

**RING CONTRACTION IN THE FLUORINATION OF METHYL 2-O-BENZYL-3,6-DIDEOXY- AND METHYL 2,3-DI-O-BENZYL-6-DEOXY- $\alpha$ -D-HEXOPYRANOSIDES WITH DIETHYLAMINOSULFUR TRIFLUORIDE (DAST)**

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Fluorination of methyl 2-O-benzyl-3,6-dideoxy- $\alpha$ -D-ribo- and  $\alpha$ -D-arabino-hexopyranosides (1 and 4) with diethylaminosulfur trifluoride (DAST) yielded methyl 2-O-benzyl-3,5,6-trideoxy-5-fluoro- $\beta$ -L-arabino- and  $\beta$ -L-ribo-hexofuranosides (3 and 6), respectively, along with the corresponding 4-deoxy-4-fluoro- $\alpha$ -D-hexopyranosides with retained configuration at C-4. The reaction of methyl 2,3-di-O-benzyl-6-deoxy- $\alpha$ -D-glucopyranoside (7) with DAST predominantly afforded methyl 2,3-di-O-benzyl-5,6-dideoxy-5-fluoro- $\beta$ -L-altrofuranside (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.<sup>1-4)</sup> However, unusual reactions caused by the action of DAST have also been reported.<sup>4)</sup>

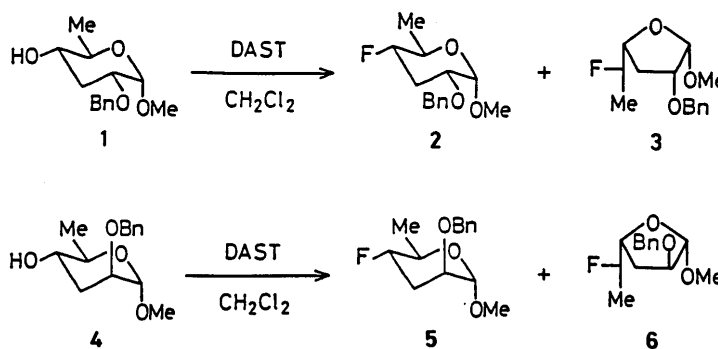
In our attempts at direct fluorination using DAST at 4-position of 3,6-dideoxyhexopyranosides, it was found that the substitution of the equatorial 4-hydroxyl group by fluorine proceeded with exclusive retention of configuration.<sup>5)</sup> Investigation of the by-products in those reactions revealed 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-O-isopropylidene- $\alpha$ -L-rhamnopyranoside,<sup>6)</sup> the deamination of the 4-amino derivatives of methyl  $\alpha$ -L-manno-<sup>7)</sup> and  $\alpha$ -D-glucopyranosides,<sup>8)</sup> and the hydrolysis of methyl 4-O-(4-nitrobenzenesulfonyl)- $\alpha$ -D-glucopyranoside.<sup>9)</sup> The ring-contracted 5-fluorides were obtained in the fluorination of racemic methyl N-acetylacosaminides with sulfur tetrafluoride-hydrogen fluoride.<sup>10)</sup> This communication provides an example of ring contraction of hexopyranoside induced by DAST.

When methyl 2-O-benzyl-3,6-dideoxy- $\alpha$ -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-O-benzyl-3,4,6-trideoxy-4-fluoro- $\alpha$ -D-ribo-hexopyranoside (2) and methyl 2-O-benzyl-3,5,6-trideoxy-5-fluoro- $\beta$ -L-arabino-hexofuranoside

(3) were isolated through silica gel column

chromatography in yields of 66% and 17%, respectively. The reaction of the  $\alpha$ -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-O-benzyl-3,5,6-trideoxy-5-fluoro- $\beta$ -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-O-benzyl derivative 7,<sup>11)</sup> methyl 2,3-di-O-benzyl-5,6-dideoxy-5-fluoro- $\beta$ -L-altrofuranside (9) was obtained in 38% yield as the major product along with

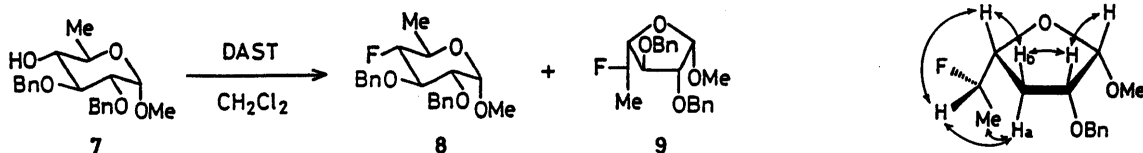
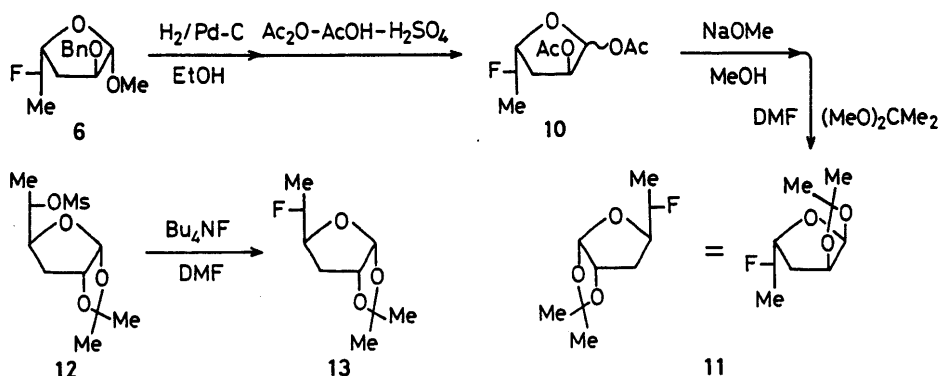


Fig. 1. NOEs observed for 3

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

The  $^1\text{H}$ - and  $^{13}\text{C}$ -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 acetylation into the 1,2-diacetate 10, which was deacetylated and then isopropylidened to form 11. The  $^1\text{H}$ -NMR spectrum of 11 was identical with that of 13 independently prepared by the reaction of 3,6-dideoxy-1,2-O-isopropylidene-4-O-methanesulfonyl- $\beta$ -L-*lyxo*-hexofuranose (12,  $[\alpha]_D^{20} -31.8^\circ$  (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  $+25.4^\circ$  and  $-25.7^\circ$ , 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 furanoid structure through migration of a sulfonyloxy group from C-4 to C-5,<sup>1,2)</sup> seems to be more presumable to the predominant formation of 9. Further experiments for elucidating the mechanisms are in progress.

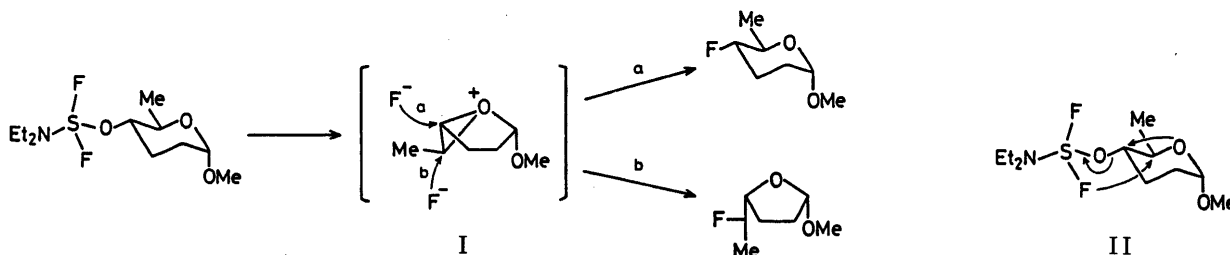


Chart 1

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