965 cm^{-1}; ^{1}H NMR δ 5.77 (AB q, 2 H, J = 17 Hz), 5.60 (br s, 1 H), 5.58 (AB q, 2 H, J = 15 Hz), 5.13 (dt, 2 H, J = 15 and 5 Hz), 4.85 (br s, 2 H), 3.62 (s, 3 H), 2.81 (br d, 2 H, J = 5 Hz), 2.12 (d, 3 H, J = 1 Hz), 1.81 (br s, 3 H), 1.16 (s, 6 H). Anal. Calcd for $C_{16}H_{24}O_2$: C, 77.38; H, 9.74. Found: C, 77.75; H, 9.77.

3,3,6,6,7,7-Hexamethyl-4,8-nonadienal (36) was obtained in 45% yield from **3** and **28** by the chromatographic separation with 2% EtOAc-hexane: IR 2720, 1725, 990, 965, 910 cm^{-1}; ^{1}H NMR δ 9.61 (t, 1 H, J = 3 Hz), 5.75 (dd, 1 H, J = 16 and 9 Hz), 5.42 (AB q, 2 H, J = 18 Hz), 4.92 and 4.87 (dd, each 1 H, J = 9 and 1.5 Hz, and 18 and 1.5 Hz, respectively), 2.26 (d, 2 H, J = 3 Hz), 1.13, 0.98 and 0.95 (s, each 6 H). Anal. Calcd for $C_{15}H_{26}O$: C, 81.02; H, 11.78. Found: C, 80.79; H, 12.01.

Methyl 2-isopropyl-5,5,8-trimethyl-3,6,8-nonatrienoate (37) was obtained in 30% yield from **3** and **29** by the chromatographic separation with 2% EtOAc-hexane: IR 3060, 1730, 1635, 1600, 965, 880 cm^{-1}; ^{1}H NMR 5.75 (AB q, 2 H, J = 17 Hz), 5.59 (dd, 1 H, J = 17 and 1.5 Hz), 5,28 (dd, 1 H, J = 17 and 6 Hz), 4.84 (br s, 2 H), 3.62 (s, 3 H), 2.58 (td, 1 H, J = 6 and 1.5 Hz), 1.81 (br s, 3 H), 1.40-2.35 (m, 1 H), 1.16 (s, 6 H), 0.90 and 0.88 (d, each 3 H, J = 7 Hz). Anal. Calcd for $C_{16}H_{26}O_2$: C, 76.75; H, 10.47. Found: C, 76.40; H, 10.82.

3,3,6,6,9-Pentamethyl-8-oxo-4-decenal (38) was obtained in 55% yield from **3** and **30** by the chromatographic separation with 5% EtOAc-hexane: IR 2720, 1735, 1700, 965 cm^{-1}; ^{1}H NMR δ 9.61 (t, 1 H, J = 3 Hz), 5.42 (AB q, 2 H, J = 16 Hz), 2.46 (septet, 1 H, J = 7 Hz), 2.37 (s, 2 H), 2.25 (d, 2 H, J = 3 Hz), 1.13 and 1.10 (s, each 6 H), 1.01 (d, 6 H, J = 7 Hz). Anal. Calcd for $C_{15}H_{26}O_2$: C, 75.58; H, 10.99. Found: C, 75.73; H, 10.84.

Preparation of 40. To a suspension of prenylmagnesium chloride in ether (10 mL) prepared from prenyl chloride (523 mg, 5 mmol) and Mg powder (365 mg, 15 matom) was added a solution of *trans*-**3** (304 mg, 2 mmol) in ether (2 mL) at 0 °C under an atmosphere of nitrogen, and the mixture was stirred overnight at room temperature. The products were extracted with ether after being poured into cold aqueous NH_4Cl and were dried over Na_2SO_4. Evaporation of the solvent left an oil, which was chromatographed with 5% EtOAc-hexane to give 350 mg (79% yield) of **39**, which had absorptions at 3450, 3080, 1670, 1640, 970, 905, and 860 cm^{-1} in the IR spectrum. This alcohol was silylated by stirring with bis(trimethylsilyl)acetamide (0.75 mL, 3 mmol) at room temperature for 12 h, and the product was purified by the chromatography with hexane to give 380 mg (82%) of **40** as an oil: IR 3080, 1640, 1250, 1080, 1000, 915, 850 cm^{-1}; ^{1}H NMR δ 6.83 (dd, 1 H, J = 18 and 10 Hz), 4.85 and 4.80 (dd, each 1 H, J = 10 and 2 Hz, and 18 and 2 Hz, respectively), 4.66 (br d, 1 H, J = 8 Hz), 3.06 (d, 1 H, J = 9 Hz), 1.70 and 1.62 (br s, each 3 H), 1.14 and 1.00 (s, each 3 H), 1.00 (dd, 1 H, J = 8 and 6 Hz, superimposed with the methyl group), 0.96 (s, 6 H), 0.58 (dd, 1 H, J = 9 and 6 Hz), 0.10 (s, 9 H). Anal. Calcd for $C_{18}H_{34}OSi$: C, 73.40; H, 11.63. Found: C, 73.43; H, 11.60.

2,5,5,8,8,11,11-Heptamethyl-6,9,12-tridecatrien-3-one (41) was obtained in 53% yield from **40** and **30** by the same procedure as employed for the reaction of **5b**: IR 3070, 1710, 1640, 980, 910 cm^{-1}; ^{1}H NMR δ 5.81 (dd, 1 H, J = 18 and 10 Hz), 5.30 (AB q, 2 H, J = 16 Hz), 5.26 (AB q, 2 H, J = 18 Hz), 4.84 and 4.81 (dd, each 1 H, J = 10 and 2 Hz, and 18 and 2 Hz, respectively), 2.34 (septet, 1 H, J = 7.5 Hz), 2.33 (s, 2 H), 1.08 (s, 12 H) 1.05 (s, 6 H), 1.00 (d, 6 H, J = 7.5 Hz). Anal. Calcd for $C_{20}H_{34}O$: C, 82.69; H, 11.80. Found: C, 82.62; H, 11.87.

Preparation of 42. To a solution of lithium diisopropylamide in THF (6 mL) prepared from *n*-butyllithium (1.9 mL of 15% hexane solution, 3 mmol) and diisopropylamine (0.42 mL, 3 mmol) was added methyl isopropyl ketone (250 mg, 2.9 mmol) at -78 °C under an atmosphere of nitrogen, and the solution was stirred for 1 h. Then, to this solution was added **3** (456 mg, 3 mmol) at this temperature, and the mixture was stirred at room temperature for 3 h. The products were extracted with ether after being poured into brine and were dried over Na_2SO_4. Evaporation of the solvent left an oil, which was chromatographed with 5% EtOAc-hexane to give 462 mg (70% yield) of **42** as an oil: IR 1690, 1660, 1610, cm^{-1}; ^{1}H NMR δ 6.50 (dd, 1 H, J = 15 and 9 Hz), 6.12 (d, 1 H, J = 15 Hz), 4.87 (br d, 1 H, J = 8 Hz), 2.62 (septet, 1 H, J = 7 Hz), 1.68 (br s, 6 H), 0.90-1.58 (m, 2 H), 1.22 and 1.12 (s, each 3 H), 1.07 (d, 6 H, J = 7 Hz). Anal. Calcd for $C_{15}H_{24}O$: C, 81.76; H, 10.98. Found: C, 81.80; H, 10.94.

2,7,7,10,10,13-Hexamethyl-5,8-tetradecadiene-3,12-dione (43) was obtained in 40% yield from **42** and **30** by the same procedure as employed for the reaction of **4**: IR 1710, 1670 cm^{-1}; ^{1}H NMR δ 5.52 (dt, 1 H, J = 16 and 4 Hz), 5.32 (AB q, 2 H, J = 16 Hz), 5.25 (dd, 1 H, J = 16 and 1 Hz), 3.07 (dd, 2 H, J = 4 and 1 Hz), 2.60 (septet, 2 H, J = 7 Hz), 2.35 (s, 2 H), 1.06 and 0.98 (d, each 6 H, J = 7 Hz), 1.08 (s, 12 H). Anal. Calcd for $C_{20}H_{34}O_2$: C, 78.38; H, 11.18. Found: C, 78.52; H, 11.04.

Chiral Synthons for the Total Synthesis of Fluoro Amino Acids and Fluoro Analogues of Antibiotic Sugars

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Configurationally different 3-azido-2,3-dideoxy-2-fluoro and 2-azido-2,3-dideoxy-3-fluoro sugars, synthetic precursors of biologically important fluoro amino acids, were synthesized. Axial alcohols involved in vicinal diaxial systems undergo fluorodehydroxylation with configurational retention in the presence of (diethylamino)sulfur trifluoride.

Appropriate synthetic schemes for the preparation of optically active β-fluorinated α amino acids are of considerable importance in view of the potential for a variety of these compounds to act as enzyme-activated irreversible inhibitors[1] or suicide substrates with interesting biological properties. During recent years, several methods involving fluorodehydroxylation,[2] photofluoration,[3] or aziridine ring

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(3) Kollonitsch, J.; Barash, L. *J. Am. Chem. Soc.* **1976**, *98*, 5591.

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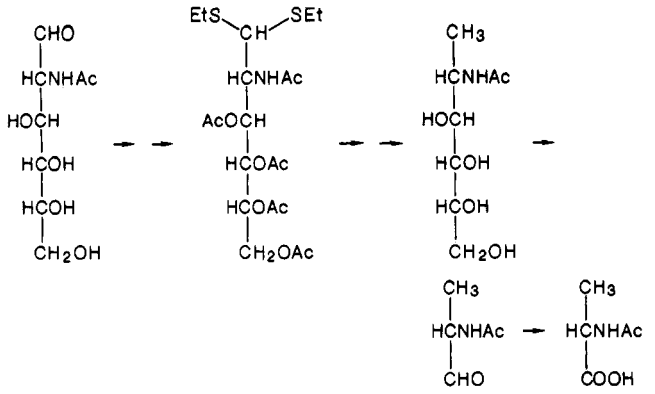
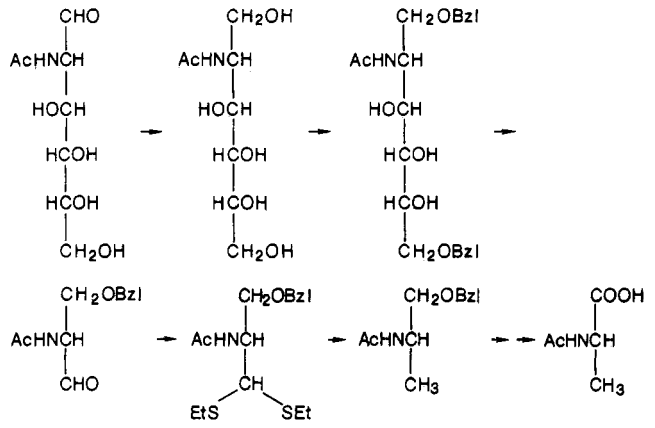
Scheme I



Scheme II



opening[4] have been developed for fluorine introduction to prepare such compounds as racemates. However, their enzymatic resolution[5] does not appear to be a straightforward process. Although, relatively little studied, α-fluorinated β amino acids might also be of some importance. For example, α-fluoro-β-alanine is a metabolite of the antitumor agent 5-fluorouracil.[6]

In view of the considerable current interest in the synthesis of fluorine-containing compounds of biological significance, we have prepared various azido fluoro sugars that are synthetic precursors of some chiral enzyme inhibitors. These azido fluoro sugars are potential intermediates in the synthesis of fluorinated analogues of carbohydrate components of antibiotics as well.

Results and Discussion

In an investigation, published in the late 1940s, Wolfrom, Lemieux, and Olin described[7] the configurational correlation of D-glucosamine with L-alanine by a direct chemical method (Scheme I).

Applying similar appropriate transformations, it appears obvious that *N*-acetyl-D-mannosamine could be also a good starting material for the preparation of *N*-acetyl L-alanine or other α amino acids of the L series (Scheme II). However, this scheme requires the β-carbon of the amino acid and its carboxyl carbon to be generated, respectively, from C-3 and from the anomeric carbon of the D-mannosamine derivative. Actually, this strategy is even more attractive than scheme I—except for the preparation of L-alanine—since it may utilize the chirality of the sugar carbons and would avoid the construction of the amino acid side chain via Wittig reaction. As a consequence, 2-amino- or 2-azido-2,3-dideoxy-3-fluoro-D-hexopyranosides with an axial azide are suitable precursors for the synthesis of a variety of β-fluoro α amino acids of the L series, which represent some of our target molecules. In the discussion of the synthesis of amino acids from carbohydrates, for the sake of simplicity, we differentiate the indicated two approaches as follows: We call process A the technique in which in a Fischer representation of the carbohydrate the amino acid β-carbon is above the amine-bearing carbon center.[7] We designate process B the method where in a Fischer representation of the sugar the amino acid β-carbon is below the carbon atom to which the amine is attached.

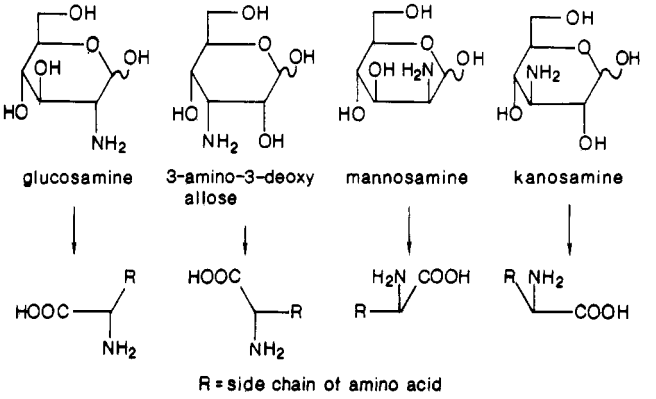


Figure 1. Stereochemical correlation of deoxy amino sugars to amino acids of the L series.

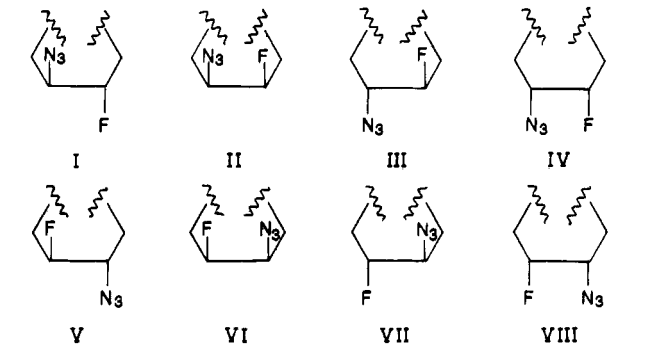


Figure 2. Stereostructures: I–IV, type A; V–VIII, type B.

It appears that the less readily available 3-amino-3-deoxy sugars can also be used for modified L amino acid synthesis. According to process A 3-amino- or 3-azido-2,3-dideoxy-2-fluoro-D-hexopyranosides with an axial azide are suitable starting materials for the synthesis of β-fluorinated α amino acids and α-fluorinated β amino acids. According to process B the synthesis of α-fluorinated β amino acids belonging to the L series require 3-amino- or 3-azido-2,3-dideoxy-2-fluoro-D-hexopyranosides having an equatorial azide as intermediates (Figure 1).

With these considerations in mind, we were particularly interested in developing suitable methods for the preparation of 3-azido-2,3-dideoxy-2-fluoro-D-hexopyranosides of type A (I–IV) and to a lesser extent of 2-azido-2,3-dideoxy-3-fluoro-D-hexopyranosides of type B (V–VIII) (Figure 2). These stereostructures (I–VIII) could be starting materials to fluoro amino acids of the D series as well.

Carbohydrates related to III and IV are synthetic precursors of fluorinated analogues of the sugar components of antitumor antibiotics[8] (daunomycin–daunosamine).

(4) Wade, T. N. *J. Org. Chem.* **1980**, *45*, 5328. Alvernhe, G. M.; Ennakoua, C. M.; Lacombe, S. M.; Laurant, A. J. *J. Org. Chem.* **1981**, *46*, 4938.
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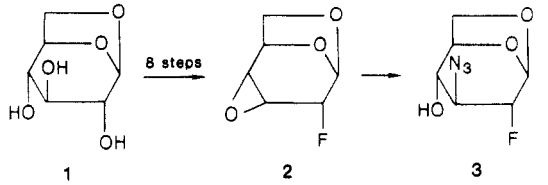
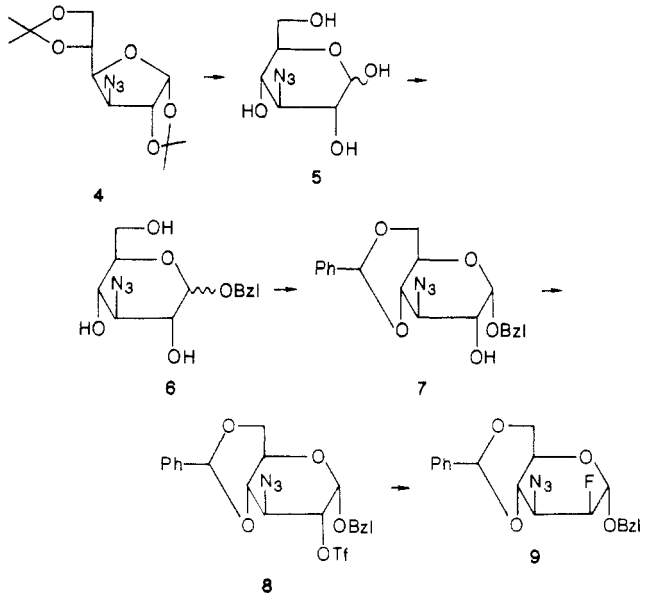
Scheme III



Scheme IV

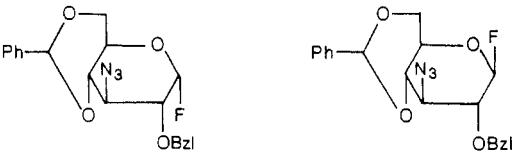


Structures representing I and II contain the appropriate stereochemistry of fluorinated analogues of carbohydrate components of 14- and 16-membered macrolide antibiotics[9] (erythromycin–desosamine, leucomycin–micaminose) and glycopeptide antibiotic constituents[10] (ristomycin–ristosamine). Sugars corresponding to stereostructures V and VIII may be considered as intermediates in the synthesis of fluorinated analogues of the carbohydrate components of aminocyclitol aminoglycoside antibiotics[11] (tobramycin–tobrosamine, gentamycin–purpurosamine).

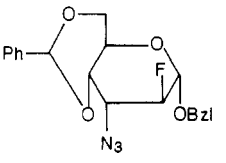
Access to 3-Azido-2,3-dideoxy-2-fluoro-D-hexopyranosides. The synthesis of these compounds, corresponding to stereostructures II–IV, was carried out with benzyl group protection of the anomeric hydroxyl of the sugars. The use of a benzyl protecting group was motivated by the extremely strong anomeric linkage in 2-deoxy-2-fluoro sugars[12] and the necessity for the ultimate easy liberation of their anomeric hydroxy function. Azido fluoro structure I was prepared in the 1,6-anhydro-β-D sugar series. According to a recent work, opening of the 1,6-anhydro bridge of such compounds can be accomplished with satisfactory yields under not too drastic conditions.[13]

Synthesis of Stereostructure I. This stereostructure, under the form of 1,6-anhydro-3-azido-2-fluoro-2,3-dideoxy-β-D-glucopyranose (**3**), was easily prepared in 87% yield (Scheme III) by azidolysis of the known 1,6:3,4-dianhydro-2-deoxy-2-fluoro-β-D-allopyranose (**2**) available in eight steps from 1,6-anhydro-β-D-glucopyranose (**1**).[14]

Synthesis of Stereostructure II. This stereostructure, under the form of benzyl 3-azido-4,6-*O*-benzylidene-2,3-dideoxy-2-fluoro-α-D-mannopyranoside (**9**), was prepared in 60% yield (Scheme IV) by an S_N2 reaction, in the presence of cesium fluoride, from benzyl 3-azido-4,6-*O*-benzylidene-3-deoxy-2-*O*-[(trifluoromethyl)-sulfonyl]-α-D-glucopyranoside (**8**) synthesized from **4**[15] as shown. Direct (diethylamino)sulfur trifluoride treatment of **7** gave the fluoro sugar **9** only with a very moderate yield (16%). The major reaction product (44%) was a mixture of the benzyl migration structures **10** and **11**.

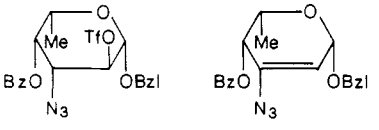


Synthesis of Stereostructure III. We reported recently the preparation of this stereostructure, under the form of benzyl 3-azido-4,6-*O*-benzylidene-2,3-dideoxy-2-fluoro-α-D-altropyranoside (**12**), in connection with a synthesis of *C*-2′β-fluorodaunomycin.[16]



Synthesis of Stereostructure IV. Preliminary attempts, worthy of mention, to prepare a compound exhibiting this stereostructure failed.

(a) Reaction of fluorine-containing nucleophilic reagents with azido sugar **13**, readily available from D-glucose, afforded invariably the elimination product **14**.



(b) Both sodium hydride and potassium *tert*-butoxide treatment of carbamate **15**, readily available from 1,6-anhydro-2-deoxy-2-fluoro-4-*O*-benzyl-β-D-glucopyranose, furnished quantitatively epoxide **2**. Surprisingly, no trace of cyclic carbamate **16** was evident in the crude reaction product. This experiment was inspired from a recent report in which carbamate **17** gave, in the presence of potassium *tert*-butoxide, the cyclic carbamate **18**.[17]

Stereostructure IV was finally prepared, under the form of benzyl 3-azido-4,6-*O*-benzylidene-2,3-dideoxy-2-fluoro-

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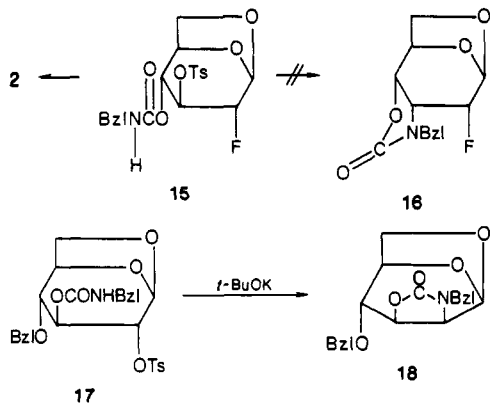
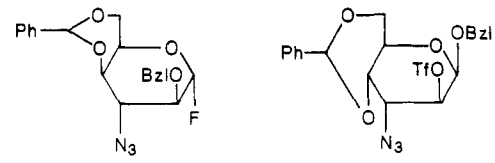


β-D-gulopyranoside (**22**; Scheme V). Azidolysis of benzyl 2,3-anhydro-4,6-*O*-benzylidene-β-D-talopyranoside (**19**)[18] gave the alcohol **20** in 84% yield. (Diethylamino)sulfur trifluoride treatment of **20** furnished the benzyl migration

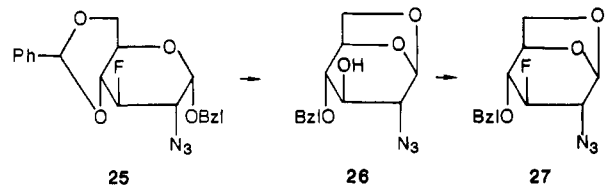


product **23** in 82% yield. However, the triflate **21** afforded **22** in 71% yield in the presence of cesium fluoride. It is of interest to note that the nucleophilic substitution reaction proceeds smoothly from the triflate of the *cis*-decaline type D ido structure **21**. Under identical conditions the epimeric *trans*-decalin type D altro structure **24** remains unchanged.

Access to 2-Azido-2,3-dideoxy-3-fluoro-D-hexopyranosides. Although acid-catalyzed liberation of the anomeric hydroxyl group of alkyl 2-azido-2-deoxypyranosides can be carried out under relatively mild conditions,[19] it appeared advisable in the synthesis of these compounds to use—whenever possible—benzyl protection at the anomeric centers.

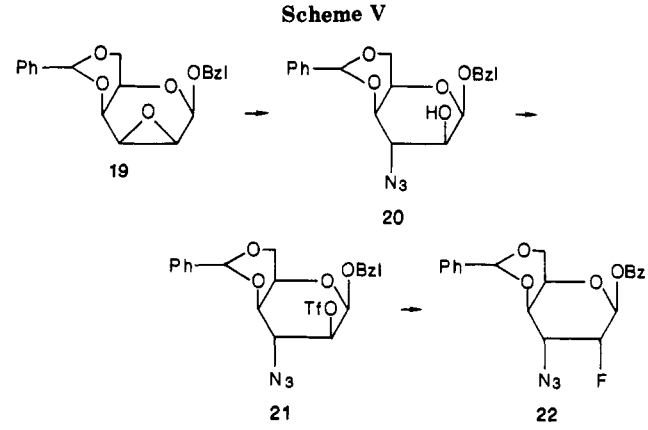
No short, practical scheme permitting an easy access with satisfactory yields to stereostructure VIII can be proposed at the moment. In view of the relatively little importance of this stereostructure for the synthesis of β-fluorinated α amino acids of the L series, no special effort was devoted to its preparation.

Synthesis of Stereostructure V. The preparation of this stereostructure under the form of benzyl 2-azido-4,6-*O*-benzylidene-2,3-dideoxy-3-fluoro-α-D-glucopyranoside (**25**) was described[16] as a side product (40% yield) in our

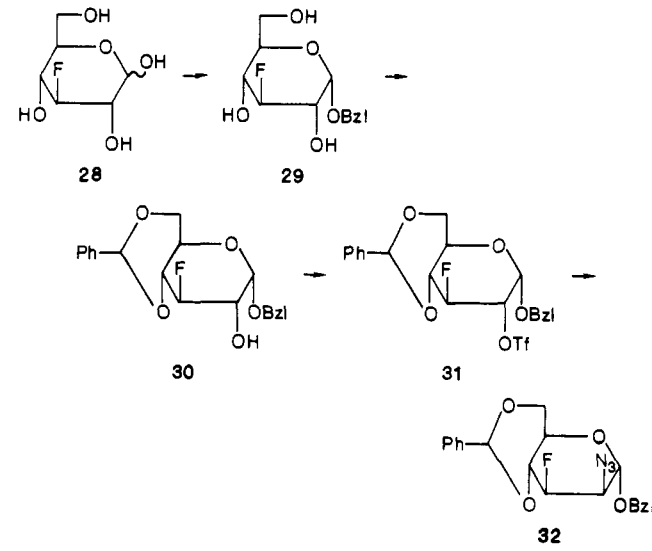


recent work on the synthesis of *C*-2′β-fluorodaunomycin. We report here a considerable improvement to get access to this stereostructure. (Diethylamino)sulfur trifluoride treatment of the readily available 1,6-anhydro-2-azido-2-deoxy-4-*O*-benzyl-β-D-glycopyranose (**26**)[20] afforded in 78% yield 1,6-anhydro-2-azido-2,3-dideoxy-4-*O*-benzyl-3-fluoro-β-D-glucopyranose (**27**) with configurational retention. Stereochemical proof for the fluorine atom of **27** was provided by the large geminal coupling constants $^2J_{C\text{-}2,F}$ = 24.9 Hz and $^2J_{C\text{-}4,F}$ = 25.9 Hz that reveal a trans-diaxial relationship between the substituents of the pyranose ring.[21] Additional support was provided by the very small vicinal coupling constants $^3J_{C\text{-}1,F} \cong {}^3J_{C\text{-}5,F} < 1$ Hz, indicating a cis arrangement of the fluorine atom with respect to both C-1 and C-5.

Scheme V



Scheme VI



Synthesis of Stereostructure VI. This stereostructure was prepared under the form of benzyl 2-azido-4,6-*O*-benzylidene-2,3-dideoxy-3-fluoro-α-D-mannopyranoside (**32**) from 3-deoxy-3-fluoro-D-glucose (**28**)[22] as shown in Scheme VI. Azide introduction in the last step of the scheme proceeded in 90% yield.

Synthesis of Stereostructure VII. This stereostructure was prepared under the form of benzyl 2-azido-4,6-*O*-benzylidene-2,3-dideoxy-3-fluoro-α-D-altropyranoside (**35**) from the readily available benzyl 2,3-anhydro-4,6-*O*-benzylidene-α-D-allopyranoside (**33**)[23] by (diethylamino)-sulfur trifluoride treatment of its azidolysis product **34**.

Stereochemical proof for the configurational retention in the fluorine introduction step was provided by both the proton and carbon-13 NMR spectra of **35**.[21] The proton

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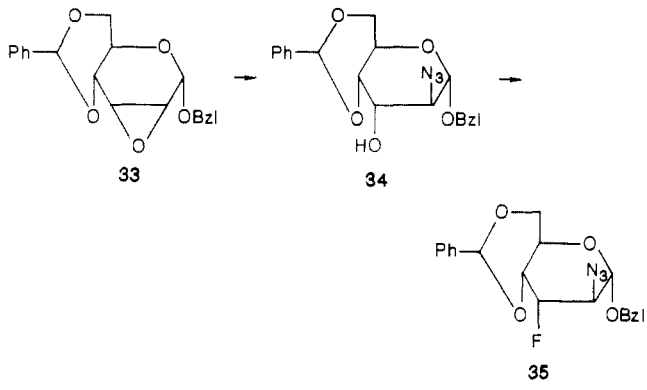

spectrum exhibited a small vicinal coupling $^3J_{H\text{-}4,H\text{-}3}$ = 2 Hz, and the carbon-13 spectrum revealed large ($^2J_{C\text{-}2,F}$ = 25.9 Hz) and relatively small ($^2J_{C\text{-}4,F}$ = 16.8 Hz) geminal coupling constants, furnishing evidence about the relationship of the fluorine atom with respect to the substituents of C-2 and C-4.

Conclusion. For fluorine introduction into the hexopyranoside systems three types of reactions were used: (a) epoxide opening with KHF_2 as described by Pacak et al. (stereostructure I); (b) tetrabutylammonium fluoride or cesium fluoride treatment of triflates of alcohols appropriately disposed for S_N2 reactions (stereostructures II, IV, and VI) [such reactions at position C-2 were considered only a few years ago as extremely difficult from the corresponding tosylates or mesylates];[24] (c) (diethylamino)-sulfur trifluoride treatment of axially configurated alcohols involved in vicinal diaxial systems [these reactions allowed fluorine introduction in high yields with configurational retention (stereostructures III, V, and VII)].

Experimental Section

General Methods. Melting points were determined with a Buchi apparatus and are uncorrected. A Perkin-Elmer Model 141 MC polarimeter and 1-dm tubes were used for measurement of specific rotations. Unless otherwise indicated ^1H NMR spectra were recorded in chloroform-*d* solution at 400, 200, and 80 MHz. ^{13}C NMR spectra were measured in chloroform solution at 100.62 and 50.31 MHz with respectively Bruker WM-400 and WP-200 spectrometers. Chemical shifts for ^1H and ^{13}C NMR are given in ppm, and tetramethylsilane was the internal standard (δ 0.000). Carbon-13 shifts for sp^2-hybridized atoms are not given. ^{19}F NMR spectra were recorded in chloroform-*d* solution at 84.24 MHz with a JEOL FX-90 Q spectrometer, and chemical shifts are given in ppm, upfield with respect to trifluorotoluene used as an internal standard. Microanalyses were performed by the Service Central de Microanalyse du CNRS. Silica gel 60 PF_{254} (Merck) activated at 120 °C was the support for TLC and for column chromatography. The term "standard workup" means that the organic layer was washed with water, dried over Na_2SO_4, and filtered and the solvent was removed at reduced pressure.

1,6-Anhydro-3-azido-2,3-dideoxy-2-fluoro-β-D-glucopyranose (3). To a solution of **2** (40 mg, 0.27 mmol) in a mixture of 2-methoxyethanol–water (5:1) (6 mL) were added sodium azide (93 mg, 1.4 mmol) and ammonium chloride (93 mg, 1.7 mmol), and the mixture was kept at 130 °C overnight. After standard workup, the crude product was chromatographed, giving pure **3** [45 mg (87%)] as a syrup: $[\alpha]^{22}_D$ −72° (*c* 0.77, chloroform); mass spectrum, *m/z* 189 ($M^{\bullet+}$); ^1H NMR δ 5.54 (br s, 1 H, H-1), 4.58 (d, $J_{5,6}$ = 7 Hz, H-5), 4.34 (d, $J_{2,F}$ = 45 Hz, H-2), 4.09 (d, $J_{6,6'}$ = 7 Hz, H-6'), 3.90 (d, $J_{3,F}$ = 17 Hz, H-3), 3.78 (t, $J_{6,6'} = J_{5,6}$ = 7 Hz, H-6), 3.58 (d, 1 H, $J_{4,F}$ = 3,3 Hz, H-4), 2.86 (br s, 1 H, OH); ^{13}C NMR δ 100.0 (d, $J_{1,F}$ = 28.6 Hz, C-1), 87.0 (d, $J_{2,F}$ = 183.5 Hz, C-2), 76.6 (C-5), 69.3 (C-4), 65.5 (C-6), 61.7 (d, $J_{3,F}$ = 24.7 Hz, C-3); ^{19}F NMR −122,2 (dq, $J_{F,2}$ = 45 Hz, $J_{F,3}$ = 17 Hz, $J_{F,4}$ = 3.3 Hz, $J_{F\text{-}1}$ = 1,3 Hz). Anal. Calcd for $C_6H_8FN_3O_3$: C, 38.12; H, 4.23; F, 10.04; N, 22.22. Found: C, 38.05; H, 4.01; F, 9.95; N, 22.14.

Benzyl 3-Azido-4,6-*O*-benzylidene-3-deoxy-α-D-glucopyranoside (7). To a solution of the diacetal **4** (1.05 g, 3.6 mmol) in water (50 mL) was added amberlite IR-120 (M^+) resin (10 g), and the mixture was stirred at 40 °C for 20 h. Removal of the resin and solvent furnished the free sugar **5** [0.74 g (98%)], which was purified by rapid filtration on a silica gel column. To a solution of the free sugar **5** (0.92 g, 4.1 mmol) in dry benzyl alcohol (30 mL) was added boron trifluoride etherate (0.3 mL), and the mixture was heated to 100 °C for 90 min with stirring. After standard workup and column chromatography, the benzyl glycoside **6** was obtained as a mixture of α and β anomers [0.91 g (68%)]. To the mixture of anomers **6** (5.2 g, 17.6 mmol) in dry *N,N'*-dimethylformamide (75 mL) was added α,α-dimethoxytoluene (3 g, 20 mmol) and *p*-toluenesulfonic acid monohydrate (15 mg), and the procedure of Evans[10] for 4,6-*O*-benzylidene formation was applied. After standard workup and chromatography of the residue the α-glycoside **7** [3.31 g (49%)] was obtained as fine needles: mp 136–138 °C; $[\alpha]^{22}_D$ +135° (*c* 0.6, chloroform); mass spectrum, *m/z* 383 ($M^{\bullet+}$); ^1H NMR δ 7.60 and 7.20 (m, 10 H, Ph), 5,52 (s, 1 H, H-7), 4.95 (d, 1 H, $J_{1,2}$ = 3 Hz, H-1), 4.78 and 4.52 (2 d, 2 H, J_{gem} = 12 Hz, CH_2Ph), 4.30 and 3.30 (m, 6 H, H-2, H-3, H-4, H-5, H-6, and H-6'), 2.30 (d, 1 H, $J_{2,OH}$ = 8 Hz, OH). Anal. Calcd for $C_{20}H_{21}N_3O_5$: C, 62.69; H, 5.48; N, 10.96. Found: C, 62.86; H, 5.44; N, 11.00.

Benzyl 3-Azido-4,6-*O*-benzylidene-3-deoxy-2-*O*-[(trifluoromethyl)sulfonyl]-α-D-glucopyranoside (8). To a solution of **7** (100 mg, 0.26 mmol) in dry pyridine (5 mL) was added at 0 °C in an argon atmosphere trifluoromethanesulfonic anhydride (0.2 mL, 1.18 mmol), and the mixture was kept at room temperature for 3 h. After standard workup, the crude product was crystallized from ether–hexane giving pure **8** [118 mg (88%)] as fine needles: mp 98–100 °C; $[\alpha]^{22}_D$ +82° (*c* 1.65, chloroform); mass spectrum, *m/z* 515 ($M^{\bullet+}$); ^1H NMR δ 7.27 (br s, 10 H, Ph), 5.46 (s, 1 H, H-7), 5.06 (d, $J_{1,2}$ = 3 Hz, H-1), 4.70 and 4.45 (2 d, 2 H, J_{gem} = 12 Hz, CH_2Ph), 4.17 (dd, $J_{6,6'}$ = 9 Hz, $J_{6,5}$ = 4 Hz, H-6), 4.06 and 3.31 (m, 5 H, H-2, H-3, H-4, H-5, and H-6').

Benzyl 3-Azido-4,6-*O*-benzylidene-2,3-dideoxy-2-fluoro-α-D-mannopyranoside (9). (a) To a solution of **8** (85 mg, 0.15 mmol) in *N,N'*-dimethylformamide (5 mL) was added cesium fluoride (100 mg, 0.66 mmol), and the mixture was kept in a nitrogen atmosphere at 120 °C for 7 h. After standard workup, the crude product was chromatographed, giving pure **9** [38 mg, (60%)] as fine needles: mp 108–111 °C; $[\alpha]^{22}_D$ +37° (*c* 0.8, chloroform); mass spectrum, *m/z* 385 ($M^{\bullet+}$); ^1H NMR δ 7.53 and 7.31 (m, 10 H, Ph), 5.66 (s, 1 H, H-7), 5.04 (dd, 1 H, $J_{1,F}$ = 8 Hz, $J_{1,2}$ = 2 Hz, H-1), 4.73 (ddd, 1 H, $J_{2,F}$ = 48.5 Hz, $J_{2,3}$ = 3 Hz, $J_{1,2}$ = 2 Hz, H-2), 4.76 and 4.56 (2 d, 2 H, J_{gem} = 12 Hz, CH_2Ph), 4.30 (dd, 1 H, $J_{6,6'}$ = 10 Hz, $J_{5,6}$ = 4 Hz, H-6), 4.12 (t, 1 H, $J_{4,5} = J_{3,4}$ = 10 Hz, H-4), 4.02 and 3.95 (m, 2 H, H-3 and H-5), 3.87 (t, 1 H, $J_{6,6'} = J_{5,6'}$ = 10 Hz, H-6'); ^{13}C NMR δ 102.0 (C-7), 96.9 (d, $J_{1,F}$ = 30.5 Hz, C-1), 89.0 (d, $J_{2,F}$ = 180.3 Hz, C-2), 77.0 (d, $J_{4,F}$ = 7.8 Hz, C-4), 70.1 (C-6), 68.9 (CH_2Ph), 64.5 (C-5), 58.7 (d, $J_{3,F}$ = 16.6 Hz, C-3); ^{19}F NMR −138,4 (ddd, $J_{F,2}$ = 48.5 Hz, $J_{F,3}$ = 31 Hz, $J_{F,1}$ = 8.0 Hz). Anal. Calcd for $C_{20}H_{20}FN_3O_4$: C, 62.36; H, 5.19; F, 4.93; N, 10.90. Found: C, 62.40; H, 5.22; F, 4.94; N, 10.96.

(b) To a solution of **7** (130 mg, 0.38 mmol) in benzene (10 mL) was added (diethylamino)sulfur trifluoride (0.2 mL, 1.64 mmol), and the mixture was refluxed for 2 h. After dilution with a saturated aqueous solution (10 mL) of sodium hydrogen carbonate and standard workup, chromatography of the crude product gave pure **9** [16 mg (16%)] and a mixture [43 mg (44%)] consisting of 3-azido-4,6-*O*-benzylidene-3-deoxy-β-D- (**10**) and -α-D-glucopyranosyl fluoride (**11**) as a syrup: mass spectrum, *m/z* 385 ($M^{\bullet+}$).

Benzyl 3-Azido-4,6-*O*-benzylidene-3-deoxy-β-D-idopyranoside (20). To a solution of **19** (350 mg, 1.03 mmol) in a mixture of 2-methoxyethanol–water (5:1) (18 mL) were added sodium azide (200 mg, 3.08 mmol) and ammonium chloride (200 mg, 3.74 mmol), and the mixture was kept at 140 °C overnight. After standard workup, the crude product was chromatographed, giving pure **20** [331 mg (84%)] as a syrup: $[\alpha]^{22}_D$ −47° (*c* 1.0, chloroform); mass spectrum, *m/z* 383 ($M^{\bullet+}$); ^1H NMR δ 7.51 (m, 10 H, Ph), 5.54 (s, 1 H, H-7), 4.72 (s, 1 H, H-1), 5.01 and 4.70 (2 d, 2 H, J_{gem} = 12 Hz, CH_2Ph), 4.42 (d, $J_{6,6'}$ = 12 Hz, H-6), 4.14 and 4.09 (m, 3 H, H-2, H-3 and H-6'), 3.97 (br s, 1 H, H-4), 3.76

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(s, 1 H, OH), 3.66 (br s, 1 H, H-5). Anal. Calcd for $C_{20}H_{21}N_3O_5$: C, 62.39; H, 5.48; N, 10.96. Found: C, 62.52; H, 5.23; N, 10.81.

Benzyl 3-Azido-4,6-*O*-benzylidene-3-deoxy-2-*O*-[(trifluoromethyl)sulfonyl]-β-D-idopyranoside (21). To a solution of **20** (50 mg, 0.13 mmol) in dry pyridine (3 mL) was added at 0 °C in an argon atmosphere trifluoromethanesulfonic anhydride (0.1 mL, 0.58 mmol), and the mixture was kept at room temperature for 5 h. After standard workup, the crude product was chromatographed, giving pure **21** [60 mg (90%)] as fine needles: mp 114–116 °C; $[\alpha]^{22}_D$ −30° (*c* 0.85, chloroform); mass spectrum, *m/z* 515 ($M^{\bullet+}$); ^1H NMR δ 7.26 (br s, 10 H, Ph), 5.39 (s, 1 H, H-7), 4.94 and 4.68 (2 d, 2 H, J_{gem} = 12 Hz, CH_2Ph), 4.64 (s, 1 H, H-1), 4.50 and 4.00 (m, 4 H, H-2, H-3, H-6, H-6′), 3.82 (br s, 1 H, H-4), 3.54 (br s, 1 H, H-5).

Benzyl 3-Azido-4,6-*O*-benzylidene-2,3-dideoxy-2-fluoro-β-D-gulopyranoside (22). To a solution of **21** (30 mg, 0.06 mmol) in *N,N′*-dimethylformamide (3 mL) was added cesium fluoride (9 mg, 0.06 mmol), and the mixture was kept in a nitrogen atmosphere at 70 °C for 5 h. After standard workup, the crude product was chromatographed, giving pure **22** [16 mg (71%)] as a syrup: $[\alpha]^{22}_D$ −25° (*c* 1.1, chloroform); mass spectrum, *m/z* 385 ($M^{\bullet+}$); ^1H NMR [in $(CD_3)_2CO$] δ 7.51 and 7.27 (m, 10 H, Ph), 5.67 (s, 1 H, H-7), 5.05 (d, $J_{1,2}$ = 8 Hz, H-1), 4.94 and 4.71 (2 d, 2 H, J_{gem} = 12 Hz, CH_2Ph), 4.70 (ddd, 1 H, $J_{2,F}$ = 48.5 Hz, $J_{1,2}$ = 8 Hz, $J_{2,3}$ = 4 Hz, H-2), 4.52 (m, 1 H, H-3), 4.26 (dd, 1 H, $J_{4,5}$ = 3 Hz, $J_{3,4}$ = 1 Hz, H-4), 4.24 (d, 1 H, H-6), 4.15 (d, 1 H, H-6′), 3.77 (br s, 1 H, H-5); ^{13}C NMR δ 101.6 (C-7), 97.1 (d, $J_{1,F}$ = 22.7 Hz, C-1), 88.2 (d, $J_{2,F}$ = 188.8 Hz, C-2), 76.1 (d, $J_{4,F}$ = 5.2 Hz, C-4), 70.8 (C-6), 69.1 (CH_2Ph), 65.5 (C-5), 61.5 (d, $J_{3,F}$ = 16.5 Hz, C-3); ^{19}F NMR δ −144.5 (d, $J_{F,2}$ = 48.5 Hz). Anal. Calcd for $C_{20}H_{20}FN_3O_4$: C, 62.36; H, 5.19; F, 4.93; N, 10.90. Found: C, 62.29; H, 5.02; F, 4.89; N, 10.84.

3-Azido-2-*O*-benzyl-4,6-*O*-benzylidene-3-deoxy-α-D-idopyranosyl Fluoride (23). To a solution of **20** (30 mg, 0.08 mmol) in benzene (2.5 mL) was added (diethylamino)sulfur trifluoride (0.1 mL, 0.82 mmol), and the mixture was refluxed for 1 h. After dilution with a saturated solution (10 mL) of sodium hydrogen carbonate and standard workup, chromatography of the crude product gave pure **23** [24 mg (85%)] as a syrup: $[\alpha]^{22}_D$ +31° (*c* 1.0, chloroform); mass spectrum, *m/z* 385 ($M^{\bullet+}$); ^1H NMR δ 7.51 and 7.24 (m, 10 H, Ph), 5.73 (dd, 1 H, $J_{1,F}$ = 56 Hz, $J_{1,2}$ = 4 Hz, H-1), 5.52 (s, 1 H, H-7), 4.80 and 4.71 (2 d, 2 H, J_{gem} = 12 Hz, CH_2Ph), 4.37 (d, 1 H, $J_{6,6'}$ = 12 Hz, H-6), 4.13 (dd, 1 H, $J_{6,6'}$ = 12 Hz, $J_{5,6'}$ = 2 Hz, H-6′), 4.00 and 3.82 (m, 3 H, H-3, H-4, and H-5), 3.68 (m, 1 H, H-2); ^{13}C NMR δ 110.1 (d, $J_{1,F}$ = 226.0 Hz, C-1), 100.8 (C-7), 75.6 (C-4), 73.4 (CH_2Ph), 68.5 (C-6), 63.4 (C-5), 61.7 (d, $J_{3,F}$ = 5.8 Hz, C-3); ^{19}F NMR δ −61.3 (dd, $J_{F,1}$ = 56 Hz, $J_{F,2}$ = 12 Hz). Anal. Calcd for $C_{20}H_{20}FN_3O_4$: C, 62.36; H, 5.19; F, 4.93; N, 10.90. Found: C, 62.21; H, 4.98; F, 4.86; N, 10.94.

1,6-Anhydro-2-azido-4-*O*-benzyl-2,3-dideoxy-3-fluoro-β-D-glucopyranose (27). To a solution of **26** (50 mg, 0.18 mmol) in benzene (3 mL) was added (diethylamino)sulfur trifluoride (0.2 mL, 1.64 mmol), and the mixture was refluxed for 0.5 h. After dilution with a saturated solution (10 mL) of sodium hydrogen carbonate and standard workup, chromatography of the crude product gave pure **27** [39 mg (78%)] as a syrup: $[\alpha]^{22}_D$ +22° (*c* 1.5, chloroform); mass spectrum, *m/z* 279 ($M^{\bullet+}$); ^1H NMR δ 7.43 and 7.33 (m, 5 H, Ph), 5.54 (s, 1 H, H-1), 4.76 and 4.70 (2 d, 2 H, J_{gem} = 12 Hz, CH_2Ph), 4.67 (d, $J_{5,6}$ = 7 Hz, H-5), 4.69 (d, 1 H, $J_{3,F}$ = 45 Hz, H-3), 3.92 (d, 1 H, $J_{6,6'}$ = 7 Hz, H-6), 3.74 (t, 1 H, $J_{5,6'} = J_{6,6'}$ = 7 Hz), 3.50 (d, 1 H, $J_{2,F}$ = 18.0 Hz, H-2), 3.32 (d, 1 H, $J_{4,F}$ = 18 Hz, H-4); ^{13}C NMR δ 100.1 (C-1), 89.1 (d, $J_{3,F}$ = 183.3 Hz, C-3), 74.7 (d, $J_{4,F}$ = 18.0 Hz, C-4), 74.0 (C-5), 73.6 (CH_2Ph), 71.7 (C-6), 59.3 (d, $J_{2,F}$ = 24.9 Hz, C-2); ^{19}F NMR δ −116.4 (dt, $J_{F,3}$ = 45 Hz, $J_{F,2} = J_{F,4}$ = 18 Hz). Anal. Calcd for $C_{13}H_{14}FN_3O_3$: C, 55.94; H, 5.02; F, 6.80; N, 15.05. Found: C, 56.01; H, 5.11; F, 6.75; N, 15.12.

Benzyl 4,6-*O*-Benzylidene-3-deoxy-3-fluoro-α-D-glucopyranoside (30). To a solution of 3-deoxy-3-fluoro-D-glucose (**28**; 500 mg, 1.8 mmol) in benzylic alcohol (5 mL) was added *p*-toluenesulfonic acid (50 mg, 0.26 mmol), and the mixture was kept at 100 °C for 5 h, then cooled, and diluted with ether (300 mL). The ethereal solution was vigorously stirred for 20 min and then left aside for 24 h. The upper phase was separated, and the remaining syrupy residue, consisting of benzyl 3-deoxy-3-fluoro-α-D-glucopyranoside (**29**), was added to a mixture of zinc chloride (1.5 g) and benzaldehyde (20 mL). This mixture was stirred at room temperature for 6 h and then poured slowly into a mixture of water (150 mL) and hexane (150 mL), and the solution was stirred for 30 min. The separated solid residue was washed several times with water and hexane and then crystallized from ethanol, giving pure **30** [0.48 g (50%)] as fine needles: mp 98–100 °C; $[\alpha]^{22}_D$ +49° (*c* 2.0, chloroform); mass spectrum, *m/z* 360 ($M^{\bullet+}$); ^1H NMR δ 7.52 and 7.26 (m, 10 H, Ph), 5.53 (s, 1 H, H-7), 5.02 (br s, 1 H, H-1), 4.70 (dt, $J_{3,F}$ = 55 Hz, $J_{2,3} = J_{3,4}$ = 9 Hz, H-3), 4.73 and 4.54 (2 d, 2 H, J_{gem} = 12 Hz, CH_2Ph), 4.23 (ddd, 1 H, $J_{6,6'}$ = 10 Hz, $J_{5,6}$ = 5 Hz, $J_{6,F}$ = 2 Hz, H-6), 3.74 (t, 1 H, $J_{5,6} = J_{6,6'}$ = 10 Hz, H-6′), 3.90 and 3.66 (m, 3 H, H-2, H-4, and H-5). Anal. Calcd for $C_{30}H_{21}FO_5$: C, 66.69; H, 5.83; F, 5.27. Found: C, 66.60; H, 5.79; F, 5.12.

Benzyl 4,6-*O*-Benzylidene-3-deoxy-3-fluoro-2-*O*-[(trifluoromethyl)sulfonyl]-α-D-glucopyranoside (31). To a solution of **30** (100 mg, 0.28 mmol) in dry pyridine (3 mL) was added at −10 °C in an argon atmosphere trifluoromethanesulfonic anhydride (0.2 mL, 1.18 mmol), and the mixture was kept at room temperature for 4 h. After standard workup, the crude product was chromatographed to give pure **31** [192 mg (92%)]. Crystallization from methanol yielded fine needles: mp 120–123 °C; $[\alpha]^{22}_D$ +39 (*c* 0.93, chloroform); mass spectrum, *m/z* 492 ($M^{\bullet+}$); ^1H NMR δ 7.49 and 7.19 (m, 10 H, Ph), 5.47 (s, 1 H, H-7), 5.10 (br s, 1 H, H-1), 4.44 and 3.92 (m, 4 H, CH_2Ph, H-2 and H-3), 4.22 (m, 1 H, H-6), 3.95 and 3.55 (m, 3 H, H-4, H-5 and H-6′).

Benzyl 2-Azido-4,6-*O*-benzylidene-2,3-dideoxy-3-fluoro-α-D-mannopyranoside (32). To a solution of **31** (100 mg, 0.20 mmol) in *N,N′*-dimethylformamide (4 mL) was added sodium azide (40 mg, 0.60 mmol) and the mixture kept in a nitrogen atmosphere at 80 °C for 3 h. After standard workup, the crude product was chromatographed to give pure **32** [0.07 g (90%)] as a syrup: $[\alpha]^{22}_D$ +71 (*c* 104, chloroform); mass spectrum, *m/z* 385 ($M^{\bullet+}$); ^1H NMR δ 7.53 and 7.23 (m, 10 H, Ph), 5.63 (s, 1 H, H-7), 5.13 (ddd, $J_{3,F}$ = 50 Hz, $J_{2,3}$ = 4 Hz, $J_{3,4}$ = 9 Hz, H-3), 4.92 (d, $J_{1,F}$ = 2 Hz, H-1), 4.71 and 4.51 (2 d, 2 H, J_{gem} = 12 Hz, CH_2Ph), 4.27 and 4.19 (m, 3 H, H-2, H-4, and H-6), 3.89 and 3.84 (m, 2 H, H-5 and H-6′); ^{13}C NMR δ 102.1 (C-7), 98.7 (d, $J_{1,F}$ = 6.4 Hz, C-1), 88.7 (d, $J_{3,F}$ = 191.1 Hz, C-3), 77.2 (d, $J_{4,F}$ = 17.0 Hz, C-4), 69.9 (C-6), 68.6 (CH_2Ph), 63.6 (d, $J_{5,F}$ = 7.3 Hz, C-5), 62.7 (d, $J_{2,F}$ = 17.6 Hz, C-2); ^{19}F NMR δ −138.6 (m, $J_{F,3}$ = 50.0 Hz). Anal. Calcd for $C_{20}H_{20}FN_3O_4$: C, 62.36; H, 5.19; F, 4.93; N, 10.90. Found: C, 62.40; H, 5.22; F, 4.99; N, 10.94.

Benzyl 2-Azido-4,6-*O*-benzylidene-2-deoxy-α-D-altropyranoside (34). To a solution of **33** (30 mg, 0.09 mmol) in a mixture of 2-methoxyethanol–water (5:1) (5 mL) were added sodium azide (30 mg, 0.46 mmol) and ammonium chloride (30 mg, 0.56 mmol), and the mixture was kept at 130 °C overnight. After standard workup, the crude product was chromatographed, giving pure syrupy **34**: 29 mg (87%); $[\alpha]^{22}_D$ +93 (*c* 1.0, chloroform); mass spectrum, *m/z* 383 ($M^{\bullet+}$); ^1H NMR δ 7.22 (br s, 10 H, Ph), 5.52 (s, 1 H, H-7), 4.78 (s, 1 H, H-1), 4.72 and 4.45 (2 d, 2 H, J_{gem} = 12 Hz, CH_2Ph), 4.45 and 3.68 (2 m, 6 H, H-2, H-3, H-4, H-5, H-6, and H-6′), 3.00 (br s, 1 H, OH). Anal. Calcd for $C_{20}H_{21}N_3O_5$: C, 62.69; H, 5.48; N, 10.96. Found: C, 62.83; H, 5.64; N, 11.02.

Benzyl 2-Azido-4,6-*O*-benzylidene-2,3-dideoxy-3-fluoro-α-D-altropyranoside (35). To a solution of **34** (25 mg, 0.06 mmol) in dry methylene chloride (2.5 mL) was added in a nitrogen atmosphere (diethylamino)sulfur trifluoride (0.1 mL, 0.82 mmol), and the mixture was kept at room temperature for 5 h. After dilution with a saturated solution (10 mL) of sodium hydrogen carbonate and standard workup, chromatography of the crude product gave pure **35** [19 mg (75%)] as a syrup: $[\alpha]^{22}_D$ +55 (*c* 0.45, chloroform); mass spectrum, *m/z* 385 ($M^{\bullet+}$); ^1H NMR δ 7.53 and 7.33 (m, 10 H, Ph), 5.61 (s, 1 H, H-7), 4.91 (s, 1 H, H-1), 4.89 (ddd, $J_{3,F}$ = 49 Hz, $J_{2,3}$ = 3 Hz, $J_{3,4}$ = 2 Hz, H-3), 4.80 and 4.57 (2 d, 2 H, J_{gem} = 12 Hz, CH_2Ph), 4.35 (dt, 1 H, $J_{4,5} = J_{5,6}$ = 10 Hz, $J_{5,6'}$ = 5 Hz, H-5), 4.26 (dd, 1 H, $J_{6,6'}$ = 10 Hz, $J_{5,6}$ = 5 Hz, H-6), 4.06 (dd, $J_{2,F}$ = 8 Hz, $J_{2,3}$ = 3 Hz, H-2), 3.89 (ddd, $J_{4,F}$ = 30 Hz, $J_{4,5}$ = 10 Hz, $J_{3,4}$ = 2 Hz, H-4), 3.77 (dt, 1 H, $J_{6,6'} = J_{5,6'}$ = 10 Hz, $J_{6',F}$ = 1 Hz, H-6′); ^{13}C NMR δ 102.7 (C-7), 97.2 (C-1), 85.8 (d, $J_{3,F}$ = 189.4 Hz, C-3), 75.8 (d, $J_{4,F}$ = 16.8 Hz, C-4), 70.0 (CH_2Ph), 69.1 (C-6), 61.0 (d, $J_{2,F}$ = 25.9 Hz, C-2), 58.7 (d, $J_{5,F}$ = 1.9 Hz, C-5); ^{19}F NMR δ −138.1 (ddd, $J_{F,3}$ = 49 Hz, $J_{F,4}$ = 30 Hz, $J_{F,2}$ = 8 Hz). Anal. Calcd for $C_{20}H_{20}FN_3O_4$: C, 62.36; H, 5.19; F, 4.93; N, 10.90. Found: C, 62.29; H, 5.12; F, 4.89; N, 11.02.

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Three New Rearranged Spongian Diterpenes from *Chromodoris macfarlandi*: Reappraisal of the Structures of Dendrillolides A and B

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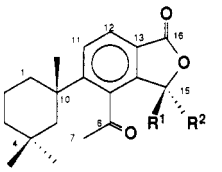
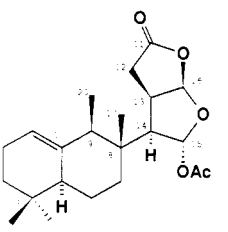
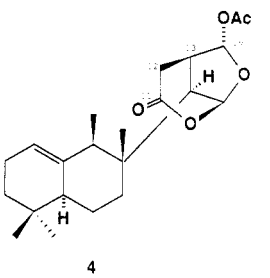
Chromodoris macfarlandi collected at Scripps Canyon, La Jolla, was found to contain three new diterpene acetates. The structure of macfarlandin C (3) was determined by a single-crystal X-ray diffraction analysis. The structures of macfarlandin D (4) and macfarlandin E (5) were elucidated from spectral data. Comparison of the spectral data of macfarlandin D (4) with those of dendrillolide A indicates that the proposed structure for the latter compound is incorrect.

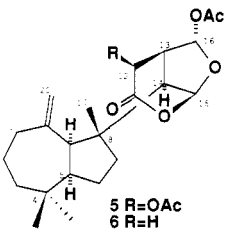
We recently reported[1] the isolation and structure elucidation of two new aromatic spongian-related norditerpenes, macfarlandins A (1) and B (2), from the acetone extract of *Chromodoris macfarlandi*, a dorid nudibranch which inhabits the coastal waters of California. It was shown that these compounds are closely related to aplysulphurin,[2] a metabolite of an Australian sponge *Aplysilla* (= *Darwinella*) *sulphurea*. We now report three new rearranged diterpene acetates from *C. macfarlandi*, macfarlandins C (3), D (4), and E (5). Comparison of the spectral data of dendrillolides A (6) and B (7)[3] with those of norrisolide (8)[4] and macfarlandins C (3) and D (4) reveals that the proposed structure of dendrillolide A is incorrect and raises doubts about the proposed structure of dendrillolide B.

The more polar fraction obtained from chromatography of the dichloromethane soluble portion of the acetone extract of *C. macfarlandi* was separated by LC on Partisil (3:2 ether/hexanes) to afford, in order of elution, macfarlandins E (5), C (3), and D (4). Macfarlandin C (3), mp 195–196 °C, is a diterpene acetate of molecular formula $C_{22}H_{32}O_5$. The molecular formula was derived from the ^{13}C NMR spectrum coupled with the exact mass of the fragment ion at m/z 316.2041 ($C_{20}H_{28}O_3$, M − AcOH). Infrared bands at 1798 and 1748 cm^{-1} were assigned to a γ-lactone and an ester, respectively. The ^1H NMR spectrum contained a six-proton spin system (Table I) that was consistent with either A, a substructure found in norrisolide (8), or B, a substructure assigned to dendrillolide A (6). We were presented with a dilemma because the proton coupling constants were almost identical with those of dendrillolide A (6) while the infrared spectrum required a γ-lactone. The remaining $C_{14}H_{28}$ portion of macfarlandin C (3) is bicyclic and contains a trisubstituted olefinic bond [^{13}C NMR δ 140.2 (s), 118.3 (d)]. The ^1H NMR spectrum contained four methyl signals at δ 0.82 (s, 3 H), 0.84 (s, 3 H), 0.88 (s, 3 H), and 1.01 (d, 3 H, J = 7 Hz). The methyl doublet was coupled to an allylic proton signal at δ 1.90 (br q, 1 H, J = 7 Hz) that was in turn allylically coupled to an olefinic proton signal at 5.32 (br t, 1 H, J = 4 Hz). In a key NOEDS experiment (Table









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