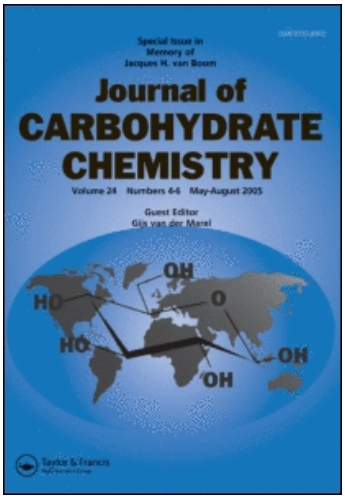

Journal of Carbohydrate Chemistry
Publication details, including instructions for authors and subscription information:
http://www.informaworld.com/smpp/title~content=t713617200

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To cite this Article Hasegawa, Akira , Goto, Makoto and Kiso, Makoto(1985) 'An Unusual Behavior of Methyl or Benzyl 3-Azido-5-O-Benzoyl-3,6-Di-Deoxy-α-L-Talofuranoside with (Dimethylamino)Sulfur Trifluoride; Migration of the Alkoxyl Group from the C-1 to the C-2 Position', Journal of Carbohydrate Chemistry, 4: 4, 627 — 638
To link to this Article: DOI: 10.1080/07328308508082680
URL: http://dx.doi.org/10.1080/07328308508082680

J. CARBOHYDRATE CHEMISTRY, 4(4), 627-638 (1985)

AN UNUSUAL BEHAVIOR OF METHYL OR BENZYL 3-AZIDO-5-O-BENZOYL-3,6-DIDEOXY-α-L-TALOFURANOSIDE WITH (DIMETHYLAMINO)SULFUR TRIFLUORIDE; MIGRATION OF THE ALKOXYL GROUP FROM THE C-1 TO THE C-2 POSITION

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Received October 10, 1985 - Final Form December 4, 1985

ABSTRACT

The reaction of methyl or benzyl 3-azido-5-O-benzoyl-3,6-dideoxy-α-L-talofuranoside with (diethylamino)sulfur trifluoride (DAST) in toluene at 60°C resulted in the formation of 3-azido-5-O-benzoyl-3,6-dideoxy-2-O-methyl (or 2-O-benzyl)-β-L-galactofuranosyl fluoride in good yield. In this reaction the alkoxyl group at C-1 migrated to the C-2 position and a fluorine atom entered into the C-1 position. The furanosyl fluoride was converted, via reduction of the azido group followed by N-trifluoroacetylation, acetolysis, and O-deacetylation, into 3,6-dideoxy-2-O-methyl-3-trifluoroacetamido-L-galactopyranose (2-methoxy-Daunosamine derivative).

INTRODUCTION

There has been a great deal of activity in recent years in the synthesis[1-13] of fluorinated carbohydrates. These sugars are interesting, not only from the point of view of the chemistry involved and the utility of glycosyl fluoride for glycoside synthesis[5,6,8,14], but also for their various biological activities.[15-18] Recently, Somawardhana and Brunngraber[19] have shown the utility of (diethylamino)sulfur

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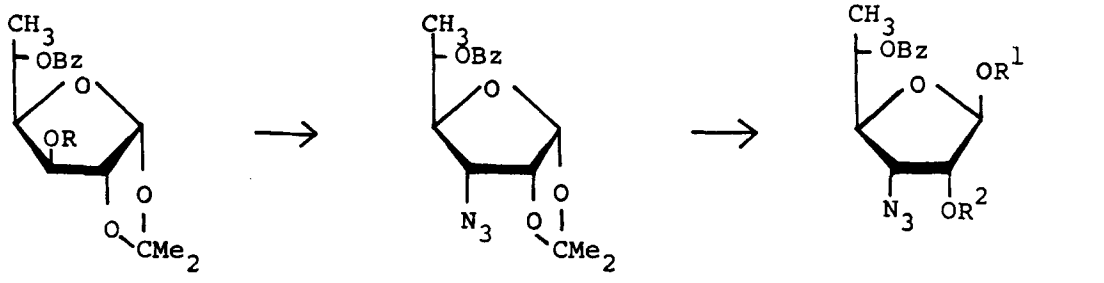
trifluoride (DAST) as a fluorinating agent for the synthesis of specific deoxyfluoro sugars, because of its stereo- and regio-selectivity.

Furthermore, the reagent has been found to react with the anomeric hydroxyl group of various, suitably protected aldoses and ketoses to give glycosyl fluorides.[20,21] We have examined the reactivity of DAST as a fluorinating agent for hexofuranosides. Methyl or benzyl 3-azido-5-O-benzoyl-3,6-dideoxy-α-L-talofuranoside reacted with DAST, and interestingly afforded the β-hexofuranosyl fluoride in good yields. In this reaction the anomeric alkoxyl groups migrated to the C-2 position and a fluorine atom entered into the anomeric carbon from the β-side.

RESULTS AND DISCUSSION

Reductive removal of the benzyl group in 5-O-benzoyl-3-O-benzyl-6-deoxy-1,2-O-isopropylidene-β-L-idofuranose (1), derived from 3-O-benzyl-6-deoxy-1,2-O-isopropylidene-β-L-idofuranose[22] by benzoylation, with hydrogen in the presence of 10% Pd-C catalyst gave the 3-OH derivative (2) in quantitative yield. Treatment of 2 with trifluoromethanesulfonic anhydride at 0°C in dichloromethane-pyridine afforded the 3-O-triflyl derivative (3) as crystals, which was converted, in 96% yield, into 3-azido-5-O-benzoyl-3,6-dideoxy-1,2-O-isopropylidene-β-L-talofuranose (4) by reacting with sodium azide for 5 h at room temperature. The NMR spectrum revealed the presence of one isopropylidene and one methyl group, H-3 as a doublet of doublets at δ 3.35 ($J_{2,3}$ 4.5, $J_{3,4}$ 10.0 Hz), H-4 as a doublet of doublets at δ 4.20 ($J_{4,5}$ 3.3 Hz), H-2 as a triplet at δ 4.73 ($J_{1,2} = J_{2,3}$ = 4.5 Hz), H-5 as a multiplet at δ 5.40, H-1 as a doublet at δ 5.84 ($J_{1,2}$ 4.5 Hz), and phenyl protons at δ 7.28-8.07, indicating the structure shown for the β-L-talofuranose derivative 4. When treated with methanol or benzyl alcohol saturated with dry hydrogen chloride, compound 4 respectively gave methyl 3-azido-5-O-benzoyl-3,6-dideoxy-α-L-talofuranoside (5) or the corresponding benzyl furanoside (6); the NMR spectra showed the presence of H-1 proton as a singlet at δ 4.89 (5) or at δ 5.05 (6), indicating the anomeric proton of trans-1,2 compound[23,24], namely α-L-talofuranoside structure.

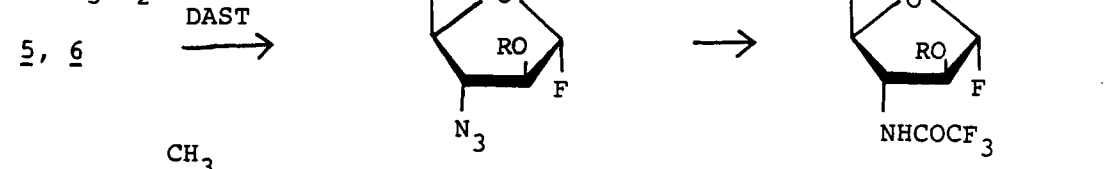
On treatment with DAST in toluene for 2 h at 60°C, compound 5 afforded unexpected glycosyl fluoride, 3-azido-5-O-benzoyl-3,6-dideoxy-2-O-methyl-β-L-galactofuranosyl fluoride (8) in 50.3% yield, in



1 R=Bn
2 R=H
3 R=Tf
Bn=Benzyl
Bz=Benzoyl
Tf=CF_3SO_2

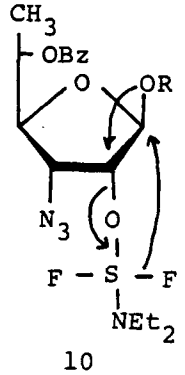
4

5 R^1=Me, R^2=H
6 R^1=Bn, R^2=H
7 R^1=Me, R^2=Tf



8 R=Me
9 R=Bn

12 R=Me
13 R=Bn



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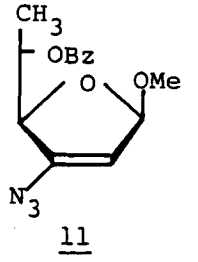

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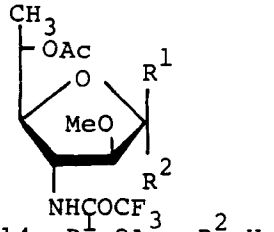
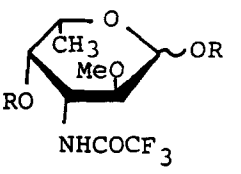


14 R^1=OAc, R^2=H
15 R^1=H, R^2=OAc



16 R=H
17 R=Ac

DAST=Diethylaminosulfur trifluoride
TBAF=Tetrabutylammonium fluoride

which the methoxyl group at the C-1 in 5 migrated to the C-2, and a fluorine atom substituted to the C-2 position from the β-side. The structure of 8 was based on ^{1}H-NMR spectroscopy and elemental analysis. The NMR spectrum exhibited the presence of one methyl, one methoxyl, and one benzoyl group, at δ 1.42 (d, $J_{Me,5}$ 6.2 Hz), 3.36 (s), and 7.28-8.07 (m), H-1 as a doublet at δ 5.74 ($J_{1,F}$ 60.0 Hz), and H-2 as a doublet of doublets at δ 3.95 ($J_{2,3}$ 3.0, $J_{2,F}$ 10.5 Hz), indicating the β-L-galactofuranosyl fluoride. Other NMR data are given in the Experimental section, and are consistent with structure 8. In the same way, treatment of 6 with DAST gave 3-azido-5-O-benzoyl-2-O-benzyl-3,6-dideoxy-β-L-galactofuranosyl fluoride (9) in 79% yield; in this reaction, again the 1-O-benzyl group in 6 migrated to the C-2 position and a fluorine atom was introduced at the C-1 position from the β-side. Considering the products, the oxygen atom of the hydroxyl group at C-2 replaces a fluorine atom of DAST, with loss of hydrogen fluoride, to form the sulfoxo group.[25,26] As shown in the scheme, the sulfoxo group in the intermediate (10) is replaced by the alkoxyl group with inversion of configuration *via* intramolecular rearrangement, and a fluorine ion may be derived from the sulfoxo group.

On the other hand, when treated with tetrabutylammonium fluoride (TBAF) in tetrahydrofuran for 2 h at -10°C, methyl 3-azido-5-O-benzoyl-3,6-dideoxy-2-O-trifluoromethanesulfonyl-α-L-talofuranoside (7), derived from 5 by 2-O-triflation, only gave an elimination product, methyl 3-azido-5-O-benzoyl-2,3,6-trideoxy-α-L-*threo*-hex-2-enofuranoside (11) in 51% yield, because of steric hindrance of the C-1 and C-4 substituents in 7.

Reduction of the azido group in 8 or 9 with hydrogen in the presence of 10% Pd-C catalyst in methanol, and subsequent N-trifluoroacetylation, respectively gave 5-O-benzoyl-3,6-dideoxy-2-O-methyl-3-trifluoroacetamido-β-L-galactofuranosyl fluoride (12) and the corresponding 2-O-benzyl derivative (13), without affecting the 1-fluorine atom. In the NMR spectra of 12 and 13, each H-1 appeared as a doublet at δ 5.87 ($J_{1,F}$ 60.0 Hz; for 12) or at δ 5.83 ($J_{1,F}$ 59.4 Hz; for 13), and H-2 as a doublet at δ 3.92 ($J_{2,F}$ 7.0 Hz; for 12), and as a doublet of doublets at δ 4.02 ($J_{2,F}$ 7.2, $J_{2,3}$ 1.0 Hz; for 13), indicating the galactofuranosyl derivatives having a 1-fluoride group

trans to the group on C-2. Other NMR data are given in the Experimental section, and are consistent with structures 12 and 13.

Acetolysis of compound 12 for 2 days at room temperature proceeded in high yield to give the mixture of anomeric 1,3-di-O-acetyl-3,6-dideoxy-2-O-methyl-3-trifluoroacetamido-L-galactofuranoses (14 and 15) (α:β ratio 1:2.3), which was separated by column chromatography. Treatment of 15 with sodium methoxide in methanol afforded crystalline 16, which was acetylated with acetic anhydride in pyridine to yield 1,4-di-O-acetyl-3,6-dideoxy-2-O-methyl-3-trifluoroacetamido-L-galactopyranose (17) (α:β ratio 1:1).

EXPERIMENTAL

General procedures. Melting points were determined with a Yanagimoto micro melting-point apparatus and are uncorrected. Specific rotations were determined with a Union MP-201 polarimeter, and IR spectra were recorded with a Jasco IR-1 spectrophotometer. NMR spectra were recorded at 90 MHz with a Hitachi R-22 spectrometer. Preparative chromatography was performed on silica gel (Waco Co.; 200 mesh) with the solvent systems specified. Evaporations were conducted in vacuo.

5-O-Benzoyl-3-O-benzyl-6-deoxy-1,2-O-isopropylidene-β-L-idofuranose (1). To a solution of 3-O-benzyl-6-deoxy-1,2-O-isopropylidene-β-L-idofuranose[22] (3.65 g) in pyridine (30 mL) was added benzoyl chloride (2.3 g), and the mixture was kept for 10 h at room temperature. The mixture was evaporated, the residue extracted with chloroform, and the extract successively washed with 2M hydrochloric acid, M sodium carbonate, and water, dried (sodium sulfate), and evaporated to give a syrup, which was purified by column chromatography on silica gel (40 g) with 1:1 chloroform-methanol. The product was obtained as a syrup in quantitative yield, $[\alpha]_D^{25}$ - 12.5° (c 0.7, chloroform).

Anal. Calcd for $C_{23}H_{26}O_6$: C, 69.33; H, 6.58. Found: C, 69.21; H, 6.71.

5-O-Benzoyl-6-deoxy-1,2-O-isopropylidene-β-L-idofuranose (2). Compound 1 (3.7 g) was dissolved in methanol (30 mL); 10% Pd-C catalyst (800 mg) was added, and hydrogen was bubbled through for 2 h

while the solution was stirred at room temperature. The catalyst was filtered off and washed with methanol. The filtrate and washings were combined, and evaporated. Crystallization from n-hexane-ether afforded 2 (2.75 g, 96%) as needles, mp 133°, $[\alpha]_D^{25}$ - 23.0° (c 0.58, chloroform); IR (Nujol): 3430 (OH), 1730 and 1260 (ester), 860 (isopropylidene), and 710 and 690 cm^{-1} (phenyl); NMR ($CDCl_3$): δ 1.29, 1.51 (2s, 6H, Me_2C), 1.41 (d, 3H, $J_{Me,5}$ 6.4 Hz, MeC), 4.10-4.29 (m, 2H, H-3,4), 4.51 (d, 1H, $J_{1,2}$ 3.3 Hz, H-2), 5.42 (m, 1H, H-5), 5.91 (d, 1H, $J_{1,2}$ 3.3 Hz, H-1), and 7.28-8.10 (m, 5H, PhCO).

Anal. Calcd for $C_{16}H_{20}O_6$: C, 62.33; H, 6.54. Found: C, 62.28; H, 6.51.

5-O-Benzoyl-6-deoxy-1,2-O-isopropylidene-3-O-trifluoromethanesulfonyl-β-L-idofuranose (3). To a solution of 2 (1.0 g) in pyridine (3 mL) and dry dichloromethane (5 mL) was added, with stirring, a solution of triflic anhydride (1.1 mL) in dry dichloromethane (4 mL) at 0°C; after 20 min, the starting material had been converted into the triflate. The mixture was extracted with chloroform, and the extract was washed with 2M hydrochloric acid and water, dried (sodium sulfate), and evaporated. Crystallization from n-hexane-ether gave 3 (1.4 g, quantitative) as needles, mp 115-116°, $[\alpha]_D^{25}$ - 5.9° (c 0.53, chloroform); IR (Nujol): 1720 and 1240 (ester), 1200 (SO_2), 840 (isopropylidene), and 720 and 690 cm^{-1} (phenyl).

Anal. Calcd for $C_{17}H_{19}O_8SF_3$: C, 46.36; H, 4.35. Found: C, 46.23; H, 4.32.

3-Azido-5-O-benzoyl-3,6-dideoxy-1,2-O-isopropylidene-β-L-talofuranose (4). To a solution of 4 (1.5 g) in dry N,N-dimethylformamide (8 mL) was added sodium azide (1.2 g), and the mixture was stirred for 5 h at room temperature, and evaporated. The residue was extracted with chloroform, and the extract was successively washed with 2M hydrochloric acid and water, dried (sodium sulfate), and evaporated. The product was purified by chromatography on a column of silica gel (30 g) with 200:1 chloroform-methanol to afford 4 (1.1 g, 96%) as a syrup, $[\alpha]_D^{25}$ + 101° (c 0.95, chloroform); IR (film): 2120 (azide), 1730 and 1260 (ester), 850 (isopropylidene), and 710 and 690 cm^{-1} (phenyl); NMR ($CDCl_3$): δ 1.33, 1.59 (2s, 6H, Me_2C), 1.47 (d, 3H, $J_{Me,5}$ 6.4 Hz, MeC), 3.35 (dd, 1H, $J_{2,3}$ 4.5, $J_{3,4}$ 10.0 Hz, H-3),

4.20 (dd, 1H, $J_{3,4}$ 10.0, $J_{4,5}$ 3.3 Hz, H-4), 4.73 (t, 1H, $J_{1,2} = J_{2,3}$ = 4.5 Hz, H-2), 5.40 (m, 1H, H-5), 5.84 (d, 1H, $J_{1,2}$ 4.5 Hz, H-1), and 7.28-8.09 (m, 5H, PhCO).

Anal. Calcd for $C_{16}H_{19}N_3O_5$: C, 57.65; H, 5.75; N, 12.61. Found: C, 57.53; H, 5.79; N, 12.48.

Methyl 3-azido-5-O-benzoyl-3,6-dideoxy-α-L-talofuranoside (5). Compound 4 (1.0 g) was dissolved in dry methanol (20 mL), and hydrogen chloride was bubbled through for 15 min at 0°C. The mixture was stirred overnight at room temperature, and neutralized with sodium hydrogen carbonate, and then evaporated. The residue was extracted with chloroform, and the extract was washed with water, dried (sodium sulfate), and evaporated to a syrup, which was purified by chromatography on a column of silica gel (30 g) with 300:1 chloroform-methanol. 5 was obtained as a syrup (570 mg, 62%), $[\alpha]_D^{25}$ - 49° (c 0.5, chloroform); IR (film): 3500 (OH), 2110 (azide), 1730 and 1260 (ester), and 710 and 690 cm^{-1} (phenyl); NMR ($CDCl_3$): δ 1.41 (d, 3H, $J_{Me,5}$ 6.2 Hz, MeC), 3.41 (s, 3H, MeO), 4.89 (s, 1H, H-1), 5.23 (m, 1H, H-5), and 7.28-8.07 (m, 5H, PhCO).

Anal. Calcd for $C_{14}H_{17}N_3O_5$: C, 54.72; H, 5.58; N, 13.67. Found: C, 54.51; H, 5.59; N, 13.58.

Benzyl 3-azido-5-O-benzoyl-3,6-dideoxy-α-L-talofuranoside (6). To a solution of 4 (2.1 g) in dry benzyl alcohol (10 mL) was bubbled hydrogen chloride for 20 min at room temperature, and the mixture was stirred for 5 h. Chloroform (200 mL) was added to the mixture, and it was successively washed with M sodium carbonate and water, dried (sodium sulfate), and evaporated. The residue was chromatographed on a column of silica gel (100 g) with chloroform to give 6 (880 mg, 36.5%) as a syrup, $[\alpha]_D^{25}$ - 19.0° (c 2.2, chloroform); IR (film): 3450 (OH), 2100 (azide), 1730 and 1270 (ester), and 740, 710, and 700 cm^{-1} (phenyl); NMR ($CDCl_3$): δ 1.50 (d, 3H, $J_{Me,5}$ 6.4 Hz, MeC), 4.00 (dd, 1H, $J_{3,4}$ 8.2, $J_{4,5}$ 5.0 Hz, H-4), 4.20 (m, 2H, H-2,3), 4.55, 4.68 (2d, 2H, J_{gem} 12.0 Hz, benzyl methylene), 5.05 (s, 1H, H-1), 5.34 (m, 1H, H-5), 7.27 (s, 5H, Ph), and 7.33-8.15 (m, 5H, PhCO).

Anal. Calcd for $C_{20}H_{21}N_3O_5$: C, 62.65; H, 5.52; N, 10.96. Found: C, 62.53; H, 5.71; N, 10.95.

3-Azido-5-O-benzoyl-3,6-dideoxy-2-O-methyl-β-L-galactofuranosyl fluoride (8). To a solution of 5 (830 mg) in dry toluene (10 mL) was added, with stirring, DAST (1.6 g) at -10°, and the mixture was heated for 2 h at 60°C; the mixture was cooled to 0°C, and methanol (1 mL) was added to decompose the reagent. The mixture was evaporated to a syrup which was chromatographed on a column of silica gel (50 g) with chloroform, and then 200:1 chloroform-methanol. The latter eluate gave 8 (420 mg, 50.3%) as a syrup, $[\alpha]_D^{25}$ + 76° (c 1.0, chloroform); IR (film): 2110 (azide), 1720 and 1270 (ester), and 710 and 680 cm^{-1} (phenyl); NMR ($CDCl_3$): δ 1.42 (d, 3H, $J_{Me,5}$ 6.2 Hz, MeC), 3.36 (s, 3H, MeO), 3.78 (dd, 1H, $J_{2,3}$ 3.0, $J_{3,4}$ 6.2 Hz, H-3), 3.95 (dd, 1H, $J_{2,3}$ 3.0, $J_{2,F}$ 10.5 Hz, H-2), 4.24 (m, $J_{3,4}$ 6.2, $J_{4,5}$ 4.2, $J_{4,F}$ 1.8 Hz, H-4), 5.36 (m, 1H, $J_{4,5}$ 4.2, $J_{5,Me}$ 6.2 Hz, H-5), 5.74 (d, 1H, $J_{1,F}$ 60.0 Hz, H-1), and 7.28-8.07 (m, 5H, PhCO).

Anal. Calcd for $C_{14}H_{16}N_3O_4F$: C, 54.37; H, 5.21; N, 13.59. Found: C, 54.19; H, 5.36; N, 13.51.

3-Azido-5-O-benzoyl-2-O-benzyl-3,6-dideoxy-β-L-galactofuranosyl fluoride (9). To a solution of 6 (220 mg) in dry toluene (5 mL) was added, with stirring, DAST (700 mg) at -10°C, and the mixture was heated for 2 h at 60°C; the course of the reaction being monitored by t.l.c.. Methanol (1 mL) was added to the mixture, and evaporated to a syrup, which was chromatographed on a column of silica gel (50 g) with chloroform to give 9 (174 mg, 79%) as a syrup, $[\alpha]_D^{25}$ + 45° (c 1.7, chloroform); IR (film): 2100 (azide), 1720 and 1270 (ester), and 730, 710, and 690 cm^{-1} (phenyl); NMR ($CDCl_3$): δ 1.41 (d, 3H, $J_{Me,5}$ 6.4 Hz, MeC), 3.95-4.60 (m, 3H, H-2,3,4), 4.53, 4.69 (2d, 2H, J_{gem} 11.4 Hz, benzyl methylene), 5.40 (m, 1H, H-5), 5.83 (d, 1H, $J_{1,F}$ 59.3 Hz, H-1), 7.27 (s, 5H, Ph), and 7.25-8.02 (m, 5H, PhCO).

Anal. Calcd for $C_{20}H_{20}N_3O_4F$: C, 62.33; H, 5.23; N, 10.90. Found: C, 62.19; H, 5.38; N, 10.81.

Methyl 3-azido-5-O-benzoyl-2,3,6-trideoxy-α-L-threo-hex-2-eno-furanoside (11). Compound 5 (100 mg) was dissolved in dry pyridine (1 mL) and dry dichloromethane (1 mL), and the solution was cooled to -20°C; a solution of triflic anhydride (0.1 mL) in dry dichloromethane (1 mL) was added. After 15 min, the starting material had been converted into the triflate, and the mixture was extracted with chloro-

form. The extract was successively washed with 2M hydrochloric acid and water, dried (sodium sulfate), and evaporated to give 7 (122 mg, 85%), which was used for the next reaction without further purification. To a solution of 7 in dry tetrahydrofuran (2 mL) was added, with stirring, a tetrahydrofuran solution of tetrabutylammonium fluoride (1.0M solution in THF) (1 mL) at -10°C, and the mixture was stirred for 2 h at -10°C. The mixture was extracted with chloroform, and the extract was successively washed with 2M hydrochloric acid, M sodium carbonate, and water, dried (sodium sulfate), and evaporated. The residue was chromatographed on a column of silica gel (30 g) with chloroform, to afford 11 (48 mg, 51%) as a syrup, $[\alpha]_D^{25}$ - 24.6° (c 0.4, chloroform); IR (film): 2120 (azide), 1720 and 1270 (ester), 1640 (C=C), and 710 and 690 cm^{-1} (phenyl); NMR ($CDCl_3$): δ 1.46 (d, 3H, $J_{Me,5}$ 6.6 Hz, MeC), 3.48 (s, 3H, MeO), 4.53 (m, 1H, H-4), 5.23 (m, 1H, $J_{4,5}$ 3.0, $J_{5,Me}$ 6.6 Hz, H-5), 5.44 (t, 1H, $J_{1,2} = J_{1,4} = 1.2$ Hz, H-1), 5.68 (t, 1H, $J_{1,2} = J_{2,4} = 1.2$ Hz, H-2), and 7.28-8.16 (m, 5H, PhCO).

Anal. Calcd for $C_{14}H_{15}N_3O_4$: C, 58.13; H, 5.23; N, 14.53. Found: C, 58.24; H, 5.39; N, 14.28.

5-O-Benzoyl-3,6-dideoxy-2-O-methyl-3-trifluoroacetamido-β-L-galactofuranosyl fluoride (12). The azido compound 8 (200 mg) was dissolved in methanol (10 mL); 10% Pd-C catalyst (100 mg) was added, and hydrogen was bubbled through the mixture, with stirring, for 1 h at room temperature. The catalyst was removed by filtration, and the filtrate was evaporated. To a solution of amino compound in dry pyridine (5 mL) was added, with stirring, trifluoroacetic anhydride (0.4 mL) at 0°C; after 15 min, the mixture was evaporated. The product was purified on a column of silica gel (30 g) with 50:1 chloroform-methanol, to give 12 (186 mg, 76%) as a syrup, $[\alpha]_D^{25}$ + 81.5° (c 0.48, chloroform); IR (film): 3300 (NH), 1720 and 1270(ester), 1690 and 1560 (amide), and 710 and 690 cm^{-1} (phenyl); NMR($CDCl_3$): δ 1.43 (d, 3H, $J_{Me,5}$ 7.0 Hz, MeC), 3.43 (s, 3H, MeO), 3.92 (d, 1H, $J_{2,F}$ 7.0 Hz, H-2), 4.35-4.58 (m, 2H, H-3,4), 5.42 (m, 1H, $J_{4,5}$ 4.0, $J_{5,Me}$ 7.0 Hz, H-5), 5.87 (d, 1H, $J_{1,F}$ 60.0 Hz, H-1), 7.32-8.11 (5H, PhCO), and 8.60 (d, 1H, $J_{NH,3}$ 4.5 Hz, NH).

Anal. Calcd for $C_{16}H_{17}NO_5F_4$: C, 50.66; H, 4.52; N, 3.69. Found: C, 50.52; H, 4.70; N, 3.65.

5-O-Benzoyl-2-O-benzyl-3,6-dideoxy-3-trifluoroacetamido-β-L-galactofuranosyl fluoride (13). By the same procedure described in the previous section, the azido group in 9 (170 mg) was reduced, and then trifluoroacetylated. Compound 13 (105 mg, 52%) was obtained as a syrup, $[\alpha]_D^{25}$ + 57.5° (c 0.35, chloroform); IR (film): 3280 (NH), 1720 and 1260 (ester), 1670 and 1560 (amide), and 740, 700, and 690 cm^{-1} (phenyl); NMR ($CDCl_3$): δ 1.42 (d, 3H, $J_{Me,5}$ 6.6 Hz, MeC), 4.04 (dd, 1H, $J_{2,3}$ 1.0, $J_{2,F}$ 7.2 Hz, H-2), 4.37 (dd, 1H, $J_{3,4}$ 4.8, $J_{4,5}$ 2.0 Hz, H-4), 4.52 (m, 1H, H-3), 4.53, 4.69 (2d, 2H, J_{gem} 11.4 Hz, benzyl methylene), 5.39 (m, 1H, $J_{4,5}$ 2.0, $J_{5,Me}$ 6.6 Hz, H-5), 5.83 (d, 1H, $J_{1,F}$ 59.4 Hz, H-1), 6.74 (d, 1H, $J_{NH,3}$ 9.0 Hz, NH), 7.27 (s, 5H, Ph), and 7.28-8.02 (m, 5H, PhCO).

Anal. Calcd for $C_{22}H_{21}NO_5F_4$: C, 58.02; H, 4.65; N, 3.08. Found: C, 57.86; H, 4.77; N, 3.05.

1,5-Di-O-acetyl-3,6-dideoxy-2-O-methyl-3-trifluoroacetamido-α-L-galactofuranose (14) and the corresponding β-anomer (15). Compound 12 (100 mg) was dissolved in a mixture of acetic anhydride (5 mL), acetic acid (2.5 mL), and sulfuric acid (0.1 mL), and the mixture was stirred for 2 days at room temperature. Sodium carbonate was then added until pH 5 was reached, and the mixture was evaporated. The residue was extracted with chloroform, and the extract was washed with water, dried (sodium sulfate), and evaporated to a syrup which was chromatographed on a column of silica gel (30 g) with chloroform, and then 100:1 chloroform-methanol. The latter eluate gave 15 (59 mg, 63%) as a faster-moving component, and 14 (26 mg, 28%) as a slower-moving component. For compound 14; mp 188-190°, $[\alpha]_D^{25}$ - 73.3° (c 0.25, chloroform); IR (Nujol): 3260 (NH), 1740 and 1240 (ester), and 1690 and 1560 cm^{-1} (amide); NMR (1:1 $CDCl_3$-CD_3OD): δ 1.22(d, 3H, $J_{Me,5}$ 6.4 Hz, MeC), 2.05, 2.16 (2s, 6H, 2AcO), 3.40 (s, 3H, MeO), 3.91 (dd, 1H, $J_{3,4}$ 9.0, $J_{4,5}$ 6.4 Hz, H-4), 4.06 (dd, 1H, $J_{1,2}$ 4.2 Hz, $J_{2,3}$ 9.0 Hz, H-2), 4.50 (t, 1H, $J_{2,3} = J_{3,4}$ = 9.0 Hz, H-3), 5.03 (q, 1H, $J_{4,5} = J_{5,Me}$ = 6.4 Hz, H-5), and 6.26 (d, 1H, $J_{1,2}$ 4.2 Hz, H-1); For compound 15; mp 167°, $[\alpha]_D^{25}$ + 49° (c 0.8, chloroform); IR (Nujol): 3300 (NH), 1740 and 1240 (ester), and 1700 and 1550 cm^{-1} (amide); NMR ($CDCl_3$): δ 1.29 (d, 3H, $J_{Me,5}$ 6.2 Hz, MeC), 2.03, 2.09 (2s, 6H, 2AcO), 3.44 (s, 3H, MeO), 3.82 (d, 1H, $J_{2,3}$ 1.8 Hz, H-2), 4.18 (t, 1H,

$J_{3,4} = J_{4,5} = 5.0$ Hz, H-4), 4.39 (m, 1H, H-3), 5.12 (m, 1H, $J_{4,5}$ 4.5, $J_{5,Me}$ 6.2 Hz, H-5), 6.22 (s, 1H, H-1), and 7.02 (d, 1H, $J_{NH,3}$ 9.5 Hz, NH).

Anal. Calcd for $C_{13}H_{18}NO_7F_3$: C, 43.70; H, 5.08; N, 3.92. Found: for 14; C, 43.75; H, 5.15; N, 3.88; and for 15; C, 43.66; H, 5.15; N, 3.90.

3,6-Dideoxy-2-O-methyl-3-trifluoroacetamido-L-galactopyranose (16). To an ice-cooled solution of 15 (100 mg) in methanol (5 mL) was added sodium methoxide (10 mg), and the solution was kept for 1 h at 0°C, and then treated with Amberlite IR-120 (H^+) resin to remove the base. The product was purified by chromatography on a column of silica gel (10 g) with 10:1 chloroform-methanol, to give 16 (70 mg, 92%) as crystals, mp 147°, $[\alpha]_D^{25}$ - 74° (c 0.55, equil.; methanol); IR (Nujol): 3450-3280 (OH, NH), and 1700 and 1560 cm^{-1} (amide).

Anal. Calcd for $C_9H_{14}NO_5F_3$: C, 39.57; H, 5.17; N, 5.13. Found: C, 39.66; H, 5.25; N, 5.15.

1,4-Di-O-acetyl-3,6-dideoxy-2-O-methyl-3-trifluoroacetamido-L-galactopyranose (17). Compound 16 (55 mg) was treated with acetic anhydride (0.3 mL)-pyridine (3 mL) overnight at room temperature. It was then evaporated to give a syrup which was purified by chromatography on a column of silica gel (10 g) with 100:1 chloroform-methanol. Compound 17 (53 mg, 74%) was obtained as a syrup, $[\alpha]_D^{25}$ - 85° (c 0.47, methanol; IR (film): 3340 (NH), 1750 and 1720 (ester), and 1700 and 1550 cm^{-1} (amide): NMR ($CDCl_3$): δ 1.11, 1.15 (2d, 3H, $J_{Me,5}$ 5.6 Hz, MeC), 2.17 (2s, 6H, 2AcO), 3.40, 3.49 (2s, 3H, MeO), 3.45 (t, $J_{1',2'} = J_{2',3} = 8.0$ Hz, H-2'), 3.65 (dd, $J_{1,2}$ 3.4, $J_{2,3}$ 10.5 Hz, H-2), 5.23, 5.38 (dd, 1H, H-4,4'), 5.61 (d, $J_{1',2'}$ 8.0 Hz, H-1β), and 6.47 (d, $J_{1,2}$ 3.4 Hz, H-1α); anomeric ratio was estimated at 1:1 from the ratio of intensity of the 2-O-methyl group.

Anal. Calcd for $C_{13}H_{18}NO_7F_3$: C, 43.70; H, 5.08; N, 3.92. Found: C, 43.58; H, 5.16; N, 3.89.

ACKNOWLEDGMENT

This work was supported in part by a Naito Research Grant.

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