]_D$[b] (*c*)	H-1, H-1′ *C-1*	*C-2*
a		64	+4 (1.00)	7.16 (6.3) *144.1*	4.34 (9.5)	8.12	72	+43 (0.98)	4.70, 4.96 *97.3*	*153.3*
b		87	+6 (0.97)	7.00[c] (6.7) *144.1*	4.14[c] (9.8)	11.6[c]	82	+74 (1.45) Lit.[12] +69 (1.00)	4.51, 4.82 *96.1*	*154.1*
c		73	−35 (2.03)	7.04 (6.8) *144.3*	3.89 (9.5)	9.07	86	−94 (0.94)	4.49, 4.69[c] *96.9*	*154.5*
d		58	+65 (1.01)	7.10[c] (5.5) *144.0*	4.87[c] (10.4)	11.48[c]	74	+29 (1.08)	4.24, 4.80 *95.7*	*151.9*
e		Inseparable mixture (probably two diastereomers)					26[d,e]	+24 (0.90)	4.44, 4.67 *87.1*	*157.7*

[a] For $CDCl_3$ solutions unless otherwise stated (δ/ppm, *J*/Hz). [b] Measured in $CHCl_3$ at room temperature. $[\alpha]_D$ Values are given in 10^{-1} deg cm^2 g^{-1}. [c] For DMSO-d_6 solutions. [d] Overall yield for the two steps. [e] For deprotonation 2 eq. of NaH was used.

DOI: 10.1039/b102963k

these transformations. These compounds are new representatives of the rather sparsely populated class of 2,5- and 2,6-anhydroaldimine derivatives.[10]

The tosylhydrazone salt formation and thermolysis were performed in one operation as suggested in the literature:[7a] a solution of **2** in 1,4-dioxane was added dropwise to boiling 1,4-dioxane containing 10 eq. of sodium hydride. *exo*-Glycals **3** were isolated by column chromatography. The reactions were rather clean and highly selective in so far as no products of 1,2-C or 1,2-O shifts could be detected in the mixtures. This was the case even with the furanoid derivative **2e**, in contrast to the ring enlargement observed with tetrahydrofuran-2-ylmethylenes.[11]

In summary, we have described a new route to *exo*-glycals from readily available glycosyl cyanides *via* 2,5- and 2,6-anhydroaldose tosylhydrazones. This method can be a useful alternative to the known procedures, especially for the preparation of acyl-protected derivatives.

Experimental

General procedure for the synthesis of 2,5- and 2,6-anhydroaldose tosylhydrazones (2)

Raney nickel (1.5 g, from an aqueous suspension, Merck) was added at room temperature to a vigorously stirred solution of pyridine (5.7 mL), acetic acid (3.4 mL), and water (3.4 mL). Then sodium hypophosphite (0.74 g, 8.4 mmol), tosylhydrazine (0.22–0.32 g, 1.2–1.7 mmol), and the corresponding glycosyl cyanide **1** (1 mmol) were added to the mixture. When the reaction was complete (TLC, eluent: ethyl acetate–hexane 1 : 1) the insoluble materials were filtered off with suction, and washed with dichloromethane (10 mL). The organic layer of the filtrate was separated, washed sequentially with water (3 mL), 10% aqueous hydrogen chloride solution (2 × 3 mL), cold, saturated sodium hydrogen carbonate solution (2 × 3 mL) and water (3 mL), and then dried on anhydrous magnesium sulfate. The solution was concentrated under reduced pressure, and traces of pyridine were removed by repeated co-evaporations with toluene. The residue was purified by column chromatography (eluent : ethyl acetate–hexane 1 : 1 or 1 : 2) to give syrupy **2a**–**d**.

General method for the synthesis of *exo*-glycals (3)

Sodium hydride (0.24 g, 10 mmol) was added to dry 1,4-dioxane (25 mL). The suspension was stirred and heated to reflux, and then a solution of a tosylhydrazone **2** (1 mmol) in dry 1,4-dioxane (25 mL) was added dropwise. When the reaction was complete (TLC, eluent: ethyl acetate–hexane 1 : 1), the mixture was cooled and the insoluble material filtered off. The solvent was removed under reduced pressure, and the residue was purified by column chromatography (eluent : gradient of ethyl acetate–hexane 1 : 2 to 1 : 1) to give *exo*-glycals **3a**–**e**.

Acknowledgements

This work was supported by the Hungarian Scientific Research Fund (Grant: OTKA T 32124).

Notes and references

1 See as leading references: (*a*) C. R. Johnson and B. A. Johns, *Synlett*, 1997, 1406; (*b*) T. Vidal, A. Haudrechy and Y. Langlois, *Tetrahedron Lett.*, 1999, **40**, 5677; (*c*) A. D. Campbell, D. E. Paterson, T. M. Raynham and R. J. K. Taylor, *Chem. Commun.*, 1999, 1599; (*d*) I. P. Smoliakova, *Curr. Org. Chem.*, 2000, **4**, 589.

2 Leading references: G. Legler, *Adv. Carbohydr. Chem. Biochem.*, 1990, **48**, 319; M. H. D. Postema, *C-Glycoside Synthesis*, CRC Press, Boca Raton, 1995, pp. 353–355.

3 C. S. Wilcox, G. W. Long and H. Suh, *Tetrahedron Lett.*, 1984, **25**, 395; T. V. RajanBabu and G. S. Reddy, *J. Org. Chem.*, 1986, **51**, 5458.

4 Y. Lakhrissi, C. Taillefumier, M. Lakhrissi and Y. Chapleur, *Tetrahedron: Asymmetry*, 2000, **11**, 417.

5 M. Brockhaus and J. Lehmann, *Carbohydr. Res.*, 1977, **53**, 21; J. Lehmann and B. Schwesinger, *Carbohydr. Res.*, 1982, **107**, 43; O. R. Martin and F. Xie, *Carbohydr. Res.*, 1994, **264**, 141; R. D. Guthrie, I. D. Jenkins, J. J. Watters, M. W. Wright and R. Yamasaki, *Aust. J. Chem.*, 1982, **35**, 2169.

6 L. Somsák, *Chem. Rev.*, 2001, **101**, 81.

7 (*a*) K.-P. Zeller and H. Gugel, in *Methoden der organischen Chemie (Houben-Weyl)*, Vol. E19b, ed. M. Regitz, Thieme, Stuttgart, 1989, pp. 225–243; (*b*) K. Maruoka and H. Yamamoto, in *Comprehensive Organic Synthesis*, Vol. 6, ed. B. M. Trost and I. Fleming, Pergamon, Oxford, 1991, pp. 776–779.

8 Z. Györgydeák and I. Pelyvás, *Monosaccharide Sugars—Chemical Synthesis by Chain Elongation, Degradation and Epimerization*, Academic Press, San Diego, 1998, pp. 316–331.

9 This method is a modification of a protocol used for the preparation of 2,5- and 2,6-anhydroaldoses from glycosyl cyanides in the presence of 1,2-dianilinoethane: H. P. Albrecht, D. B. Repke and J. G. Moffatt, *J. Org. Chem.*, 1973, **38**, 1836; H.-M. Dettinger, G. Kurz and J. Lehmann, *Carbohydr. Res.*, 1979, **74**, 301.

10 Leading references for 2,5- and 2,6-anhydroaldoximes: S. Kim, I. Y. Lee, J.-Y. Yoon and D. H. Oh, *J. Am. Chem. Soc.*, 1996, **118**, 5138; D.-P. Pham-Huu, M. Petrušová, J. N. BeMiller and L. Petruš, *Synlett*, 1998, 1319; D.-P. Pham-Huu, M. Petrušová, J. N. BeMiller and L. Petruš, *J. Carbohydr. Chem.*, 2000, **19**, 93; for nitrones of 2,5- and 2,6-anhydroaldoses: A. Dondoni, F. Junquera, F. L. Merchán, P. Merino, M.-C. Scherrmann and T. Tejero, *J. Org. Chem.*, 1997, **62**, 5484; for silyl nitronates of 2,6-anhydroaldoses: O. R. Martin, F. E. Khamis and S. P. Rao, *Tetrahedron Lett.*, 1989, **30**, 6143.

11 S. Kim, J.-Y. Yoon and C. M. Cho, *Chem. Commun.*, 1996, 909; S. Kim and J.-Y. Yoon, *Synthesis*, 2000, 1622.

12 H. Fritz, J. Lehmann and P. Schlesselmann, *Carbohydr. Res.*, 1983, **113**, 71.