

## Utility of Tris(dimethylamino)sulphonium Difluorotrimethylsilicate (TASF) for the Rapid Synthesis of Deoxyfluoro Sugars

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The fluoride ion displacement of carbohydrate trifluoromethanesulphonates using tris(dimethylamino)sulphonium difluorotrimethylsilicate (TASF) provides a convenient route to deoxyfluoro sugars; the rapidity of the reaction makes it of interest for the potential synthesis of fluorinated-carbohydrate radiopharmaceuticals for use in medical imaging.

The selective introduction of fluorine into carbohydrates is of continuing interest not only because of the synthetic challenge but also because of the possibility of a dramatic change in biological activity.<sup>1</sup> Moreover, the utility of [<sup>18</sup>F]-labelled carbohydrates, especially 2-deoxy-2-[<sup>18</sup>F]fluoro-D-glucose, in studying regional organ metabolism by positron emission tomography (p.e.t.),<sup>2</sup> has provided added impetus to the search for convenient, rapid fluorination techniques. The reagent, tris(dimethylamino)sulphonium difluorotrimethylsilicate (TASF),<sup>3</sup> has been used in the synthesis of 1-deoxy-1-fluoro-D-fructose;<sup>4</sup> here we report the utility of this reagent for the rapid introduction of fluorine into a variety of monosaccharide trifluoromethanesulphonates (triflates). The reaction time is such that an [<sup>18</sup>F]-labelled analogue of the reagent would be well-suited for the preparation of radiopharmaceuticals for p.e.t.

Compounds (1a)—(4a), respectively, were prepared as described in the literature,<sup>5–8</sup> and converted into the corresponding triflates (1b)—(4b) using the following procedure. Trifluoromethanesulphonic anhydride (2.5 mol equiv.) was added to a cold (salt bath) solution of the substrate in CH<sub>2</sub>Cl<sub>2</sub> and pyridine (3 mol equiv.); t.l.c. indicated completeness of reaction within 10 min. The reaction mixture was washed sequentially with ice-cold, dilute HCl, and water, dried (MgSO<sub>4</sub>), and evaporated. The triflate product was used directly in the displacement reaction. The use of this procedure in the case of (4a) minimized the formation of a pyridinium salt; treatment of (4a) with trifluoromethanesulphonic anhydride in pyridine solution for ca. 1.5 h at -15 °C has been reported<sup>9</sup> to produce 6-deoxy-1,2:3,4-di-O-isopropylidene-6-pyridino-α-D-galactopyranose trifluoromethanesulphonate rather than the desired triflate.

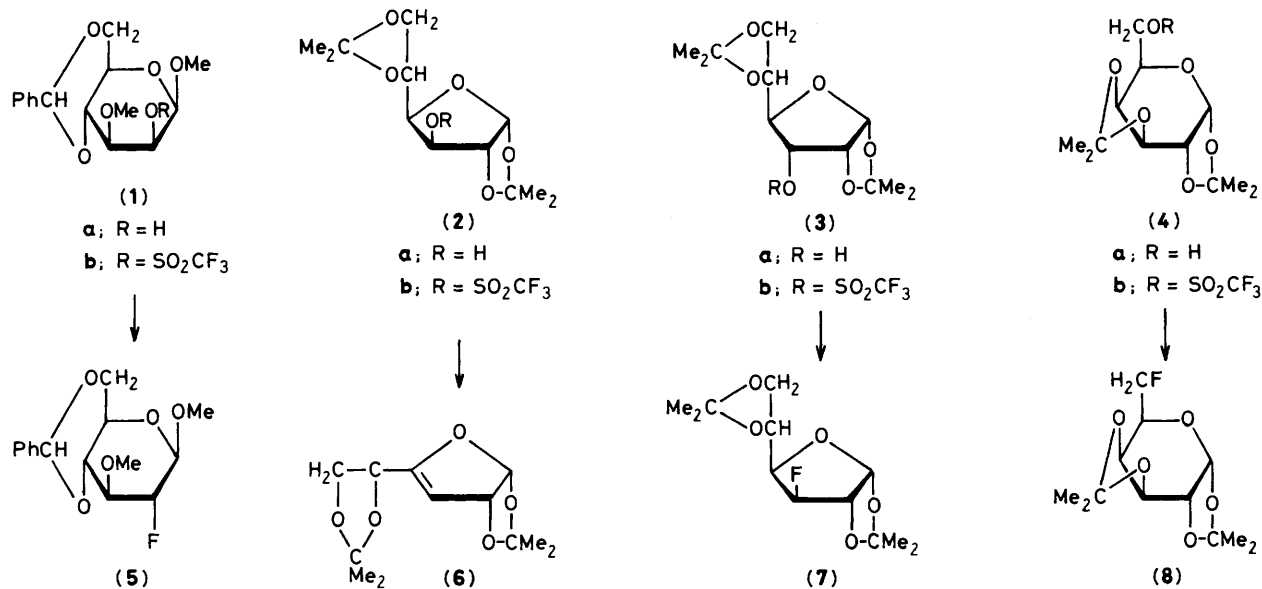


Table 1. Data for products (5)—(8).

Compound	Yield (%) <sup>a</sup>	Melting point (°C)	Specific rotation, [α] <sub>D</sub>		Solvent system for chromatography <sup>d</sup> (v/v)
			This work <sup>c</sup>	Literature	
(5)	64	107–108 <sup>b</sup>	-39.6° (c 0.79, CHCl <sub>3</sub> )	—	2 : 1 Hexanes-Et <sub>2</sub> O
(6)	83	—	+15.3° (c 1.1, EtOH)	+19.8° (c 3.03, EtOH) <sup>11</sup>	4 : 1 Hexanes-Et <sub>2</sub> O
(7)	66	—	-21.4° (c 1.15, CHCl <sub>3</sub> )	-22° (c 1.0, CHCl <sub>3</sub> ) <sup>12</sup>	4 : 1 Hexanes-Et <sub>2</sub> O
(8)	71	—	-54.8° (c 3.18, CHCl <sub>3</sub> )	-51.4° (c 1.28, CHCl <sub>3</sub> ) <sup>11</sup>	19 : 1 Toluene-Et <sub>2</sub> O

<sup>a</sup> Yields are based on the starting hydroxy compounds. <sup>b</sup> Lit.<sup>10</sup> 108 °C. <sup>c</sup> Optical rotations were measured with a Perkin-Elmer model 141 automatic polarimeter at 26 ± 3 °C. <sup>d</sup> Flash chromatography was performed on Merck Kieselgel 60 (230–400 mesh).

The reaction of each of (1b)—(4b) with tris(dimethylamino)-sulphonium difluorotrimethylsilicate† was performed in the following manner. To a cooled (salt bath) solution of the triflate in CH<sub>2</sub>Cl<sub>2</sub> was added TASF (ca. 3 mol equiv., based on the starting hydroxy compound); anhydrous conditions (argon) were maintained. The cooling bath was removed, and after 10 min, t.l.c. indicated that all of the starting material had been consumed. The reaction mixture was washed with water, dried (MgSO<sub>4</sub>), and evaporated, and the product was isolated by flash chromatography on silica gel. Triflates (1b), (3b), and (4b) afforded fluorides (5), (7), and (8), respectively, in good yield; in the case of triflate (2b), 3-deoxy-1,2:5,6-di-*O*-isopropylidene- $\alpha$ -D-erythro-hex-3-enofuranose (6) was formed, but no fluoride. Also, in the case of the reaction with triflate (1b), a more-polar (t.l.c.), minor compound was formed whose <sup>1</sup>H n.m.r. spectrum indicated the presence of only one methoxy group; this product has not been investigated further. The <sup>13</sup>C and <sup>19</sup>F n.m.r. spectra of the fluoro sugars (5), (7), and (8) are consistent with the assigned structures. Other data for these compounds and for (6) are given in Table 1.

† This reagent was purchased from Aldrich Chemical Co. whose catalogue lists it as tris(dimethylamino)sulfur (trimethylsilyl)difluoride. It has also been named tris(dimethylamino)sulphonium difluorotrimethylsilicate; see, for example, T. V. RajanBabu, *J. Org. Chem.*, 1984, **49**, 2083. We prefer to use the name given in this communication.

The authors are grateful to the Medical Research Council and the Natural Sciences and Engineering Research Council of Canada for their support of this research.

Received, 8th February 1985; Com. 169

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