dd, J = 2, 9 Hz), 7.21 (2 H, d, J = 9 Hz), 7.14 (1 H, d, J = 9 Hz), 6.78 (2 H, d, J = 9 Hz), 3.85 (2 H, obscured m), 3.85 (3 H, s), 3.30–3.15 (8 H, overlap m); ^{13}C NMR (Me_2SO-d_6) δ 156.8, 154.9, 133.8, 130.5, 130.3, 128.9, 125.1, 115.7, 113.1, 110.9, 56.3, 52.1, 51.6, 2 X ca. 40.1 (solvent obscured), 32.9, 32.1.

(2*S*,5*S*)-2-[(*o*-Iodo-*p*-methoxyphenyl)methyl]-5-[(*p*-hydroxyphenyl)methyl]piperazine Dihydrobromide (10d). IR (KBr) 3250–2800, 1510, 1250 cm^{-1}; ^{1}H NMR (Me_2SO-d_6) δ 9.33 (5 H, br s, NH, OH), 7.84 (1 H, d, J = 2 Hz), 7.42 (1 H, dd, J = 2, 8 Hz), 7.18 (2 H, d, J = 8 Hz), 7.03 (1 H, d, J = 8 Hz), 6.77 (2 H, d, J = 8 Hz), 3.83 (2 H, obscured m), 3.83 (3 H, S), 3.30–3.12 (8 H, overlap m); ^{13}C NMR (Me_2SO-d_6) δ 157.2, 156.8, 139.8, 130.8, 130.5, 129.5, 125.2, 115.8, 111.7, 86.7, 56.6, 52.1, 51.9, 2 x ca. 40.1 (solvent obscured), 32.9, 31.9.

(2*S*,5*S*)-2,5-Bis(phenylmethyl)piperazine Dihydrobromide (7a). IR (KBr) 3300–2700, 1455, 1070, 970, 740 cm^{-1}; ^{1}H NMR (Me_2SO-d_6) δ 9.43 (4 H, br s, NH), 7.42–7.32 (10 H, m), 3.89 (2 H, m), 3.43–3.18 (8 H, overlap m); ^{13}C NMR (Me_2SO-d_6) δ 135.4, 129.6, 129.0, 127.5, 51.7, ca. 40.1 (solvent obscured), 33.7.

(2*S*,5*S*)-2,5-Dimethylpiperazine Dihydrobromide (7c). IR 3450, 2900, 2550, 1440, 1400, 1360 cm^{-1}; ^{1}H NMR (Me_2SO-d_6) δ 9.50 (4 H, br s, NH), 3.76 (2 H, m), 3.47 (2 H, dd, J = 4, 14 Hz), 3.24 (2 H, dd, J = 7, 14 Hz), 1.45 (6 H, d, J = 7 Hz); ^{13}C NMR (Me_2SO-d_6) δ 46.4, 42.0, 14.2.

***trans*-2,5-Bis[(*p*-hydroxyphenyl)methyl]piperazine Dihydrobromide (11).** IR (KBr) 3300–2900, 1560, 1210 cm^{-1}; ^{1}H NMR (Me_2SO-d_6) δ 8.05 (4 H, br s, NH), 7.27 (4 H, d, J = 8 Hz), 6.85 (4 H, d, J = 8 Hz), 3.90–2.65 (10 H, overlap m); ^{13}C NMR (Me_2SO-d_6) 156.4, 130.3, 126.5, 115.5, 60.9, 59.7, 54.0, 34.0.

(2*S*,5*S*)-1,4-Dibenzoyl-2,5-dimethylpiperazine. (2*S*,5*S*)-2,5-Dimethylpiperazine dihydrobromide (**7c**) (110 mg, 0.4 mmol) was dissolved in dry pyridine (2 mL) at 80 °C and treated with benzoyl chloride (220 mg, 1.6 mmol). After 2 h of stirring the cooled mixture was partitioned between ethyl acetate (10 mL) and 1 N HCl (20 mL). The organic layer was dried with Na_2SO_4 and evaporated to leave an orange residue. Flash chromatography (R_f 0.35, 70% ethyl acetate/petroleum ether) gave 66 mg colorless solid, 50% yield; IR (KBr) 1640, 1605, 1420 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 7.42 (10 H, br s); 4.43 (2 H, m); 3.88 (2 H, dd, J = 4, 15 Hz), 2.98 (2 H, dd, J = 11, 15 Hz), 1.16 (6 H, d, J = 6 Hz). Anal. Calcd for $C_{20}H_{22}N_2O_2$: C, 74.51; H, 6.87. Found: C, 74.51; H, 6.72.

(2*S*,5*S*)-1,4-Dimethyl-2,5-bis(phenylmethyl)piperazine (7b). A suspension of (2*S*,5*S*)-bis[(*p*-hydroxyphenyl)methyl]-piperazine dihydrobromide (**7a**; 128 mg, 0.3 mmol) in 98% formic acid (700 mg) and 37% formaldehyde (800 mg) was heated at 70 °C for $^1/_2$ h. The cooled reaction mixture was partitioned between ethyl acetate (10 mL) and saturated aqueous $NaHCO_3$ (35 mL). The organic layer was dried over Na_2SO_4 and evaporated in vacuo to leave 91 mg of off-white solid. Flash chromatography (R_f 0.3, ethyl acetate) gave a colorless crystalline solid: 81 mg, 90% yield; IR, ^{1}H and ^{13}C NMR, and mass spectra were in accord with values reported.[11]

Acknowledgment. We gratefully acknowledge the financial support of the National Institutes of Health (GM-31349).

Registry No. **1**, 83858-82-6; **2**, 71812-08-3; **6a**, 2862-51-3; **6c**, 5845-61-4; **7a**·2HBr, 98778-70-2; **7b**, 81536-08-5; **7c**·2HBr, 98778-71-3; **8a**, 27513-48-0; **8b**, 98778-72-4; **8c**, 98778-73-5; **8d**, 98778-74-6; **9a**, 10125-11-8; **9b**, 98778-75-7; **9c**, 98778-76-8; **9d**, 98778-77-9; **9e**, 10125-12-9; **10a**, 98778-78-0; **10b**, 98778-79-1; **10c**, 98778-80-4; **10d**, 98778-81-5; **11**, 98854-94-5; 4-*O*-methyl-L-tyrosine, 6230-11-1; 3-bromo-4-*O*-methyl-L-tyrosine, 98778-82-6; L-tyrosine methyl ester hydrochloride, 3417-91-2; 3-bromo-L-tyrosine, 38739-13-8; 3-bromo-L-tyrosine methyl ester hydrochloride, 98778-83-7; 3-bromo-4-*O*-methyl-L-tyrosine methyl ester hydrochloride, 98778-84-8; 3-iodo-4-*O*-methyl-L-tyrosine, 98778-85-9; 3-iodo-4-*O*-methyl-L-tyrosine methyl ester hydrochloride, 98778-86-0; *N*-(*tert*-butoxycarbonyl)-L-tyrosine, 3978-80-1; L-tyrosine, 60-18-4; (2*S*,5*S*)-1,4-dibenzoyl-2,5-dimethylpiperazine, 59525-66-5; benzoyl chloride, 98-88-4; borane, 13283-31-3.

Synthesis of 2′-*C*-Fluoro-β-daunomycin. An Example of Configurational Retention in Fluorodehydroxylation with Diethylaminosulfur Trifluoride

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Fluorodehydroxylation of benzyl 3-azido-3-deoxy-4,6-*O*-benzylidene-α-D-altropyranoside in the presence of diethylaminosulfur trifluoride proceeded with configurational retention at C-2. On the basis of this reaction a new synthesis of benzyl 3-amino-2,3,6-trideoxy-2-fluoro-β-L-galactopyranoside, a C-2 fluoro analogue of daunosamine was accomplished. From the latter and daunomycinone, 2′-*C*-fluoro-β-daunomycin was stereospecifically prepared and its antitumor activity evaluated.

The antibiotic daunomycin (**1**) is a clinically useful antineoplastic agent.[1] As part of a program directed toward the synthesis of analogues of **1** modified in the amino–sugar moiety,[2,3] we now report the synthesis of 2′-*C*-fluoro-β-daunomycin (**2**). The synthesis of **2** was undertaken in the hope that strengthening of the glycosidic linkage of daunomycin would result in an improvement of its ther-

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[∥] The synthesis of the antibiotic from compound **14** is part of the Ph.D. thesis of Aimée Dessinges.

[⊥] Present address: Department of Chemistry, Duke University, Durham, North Carolina 27706. The fluorodehydroxylation reaction and the preparation of compound **14** from **5** is part of the Ph.D. thesis of Ramine Faghih.

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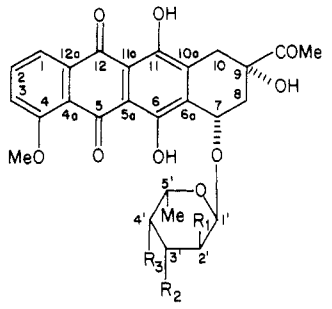
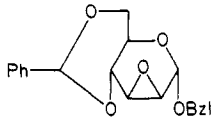


1, R_1=H; R_2=NH_2; R_3=OH
2, R_1=F; R_2=NH_2; R_3=OH
20, R_1=F; R_2=NHCOCF$_3$; R_3=OBz
21, R_1=F; R_2=NHCOCF$_3$; R_3=OH

apeutic index. For this reason, introduction of a powerful electronegative atom at C-2′, fluorine, having a volume comparable to that of hydrogen was considered.



3

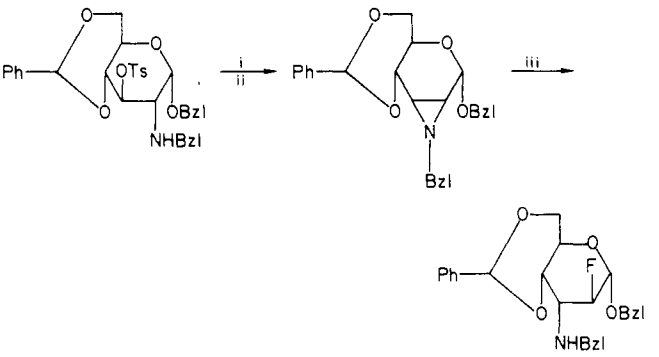
Results and Discussion

In a previous work,[4] starting from D-glucosamine, we described the synthesis of benzyl 3-benzamido-2-fluoro-2,3,6-trideoxy-β-L-galactopyranoside (18), a protected 2′-*C*-fluoro β-analogue of daunosamine. Fluorine was introduced into the carbohydrate in about 40% yield via tetrabutylammonium fluoride induced regio- and stereospecific opening of an intermediate epimine[5] (Scheme I). However, tetrabutylammonium fluoride appeared to be inconvenient for large-scale reactions. [Tetrabutylammonium fluoride is available under the form of its trihydrate. It is a rather expensive reagent and its dehydration at large scale proved to be difficult in our hands.] Therefore other techniques for the generation of a D-altro system with a nitrogen at C-3 and a fluorine at C-2 were considered using D-glucose as starting material.

Diethylaminosulfur trifluoride (DAST) has been extensively used recently for the introduction of fluorine into carbohydrates.[6] All available examples in the sugar literature report inversion of configuration during this reaction.[6] However, Meakins et al. have published[7] a few cases in the steroid field, where DAST treatment of secondary alcohols induced replacement of the hydroxy group by fluorine with configurational retention. Inspection of these examples reveal that in each case where retention of the configuration occurred, an S_N2 reaction appeared highly unfavorable for steric reasons. In the light of these results treatment of azido alcohol **4**, readily available from D-glucose, with DAST was attempted. An S_N2 reaction at C-2 of **4** was considered highly unlikely in view of the axially disposed substituents at both C-1 and C-3.

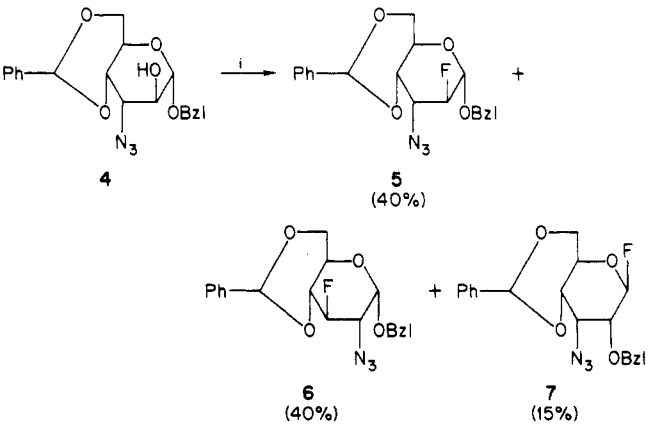
Azidolysis of the known epoxide **3**[8] furnished azido alcohol **4** in 90% yield. Treatment of the latter with 3 equiv of DAST in boiling benzene afforded a mixture (Scheme II) from which chromatography allowed the isolation of three compounds: **5** (40%), **6** (40%), and **7** (15%).

Scheme I[a]



[a] (i) OH^-; (ii) C_6H_5COCl; (iii) Bu_4NF.

Scheme II[a]



[a] (i) DAST.

Structural Determination of the Compounds Produced by DAST Treatment of Azido Alcohol 4 and Mechanism of Their Formation. The proton NMR spectrum of **5** showed its anomeric hydrogen at 4.90 ppm as a doublet ($J_{H\text{-}1,F}$ = 12 Hz). The very small value of $^3J_{H\text{-}1,H\text{-}2}$ < 1 Hz was in favor of an equatorial proton at C-2. The carbon-13 NMR spectrum of **5** afforded unambiguous proof for its structure. Although, inspection of the chemical shifts[9] [96.4 (d, $J_{C\text{-}1,F}$ = 34.3 Hz, C-1), 88.0 (d, $J_{C\text{-}2,F}$ = 174.9 Hz, C-2), 57.7 (d, $J_{C\text{-}3,F}$ = 28.9 Hz, C-3), 75.9 (C-4) ppm] furnished evidence for the presence of the fluorine atom at C-2, the shifts were not clearly indicative of the C-2 stereochemistry. The latter was deduced from $^2J_{^{13}C,F}$ and $^3J_{^{13}C,F}$ coupling constants.[9] It is well-known that $^2J_{^{13}C,F}$ exhibits a marked dependency upon the orientation of substitutents bonded to the coupled carbon.[9] Geminal couplings in absolute value higher and lower than 24 and 19 Hz characterize respectively trans diaxial and trans diequatorial or cis configurations. Since $^2J_{^{13}C,F}$ is also dependent on the electronegativity of the substitutents, the above indicated values are higher by a few Hz if the anomeric carbon is involved in the coupling. In the light of these observations the $^2J_{C\text{-}1,F}$ and $^2J_{C\text{-}3,F}$ values can be interpreted only in terms of a D-altro stereochemistry in **5**. This conclusion is corroborated also by the very small coupling constant $^3J_{C\text{-}4,F}$ < 1.5 Hz. It has been established that for vicinal coupling constants, trans and gauche orientations are characterized respectively by absolute values higher than 7.3 Hz and lower than 2.2 Hz.[9] The small

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value of $^3J_{C-4,F}$ reveals a gauche relationship between these nuclei.

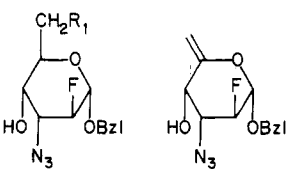
The proton NMR spectrum of **6** showed a doublet of triplets at 5.04 ppm ($^2J_{H-3,F}$ = 54 Hz, $^3J_{H-3,H-2}$ = $^3J_{H-3,H-4}$ = 9 Hz) to which double resonance experiments permitted to assign H-3. The large vicinal coupling constants were indicative of axial protons and consequently of a D-gluco configuration. Interestingly, H-6_{eq} showed up as an octet ($^2J_{H-6_{eq},H-6_{ax}}$ = 9 Hz, $^3J_{H-6_{eq},H-5}$ = 4 Hz, and $^5J_{H-6_{eq},F}$ = 2 Hz). The long-range stereospecific coupling of fluorine with H-6_{eq} appears characteristic of the 3β-configuration of the halogen. Similar results were found in the ^{1}H NMR spectrum of 3-deoxy-3-fluoro-D-glucose.[9] Carbon-13 chemical shifts of **6** and coupling constants of the type $^2J_{^{13}C,F}$ and $^3J_{^{13}C,F}$ were in excellent agreement with the proposed structure. The relatively small geminal couplings $^2J_{C-2,F}$ = 17.4 Hz and $^2J_{C-4,F}$ = 17.2 Hz were indicative of equatorial substituents on the neighbors of the fluorine-bearing carbon. On the other hand, $^3J_{C-1,F}$ = 8.8 Hz revealed a trans relationship between the halogen and the anomeric carbon atom.

The proton NMR spectrum of **7** showed its anomeric hydrogen at 5.52 ppm as a doublet of doublets: $^2J_{H-1,F}$ = 52.0 Hz and $^3J_{H-1,H-2}$ = 7 Hz. Double resonance experiments permitted to identify a signal at 3.50 ppm as H-2. The latter appeared under the form of an octet: $^3J_{H-2,F}$ = 12 Hz, $^3J_{H-2,H-1}$ = 7 Hz, and $^3J_{H-2,H-3}$ = 3 Hz. These results suggested a trans diequatorial relationship between the C-2 substituent and the fluorine atom which is bonded to the anomeric carbon. Carbon-13 chemical shifts of **7** and coupling constants of the type $^1J_{^{13}C,F}$, $^2J_{^{13}C,F}$, and $^3J_{^{13}C,F}$ fully supported the proposed structure. As a consequence of the fluorine atom, the anomeric carbon was strongly deshielded (108.5 ppm) and exhibited a very large doublet (214.9 Hz). The geminal ($^2J_{C-2,F}$ = 31.9 Hz) and vicinal ($^3J_{C-3,F}$ = 9.8 Hz) coupling constants afforded evidence for the trans relationship between the fluorine atom and both the C-2 substituent and C-3.

Fluorine-19 NMR data (see Experimental Section) were also in excellent agreement[10] with structures **5–7**.

While steric arguments appear to account for the formation of **5** by a stereospecific attack of F^- at C-2 from the less hindered β-face in the reaction of DAST with azido alcohol **4** (Scheme II), possible explanations for the formation of **6** and **7** include respectively an S_Ni reaction and a neighboring group participation.

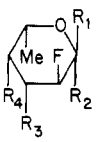
Synthesis of Benzyl 3-Amino-2,3,6-trideoxy-2-fluoro-β-L-galactopyranoside (12). The transformation of benzyl 3-azido-4,6-*O*-benzylidene-2,3-dideoxy-2-fluoro-α-D-altropyranoside (**5**) into **12** was carried out according to known methodology.[11] Acid-catalyzed debenzylidenation of **5** gave quantitatively **8**, partial mesylation of which and treatment of the resulting sulfonate **9** with sodium iodide gave the 6-deoxy-6-iodo derivative **10**. Reaction of **10** with silver fluoride afforded the unsaturated compound **11**. The double bond of **11** was saturated, with simultaneous reduction of the azide but without cleavage of the benzyl groups, by rapid hydrogenation[4] (10% Pd/C, triethylamine, methanol) to give **12** in 95% yield from **11**.



8, R_1=OH
9, R_1=OMs
10, R_1=I

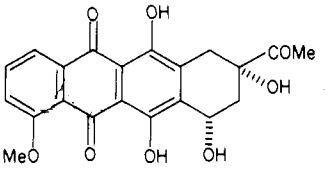
11

Stereospecific α-Glycosylation of Daunomycinone with a 2-*C*-Fluoro-β-L-sugar. Benzyl 3-amino-2,3,trideoxy-2-fluoro-β-L-galactopyranoside (**12**) was transformed into **15** in three steps via derivatives **13** and **14**. Evidence



12, R_1=H; R_2=OBzl; R_3=NH_2; R_4=OH
13, R_1=H; R_2=OBzl; R_3=NHCOCF$_3$; R_4=OH
14, R_1=H; R_2=OBzl; R_3=NHCOCF$_3$; R_4=OBzl
15, R_1=H; R_2=OH; R_3=NHCOCF$_3$; R_4=OBzl
16, R_1=OAc; R_2=H; R_3=NHCOCF$_3$; R_4=OBzl
17, R_1=H; R_2=Br; R_3=NHCOCF$_3$; R_4=OBzl
18, R_1=H; R_2=OBzl; R_3=NHBzl; R_4=OH

for the L-galacto configuration of **14** was furnished by both its ^{1}H and ^{13}C NMR spectrum. (**14** is obviously in the $^1C_4$ conformation.) The proton spectrum of **14** exhibited large and small couplings respectively for $^3J_{H-2,H-3}$ and $^3J_{H-3,H-4}$. The carbon-13 spectrum of **14** showed relatively small couplings for both $^2J_{C-3,F}$ (18.7 Hz) and $^2J_{C-1,F}$ (22.3 Hz). These values were found indicative of a trans diequatorial relationship between the fluorine atom and the substituents of both C-1 and C-3.[9] Acetylation of **15** in the presence of acetic anhydride and sodium acetate gave quantitatively **16**. Treatment of **16** with 33% hydrobromic acid in acetic acid afforded the bromo derivative **17** in 86% yield. Stereospecific α-glycosylation of daunomycinone **19** by **17** was accomplished[12] in 54% yield in methylene chloride solution in a nitrogen atmosphere, in the presence of 1 equiv of silver triflate and powdered molecular sieves (4 Å). Elimination of the base-sensitive C-3′ and C-4



19

protecting groups of **20** was found to proceed more efficiently in two steps rather than in a single step. As the free amine **2** proved to be slightly unstable, its hydrochloride **2**·HCl was prepared for the biological experiments.

Biological Results. The cytostatic activity of 2′-*C*-β-fluorodaunomycin hydrochloride (**2**·HCl) against P388 leukemia cells in vitro was approximately identical with that of daunomycin **1**. However, for the in vivo test againts P388 leukemia, the range of active doses of **2**·HCl was considerably higher than that of daunomycin **1**.

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. ^{1}H NMR spectra were recorded in chloroform-*d* solution at 400 MHz. ^{13}C NMR spectra were measured in chloroform-*d* solution at 100.62 and 50.31 MHz with respectively

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Burker 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 chemical 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.

Benzyl 3-Azido-4,6-*O*-benzylidene-3-deoxy-α-D-altropyranoside (4). To a solution of **3** (4.1 g, 12.1 mmol) in a mixture of 2-methoxyethanol–water (5:1) were added sodium azide (3.4 g, 52.3 mmol) and ammonium chloride (5.6 g, 10.5 mmol) and the mixture was kept at 140 °C overnight. After standard workup, the crude product was chromatographed giving pure **4** (3.7 g, 90%) as a syrup: $[\alpha]^{22}_D$ +88° (*c* 0.88, chrloroform); mass spectrum, *m/z* 383 (M^+·); ^1H NMR δ 7.54 and 7.36 (2 m, 10 H, 2 Ph), 5.59 (s, 1 H, H-7), 4.70 (s, 1 H, H-1), 4.77 and 4.56 (2 d, 2 H, J_{gem} = 12 Hz, CH_2Ph), 4.32 (ddd, 1 H, $J_{5,4}$ = 9 Hz, $J_{5,6}$ = 10 Hz, $J_{5,6'}$ = 5 Hz, H-5), 4.23 (dd, 1 H, $J_{6',5}$ = 5 Hz, $J_{6',6}$ = 10 Hz, H-6'), 4.13 (dd, 1 H, $J_{4,3}$ = 4 Hz, $J_{4,5}$ 9 Hz, H-4), 4.04 (dd, 1 H, $J_{3,2}$ = 3 Hz, $J_{3,4}$ = 4 Hz, H-3), 3.93 (br s, 1 H, H-2), 3.76 (t, 1 H, $J_{6,5}$ = $J_{6,6'}$ = 10 Hz, H-6).

Anal. Calcd for $C_{20}H_{21}N_3O_5$: C, 62.69; H, 5.48. Found: C, 62.60; H, 5.47.

Benzyl 3-Azido-4,6-*O*-benzylidene-2,3-dideoxy-2-fluoro-α-D-altropyranoside (5), Benzyl 2-Azido-4,6-*O*-benzylidene-2,3-dideoxy-3-fluoro-α-D-glucopyranoside (6), and 3-Azido-4,6-*O*-benzylidene-3-deoxy-β-D-allopyranosyl Fluoride (7). To a solution of **4** (3.7 g, 9.7 mmol) in dry benzene (40 mL) was added diethylaminosulfur trifluoride (DAST) (3.6 mL, 29.5 mmol), and the mixture was refluxed for 2 h. After dilution with a saturated aqueous solution (100 mL) of sodium hydrogen carbonate and standard workup, the crude product was chromatographed (8:2 hexane–ethyl acetate), giving pure **5** (1.49 g, 40%) (R_F 0.55) as a syrup and another syrup (2.16 g, 58%) (R_F 0.50), containing two compounds and which was rechromatographed (6:4 hexane–methylene chloride), giving pure **6** (1.49 g, 40%) (R_F 0.25) as a syrup and **7** (0.67 g, 15%) (R_F 0.2) as a syrup.

5: $[\alpha]^{22}_D$ +35° (*c* 1.7, chloroform); mass spectrum, *m/z* 385 (M^+·); ^1H NMR δ 7.54 and 7.37 (2 m, 10 H, 2 Ph), 5.62 (s, 1 H, H-7), 4.90 (d, 1 H, $J_{1,F}$ = 11.5 Hz, H-1), 4.63 (dd, 1 H, $J_{2,F}$ = 43.5 Hz, $J_{2,3}$ = 2.5 Hz, H-2), 4.80 and 4.60 (2 d, 2 H, J_{gem} = 12 Hz, CH_2Ph), 4.29 (m, 3 H, H-3, H-5, and H-6'), 4.09 (ddd, 1 H, $J_{4,F}$ = 3 Hz, $J_{4,3}$ = 4 Hz, $J_{4,5}$ = 9.5 Hz, H-4), 3.77 (t, 1 H, $J_{6,5}$ = $J_{6,6'}$ = 10.5 Hz, H-6); ^{13}C NMR δ 102.6 (C-7), 96.4 (d, $J_{1,F}$ = 34.3 Hz, C-1), 88.0 (d, $J_{2,F}$ = 174.9 Hz, C-2), 75.9 (C-4), 70.0 (CH_2Ph), 69.2 (C-6), 59.3 (C-5), 57.7 (d, $J_{3,F}$ = 28.9 Hz, C-3); ^{19}F NMR −126.9 dt, J = 43.5 Hz, $J_{F,1}$ = $J_{F,3}$ = 11.5 Hz, F-2) ppm.

Anal. Calcd for $C_{20}H_{20}FN_3O_4$: C, 62.36; H, 5.19; F, 4.93; N, 10.90. Found: C, 62.32; H, 5.21; F, 4.98; N, 11.03.

6: $[\alpha]^{22}_D$ +80° (*c* 1.2, chloroform); mass spectrum, *m/z* 385 (M^+·); ^1H NMR δ 7.52 and 7.33 (m, 10 H, 2 Ph), 5.57 (s, 1 H, H-7), 5.03 (dd, 1 H, $J_{1,F}$ = 5.5 Hz, $J_{1,2}$ = 4 Hz, H-1), 5.03 (dt, 1 H, $J_{3,F}$ = 54.5 Hz, $J_{3,2}$ = $J_{3,4}$ = 9 Hz, H-3), 4.76 and 4.61 (2 d, 2 H, J_{gem} = 12 Hz, CH_2Ph), 4.26 (ddd, 1 H, $J_{6',F}$ = 2 Hz, $J_{6',5}$ = 4.5 Hz, $J_{6',6}$ = 10 Hz, H-6'), 3.91 (td, 1 H, $J_{5,4}$ = $J_{5,6}$ = 9 Hz, $J_{5,6'}$ = 4.5 Hz, H-5), 3.78 (m, 2 H, H-4 and H-6), 3.47 (td, 1 H, $J_{2,F}$ = $J_{2,3}$ = 9 Hz, $J_{2,1}$ = 4 Hz, H-2); ^{13}C NMR δ 102.0 (C-7), 98.0 (d, $J_{1,F}$ = 8.8 Hz, C-1), 88.7 (d, $J_{3,F}$ = 189.1 Hz, C-3), 80.1 (d, $J_{4,F}$ = 17.2 Hz, C-4), 70.4 (CH_2Ph), 68.8 (C-6), 62.6 (d, $J_{5,F}$ = 7.6 Hz, C-5), 62.3 (d, $J_{2,F}$ = 17.4 Hz, C-2); ^{19}F NMR −134.2 (m, $J_{F,3}$ = 54.5 Hz, $J_{F,2}$ = $J_{F,4}$ = 9 Hz, $J_{F,6'}$ = 2 Hz, F-3) ppm.

Anal. Calcd for $C_{20}H_{20}FN_3O_4$: C, 62.36; H, 5.19; F, 4.93; N, 10.90. Found: C, 62.41; H, 5.17; F, 4.99; N, 10.82.

7: $[\alpha]^{22}_D$ −84° (*c* 0.9, chloroform); mass spectrum, *m/z* 385 (M^+·); ^1H NMR δ 7.53 and 7.32 (m, 10 H, 2 Ph), 5.50 (s, 1 H, H-7), 5.53 (dd, 1 H, $J_{1,F}$ = 52 Hz, $J_{1,2}$ = 8 Hz, H-1), 4.85 and 4.67 (2 d, 2 H, J_{gem} = 12 Hz, CH_2Ph), 4.37 (dd, $J_{6',5}$ = 5 Hz, $J_{6',6}$ = 9 Hz, H-6'), 4.20 (m, 1 H, H-3), 3.99 (td, 1 H, $J_{5,4}$ = $J_{5,6}$ = 9 Hz, $J_{5,6'}$ = 5 Hz, H-5), 3.72 (t, 1 H, $J_{6,5}$ = $J_{6,6'}$ = 9 Hz, H-6), 3.60 (dd, 1 H, $J_{4,3}$ = 3 Hz, $J_{4,5}$ = 9 Hz, H-4), 3.50 (ddd, 1 H, $J_{2,F}$ = 12.5 Hz, $J_{2,1}$ = 8 Hz, $J_{2,3}$ = 3.5 Hz, H-2); ^{13}C NMR δ 108.5 (d, $J_{1,F}$ = 214.9 Hz, C-1), 102.2 (C-7), 77.1 (C-4), 76.7 (d, $J_{2,F}$ = 22.9 Hz, C-2), 73.1 (CH_2Ph), 67.8 (C-6), 64.1 (d, $J_{5,F}$ = 4.6 Hz, C-5), 61.4 (d, $J_{3,F}$ = 9.8 Hz, C-3); ^{19}F NMR −83.4 (ddd, $J_{F,1}$ = 52 Hz, $J_{F,2}$ = 12.5 Hz, $J_{F,3}$ = 3.4 Hz, F-1) ppm.

Anal. Calcd for $C_{20}H_{20}FN_3O_4$: C, 62.36; H, 5.19. Found: C, 62.45; H, 5.23.

Benzyl 3-Azido-2,3-dideoxy-2-fluoro-α-D-altropyranoside (8). A solution of **5** (1.4 g, 3.6 mmol) in ethanol (250 mL) containing hydrochloric acid (0.1 M) was stirred at room temperature for 48 h, then neutralized to pH 5 by dropwise addition of cold saturated aqueous sodium hydrogen carbonate, filtered, and concentrated. The residue was washed with water, and standard workup gave a syrup **8**: mass spectrum, *m/z* 297 (M^+·).

Benzyl 3-Azido-2,3-dideoxy-2-fluoro-6-*O*-(methylsulfonyl)-α-D-altropyranoside (9). To a solution of crude **8** (1.045 g, 3.5 mmol) in dry pyridine (15 mL) at 0 °C was added methanesulfonyl chloride (0.3 mL, 3.5 mmol). The mixture was stirred at room temperature for 6 h and then poured into ice–water (100 mL). After standard workup, the crude product was chromatographed (6:4 toluene–ethyl acetate), giving pure **9** (1.14 g, 87%) as a syrup: $[\alpha]^{22}_D$ +79° (*c* 1.06, chloroform); mass spectrum, *m/z* 375 (M^+·); ^1H NMR δ 7.33 (br s, 5 H, Ph), 4.92 (d, 1 H, $J_{1,F}$ = 12 Hz, H-1), 4.67 (dd, 1 H, $J_{2,F}$ = 43 Hz, $J_{2,3}$ = 2 Hz, H-2), 4.73 and 4.57 (2 d, 2 H, J_{gem} = 12 Hz, CH_2Ph), 4.46 (d, 1 H, $J_{6,6'}$ = 10 Hz, H-6), 4.29 (d, 1 H, $J_{6,6'}$ = 10 Hz, H-6'), 4.17 (m, 1 H, H-5), 4.04 (m, 2 H, H-3 and H-4), 3.02 (s, 3 H, $MeSO_2$).

Anal. Calcd for $C_{14}H_{18}FN_3O_6S$: C, 44.82; H, 4.79; F, 5.06; N, 11.19; S, 8.54. Found: C, 44.75; H, 4.63; F, 4.92; N, 11.03; S, 8.42.

Benzyl 3-Azido-2-fluoro-6-iodo-2,3,6-trideoxy-α-D-altropyranoside (10). To a solution of **9** (1.13 g, 3 mmol) in ethyl methyl ketone (25 mL) was added sodium iodide (1.08 g, 7.2 mmol). The mixture was stirred for 16 h at 85 °C and then concentrated, and a solution of the residue in hexane–ethyl acetate (1:1) was filtered through a silica gel column to give pure **10** (1.16 g, 95%) as a syrup: $[\alpha]^{22}_D$ +82% (*c* 1.54, chloroform); mass spectrum, *m/z* 407 (M^+·); ^1H NMR δ 7.30 (br s, 5 H, Ph), 4.88 (d, 1 H, $J_{1,F}$ = 12 Hz, H-1), 4.67 (dd, 1 H, $J_{2,F}$ = 44 Hz, $J_{2,3}$ = 3 Hz, H-2), 4.82 and 4.57 (2 d, 2 H, J_{gem} = 12 Hz, CH_2Ph), 4.06 (td, 1 H, $J_{5,4}$ = $J_{5,6}$ = 10.5 Hz, $J_{5,6'}$ = 2.5 Hz, H-5), 3.71 (M, 2 H, H-3 and H-4), 3.45 (dd, 1 H, $J_{6,5}$ = 2.5 Hz, $J_{6,6'}$ = 11 Hz, H-6), 3.21 (dd, 1 H, $J_{6',5}$ = 10.5 Hz, $J_{6',6}$ = 11 Hz, H-6').

Anal. Calcd for $C_{13}H_{15}FIN_3O_3$: C, 38.36; H, 3.68; N, 10.32. Found: C, 38.47; H, 3.72; N, 10.30.

Benzyl 3-Azido-2-fluoro-2,3,6-trideoxy-α-D-*arabino*-hex-5-enopyranoside (11). To a solution of **10** (1.15 g, 2.8 mmol) in dry pyridine (15 mL) was added silver fluoride (1.07 g, 8.4 mmol). The mixture was stirred in the dark at room temperature for 16 h, then diluted with ether (200 mL), filtered through a column of silica gel, and concentrated. Preparative TLC (7:3 hexane–ethyl acetate) of the residue gave pure **11** (0.4 g, 51%) as a syrup: $[\alpha]^{22}_D$ +74° (*c* 0.82, chloroform); mass spectrum, *m/z* 279 (M^+·); ^1H NMR δ 7.23 and 7.08 (m, 5 H, Ph), 4.67 (dd, 1 H, $J_{1,F}$ = 11 Hz, $J_{1,2}$ = 4 Hz, H-1), 4.66 (s, 1 H, H-6), 4.62 (ddd, 1 H, $J_{2,F}$ = 47 Hz, $J_{2,1}$ = 4 Hz, $J_{2,3}$ = 7 Hz, H-2), 4.44 (s, 1 H, H-6'), 4.68 and 4.31 (2 d, 2 H, J_{gem} = 12 Hz, CH_2Ph), 3.94 (br s, 1 H, H-4), 3.11 (ddd, 1 H, $J_{3,F}$ = 12.5 Hz, $J_{3,2}$ = 7 Hz, $J_{3,4}$ = 3.5 Hz, H-3).

Anal. Calcd for $C_{13}H_{14}FN_3O_3$: C, 55.94; H, 5.01. Found: C, 55.82; H, 4.85.

Benzyl 3-Amino-2-fluoro-2,3,6-trideoxy-β-L-galactopyranoside (12). A stirred solution of **11** (0.35 g, 1.2 mmol) in methanol (50 mL) containing triethylamine (1 mL) was hydrogenated for 1 h in the presence of 10% Pd/C (0.35 g) at normal pressure, then filtered through Kieselguhr (Merck), and concentrated, giving pure **12** (0.3 g, 95%) as a syrup: $[\alpha^{22}_D$ +28° (*c* 0.5, methanol); mass spectrum, *m/z* 255 (M^+·); ^1H NMR δ 7.41 (m, 5 H, Ph), 4.85 (dd, 1 H, $J_{1,F}$ = 8 Hz, $J_{1,2}$ = 7 Hz, H-1), 5.13 and 4.82 (2 d, 2 H, J_{gem} = 12 Hz, CH_2Ph), 4.77 (ddd, $J_{2,F}$ = 52 Hz, $J_{2,1}$ = 7 Hz, $J_{2,3}$ = 8 Hz, H-2), 3.88 (dd, 1 H, $J_{4,F}$ = 3 Hz, $J_{4,3}$ = 4 Hz, H-4), 3.78 (q, 1 H, $J_{5,6}$ = 7 Hz, H-5), 3.15 (m, 1 H, H-3), 1.47 (d, 3 H, $J_{6,5}$ = 7 Hz, Me).

Benzyl 2-Fluoro-2,3,6-trideoxy-3-(trifluoroacetamido)-β-L-galactopyranoside (13). To a solution of **12** (0.28 g, 1.1 mmol) in a mixture of methylene chloride–pyridine (5:1) (18 mL) was added trifluoroacetic anhydride (0.5 mL, 3.5 mmol) at 0 °C. The

solution was stirred for 6 h at room temperature. Standard workup gave a residue, which was purified by preparative TLC (6:4 toluene–ethyl acetate). Pure **13** (0.38 g, 98%) was obtained as fine needles: mp 140–141 °C; $[\alpha]^{22}_D$ +20° (*c* 1.0, chloroform); mass spectrum, *m/z* 351 ($M^{+\cdot}$); ^{1}H NMR δ 7.37 (br s, 5 H, Ph), 6.89 (d, 1 H, $J_{NH,3}$ = 7 Hz, NH), 4.95 and 4.71 (2 d, 2 H, J_{gem} = 12 Hz, CH_2Ph), 4.63 (dd, 1 H, $J_{1,F}$ = 9 Hz, $J_{1,2}$ = 7.5 Hz, H-1), 4.37 (ddd, 1 H, $J_{2,F}$ = 51 Hz, $J_{2,1}$ = 7.5 Hz, J_{23} = 9 Hz, H-2), 4.29 (m, 1 H, H-4), 3.78 (q, 1 H, $J_{5,6}$ = 7 Hz, H-5), 3.75 (m, 1 H, H-3), 1.33 (d, 3 H, $J_{6,5}$ = 7 Hz, Me).

Anal. Calcd for $C_{15}H_{17}F_4NO_4$: C, 51.31; H, 4.84. Found: C, 51.45; H, 4.92.

Benzyl 4-*O*-Benzoyl-2-fluoro-2,3,6-trideoxy-3-(trifluoroacetamido)-β-L-galactopyranoside (14). To a solution of **13** (0.36 g, 1 mmol) in dry pyridine (10 mL) was added benzoyl chloride (0.3 mL, 3.1 mmol) dropwise at 0 °C. The mixture was stirred at room temperature for 48 h and then poured into ice–water (100 mL). After standard workup, the crude product was chromatographed (8:2 hexane–ethyl acetate), giving pure **14** (0.45 g, 96%) as a syrup: $[\alpha]^{22}_D$ −71° (*c* 1, chloroform); mass spectrum, *m/z* 455 ($M^{+\cdot}$); ^{1}H NMR δ 8.09 and 7.25 (m, 10 H, Ph), 6.63 (d, 1 H, $J_{NH,3}$ = 7 Hz, NH), 5.52 (dd, 1 H, $J_{4,F}$ = 5 Hz, $J_{4,3}$ = 3 Hz, H-4), 5.01 and 4.75 (2 d, 2 H, J_{gem} = 12 Hz, CH_2Ph), 4.71 (dd, 1 H, $J_{1,F}$ = 8 Hz, $J_{1,2}$ = 7 Hz, H-1), 4.49 (m, 1 H, H-3), 4.57 (ddd, 1 H, $J_{2,F}$ = 54 Hz, $J_{2,1}$ = 7 Hz, $J_{2,3}$ = 10 Hz, H-2), 3.90 (q, 1 H, $J_{5,6}$ = 7 Hz, H-5), 1.24 (d, 3 H, $J_{6,5}$ = 7 Hz, Me); ^{13}C NMR δ 99.8 (d, $J_{1,F}$ = 22.3 Hz, C-1), 88.2 (d, $J_{2,F}$ = 189.1 Hz, C-2), 72.2 (d, $J_{4,F}$ = 7.1 Hz, C-4), 71.1 (C-5), 70.9 (CH_2Ph), 53.1 (d, $J_{3,F}$ = 18.7 Hz, C-3), 16.4 (C-6); ^{19}F NMR −129.5 (ddd, $J_{F,2}$ = 54.0 Hz, $J_{F,1}$ = 8 Hz, $J_{F,4}$ = 5 Hz, F-2), +13.1 ($NHCOCF_3$) ppm.

Anal. Calcd for $C_{22}H_{21}F_4NO_5$: C, 58.05; H, 4.61; F, 16.69; N, 3.08. Found: C, 58.12; H, 4.77; F, 16.81; N, 3.11.

4-*O*-Benzoyl-2-fluoro-2,3,6-trideoxy-3-(trifluoroacetamido)-L-galactopyranose (15). To a solution of **14** (0.19 g, 0.4 mmol) in methanol (50 mL) was added 10% Pd/C (0.2 g), and the mixture was hydrogenated overnight at normal pressure, then filtered, and concentrated to give pure **15** (0.14 g, 91%) as a syrup: chemical ionization mass spectrum, *m/z* 366 (MH^+).

Acetyl 4-*O*-Benzoyl-2-fluoro-2,3,6-trideoxy-3-(trifluoroacetamido)-β-L-galactopyranoside (16). To a solution of sodium acetate (80 mg, 1.2 mmol) in acetic anhydride (5 mL) was added dropwise a solution of **15** (0.14 g, 0.38 mmol) in acetic anhydride (1 mL). The mixture was refluxed for 0.5 h. Standard workup gave pure **16** (0.15 g, 96%) as a syrup: $[\alpha]^{22}_D$ −103° (*c* 0.7, chloroform); mass spectrum, *m/z* 408 ($M^{+\cdot}$); ^{1}H NMR δ 8.20 and 7.50 (m, 5 H, Ph), 6.90 (d, 1 H, $J_{NH,3}$ = 8 Hz, NH), 5.90 (dd, 1 H, $J_{1,F}$ = 4 Hz, $J_{1,2}$ = 8 Hz, H-1), 5.63 (dd, 1 H, $J_{4,3}$ = 2 Hz, $J_{4,5}$ = 1 Hz, H-4), 4.70 (ddd, 1 H, $J_{2,F}$ = 45 Hz, $J_{1,2}$ = 8 Hz, $J_{2,3}$ = 10 Hz, H-2), 4.60 (m, 1 H, H-3), 4.13 (qd, 1 H, $J_{5,6}$ = 7 Hz, $J_{5,4}$ = 1 Hz, H-5), 2.20 (s, 3 H, OCOMe), 1.26 (d, 3 H, $J_{6,5}$ = 7 Hz, Me).

4-*O*-Benzoyl-2-fluoro-2,3,6-trideoxy-3-(trifluoroacetamido)-α-L-galactopyranosyl Bromide (17). To a solution of 33% hydrobromic acid in acetic acid (1 mL) was added **16** (0.067 g, 0.16 mmol) at 0 °C, and then the mixture was stirred at room temperature for 1 h. After dilution of the reaction mixture with methylene chloride (10 mL) and water (10 mL) and neutralization with a cold solution of saturated aqueous sodium hydrogen carbonate, standard workup gave unstable **17** (0.063 g, 86%) as a syrup: ^{1}H NMR δ 8.0 and 7.20 (m, 5 H, Ph), 6.68 (d, 1 H, $J_{1,2}$ = 4 Hz, H-1), 6.46 (d, 1 H, $J_{NH,3}$ = 8 Hz, NH), 5.63 (br s, 1 H, H-4), 4.93 (m, 1 H, H-3), 4.78 (ddd, 1 H, $J_{2,F}$ = 50 Hz, $J_{1,2}$ = 4 Hz, $J_{2,3}$ = 10 Hz, H-2), 4.50 (q, 1 H, $J_{5,6}$ = 7 Hz, H-5), 1.23 (d, 3 H, $J_{6,5}$ = 7 Hz, Me).

7-*O*-[4-*O*-Benzoyl-2-fluoro-2,3,6-trideoxy-3-(trifluoroacetamido)-α-L-galactopyranosyl]daunomycinone (20). To a solution of daunomycinone **19** (0.3 g, 0.74 mmol) in dry methylene chloride (15 mL) were added in the dark and in a nitrogen atmosphere silver triflate (0.22 g, 0.8 mmol) and powdered molecular sieves (4 Å) (600 mg). To this mixture cooled to −80 °C was added dropwise a solution of **17** (0.37 g, 0.86 mmol) in dry methylene chloride (2 mL). Stirring at −80 °C was maintained for 45 min, and then the temperature was allowed to increase slowly (in 45 min) to −20 °C. The mixture was then filtered through Kieselguhr (Merck) and standard workup gave a residue, which was purified by preparative TLC using methylene chloride–methanol (97:3). Pure **20** (0.35 g, 54%) (R_f 0.4) was obtained as red crystals and **19** (0.11 g) was also recovered. **20** was recrystallized from methanol–ether: mp 173–176 °C; $[\alpha]^{22}_D$ +21° (*c* 0.7, chloroform); chemical ionization mass spectrum, *m/z* 348 (M − 397); ^{1}H NMR δ 14.0 and 13.3 (2 s, 2 H, 6-OH and 11-OH), 8.15, 7.70, and 7.57 (5 H, Ph), 8.10 (d, 1 H, $J_{1,2}$ = 8 Hz, H-1), 7.85 (t, 1 H, $J_{2,1}$ = $J_{2,3}$ = 8 Hz, H-2), 7.35 (d, 1 H, $J_{3,2}$ = 8 Hz, H-3), 6.47 (d, 1 H, $J_{NH,3'}$ = 8 Hz, NH), 5.83 (d, 1 H, $J_{1',2'}$ = 4 Hz, H-1′), 5.47 (dd, 1 H, $J_{7,8a}$ = 2 Hz, $J_{7,8b}$ = 4 Hz, H-7), 4.85 (ddd, 1 H, $J_{2',F}$ = 48 Hz, $J_{2',1'}$ = 4 Hz, $J_{2',3'}$ = 10 Hz, H-2′), 4.70 (td, 1 H, $J_{4',F}$ = 2 Hz, $J_{4',3'}$ = $J_{4',5'}$ = 1 Hz, H-4′), 4.67 (, 1 H, H-3′), 4.54 (qd, 1 H, $J_{5',4'}$ = 1 Hz, $J_{5',6'}$ = 7 Hz, H-5′), 4.10 (s, 3 H, OMe), 4.02 (s, 1 H, 9-OH), 3.27 and 3.01 (2 d, 2 H, J_{gem} = 19 Hz, H-10a and H-10b), 2.45 (s, 3 H, Me-14), 2.37 (dd, 1 H, $J_{8a,7}$ = 2 Hz, J_{gem} = 17 Hz, H-8a), 2.25 (dd, 1 H, $J_{8b,7}$ = 4 Hz, J_{gem} = 17 Hz, H-8b), 1.24 (d, 3 H, $J_{6',5'}$ = 7 Hz, Me); ^{13}C NMR δ (carbohydrate carbons) 97.8 (d, $J_{1',F}$ = 20.9 Hz, C-1′), 85.1 (d, $J_{2',F}$ = 195.0 Hz, C-2′), 72.7 (d, $J_{4',F}$ = 6.5 Hz, C-4′), 66.4 (C-5′), 49.6 (d, $J_{3',F}$ = 18.0 Hz, C-3′), 16.2 (C-6′).

Anal. Calcd for $C_{36}H_{31}F_4NO_{12}\cdot H_2O$: C, 56.61; H, 4.32; F, 9.93; N, 1.88. Found: C, 56.67; H, 4.35; F, 9.90; N, 1.79.

7-*O*-[2-Fluoro-2,3,6-trideoxy-3-(trifluoroacetamido)-α-L-galactopyranosyl]daunomycinone (21). To a solution of **20** (0.07 g, 94 μmol) in methanol (5 mL) was added in an argon atmosphere 0.1 N sodium hydroxyde (5 mL). After being stirred for 10 min, the solution was neutralized by 0.1 N hydrochloric acid and then diluted with methylene chloride (50 mL). Standard workup gave a residue, which was purified by preparative TLC (97:3 methylene chloride–methanol). Pure **21** (0.05 g, 83%); mp 112–115 °C; $[\alpha]^{22}_D$ +109° (*c* 0.85, chloroform) was obtained: chemical ionization mass spectrum, *m/z* 244 (M − 397).

Anal. Calcd for $C_{29}H_{27}F_4NO_{11}\cdot H_2O$: C, 52.81; H, 4.40; F, 11.53; N, 2.12. Found: C, 52.91; H, 4.41; F, 11.50; N, 2.13.

7-*O*-[2-Fluoro-2,3,6-trideoxy-α-L-galactopyranosyl]daunomycinone Hydrochloride (2·HCl). To a solution of **21** (0.03 g, 45 μmol) in methanol (3 mL) was added in a nitrogen atmosphere 0.1 N barium hydroxyde (3 mL). After being stirred for 90 min, the solution was neutralized by 0.1 N hydrochloric acid to pH 4 and washed with methylene chloride (3 × 3 mL). The aqueous layer was then treated with a saturated aqueous solution of sodium hydrogen carbonate until pH 8.4 was obtained. Extraction and standard workup gave unstable free amine **2**, which was dissolved in dry methylene chloride (5 mL). To this solution was added a 0.25 M solution of dry hydrochloric acid in methylene chloride (1 mL). The solvent was then evaporated under reduced pressure and the residue recrystallized from methanol–ether, giving highly hygroscopic **2**·HCl (0.019 g, 70%). The red crystals were collected by centrifugation to avoid exposure to air: mp 231–232 °C; $[\alpha]^{22}_D$ −37° (*c* 0.27, methanol); ^{1}H NMR (Me_2SO-d_6) δ 7.92 (m, 2 H, H-1 and H-2), 7.66 (d, 1 H, $J_{3,2}$ = 8 Hz, H-3), 5.43 (d, 1 H, $J_{1',2'}$ = 4 Hz, H-1′), 5.08 (br s, 1 H, H-7), 4.58 (ddd, 1 H, $J_{2',F}$ = 48 Hz, $J_{2',1'}$ = 4 Hz, $J_{2',3'}$ = 10 Hz, H-2′), 4.33 (q, 1 H, $J_{5',6'}$ = 7 Hz, H-5′), 4.00 (s, 3 H, OMe), 3.72 (br s, 1 H, H-4′), 3.33 (m, 1 H, H-3′), 3.00 (s, 2 H, H-10a and H-10b), 2.32 (s, 3 H, Me-14), 2.25 (d, 1 H, J_{gem} = 13 Hz, H-8a), 2.12 (dd, 1 H, $J_{8b,7}$ = 4 Hz, J_{gem} = 13 Hz, H-8b), 1.17 (d, 3 H, $J_{6',5'}$ = 7 Hz, Me).

Anal. Calcd for $C_{27}H_{23}FClNO_{10}\cdot H_2O$: C, 54.04; H, 5.17; N, 2.33. Found: C, 54.20; H, 5.19; N, 2.35.

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Note Added in Proof While the biological study on our antibiotic was under investigation, three papers were published on the synthesis of its amino sugar constituent.[13]