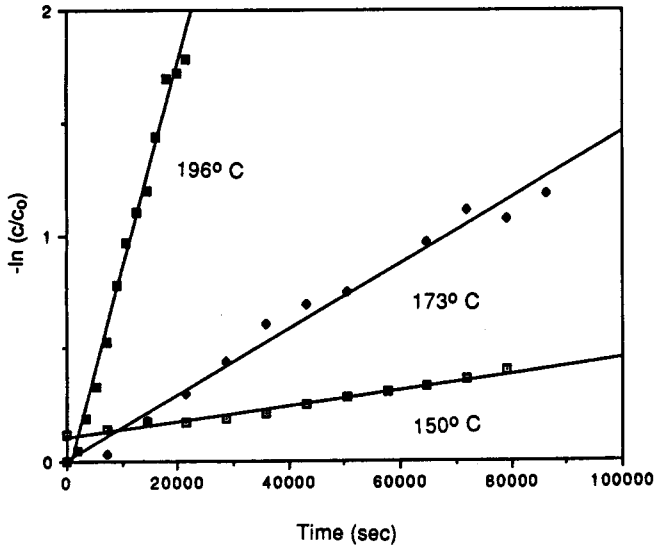


Figure 2. First-order kinetic plots for the rearrangement of TBMA to TBB at 150, 173, and 196 °C.

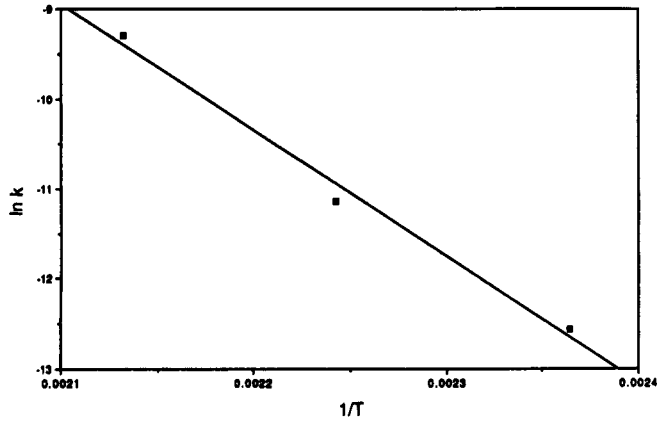


Figure 3. Plot of ln k versus $1/T$ for the rearrangement of TBMA to TBB.

shown in Figure 2 are for data obtained at longer reaction times, which enabled more reliable integration of the NMR spectra and calculation of the TBMA to TBB ratios.) The plot of ln k versus $1/T$ is shown in Figure 3, which gives values for the activation parameters for this reaction of $\Delta H^{\ddagger} = 27.9 \pm 1.0$ kcal mol^{-1} and $\Delta S^{\ddagger} = +1.4 \pm 1.5$ eu. The linearity of this plot suggests that this reaction is a true unimolecular process and is not "catalyzed" by some adventitious acid or base that might be present in the solutions. The apparent driving force for this reaction is the loss of the very high positive heat of formation of the allenic carbon atom of the TBMA (+34.2 kcal mol^{-1}), the calculated change in the heat of formation, ΔH_f, and entropy, ΔS_f, for the reaction at 298 °C being −18.3 kcal mol^{-1} and +16.4 eu (ΔG_{298} −23.2 kcal mol^{-1}),[9] both being highly favorable for the reaction. The rather high $\Delta H^{\ddagger}$ for the rearrangement compared to the rather exothermic nature of the process reflects the poor overlap between the 2p AO's on the terminal carbon atoms of the ultimate 1,3-diene, which are undergoing rotation in the transition state for the rearrangement.

Experimental Section

The preparation of 1-*tert*-butyl-3-methylallene (TBMA) was carried out by the procedure of Elsevier and Vermeer.[10] 1-*tert*-Butyl-1,3-butadiene (TBB) has been previously prepared and characterized by Corey and Cane.[11]

Thermal Rearrangement of TBMA. Solutions of 10 mg (0.09 mmol) of TBMA in 0.5 mL of bromobenzene-d_5 in NMR tubes were triply freeze–degassed, and the NMR tubes were sealed under reduced pressure. The NMR tubes were suspended in the refluxing vapors of nonane (150 °C), decane (173 °C), and undecane (196 °C). The NMR tubes were periodically removed from the vapors of the refluxing solvents, and the 200-MHz ^{1}H NMR spectra of the solutions were recorded and integrated. Resonances corresponding to only TBMA and the product TBB were observed in the NMR spectra. The relative ratios of the TBMA and TBB were converted to relative concentrations, resulting in the first-order kinetic plots shown in Figure 2 (k_{150} 3.49×10^{-6} s^{-1}, k_{173} 1.45×10^{-5} s^{-1}, k_{196} 9.15×10^{-5} s^{-1}). 300-MHz ^{1}H NMR spectrum of TBMA: ($CDCl_3$) δ 1.01 (s, 9 H), 1.65 (dd, J = 6.82, 3.37 Hz, 3 H), 5.04 (dq, J = 6.73, 3.37 Hz, 1 H), 5.09 (dq, J = 6.73, 6.82 Hz, 1 H). 300-MHz ^{1}H NMR spectrum of TBB: δ 0.96 (s, 9 H), 4.95 (dddd, J = 10.11, 1.79, 0.76, 0.55 Hz, 1 H), 5.10 (dddd, J = 16.92, 1.79, 1.03, 0.67 Hz, 1 H), 5.65 (dddd, J = 15.41, 0.76, 0.68, 0.67 Hz, 1 H), 5.99 (dddd, J = 15.41, 10.13, 1.03, 0.55 Hz, 1 H), 6.29 (dddd, J = 16.92, 10.13, 10.11, 0.68 Hz, 1 H).

Acknowledgment. This research was supported by a grant from the National Science Foundation (CHE-8709725).

(9) Calculated by the method of Benson: Benson, S. W. *Thermochemical Kinetics*, 2nd ed.; John Wiley & Sons: New York, 1976).

(10) Elsevier, C. J.; Vermeer, P. *J. Org. Chem.* **1989**, *54*, 3726.
(11) Corey, E. J.; Cane, D. E. *J. Org. Chem.* **1969**, *34*, 3053.

gem-Difluorination versus 1,2-Migration and Fragmentation in the Reaction of 2- and 3-Uloses with DAST. Influence of Stereochemistry at the Anomeric Carbon Atom

Anas El-Laghdach, Raouf Echarri, M. Isabel Matheu, M. Isabel Barrena, and Sergio Castillón*

Departament de Quimica, Facultat de Ciencies Quimiques de Tarragona, Universitat de Barcelona, Psa. Imperial Tarraco 1, 43005 Tarragona, Spain

Jordi Garcia

Departament de Quimica Orgânica, Facultat de Quimica, Universitat de Barcelona, Martí i Franquès 1, 08028 Barcelona, Spain

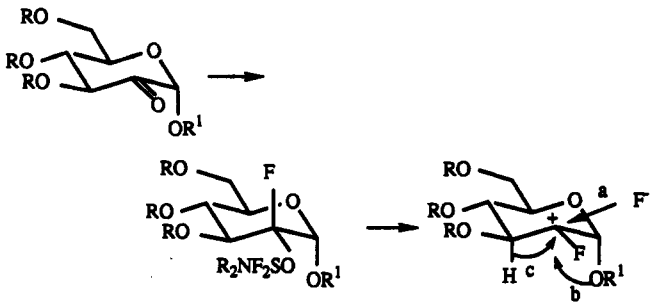
Received October 1, 1990 (Revised Manuscript Received March 18, 1991)

Introduction of fluorine into biologically active organic compounds is one of the most simple structural modifications in order to increase their activity.[1] Recently, many reagents[2] have been developed for the synthesis of mono- and *gem*-difluorinated compounds, looking for higher yields and selectivities. The difluoromethylene group has a steric profile similar to that of methylene and is frequently prepared from a carbonyl group; among the reagents commonly utilized for this transformation—SF_4,[3] SeF_4,[4] MoF_6,[5] $PhSF_3$,[6] and (diethylamino)sulfur trifluoride

(1) (a) Schlosser, M. *Tetrahedron* **1978**, *34*, 3. (b) *Fluorinated Carbohydrates, Chemical and Biochemical Aspects*; Taylor, N. F., Ed.; American Chemical Society: Washington DC, 1988.
(2) Gerstenberger, M. R. C.; Haas, A. *Angew. Chem., Int. Ed. Engl.* **1981**, *20*, 647.
(3) (a) Boswell, G. A.; Ripko, W. C.; Scribner, R. M.; Tullock, C. W. *Org. React. (N.Y.)* **1974**, *21*, 20–30. (b) Wang, C.-L. *J. Org. React. (N.Y.)* **1985**, *34*, 319.
(4) Kent, P. W.; Wood, K. R. British Patent 1968, 1 136075.
(5) Mathey, F.; Bensoam, J. *Tetrahedron* **1971**, *27*, 3965.
(6) Sheppard, W. A. *J. Am. Chem. Soc.* **1962**, *84*, 3058.

0022-3263/91/1956-4556$02.50/0

Scheme I



(DAST)[7,8]—only the last one is commercially available. On the other hand, *gem*-difluoro compounds have also been recently prepared from 1,3-dithiolanes by action of pyridinium poly(hydrogen fluoride).[9]

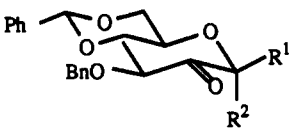
In the carbohydrate field the interest in C-2 fluoro analogues is justified by the unusual stability to acidic hydrolysis of α-fluoro ketals and acetals,[10,11] which implies a resistance to the degradation of carbohydrate-containing antibiotics. Few 2-deoxy-2,2-difluorinated carbohydrates have been reported so far; they were obtained either by addition of trifluorofluoroxymethane (CF_3OF) to the 2-fluoroglycals,[12,13] via Reformatskii reaction with ethyl bromodifluoroacetate[11,14] and bromodifluoromethylacetylene[15] in acyclic precursors, or by reaction of carbonyl groups with DAST.[16] The last one appears to be the most direct method; nevertheless, different reports describe the very peculiar behavior of this reaction,[13,17] suggesting that transposition and/or anomerization does take place. A 1,2-migration has been described[18] when 2-hydroxy carbohydrates are treated with DAST involving a stereoselective entry of fluorine at position 1 of the sugar.

Due to our interest in the synthesis of difluorinated analogues of glycosides and nucleosides, we decided to undertake a systematic study of the reaction of different 2- and 3-uloses with DAST to know when *gem*-difluorination or migration occurs.

Results and Discussion

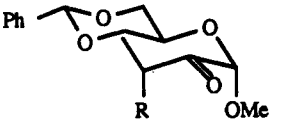
In the light of the mechanism proposed for the *gem*-difluorination reaction with DAST,[7] in which some elimination products, suggesting carbocation intermediates, have been observed, we reasoned that the stereochemistry of neighboring groups to the carbonyl could change the reaction course, favoring either the addition/substitution (Scheme I, see arrow a), migration (see b), or elimination (see c) pathway.

Methyl 3-*O*-benzyl-4,6-*O*-benzylidene-β-D-*arabino*-hexopyranosid-2-ulose[19] (1) and its α anomer[20] 2, methyl 4,6-*O*-benzylidene-3-*O*-methyl-α-D-*ribo*-hexopyranosid-2-ulose[21] (3), methyl 3,4-*O*-isopropylidene-β-D-*erythro*-pentopyranosid-2-ulose[17,22] (5) and its α anomer[23] 6, and methyl 2-*O*-benzyl-4,6-*O*-benzylidene-β-D-*ribo*-hexopyranosid-3-ulose[24] (7) and its α anomer[25] 8 were synthesized in order to determine the effect of the stereochemistry of the anomeric substituent in the pyranose series.



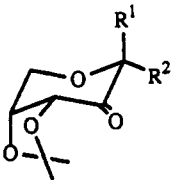
1 R^1=OMe; R^2=H

2 R^1=H; R^2=OMe



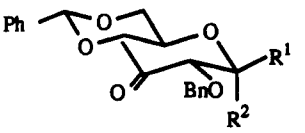
3 R=OMe

4 $R=N_3$



5 R^1=OMe; R^2=H

6 R^1=H; R^2=OMe



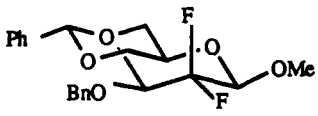
7 R^1=OMe R^2=H

8 R^1=H; R^2=OMe

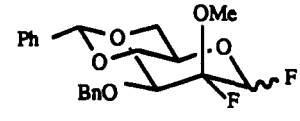
The reactions with DAST were carried out at room temperature, when possible, and using dichloromethane or benzene as solvents, looking for the most advantageous conditions for the synthesis of *gem*-difluoro compounds.[7] When the reaction of 1 with DAST was carried out in dichloromethane for 24 h only the *gem*-difluorinated compound 9 was obtained, in 80% yield. A triplet at 116 ppm in the ^{13}C NMR spectrum (J = 253 Hz) clearly showed the presence of the difluoromethylene group. On the other hand, the α isomer 2 did not react with DAST in dichloromethane or benzene at room temperature. When the solution was refluxed in benzene, a new product slowly appeared, which was identified as an anomeric mixture corresponding to the migration product 10. No improvement was observed on heating in toluene or dichloroethane. The structure of compound 10 was established by ^1H, ^{13}C, and ^{19}F NMR spectroscopy on the basis of the following facts: (1) chemical shifts and coupling constants for protons H-1 show a geminal relation F/H;[26] (2) three different groups of signals (double doublets) in the ^{13}C NMR spectrum appear in the 100–110-ppm region corresponding to the C-1 and C-2 of the main isomer and to C-1 of the minor isomer (C-2 cannot be seen); the high value (~225 Hz) for the $^1J_{F,C}$ coupling constant indicates a fluoroalkoxy substitution for these carbons;[27] (3) the coupling constants H-1/F-2 and H-3/F-2 indicate an equatorial orientation for the fluorine. The structure of

(7) Middleton, W. J. *J. Org. Chem.* **1975**, *40*, 574.
(8) Hudlicky, M. *Org. React. (N.Y.)* **1988**, *35*, 513.
(9) Sandej, S. C.; Katzenellenbogen, J. A. *J. Org. Chem.* **1986**, *51*, 3508.
(10) Simmons, H. E.; Wiley, D. W. *J. Am. Chem. Soc.* **1960**, *82*, 2288.
(11) Fried, J.; Ann Hallinan, E.; Szwedo, M. J., Jr. *J. Am. Chem. Soc.* **1984**, *106*, 3871.
(12) Adamson, J.; Foster, A. B.; Westwood, J. H. *Carbohydr. Res.* **1971**, *18*, 345.
(13) Dessinges, A.; Cabrera Escribano, F.; Lukacs, G.; Olesker, A.; That Thang, T. *J. Org. Chem.* **1987**, *52*, 1633.
(14) Wohlrab, F.; Jamieson, A. T.; Hay, J.; Mengel, R.; Guschlbauer, W. *Biochem. Biophys. Acta* **1985**, *824*, 233.
(15) Hanzawa, Y.; Izanawa, K.; Kon, A.; Aoki, H.; Kobayhasi, Y. *Tetrahedron Lett.* **1987**, *28*, 659.
(16) Sharma, R. A.; Kavai, I.; Fu, Y. L.; Bobek, M. *Tetrahedron Lett.* **1977**, 3433.
(17) An, S.; Bobeck, M. *Tetrahedron Lett.* **1986**, 3219.
(18) Nicolau, K. C.; Ladduwahetty, T. Randall, J. L.; Chucholowsky, A. *J. Am. Chem. Soc.* **1986**, *108*, 2466.
(19) Lee, E. E.; Kaeveney, G.; O'Colla, P. S. *Carbohydr. Res.* **1977**, *59*, 268.
(20) (a) Takamoto, T.; Sudoh, R. *Bull. Soc. Chim. Jpn.* **1975**, *48*, 3413. (b) Morris, Ph. E.; Kiely, D. E.; Vigee, G. S.; Kovac, P. *J. Carbohydr. Chem.* **1990**, 661.
(21) Bissember, B. B.; Wightman, R. H. *Carbohydr. Res.* **1980**, *81*, 187.
(22) Roshental, A.; Sprinzl, M. *Can. J. Chem.* **1970**, *48*, 3253.
(23) (a) Wolfrom, M. L.; Otani, S. *Carbohydr. Res.* **1986**, *153*, 150. (b) Collins, P. M.; Gupta, P.; Jyer, R. *J. Chem. Soc., Perkin Trans. I* **1972**, 1670.
(24) Klemer, A.; Klaffike, W. *Liebigs Ann. Chem.* **1987**, 759.
(25) Yoshimura, J.; Sato, K.; Funabashi, M. *Bull. Soc. Chim. Jpn.* **1979**, *52*, 2630.
(26) Phillips, L.; Wray, V. *J. Chem. Soc., Perkin Trans. II* **1974**, 928.
(27) Wray, V. *J. Chem. Soc., Perkin Trans. II* **1976**, 1598.

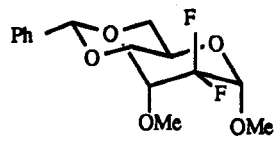
10 suggests that migration of OMe takes place in the first stage of the reaction with DAST, as shown in Scheme II. When compound 3 (drawn, for the sake of simplicity, with both substituents axials) was refluxed in dichloromethane, difluoro compound 11 is obtained as the main product in 38% yield, indicating a twist-boat conformation to avoid the destabilizing 1,3-interaction. On the other hand, compound 4 gave a complex mixture where no difluoro compound was detected, as previously reported.[13]



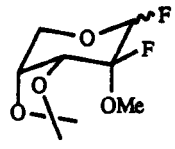
9



10



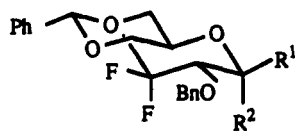
11



12

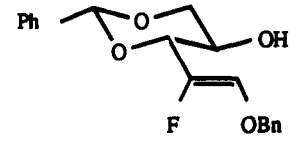
The ulose 5 gave an anomeric mixture of migration products 12 when it was treated with DAST in benzene at room temperature, in which the β-fluoro isomer predominated. The 1,2-difluoro-2-methoxy substitution pattern and the equatorial orientation for F-2 were established as in the case of 10, which implies that the migration of OMe takes place first again (Scheme II). Curiously, the ulose 6 afforded the same product (but in different α/β ratio) as the ulose 5 (12) when treated with DAST; a possible explanation for this fact is the rapid chair inversion in this conformationally mobile compound.[23b]

When the 3-uloses 7 and 8 were treated with DAST, *gem*-difluorinated compounds 13 and 14 were obtained as the main products in moderate 40% and 48% yields, respectively. Compound 15 was isolated as a byproduct in



13 R^1=OMe; R^2=H

14 R^1=H; R^2=OMe



15

both cases, in 17% and 10% yields, respectively, resulting from a Grob-type fragmentation induced either by a carbocation at position 3 or through a concerted path[28] (Scheme III). The fragmentation process is observed in several solvents even at room temperature.[29]

In conclusion, *gem*-difluorination of 2-uloses can be performed with DAST, in a preparative way if both neighboring groups are equatorial or axial. Axial orientation of the anomeric group gives rise to 1,2-migrations to afford 1,2-difluoro-2-alkoxy compounds. 3-Uloses can be *gem*-difluorinated with DAST only in moderate yields due to a competitive Grob-type fragmentation.

(28) A similar fragmentation process was observed for carbohydrate analogues with a triflate group in position 3; see ref 11.

(29) When methyl 4,6-*O*-benzylidene-2-*O*-methyl-β-D-*arabino*-hexopyranosid-3-ulose, which epimerizes easily at position 2, was treated with DAST a mixture of fragmentation products with a trans arrangement of F and OMe groups in the double bond was obtained. This suggests a stereospecific fragmentation reaction.

Experimental Section

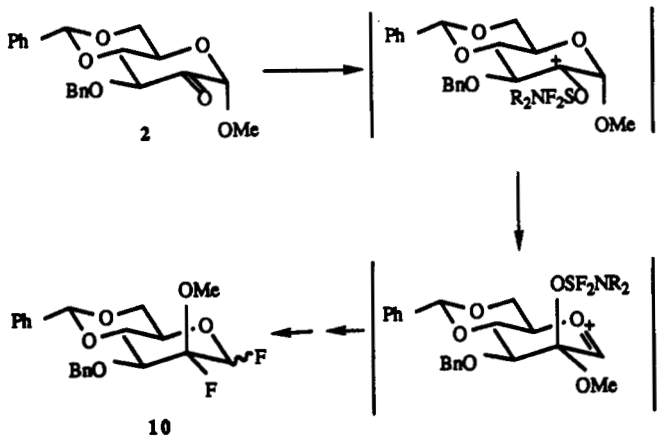
General Procedures. Melting points appear uncorrected. ^{1}H NMR, ^{13}C NMR, and ^{19}F NMR (188 MHz) spectra were recorded in $CDCl_3$, using Me_4Si, with the central solvent peak at δ 77.0 ppm and $CFCl_3$, respectively, as internal reference. Elemental analyses were determined at the Servei de Microanalisi del CSIC (Barcelona). Flash column chromatography was performed on silica gel 60 A CC. Preparative thin layer chromatography was performed on silica gel 60. All reactions were carried out under an atmosphere of dry N_2 in oven-dried glassware. Reaction temperatures were recorded as bath temperatures. Solvents for chromatography were distilled at atmospheric pressure prior to use. Anhydrous CH_2Cl_2 was distilled from CaH_2. Benzene was dried by distillation from Na ribbon and stored over 4-Å molecular sieves and under argon. Standard workup means the following: after pouring the reaction mixture into cold saturated aqueous $NaHCO_3$, the organic layer was separated, the aqueous layer was extracted with CH_2Cl_2 (3 × 10 mL), and the combined layers were dried ($MgSO_4$) and evaporated. Reported yields refer to chromatographically and spectrocopically homogeneous material.

Methyl 3-*O*-Benzyl-4,6-*O*-benzylidene-2-deoxy-2,2-difluoro-β-D-*arabino*-hexopyranoside (9). To a solution of the ulose 1 (100 mg, 0.27 mmol) in anhydrous dichloromethane (2 mL) was added DAST (0.15 mL, 1.13 mmol) dropwise at room temperature. After 24 h standard workup given an oil, which was purified by preparative thin layer chromatography (5/1 hexane/ethyl acetate), yielding the difluoro compound 9 (85 mg, 80%) as a white solid: mp 164–166 °C; $[\alpha]_D$ −25.5° (*c* 0.4 $CHCl_3$); ^{1}H NMR (300 MHz) δ 7.50 and 7.30 (m, 10 H, Ph), 5.58 (s, 1 H, H-7), 4.90 (d, J = 12 Hz, CH_2PH), 4.86 (d, 1 H, CH_2Ph), 4.46 (d, 1 H, $J_{1,Fax}$ = 14.6 Hz, H-1), 4.38 (dd, 1 H, $J_{6eq,6ax}$ = 10 Hz, $J_{6eq,5}$ = 5 Hz, H-6eq), 3.95–3.78 (m, 3 H, H-3, H-4, H-6ax) 3.68 (s, 3 H, Me), 3.46 (td, 1 H, $J_{5,6ax}$ = 10 Hz, H-5); ^{13}C NMR (75.4 MHz) δ 137.1–126.0 (Ph), 116.0 (t, $J_{C,F}$ = 253 Hz, C-2), 101.4 (C-7), 100.2 (dd, $J_{C,F}$ = 28 Hz, $J_{C,F}$ = 20 Hz, C-1), 79.2 (d, $J_{C,F}$ = 8.7 Hz, C-4), 77.4 (C-3), 74.7 (d, $J_{C,F}$ = 1.5 Hz, C-5), 68.3 (C-6), 66.5 (CH_2Ph), 58.2 (Me); ^{19}F NMR δ −118.9 (d, $J_{F,F}$ = 251.5 Hz, Feq), −136.5 (dt, $J_{Fax,1}$ = $J_{Fax,3}$ = 15 Hz, Fax). Anal. Calcd for $C_{21}H_{22}F_2O_5$: C, 64.27; H, 5.66. Found: C, 64.48; H, 5.76.

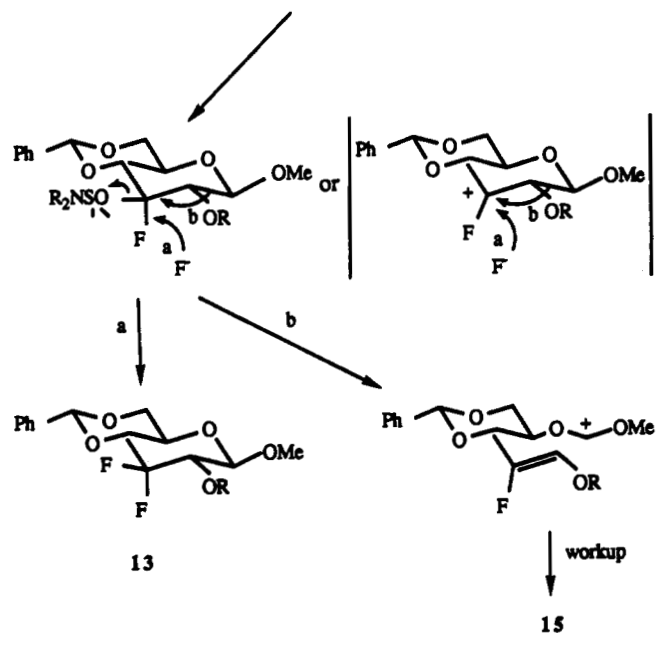
3-*O*-Benzyl-4,6-*O*-benzylidene-2-*O*-methyl-α- and -β-D-*manno*-hexopyranosyl Fluoride (10). To a solution of the ulose 2 (150 mg, 0.4 mmol) in anhydrous benzene (4 mL) was added DAST (0.53 mL, 4 mmol) dropwise at room temperature. After 10 h at reflux the reaction mixture was cooled. The standard workup give a residue, which was chromatographed (4/1 hexane/ethyl acetate), giving the glycosyl fluorides 10 (68 mg, 43%) as an α,β mixture. Major isomer (α, axial F in C_1): ^{1}H NMR (500 MHz) δ 7.50 and 7.30 (m, 10 H, Ph), 5.65 (dd, 1 H, $J_{1,F1}$ = 50.5 Hz, $J_{1,F2}$ = 2 Hz, H-1), 5.59 (s, 1 H, H-7), 4.92 (d, 1 H, J = 11.5 Hz, CH_2Ph), 4.87 (d, 1 H, CH_2Ph), 4.36 (dd, 1 H, $J_{6eq,6ax}$ = 10 Hz, $J_{6eq,5}$ = 5.5 Hz, H-6eq), 4.10–3.90 (m, 3 H, H-3, H-4, H-5), 3.81 (t, 1 H, $J_{6ax,5}$ = 10 Hz, H-6ax), 3.62 (d, 3 H, $J_{Me,F}$ = 1 Hz, Me); ^{13}C NMR (101 MHz) δ 138.0–126.0 (Ph), 109.7 (dd, $^1J_{C,F}$ = 225.5 Hz, $^2J_{C,F}$ = 33.6 Hz, C-2), 104.0 (dd, $^1J_{C,F}$ = 229 Hz, $^2J_{C,F}$ = 50.6 Hz, C-1), 78.7 (d, $J_{F,C}$ = 31 Hz, H-3), 78.5 (C-4), 75.4 (CH_2Ph), 68.2 (C-6), 65.2 (d, $J_{C,F}$ = 3.4 Hz, C-5), 65.2 (d, $J_{Me,F}$ = 4.6 Hz); ^{19}F NMR δ −137 (d, J = 18 Hz, F-2), −145.7 (d, J = 51 Hz, F-1). Minor isomer (β, equatorial F in C_1): ^{1}H NMR (500 MHz) δ 7.50 and 7.30 (m, 10 H, Ph), 5.58 (s, 1 H, H-7), 5.43 (dd, 1 H, $J_{1,F1}$ = 53.3 Hz, $J_{1,F2}$ = 7.8 Hz, H-1), 4.98 (d, 1 H, J = 12.5 Hz, CH_2Ph), 4.86 (d, 1 H, CH_2Ph), 4.39 (dd, 1 H, $J_{6eq,6ax}$ = 10 Hz, $J_{6eq,5}$ = 4.4 Hz, H-6eq), 4.10–3.90 (m, 3 H, H-3, H-4, H-5), 3.82 (t, 1 H, $J_{6ax,5}$ = 10 Hz, H-6ax), 3.59 (dd, 3 H, $J_{Me,F2}$ = 1.5 Hz, $J_{Me,F1}$ = 1 Hz, Me); ^{13}C NMR (101 MHz) δ 138.0–126.0 (Ph), 105.9 (dd, $^1J_{C,F}$ = 227.4 Hz, $^2J_{C,F}$ = 33 Hz, C-1), 101.3 (C-7), 78.8 (C-3), 77.2 (C-4), 74.6 (CH_2Ph), 68.2 (C-6), 65.5 (C-5), 51.8 (Me); ^{19}F NMR δ −138.6 (dd, $J_{F,H1}$ = 53 Hz, $J_{F,F}$ = 12 Hz, F-1), −146.2 (d, F-2).

Methyl 4,6-*O*-Benzylidene-2-deoxy-2,2-difluoro-3-*O*-methyl-α-D-*ribo*-hexopyranoside (11). To a solution of the ulose 3 (200 mg, 6.8 mmol) in dichloromethane (5 mL) was added DAST (0.9 mL, 6.8 mmol) dropwise at room temperature. The

Scheme II



Scheme III



reaction mixture was refluxed for 7 h. After cooling and standard workup, the residue was chromatographed on silica (3/1 hexane/ethyl acetate) to give the difluorinated compound **11** (82 mg, 39%) as a white solid: mp 97–98 °C (from hexane); $[\alpha]_D$ +85.1° (*c* 0.55 $CHCl_3$); ^1H NMR (300 MHz) ∂ 7.50 and 7.30 (m, 5 H, Ph), 5.60 (s, 1 H, H-7), 4.60 (dt, 1 H, $J_{1,Fax}$ = 9 Hz, $J_{1,Feq}$ = 1 Hz, $J_{1,3}$ = 1 Hz, H-1), 4.30 (dd, 1 H, $J_{6eq,6ax}$ = 10 Hz, $J_{6eq,5}$ = 5.5 Hz, H-6eq), 4.25 (td, 1 H, $J_{5,6ax}$ = 10 Hz, $J_{5,4}$ = 10 Hz, H-5), 3.84 (m, 1 H, H-3), 3.77 (m, 1 H, H-4), 3.69 (t, 1 H, H-6ax), 3.58 (s, 3 H, Me), 3.46 (s, 3 H, Me); ^{13}C NMR (75.4 MHz) ∂ 137.7, 129.8, 128.9, 126.8, 115.8 (dd, $J_{C,F1}$ = 268 Hz, $J_{C,F2}$ = 240 Hz, C-2), 102.9 (C-7), 100.0 (dd, $J_{C,F1}$ = 40 Hz, $J_{C,F2}$ = 28 Hz, C-1), 78.2 (dd, $J_{C,F1}$ = 32 Hz, $J_{C,F2}$ = 21 Hz, C-3), 78.5 (d, $J_{C,F}$ = 7 Hz, C-4), 69.6 (C-6), 62.4 (C-5), 58.9 (Me), 57.0 (Me); ^{19}F NMR ∂ −107.1 (d, $J_{F,F}$ = 271 Hz, Feq), −116.9 (d, Fax). Anal. Calcd for $C_{15}H_{18}O_5F_2$: C, 56.96; H, 5.69. Found: C, 56.79; H, 5.73.

3,4-Isopropylidene-2-fluoro-2-*O*-methyl-α- and -β-D-*ribo*-pentopyranosyl Fluoride (12). To a solution of the ulose **5** (202 mg, 1 mmol) in dichloromethane (5 mL) was added DAST (0.54 mL, 4 mmol) dropwise at room temperature. After 8 h at room temperature the standard procedure give a crude oil, which was chromatographed (4/1 hexane/ethyl acetate) giving the glycosyl fluoride **12** (161 mg, 72%) as an α,β mixture. Major isomer (β, axial F in C_1): ^1H NMR (400 MHz) ∂ 5.22 (dd, 1 H, $J_{1,F1}$ = 64.6 Hz, $J_{1,F2}$ = 0.6 Hz, H-1), 4.95–4.75 (m, 2 H, H-3, H-4), 4.30–4.10 (m, 2 H, H-5eq, H-5ax), 3.58 (d, 3 H, $J_{Me,F}$ = 1.5 Hz, OMe), 1.55 (s, 3 H, Me), 1.35 (s, 3 H, Me); ^{13}C NMR (101 MHz) ∂ 115.4 (C-6), 112.1 (dd, $^1J_{C,F}$ = 223.3 Hz, $^2J_{C,F}$ = 28 Hz, C-2), 109.1 (dd, $^1J_{C,F}$ = 237.5 Hz, $^2J_{C,F}$ = 45.4 Hz, C-1), 79.2 (d, $J_{C,F}$ = 19.8 Hz, C-3), 78.1 (C-4), 72.4 (C-5), 57.7 (OMe), 25.8 (Me), 25.4 (Me); ^{19}F NMR ∂ −124.0 (t, $J_{F,F}$ = $J_{F,3}$ = 10.6 Hz, F_2), −142,90 (dd, $J_{F,1}$ = 64.3 Hz, $J_{F,F}$ = 10.6 Hz, F-1). Minor isomer (α, equatorial F in C_1): ^1H NMR (400 MHz) ∂ 5.21 (dd, 1 H, $J_{1,F1}$ = 63.4 Hz, $J_{1,F2}$ = 2.3 Hz, H-1), 4.95–4.75 (m, 2 H, H-3, H-4), 4.30–4.10 (m, 2 H, H-5eq, H-5ax), 3.62 (d, $J_{Me,F}$ = 1.5 Hz, OMe), 1.55 (s, 3 H, Me), 1.35 (s, 3 H, Me); ^{13}C NMR (101 MHz) ∂ 115.3 (C-6), 79.1 (d, $J_{C,F}$ = 19.8 Hz, C-3), 78.2 (C-4), 72.5 (C-5), 57.5 (OMe); ^{19}F NMR ∂ −123.0 (br s, F-2), −143.7 (br d, $J_{F,1}$ = 63.5 Hz, F-1).

Methyl 2-*O*-Benzyl-4,6-benzylidene-3-deoxy-3,3-difluoro-β-D-*ribo*-hexopyranoside (13). To a solution of the ulose **7** (150 mg, 0.4 mmol) in anhydrous benzene (2 mL) was added DAST (0.23 mL, 1.7 mmol) dropwise at room temperature. The reaction mixture was refluxed for 2 h. After cooling and standard workup, the residue was chomatographed on silica gel (6/1 hexane/ethyl acetate) to gave the difluoro compound **13** (64 mg, 40%) as a white solid: mp 110–111 °C (from hexane); $[\alpha]_D$ −25.6° (*c* 0.79, $CHCl_3$); ^1H NMR (200 MHz) ∂ 7.50 and 7.30 (m, 10 H, Ph), 5.52 (s, 1 H, H-7), 4.86 (s, 2 H, CH_2Ph), 4.56 (dd, 1 H, $J_{1,2}$ = 7.5 Hz, $J_{1,F}$ = 1.5 Hz, H-1), 4.42 (dd, 1 H, $J_{6eq,6ax}$ = 4.7 Hz, $J_{6eq,5}$ = 10 Hz, H-6eq), 3.60–3.80 (m, 3 H, H-4, H-5, H-6ax), 3.58 (s, 3 H, Me), 3.50 (ddd, $J_{2,Fax}$ = 20 Hz, $J_{2,Feq}$ = 4.5 Hz, H-2); ^{13}C NMR (50.3 MHz) ∂ 137.1, 136.4, 129.4, 128.4, 128.3, 128.0, 127.9, 126.3, 118.7 (t, $J_{C,F}$ = 250 Hz, C-3), 101.9 (C-7), 103.5 (d, $J_{C,F}$ = 9.6 Hz, C-1), 78.3 (t, $J_{C,F}$ = 23.3 Hz, C-4), 77.7 (t, $J_{C,F}$ = 23.3 Hz, C-2), 74.9 (CH_2Ph), 68.5 (C-6), 63.1 (d, $J_{C,F}$ = 6.6 Hz), 57.6 (Me); ^{19}F NMR ∂ −118.5 (d, $J_{F,F}$ = 241.7 Hz, Feq), −132.7 (dt, $J_{F,2}$ = $J_{F,4}$ = 20 Hz, Fax). Anal. Calcd for $C_{21}H_{22}F_2O_5$: C, 64.27; H, 5.66. Found: C, 63.97; H, 5.62.

Methyl 2-*O*-Benzyl-4,6-*O*-benzylidene-3-deoxy-3,3-difluoro-α-D-*ribo*-hexopyranoside (14). To a solution of the ulose **8** (150 mg, 0.4 mmol) in anhydrous benzene (4 mL) was added DAST (0.54 mL, 4 mmol) dropwise at room temperature. Ten hours later, the reaction mixture was submitted to the standard workup to give an oil, which was purified by preparative thin-layer chromatography (4/1 hexane/ethyl acetate) to afford (76 mg, 48%) of the difluoro compound **14** as a white solid: mp 107–108 °C (from hexane); $[\alpha]_D$ −20.0° (*c* 0.50 $CHCl_3$); ^1H NMR (300 MHz) ∂ 7.50 and 7.30 (m, 10 H, Ph), 5.43 (s, 1 H, H-7), 4.86 (d, 1 H, *J* = 12.4 Hz, CH_2Ph), 4.54 (d, 1 H, CH_2Ph), 4.54 (t, 1 H, $J_{1,2}$ = 4 Hz, $J_{1,F}$ = 4 Hz, H-1), 4.23 (ddd, 1 H, $J_{6eq,6ax}$ = 10.3 Hz, $J_{6eq,5}$ = 5 Hz, $J_{6eq,F}$ = 2.5 Hz, H-6eq), 4.00 (dt, 1 H, $J_{5,6ax}$ = 10.2 Hz, $J_{5,4}$ = 10.2 Hz, H-5), 3.70–3.50 (m, 3 H, H-2, H-4, H-6ax), 3.33 (s, 3 H, Me); ^{13}C NMR (75.4 MHz) ∂ 136.9–126.3 (Ph), 118.1 (t, $J_{C,F}$ = 245 Hz, C-3), 102.0 (C-7), 99.0 (d, $J_{C,F}$ = 3 Hz, C-1), 77.8 (t, $J_{C,F}$ = 18.5 Hz, C-4), 74.8 (t, $J_{C,F}$ = 18.5 Hz, C-2), 74.1 (CH_2Ph), 68.7 (C-6), 60.3 (C-5), 56.1 (Me); ^{19}F NMR ∂ −115.28 (d, $J_{F,F}$ = 236.7 Hz, Feq), −130.23 (dt, $J_{Fax,2}$ = $J_{Fax,4}$ = 18.5 Hz, Fax). Anal. Calcd for $C_{21}H_{22}F_2O_5$: C, 64.27; H, 5.66. Found: C, 64.11; H, 5.61.

(2*R*,3*R*,4*Z*)-5-(Benzyloxy)-4-fluoro-4-pentene-1,2,3-triol 1,3-(Benzylidene acetal) (15). Compound **15** was obtained as byproduct in the synthesis of **13** and **14**: mp 121–122 °C (from CH_2Cl_2–hexane); $[\alpha]_D$ −55.4° (*c* 0.61 $CHCl_3$); ^1H NMR (200 MHz) ∂ 7.50 and 7.30 (m, 10 H, Ph), 5.98 (d, 1 H, $J_{H,F}$ = 21 Hz, H-5), 5.46 (s, 1 H, CH-Ph), 4.88 (s, 2 H, CH_2Ph), 4.34 (dd, 1 H, $J_{H1eq,H1ax}$ = 10.8 Hz, H-1eq), 4.01 (dt, 1 H, $J_{H2,H3}$ = 9.5 Hz, $J_{H2,H1ax}$ = 9.5 Hz, H-1), 3.80 (dd, 1 H, $J_{H3,F}$ = 23.5 Hz, H-3), 3.58 (dd, 1 H, H-1ax); ^{13}C NMR (50.3 MHz) ∂ 140.2 (d, $J_{C4,F}$ = 249 Hz, C-4), 131.6 (d, $J_{C5,F}$ = 22.5 Hz, C-5), 125.8–136.6 (Ph), 100.8 (CH-Ph), 79.1 (d, $J_{C3,F}$ = 22.8 Hz, C-3), 74.1 (C-1), 69.9 (CH_2Ph), 60.4 (C-2); ^{19}F NMR ∂ −152.34 (t, 1 F, $J_{F,H3}$ = $J_{F,H5}$ = 22.5 Hz). Anal. Calcd for $C_{19}H_{19}FO_4$: C, 69.09; H, 5.75. Found: C, 68.83; H, 5.67.

Acknowledgment. Financial support by DGICYT (PB 86-0137-C02) is gratefully acknowledged. We thank Dr. G. Lukacs (CNRS Gif-sur-Yvette) and Dr. J. Vilarrasa (University of Barcelona) for many fruitful discussions. Thanks are also due to Dr. D. Carmona (University of Zaragoza) for recording ^{19}F NMR spectra.

Registry No. **1**, 129706-94-1; **2**, 130983-50-5; **3**, 74410-52-9; **5**, 4096-64-4; **7**, 134175-76-1; **8**, 109010-30-2; **9**, 134131-55-8; **α-10**, 134110-36-4; **β-10**, 134110-41-1; **11**, 134110-37-5; **α-12**, 134110-38-6; **β-12**, 134110-42-2; **13**, 134131-07-0; **14**, 134110-39-7; **15**, 134110-40-0.