RING CONTRACTION IN THE FLUORINATION OF METHYL 2-0-BENZYL-3,6-DIDEOXY- AND METHYL 2,3-DI-0-BENZYL-6-DEOXY- α -D-HEXOPYRANOSIDES WITH DIETHYLAMINOSULFUR TRIFLUORIDE (DAST)

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Fluorination of methyl 2-0-benzyl-3,6-dideoxy- α -D-ribo- and α -D-arabino-hexopyranosides (1 and 4) with diethylaminosulfur trifluoride (DAST) yielded methyl 2-0-benzyl-3,5,6-trideoxy-5-fluoro- β -L-arabino- and β -L-ribo-hexofuranosides (3 and 6), respectively, along with the corresponding 4-deoxy-4-fluoro- α -D-hexopyranosides with retained configuration at C-4. The reaction of methyl 2,3-di-0-benzyl-6-deoxy- α -D-glucopyranoside (7) with DAST predominantly afforded methyl 2,3-di-0-benzyl-5,6-di-deoxy-5-fluoro- β -L-altrofuranoside (9).

KEYWORDS ring contraction; fluorination; DAST; fluorinated carbohydrate; 5,6-dideoxy-5-fluoro-hexofuranose; 3,5,6-trideoxy-5-fluoro-hexofuranose

Among a large number of strategies for the introduction of fluorine into carbohydrates, diethylaminosulfur trifluoride (DAST) is known as a useful reagent for the direct replacement of hydroxyl group by fluorine. However, unusual reactions caused by the action of DAST have also been reported.

In our attempts at direct fluorination using DAST at 4-position of 3,6-dideoxyhexopyranosides, it was found that the substitution of the equatorial 4-hydroxyl group by fluorine proceeded with exclusive retention of configuration. Investigation of the by-products in those reactions revealed the formation of the fluorides having furanoid structure such as 3 and 6. There have been reports of similar results on the iodination of methyl 2,3-0-isopropyridene- α -L-rhamnopyranoside, the deamination of the 4-amino derivatives of methyl α -L-manno- α and α -D-glucopyranosides, and the hydrolysis of methyl 4-0-(4-nitrobenzenesulfonyl)- α -D-glucopyranoside. The ring-contracted 5-fluorides were obtained in the fluorination of racemic methyl N-acetylacosaminides with sulfur tetrafluoride-hydrogen fluoride. This communication provides an example of ring contraction of hexopyranoside induced by DAST.

When methyl 2-0-benzyl-3,6-dideoxy- α -D-ribo-hexopyranoside (1) was treated with 1.2 molar equivalents of DAST in dichloromethane at -13°C for 0.5 h and then at room temperature for 1.5 h, methyl 2-0-benzyl-3,4,6-trideoxy-4-fluoro- α -D-ribo-hexopyranoside (2) and methyl 2-0-benzyl-3,5,6-trideoxy-5-fluoro- β -L-arabino-hexofuranoside

(3) were isolated through silica gel column chromatography in yields of 66% and 17%, respectively. The reaction of the α -D-arabino isomer 4 with DAST under the same reaction conditions as those for 1 gave the 4-fluoride 5 in 28% yield and methyl 2-0-benzyl-3,5,6-trideoxy-5-fluoro- β -L-ribo-hexofuranoside (6) in 21% yield along with 34% recovery of 4. No 5-epi-fluoride was isolated from both reactions.

In a similar reaction of the 2,3-di-0-benzyl derivative 7,¹¹⁾ methyl 2,3-di-0-benzyl-5,6-di-deoxy-5-fluoro- β -L-altrofuranoside (9) was obtained in 38% yield as the major product along with

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Fig. 1. NOEs observed for 3

only 2% yield of the 4-fluoride 8, and 7 recovered (39%); no α -D-galacto isomer of 9 was produced.

The ¹H- and ¹³C-NMR spectral data of the ring-contracted compounds (3, 6, and 9) are summarized in Tables I and II, respectively. The NOEs observed for the protons of 3 are shown in Fig. 1. The stereochemistry at C-4 of 3 was determined by the presence of the NOEs between H-2 and H-3b, H-3b and H-4, H-3a and H-5, and H-3a and H-6's. Similarly, the NOEs observed between H-2 and H-3a, and H-3b and H-4 of 6, and that observed between H-3 and H-5 of 9 were reasonable for their proposed configuration at C-4.

The absolute configuration at C-5 was verified in the following synthetical manner. The compound 6 was readily converted through hydrogenolysis and subsequent acetolysis into the 1,2-diacetate 10, which was deacetylated and then isopropylidenated to form 11. The ¹H-NMR spectrum of 11 was identical with that of 13 independently prepared by the reaction of 3,6-dideoxy-1,2-0-isopropylidene-4-0-methanesulfonyl- β -L-lyxo-hexofuranose (12, $[\alpha]_{p}^{20}$ -31.8° (c 0.9, chloroform)) with tetrabutylammonium fluoride in N,N-dimethylformamide. The specific rotations for 11 and 13, measured in chloroform at 20°C, are +25.4° and -25.7°, respectively. Thus, it is ascertained that 11 is the enantiomer of 13, and this indicates that the proposed structure of 6 is correct. Details of the syntheses of 1, 4, 11, 12, and 13 are to be published elsewhere.

Stereospecific formation of single isomers of both the 4- and the 5-fluorides suggests that the bicyclic oxonium ion I (Chart 1) formed by the participation of ring oxygen is a plausible intermediate for the production of the 4-fluoride (route a) and the 5-fluoride (route b). However, the ring contraction concerted with the intramolecular attack of fluorine at C-5 (depicted as II), being analogous to the formation of a furancial structure through migration of a sulfonyloxyl group from C-4 to C-5, 12) seems to be more presumable to the predominant formation of 9. Further experiments for elucidating the mechanisms are in progress.

$$\begin{array}{c} F \\ Et_2N \\ \hline \end{array}$$

$$\begin{array}{c} Me \\ OMe \\ \hline \end{array}$$

$$\begin{array}{c} Me \\ OMe \\ \hline \end{array}$$

$$\begin{array}{c} Me \\ OMe \\ \hline \end{array}$$

$$\begin{array}{c} F \\ OMe \\ \hline \end{array}$$

$$\begin{array}{c} Me \\ OMe \\ \hline \end{array}$$

$$\begin{array}{c} I \\ OMe \\ \hline \end{array}$$

$$\begin{array}{c} I \\ OMe \\ \hline \end{array}$$

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Table I. ¹H-NMR Data for 3, 6, 9, and 11(13) (Measured at 300 MHz in CDCl₃)

Compound	δ (ppm) J _{H, H} (Hz) (J _{F, H} (Hz))								
•	H-1	H-2	H-3a^	H-3b	H-4	H-5	H-6's		
3		.010	1.99 1.8————————————————————————————————————	6	.5——6 .0—		. 2 —		
6		4 ــــا نــــ 4	2.04 .9————————————————————————————————————	.4——6	4.28 .6———6	4.57	.2—1.38		
9			4.27	— 5.2 —	7		. 2 —		
11(13)		3.7	1.84	2 — — 4	.7 — — 3 .4 —		. 4 —		

[^] H-3a represents a H-3 oriented to the same side as C-5.

Table II. 13 C-NMR Data for 3, 6, 9, and 11 (Measured at 75.4 MHz in CDCl₃)

Compound	δ (ppm) (J _{c. F} (Hz))								
	C-1	C-2	C-3	C-4	C-5	C-6			
3	101.7	78.3	30.5 (2.8)	78.7 (26.5)	91.9 (169.3)	17.3 (22.1)			
6	107.0	82.9	31.4 (3.2)	81.5 (25.1)	91.5 (170.2)	(22.0)			
9	101.8	84.3	82.9	83.1 (27.5)	90.3	17.5 (22.0)			
11	105.5	80.3	32.8 (4.6)	80.1 (22.6)	89.5 (171.5)	17.5 (22.1)			

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