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REACTIONS ON METHYL 2-DEOXY-2-TRIFLUOROACETAMIDO-3-*O*-TRIFLUOROMETHYLSULFONYL-α-D-GLUCOPYRANOSIDE DERIVATIVES: FORMATION OF RING-CONTRACTION COMPOUNDS

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ABSTRACT

The behavior of methyl 4,6-*O*-cyclohexylidene-2-deoxy-2-trifluoroacetamido-3-*O*-trifluoromethylsulfonyl-α-D-glucopyranoside (**6**) with several reagents was examined. By reaction of **6** with lithium chloride or sodium iodide in *N,N*-dimethylformamide, the corresponding 3-chloro-3-deoxy- and 3-deoxy-3-iodo-allopyranosides were readily obtained. Treatment of **6** with sodium benzoate in *N,N*-dimethylformamide, or sodium methoxide in methanol, gave several products derived from an initially formed 2,3-*allo*-epimine. The difference in the foregoing reactions is explained on the basis of hydrogen bonding between 2-N*H*COCF$_3$ and 1-*O*Me. Solvolysis of **6** and methyl 6-benzyloxycarbonylamino-2,6-dideoxy-2-trifluoroacetamido-3-*O*-trifluoromethylsulfonyl-α-D-glucopyranoside (**26**) in hot (100°) methanol gave ring-contraction products (**18**, **27**) having bicyclic D-xylofuranoside structures.

INTRODUCTION

Deoxygenation reactions[1,2] at C-3′ and other equivalent positions of kanamycins and other related aminoglycoside antibiotics that are susceptible to modification by resistant bacteria are the most effective procedures to convert the mother antibiotics into derivatives active against the resistant bacteria. Since 1975, a number of successful 3′-deoxygenation procedures have been reported[3]. We have also been searching for new and effective methods to deoxygenate or halogenate the 3′-positions of these antibiotics; regarding the latter, halo derivatives effective against resistant bacteria are to be expected when the hydroxyl groups to be modified by the bacteria are absent. As basic studies related to this problem, we report here several reactions at C-3 of a model compound, methyl 4,6-*O*-cyclohexylidene-2-deoxy-2-trifluoroacetamido-3-*O*-trifluoromethylsulfonyl-α-D-glucopyranoside (**6**).

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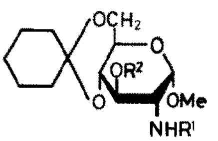
RESULTS AND DISCUSSION

Compound **6** was prepared by trifluoromethylsulfonylation of methyl 4,6-*O*-cyclohexylidene-2-deoxy-2-trifluoroacetamido-α-D-glucopyranoside (**4**), which, in turn, was prepared from methyl 2-amino-4,6-*O*-cyclohexylidene-2-deoxy-α-D-glucopyranoside[4] (**1**) by *N*-trifluoroacetylation.

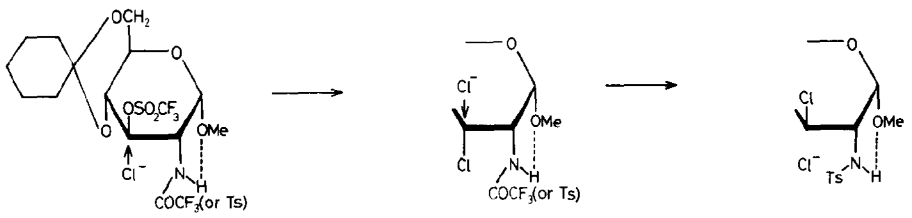
Reaction with halides. — When **6** was treated with lithium chloride in *N,N*-dimethylformamide, the 3-chloro-3-deoxy-*allo* derivative (**8**) was readily formed by inversion of configuration at C-3. Similar treatment of **6** with sodium iodide also gave the 3-deoxy-3-iodo-*allo* derivative (**10**), together with a trace of 3-deoxy-3-iodo-*gluco* isomer (**11**). To examine the roles of the 2-*N*-trifluoroacetyl and the 3-*O*-trifluoromethylsulfonyl groups in these halogenations, the structurally related 2-*N*-acetyl-3-*O*-trifluoromethylsulfonyl (**3**) [prepared from the corresponding *N*-acetyl compound (**2**)] and the 2-*N*-trifluoroacetyl-3-*O*-methylsulfonyl compounds (**5**) were prepared, and they were subjected to reaction with lithium chloride. In this instance, however, no reaction was observed to occur (in the case of **5**) or several unidentified products were formed simultaneously (in the case of **3**). These unsuccessful reactions are understandable in that S_N2 reaction at C-3 is hindered[5] by the axial methoxyl group at C-1, and this clearly means that both *N*-trifluoroacetyl and *O*-trifluoromethylsulfonyl groups of **6** are essential for the displacement reactions at C-3.

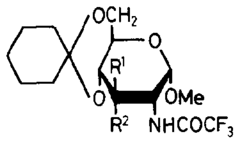
In a previous paper[4] we reported that, by similar treatment with lithium chloride, a 2-*N*-tosyl-3-*O*-tosyl derivative of methyl 2-amino-4,6-*O*-cyclohexylidene-2-deoxy-α-D-glucopyranoside gave the corresponding 3-chloro-3-deoxy-*gluco* derivative *via* the corresponding intermediate 3-chloro-3-deoxy-*allo* derivative. This ready substitution at C-3 was explained[4] on the basis of hydrogen bonding between the 2-N*H*-tosyl and the 1-*O*-Me groups; this bonding would decrease the negativity of the oxygen atom at the 1-methoxyl group, thus facilitating approach of the chloride ion from the α side to give the 3-chloro-3-deoxy-α-D-allopyranoside, with subsequent removal of the axial chloro atom by attack of another chloride ion from the β side to give the 3-chloro-3-deoxy-α-D-glucopyranoside.

In the present chlorination of **6**, however, reaction stopped at the stage of the 3-chloro-3-deoxy-*allo* derivative (**8**). Even after a prolonged reaction-period, no 3-chloro-3-deoxy-*gluco* derivative (**9**) was obtained, although the corresponding 3-

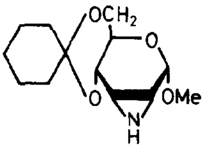


	R^1	R^2
1	H	H
2	$COCH_3$	H
3	$COCH_3$	SO_2CF_3
4	$COCF_3$	H
5	$COCF_3$	SO_2Me
6	$COCF_3$	SO_2CF_3
7	$COCF_3$	Bz





	R^1	R^2
8	H	Cl
9	Cl	H
10	H	I
11	I	H
12	H	H
13	H	OH
14	H	OSO_2CF_3
15	H	OBz



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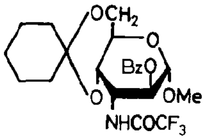

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deoxy-3-iodo-*gluco* derivative (**11**) was formed in low yield on iodination. This behavior may be explained on the basis of the assumption that hydrogen bonding between the 2-N*H*COCF$_3$ and the 1-*O*-Me groups is also present, but is weaker than that between the 2-N*H*-tosyl and 1-*O*-Me groups. As a chloride ion is a weaker leaving group than a trifluoromethylsulfonyloxy group, 1,3-diaxial electronic repulsion between the 1-methoxyl group (although the negativity is partly offset by hydrogen bonding) and the 3-chloro atom (the negativity of the chloro atom being increased when the system approaches the transition state for the expected reaction) should suppress further reaction. Treatment of **8** with tributylstannane according to Barton *et al.*[6] gave, as expected, the corresponding 3-deoxy derivative (**12**).

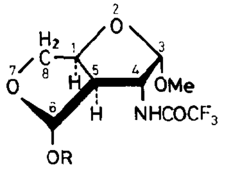
To substantiate the foregoing assumption, a similar SN2 reaction was examined with respect to an α-D-allopyranoside (**14**) carrying a trifluoromethylsulfonyloxy group at C-3. For that purpose, methyl 4,6-*O*-cyclohexylidene-2-deoxy-2-trifluoroacetamido-α-D-allopyranoside (**13**) (see later) was treated with trifluoromethanesulfonic anhydride to give the 3-trifluoromethanesulfonate (**14**). Treatment of **14** with lithium chloride in *N*,*N*-dimethylformamide readily gave the 3-chloro-3-deoxy-*gluco* derivative (**9**) in moderate yield. This result supports the foregoing assumption and, taken with the result of the chlorination of **6**, shows that chlorine substitution of the 3-*O*-trifluoromethylsulfonyl derivatives (**6** and **14**) occurs from either side, as long as their 2-amino groups are protected by an electron-withdrawing trifluoroacetyl group. The foregoing synthetic route will be advantageous for preparing a 2-amino-3-chloro-2,3-dideoxy-α-D-glucopyranoside derivative from the corresponding 2-amino-2-deoxy-α-D-glucopyranoside precursor.

Reaction with alkaline reagents. — The reaction of **6** with sodium benzoate in *N,N*-dimethylformamide was studied next. By this reaction, the expected 3-*O*-benzoyl-*allo* derivative (**15**) was formed in only low yield (4%), and, instead, the 2-*O*-benzoyl-3-deoxy-3-trifluoroacetamido-*altro* (**17**, 62%) and 3-*O*-benzoyl-2-deoxy-2-trifluoroacetamido-*gluco* derivatives (**7**, 17%) were formed, possibly by way of a 2,3-dideoxy-*N*-trifluoroacetyl-*allo*-epimine intermediate that undergoes ring opening *via* attack of the benzoate ion at C-2 (to give **17**) or C-3 (to give **7**). In order to ascertain the structure of **15**, it was prepared by an unambiguous route, namely, from **13** (see later) by benzoylation.

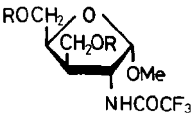
In contrast to the benzoylation of **6**, treatment of **6** with sodium methoxide in methanol gave mainly (49%) the 2,3-*allo* epimine (**16**) together with the 2-trifluoroacetamido-3-hydroxyl derivative (**13**, 25%) having the *allo* structure. As the latter compound (**13**) was not observed in the original reaction mixture, the compound may be produced during the purification step. The foregoing formation of an epimine may reasonably be explained on the basis of the absence of hydrogen bonding as a result of the alkaline environment, which would suppress the SN2 reaction at C-3 and facilitate the formation of the $^{-}NCOCF_3$ ion to give the epimine. The structures of **7, 13, 15, 16,** and **17** were confirmed by their ^{1}H-n.m.r. spectra (see Experimental section).

Solvolysis; formation of ring-contraction compounds. — Next, we intended to examine the effects of several solvents upon the substitution reactions at C-3 of **6**. As the first trial experiment, compound **6** was dissolved in hot methanol, and the formation of an unknown compound (**18**) was observed. Compound **18** was later found to be best formed when **6** was heated in methanol at 100° in a sealed tube for a short period. The structure of **18** was established as a bicyclic D-xylofuranoside formed by ring contraction; it is (1*S*,3*S*,4*R*,5*R*,6*R*)-3,6-dimethoxy-4-trifluoroacetamido-2,7-dioxabicyclo[3.3.0]octane (**18**).

The ^{1}H-n.m.r. spectrum of **18** showed the presence of two methoxyl groups, five methines, one methylene, and one NH proton. The sequence of H-3–H-4–H-5–H-1–H-8(8′) was readily determined by decoupling, initiating the irradiation



18 R = CH_3
19 R = H
20 R = Ac

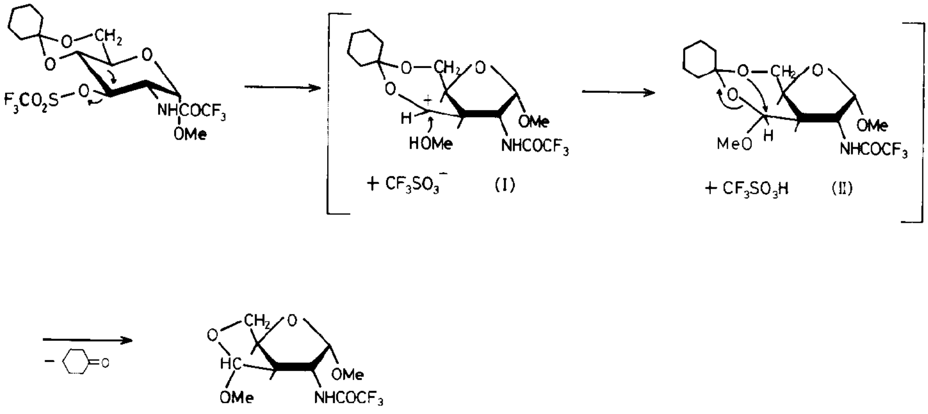


21 R = H
22 R = Ac

from the anomeric proton (H-3), which was readily distinguished from the other signals in the spectrum. The fact that the $NHCOCF_3$ group was attached to C-4 was proved by the presence of coupling between the N*H* and H-4. The signals of H-8,8′ appeared as a typical pattern for the AB part of an ABX system, suggesting that the hydrogen atoms at C-8 originated from H-6,6′ of the starting compound (**6**). It is also certain that H-3,-4 and possibly H-1 of **18** originate from H-1, -2, and -5 of **6**, respectively, and this indicates that one carbon is missing from the C-1–C-6 chain of the original compound (**6**). These results support the general structure of **18**, as proposed. That the newly formed oxolane ring has a conformation close to ^{0}E is presumed from the zero couplings of $J_{5,6}$ and $J_{1,8A}$ (see Experimental section).

As no trifluoromethylsulfonyl group was observed in **18**, and as, at the end of the reaction to form **18** from **6**, the medium became strongly acidic (suggesting the liberation of trifluoromethanesulfonic acid), compound **18** was presumed to be formed by departure of the trifluoromethylsulfonyloxy group at C-3 with concomitant attack of the C-4–C-5 bonding electrons on C-3 by a concerted process[7], as depicted here. The configuration at C-5 is, therefore, *R*; if the bonding electrons had attacked C-3 from the β side of **6** to give the *S* configuration at C-5, the resulting *trans*-1,5 product would not give a new five-membered ring readily. The proof for the furanoside structure of **18** was also confirmed, in the ^{1}H-n.m.r. spectrum, from the medium to small $^{3}J_{H,H}$ values for the ring protons.

The configuration at C-6 of **18** is next described. The carbonium ion intermediate (I) formed just after ring contraction will be attacked by methanol from the less-hindered α side to give an asymmetric center having the *R* configuration (as shown in II). This interpretation was supported by the zero coupling of $J_{5,6}$ in the ^{1}H-n.m.r. spectrum of **18**; if the methanol had attacked C-6 from the β side, the resulting product should show a $J_{5,6}$ value of at least 5 Hz.



The *R* configuration at C-6 of **18** is also reasonable from the point of view of optical rotation. In a furanoside, the most important contribution to the optical rotation is believed to be that by the anomeric center. If C-3 and C-6 are viewed from the opposite directions of the hydrogen atom attached to carbon, the directions of rotation of the sequence, ring O–OMe–C-4 (and C-5) are counter- and clock-wise, respectively; the opposite directions of rotation are expected by overall cancellation to give an optical rotation of almost zero for **18**. This assumption was proved by the experimental value ($[\alpha]_D$ 0°) of **18**. A ring-opened derivative (**21**) described later had $[\alpha]_D$ +79°, also supporting the foregoing conclusion.

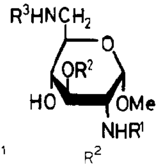
The structure of **18** was also confirmed by its ^{13}C-n.m.r. spectrum. Two resonances near δ 55 (other than those for the methoxyl carbon atoms) could be assigned, judging from the shift-values, to C-4 carrying a nitrogen, and the newly formed tertiary carbon (C-5). Two resonances near δ 105 were assignable to the anomeric carbon (C-3) and the newly formed acetal carbon (C-6). The presence of the trifluoroacetyl group was confirmed by the shift-values and the multiplicities of the trifluoromethyl (a quartet, $J_{C,F}$ = 288 Hz) and the carbonyl carbon atoms (a quartet, $J_{C,F}$ = 37 Hz).

There have been several reports dealing with ring contraction resulting from solvolysis of *O*-sulfonyl derivatives of sugar pyranosides. Austin *et al.*[8] obtained, from the solvolysis in hot water of the 3-*p*-nitrobenzenesulfonates of methyl α-D-gluco- and -mannopyranosides, the hemiacetals of methyl 3-deoxy-3-formyl-α-D-*xylo*- and -*lyxo*-furanosides, the former being identical with the nitrous acid deamination product[9] of 3-amino-3-deoxy-α-D-glucopyranoside. Stevens *et al.*[10] obtained, on refluxing methyl 6-deoxy-2,3-*O*-isopropylidene- 4-*O*-methylsulfonyl-α-D-mannopyranoside in *N,N*-dimethylformamide containing acetate ion, methyl 2,3-*O*-isopropylidene-D-talo- and L-allofuranosides. Similar ring-contraction compounds were also obtained by the reaction[7,11] of 6-deoxy-2,3-*O*-isopropylidene-4-*O*-methylsulfonyl-α-L-mannopyranoside with sodium azide in refluxing *N,N*-dimethylformamide.

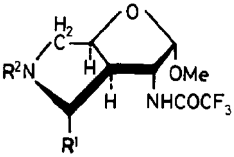
All of these ring-contraction compounds, including ours, were formed under circumstances in which the departing and the migrating groups were in an antiparallel, coplanar relationship[8]. The situation largely resembles that of the deamination process by nitrous acid[12].

In order to obtain the 6-hydroxyl derivative (**19**) of **18**, compound **18** was subjected to acidic hydrolysis, but selective removal of the 6-*O*-methyl group to give **19** did not occur. When, however, **6** was heated in methanol in the presence of cesium fluoride, compound **19** was obtained in moderate yield. The *J* values of **19** in the ^{1}H-n.m.r. spectrum showed good accordance with the respective *J* value of **18**, proving that the structure of **19** was also bicyclic, as in **18**. Acetylation of **19** gave the 6-acetate (**20**). Reduction of **19** with sodium borohydride gave a 3-*C*-hydroxymethyl-D-xylofuranoside (**21**) which, on acetylation, gave the diacetate (**22**).

Next, a similar solvolysis reaction of methyl 6-benzyloxycarbonylamino-2,6-dideoxy-2-trifluoroacetamido-3-*O*-trifluoromethylsulfonyl-α-D-glucopyranoside (**26**, which is structurally related to **18**), was examined. The compound was prepared from methyl 2,6-diamino-2,6-dideoxy-α-D-glucopyranoside[13] (**23**). Treatment of **23** with *N*-(benzyloxycarbonyloxy)succinimide[14] in *N,N*-dimethylformamide gave (fairly selectively) the corresponding 6-*N*-benzyloxycarbonyl deriva-



	R^1	R^2	R^3
23	H	H	H
24	H	H	CO_2CH_2Ph
25	$COCF_3$	H	CO_2CH_2Ph
26	$COCF_3$	SO_2CF_3	CO_2CH_2Ph



	R^1	R^2
27	OMe	CO_2CH_2Ph
28	H	H

tive (**24**). Treatment of **24** with ethyl trifluoroacetate[15] gave the 2-trifluoroacetamido derivative (**25**), which was then treated with trifluoromethanesulfonic anhydride. The desired 3-*O*-trifluoromethylsulfonyl derivative (**26**) was produced mainly, but, as it was too unstable for isolation, the product mixture was subjected to solvolysis without purification. By the solvolysis, (1*S*,3*S*,4*R*,5*R*,6*S*)-7-*N*-benzyloxycarbonyl-3,6-dimethoxy-4-trifluoroacetamido-7-aza-2-oxa-bicyclo-[3.3.0]octane (**27**) was obtained in good yield. The structure was determined by comparison of the ^{1}H-n.m.r. spectrum with that of **18** (see Experimental section) and by the mass spectrum, which showed a clear M$^+$ peak.

Catalytic reduction of **27** gave a bicyclic D-xylofuranoside derivative (**28**) formed by reductive cleavage of the methoxyl group at C-6 and the benzyloxycarbonyl group. Its structure was confirmed by the ^{1}H- and ^{13}C-n.m.r. spectra.

Through the foregoing studies, it was determined that compound (**6**) gives different kinds of products according to the reaction conditions, and this is presumably caused by the presence of the two, strongly electron-withdrawing, trifluoroacetyl and trifluoromethylsulfonyl groups.

EXPERIMENTAL

General methods. — Specific rotations were measured with a Perkin–Elmer Model 241 polarimeter. I.r. spectra were recorded, for potassium bromide pellets, with a JASCO A-202 grating spectrophotometer. ^{1}H- and ^{13}C-n.m.r. spectra were recorded in the F.t. mode with a Bruker WM-250 spectrometer operated at 250 and 62.9 MHz, respectively, and the shift values were both calculated from an internal reference of tetramethylsilane. Multiplicities of the ^{13}C spectra obtained by the off-resonance technique are given in parentheses. Thin-layer chromatography (t.l.c.) was performed on precoated Kieselgel 60, Merck, with sulfuric acid as the spray for visual detection. For column separation of the products, silica gel (Wakogel C-200) was used.

Methyl 2-acetamido-4,6-O-cyclohexylidene-2-deoxy-α-D-glucopyranoside (**2**). — A solution of compound[4] **1** (341 mg, as the base) and acetic anhydride (0.24 mL) in methanol (36 mL) was kept for 15 h at 27°. Evaporation with several additions of toluene gave a syrup that was precipitated from ethanol–hexane to give a solid, 347 mg (88%), $[\alpha]_D^{21}$ +58° (*c* 1, chloroform).

Anal. Calc. for $C_{15}H_{25}NO_6$: C, 57.13; H, 7.99; N, 4.44. Found: C, 57.35; H, 8.02; N, 4.23.

Methyl 2-acetamido-4,6-O-cyclohexylidene-2-deoxy-3-O-trifluoromethylsulfonyl-α-D-glucopyranoside (**3**). — Compound **2** was treated with trifluoromethanesulfonic anhydride in pyridine (−15°, 10 min → room temperature, 30 min). Conventional isolation of the product gave syrupy **3** in 97% yield, $[\alpha]_D^{21}$ +54° (*c* 1, chloroform); ^{1}H-n.m.r. ($CDCl_3$): δ 2.05 (s, 3 H, Ac), 3.39 (s, 3 H, OCH_3), 3.69 (dt, 1 H, H-5), 3.85 (t) and 3.90 (dd) (the AB part of an ABX system, H-6,6′), 3.89 (t, 1 H, H-4), 4.58 (dt, 1 H, H-2), 4.71 (d, 1 H, H-1), 4.84 (t, 1 H, H-3), and 5.90 (d,1 H, NH); $J_{1,2}$ 3.5, $J_{2,3} = J_{2,NH} = J_{3,4} = J_{4,5} = J_{5,6} = J_{6,6'} = \sim 10$, and $J_{5,6'}$ 6 Hz.

Anal. Calc. for $C_{16}H_{24}F_3NO_8S$: C, 42.95; H, 5.41; N, 3.13, S, 7.17. Found: C, 43.28; H, 5.58. N, 3.27; S, 6.94.

Methyl 4,6-O-cyclohexylidene-2-deoxy-2-trifluoroacetamido-α-D-glucopyranoside (**4**). — To an ice-cold mixture of compound[4] **1** (99.5 mg, as the base) and well-powdered sodium hydrogencarbonate (73 mg) in 1,4-dioxane (2 mL) was added trifluoroacetic anhydride (0.06 mL), and the mixture was stirred for 1.5 h at room temperature. The same amounts of trifluoroacetic anhydride and sodium hydrogencarbonate were added and the mixture was stirred for a further 1.5 h. Evaporation gave a residue that was extracted with chloroform; the organic solution was then washed with saturated aqueous sodium hydrogencarbonate, whereupon a byproduct (R_F 0.7 in t.l.c. with 2:1 benzene–ethyl acetate; *cf.* **4**: R_F 0.6) disappeared. Purification of the product by chromatography on a short column of silica gel with 20:1 chloroform–ethanol gave hygroscopic, solid **4**, 130 mg (97%), $[\alpha]_D^{22}$ +65° (*c* 1, chloroform); ν_{max}^{KBr} 1720 cm^{-1}; ^{1}H-n.m.r. ($CDCl_3$): δ 3.39 (s, 3 H, OCH_3), 4.17 (dt, 1 H, $J_{1,2}$ 3.5, $J_{2,3} = J_{2,NH} = 9.5$ Hz, dd on deuteration, H-2), and 4.75 (d, 1 H, H-1); ^{13}C-n.m.r. ($CDCl_3$): δ 22.52 (t), 22.79 (t), 25.57 (t), 27.80 (t), and 37.95 (t) (CH_2 of cyclohexylidene); 54.14 (d, C-2), 55.34 (q, OCH_3), 61.43 (t, C-6); 63.62 and 70.09 (d, each, C-4,5); 73.51 (d, C-3), 98.15 (d, C-1), 100.14 [s, $C(O)_2$ of cyclohexylidene], 115.79 (q, $^1J_{C,F}$ 288 Hz), CO*C*F$_3$), and 157.45 (q, $^2J_{C,F}$ 37 Hz, *C*OCF$_3$).

Anal. Calc. for $C_{15}H_{22}F_3NO_6$: C, 48.78; H, 6.00; N, 3.79; F, 15.43. Found: C, 48.38; H, 6.09; N, 3.49; F, 14.71.

Methyl 4,6-O-cyclohexylidene-2-deoxy-3-O-methylsulfonyl-2-trifluoroacetamido-α-D-glucopyranoside (**5**). — Compound **4** was treated with methanesulfonyl chloride in pyridine to give **5** as a thick syrup, yield 97%, $[\alpha]_D^{19}$ +50° (*c* 1, chloroform); ^{1}H-n.m.r. ($CDCl_3$): δ 3.10 (s, 3 H, SO_2CH_3), 3.45 (s, 3 H, OCH_3), 4.34 (dt, 1 H, H-2), 4.76 (t, 1 H, J ~10.5 Hz, H-3), and 4.88 (d, 1 H, $J_{1,2}$ 3.5 Hz, H-1).

Anal. Calc for $C_{16}H_{24}F_3NO_8S$: C, 42.95; H, 5.41; N, 3.13; S, 7.17. Found: C, 43.32; H, 5.42; N, 3.12; S, 6.97.

Methyl 4,6-O-cyclohexylidene-2-deoxy-2-trifluoroacetamido-3-O-trifluoromethylsulfonyl-α-D-glucopyranoside (**6**). — To a cold (−20°) solution of **4** (400 mg) in pyridine (8.0 mL), was added trifluoromethanesulfonic anhydride (0.29 mL) dropwise, and the pale-brown solution was kept for 15 h at −20°, and then for 1.5 h at room temperature. The solution was cooled to −20°, water (0.2 mL) was added, and the solution was kept for 2 min in the cold. The orange-colored solution was evaporated at room temperature to a syrup. A solution of the syrup in chloroform was washed with cold, 3% aqueous potassium hydrogensulfate, cold aqueous sodium hydrogencarbonate (saturated), and cold water, dried (anhydrous sodium sulfate), and evaporated to give a yellow solid (532 mg, 98%). The solid was unstable and gradually changed on being kept [a compound (t.l.c.: R_F 0.24 with 60:1 chloroform–ethanol) was gradually formed; compare **6**: R_F 0.29] and could not be purified by column chromatography on silica gel; ^{1}H-n.m.r. ($CDCl_3$): δ 3.44 (s, 3 H, OCH_3), 4.53 (dt, 1 H, H-2), 4.79 (d, 1 H, H-1), 4.90 (t, 1 H, H-3), and 6.61 (d, 1 H, NH); $J_{1,2}$ 3.5, $J_{2,NH} = J_{2,3} = J_{3,4} = 10$ Hz; ^{13}C-n.m.r. ($CDCl_3$): δ 22.14, 22.28, 25.46, 27.71, and 37.73 (each t, cyclohexylidene); 52.12 (d, C-2), 55.58 (q, OCH_3), 61.29 (t, C-6); 64.18 and 70.87 (each d, C-4,5), 83.83 (d, C-3), 98.61 (d, C-1), 100.86 [s, $C(O)_2$ of cyclohexylidene], 115.54 (q, $^1J_{C,F}$ 288 Hz, $COCF_3$), 118.47 (q, $^1J_{C,F}$ 319 Hz, SO_2CF_3), and 157.26 (q, $^2J_{C,F}$ 38 Hz, $COCF_3$).

*Methyl 3-chloro-4,6-O-cyclohexylidene-2,3-dideoxy-2-trifluoroacetamido-α-*D*-allopyranoside* (**8**). — A mixture of **6** (250 mg) and anhydrous lithium chloride (210 mg, 10 mol eq. for **6**) in dry *N,N*-dimethylformamide (5.8 mL) was heated for 20 min at 100°. T.l.c. with 60:1 chloroform–ethanol showed spots having R_F 0.42 (**8**), 0.25, and 0.15 (**4**, slight). Addition of triethylamine (0.05 mL) followed by evaporation gave a residue that was vigorously shaken with chloroform and water. The organic layer was evaporated, and the residue was dissolved in benzene. The solution was washed with water to remove the remaining *N,N*-dimethylformamide. The crude product obtained after evaporation was chromatographed on a column of silica gel with 20:1 benzene–ethyl acetate to give **8** as a solid, 173 mg (89%), $[\alpha]_D^{20}$ +56° (*c* 1, chloroform); ν_{max}^{KBr} 1710, 1535 cm^{-1}; ^{1}H-n.m.r. ($CDCl_3$): δ 3.41 (s, 3 H, OCH_3), 3.80 (t, 1 H, H-6), 3.94 (dd, 1 H, H-6′), 3.945 (dd, 1 H, H-4), 4.08 (dt, 1 H, H-5), 4.49 (t, 1 H, H-3), 4.51 (dt, 1 H; t on deuteration; H-2), 4.69 (d, 1 H, H-1), and 6.98 (br d, 1 H, NH); $J_{1,2} = J_{2,3}$ 4, $J_{2,NH} = {\sim}9$, $J_{3,4}$ 3.5, $J_{4,5}$ 9, $J_{5,6} = J_{6,6'} = {\sim}10$, and $J_{5,6'}$ 5.5 Hz; ^{13}C-n.m.r. ($CDCl_3$): δ 22.70 (2 C), 25.60, 28.06, 37.69 (each t, CH_2 of cyclohexylidene), 49.51 (d, C-2), 56.23 (q, OCH_3), 58.01 (d, C-3), 58.77 (d, C-5), 61.25 (t, C-6), 68.90 (d, C-4), 97.34 (d, C-1), 100.07 [s, $C(O)_2$ of cyclohexylidene], 115.70 (q, $COCF_3$), and 156.78 (q, $COCF_3$); $^1J_{C,F}$ 288, $^2J_{C,F}$ 38 Hz.

Anal. Calc. for $C_{15}H_{21}ClF_3NO_5$: C, 46.46; H, 5.46; Cl, 9.14; F, 14.70; N, 3.61. Found: C, 46.36; H, 5.17; Cl, 9.79; F, 14.14; N, 3.67.

*Methyl 4,6-O-cyclohexylidene-2,3-dideoxy-3-iodo-2-trifluoroacetamido-α-*D*-allopyranoside* (**10**) *and -glucopyranoside* (**11**). — A mixture of **6** (532 mg) and sodium iodide (1.42 g, 9 mol eq. for **6**) in dry *N,N*-dimethylformamide (10.6 mL) was heated for 20 min at 80°. T.l.c. with 6:1 benzene–ethyl acetate showed spots of R_F 0.6 (**10**), 0.5 (very slight, **11**), 0.45 (very slight, an impurity included in the starting material), 0.1, and 0. After addition of triethylamine (0.1 mL) and chloroform (20 mL), the mixture was vigorously shaken, filtered from the precipitate, and the filtrate and combined chloroform washings were evaporated. A solution of the residue in chloroform was washed with 10% aqueous sodium thiosulfate solution, and water, dried, and concentrated. The residual syrup was chromatographed on a column of silica gel with 30:1 benzene–ethyl acetate to give solids of **10**, 323 mg (64%), and **11**, 5 mg (1%).

Compound **10** had $[\alpha]_D^{20}$ +46° (*c* 1, chloroform); ^{1}H-n.m.r. (CDCl$_3$): δ 3.01 (dd, 1 H, H-4), 3.40 (s, 3 H, OCH$_3$), 3.79–4.0 (m, 3 H, H-5,6,6'), 4.12 (apparently quintet, 1 H, H-2), 4.66 (t, 1 H, H-3), 4.73 (d, 1 H, H-1), and 6.90 (slightly br d, 1 H, NH); $J_{1,2} = J_{2,3} = J_{3,4}$ 4, $J_{2,NH}$ 8, and $J_{4,5}$ 8 Hz.

Compound **11** had ^{1}H-n.m.r. (CDCl$_3$): δ 3.40 (s, 3 H, OCH$_3$), 3.6–3.83 (m, 4 H, H-4,5,6,6'), 4.05 (dd, 1 H, H-3), 4.52 (dt, 1 H, H-2), 4.61 (d, 1 H, H-1), and 6.48 (slightly br d. 1 H, NH); $J_{1,2}$ 3.5, $J_{2,3} = J_{2,NH}$ = ~10, and $J_{3,4}$ 11.5 Hz.

*Methyl 4,6-O-cyclohexylidene-2,3-dideoxy-2-trifluoroacetamido-α-*D-ribo-*hexopyranoside* (**12**). — To a solution of **8** (400 mg) in dry 1,4-dioxane (8.0 mL) were added tributylstannane (0.82 mL) and α,α'-azobisisobutanonitrile (3.6 mg), and the solution was heated for 1 h at 80° under nitrogen. T.l.c. (6:1 benzene–ethyl acetate) showed a single spot (R_F 0.45; compare **10**: R_F 0.05). Addition of triethylamine (0.1 mL) followed by evaporation gave a syrup that was purified by column chromatography on silica gel (hexane → benzene → 25:1 benzene–ethyl acetate) to give a syrup, 355 mg (97%), $[\alpha]_D^{21}$ +97° (*c* 1, methanol); ^{1}H-n.m.r. (CDCl$_3$): δ 1.06–1.51 (~5 H), 1.51–1.53 (3 H), and 1.85–2.0 (2 H) (cyclohexylidene); 1.73 (q, 1 H, H-3ax), 2.10 (dt, 1 H, H-3eq), 3.42 (s, 3 H, OCH$_3$), 3.59 (dt, 1 H, H-5), 3.72 (ddd, 1 H, H-4), 3.75 (t, 1 H, H-6), 3.83 (dd, 1 H, H-6'), 4.24 (apparent octet, 1 H, H-2), 4.61 (d, 1 H, H-1), and 6.52 (sl. br d, 1 H, NH); $J_{1,2}$ 4, $J_{2,3e} = J_{3e,4}$ 4, $J_{2,3a} = J_{3e,3a} = J_{3a,4}$ 12, $J_{2,NH}$ ~10, $J_{4,5} = J_{5,6} = J_{6,6'}$ 10, and $J_{5,6'}$ 5.5 Hz. Irradiation of H-2 collapsed the signals of H-1, -3ax, -3eq, and N*H* to a singlet, a triplet, doublet of doublets, and a singlet, respectively.

Anal. Calc. for $C_{15}H_{22}F_3NO_5$: C, 50.99; H, 6.28; N, 3.96. Found: C, 50.61; H, 6.56; N, 4.26.

*Methyl 4,6-O-cyclohexylidene-2-deoxy-2-trifluoroacetamido-α-*D*-allopyranoside* (**13**) *and methyl 4,6-O-cyclohexylidene-2,3-dideoxy-2,3-epimino-α-*D*-allopyranoside* (**16**). — To a solution of **6** (590 mg) in dry methanol (10 mL) was added 0.8M sodium methoxide in methanol (1.8 mL), and the solution was kept for 1 h at room temperature. T.l.c. with 40:1 chloroform–ethanol showed spots of R_F 0.57 (slight, **6**), 0.44, 0.25 (**4**), and 0.18 (major, **16**). After addition of 2M aqueous hydrochloric acid to pH ~1, the solution was kept for 3 min at room temperature and then made neutral with triethylamine. Evaporation gave a syrup that was extracted with chloroform. The organic solution was washed with water, dried, and evaporated. T.l.c. of the resulting syrup showed a new spot at R_F 0.33 (**13**; the spot of R_F 0.44 disappeared) in addition to the spots of **4** and **16**. Column chromatography on silica gel of the syrup with 50:1 chloroform–methanol gave **16** as a solid, 133 mg (44%) and a mixture of **4** and **13**. Separation of the mixture by column chromatography on silica gel (10:1 → 5:1 benzene–ethyl acetate) gave **13**, 111 mg (25%), and **4**, 41 mg (9%) as solids.

Compound **13** had $[\alpha]_D^{22}$ +57° (*c* 1, chloroform); ^{1}H-n.m.r. ($CDCl_3$): δ 2.61 (sl. br d, 1 H, 3-OH), 3.43 (s, 3 H, OCH_3), 3.72 (dd, 1 H, H-4), 4.11 (br, 1 H, H-3), 4.24 (ddd, 1 H, H-2), 4.76 (d, 1 H, H-1), and 7.06 (br d, 1 H, NH); $J_{1,2}$ 4, $J_{2,3}$ ~4, $J_{2,NH}$ ~9, $J_{3,4}$ 3, $J_{3,OH}$ ~4, and $J_{4,5}$ 10 Hz.

Anal. Calc. for $C_{15}H_{22}F_3NO_6$: C, 48.78; H, 6.00; F, 15.43; N, 3.79. Found: C, 48.84; H, 5.98; F, 16.10; N, 3.73.

Compound **16** had $[\alpha]_D^{23}$ +121° (*c* 1, chloroform); ^{1}H-n.m.r. ($CDCl_3$): δ 0.82 (br, 1 H, NH), 1.3–2.1 (10 Hz), 2.58 (br, width at half-height 13 Hz, 1 H, H-3), 2.68 (br, width at half-height 14 Hz, 1 H, H-2), 3.42 (s, 3 H, OCH_3), 4.02 (br, 1 H, H-4), and 4.87 (d, 1 H, $J_{1,2}$ 4 Hz, H-1). Irradiation of H-2 collapsed the doublet of H-1 to a singlet. The ^{13}C-n.m.r. spectrum ($CDCl_3$) gave: δ 22.72, 22.85, 25.74, 28.06, and 38.03 (each t, cyclohexylidene); 30.53 and 32.88 (each d, C-2,3), 55.35 (q, OCH_3), 60.60 (d, C-4 or 5), 61.96 (t, C-6), 69.29 (d, C-5 or 4), 95.89 (d, C-1), and 100.03 [s, $C(O)_2$].

Anal. Calc. for $C_{13}H_{21}NO_4$: C, 61.16; H, 8.29; N, 5.49. Found: C, 61.29; H, 8.28; N, 5.72.

*Methyl 3-chloro-4,6-O-cyclohexylidene-2,3-dideoxy-2-trifluoroacetamido-α-*D*-glucopyranoside* (**9**) *via methyl 4,6-O-cyclohexylidene-2-deoxy-2-trifluoroacetamido-3-O-trifluoromethylsulfonyl-α-*D*-allopyranoside* (**14**). — Compound **13** (50 mg) was treated with trifluoromethanesulfonic anhydride as described for **6** to give syrupy **14** almost quantitatively; ^{1}H-n.m.r. ($CDCl_3$): δ 4.40 (apparent quintet, H-2), 4.73 (d, H-1), 5.23 (t, H-3), and 6.80 (d, NH); $J_{1,2}$ 4.5, $J_{2,3}$ = $J_{3,4}$ ~3, and $J_{2,NH}$ ~8 Hz.

The syrup (60 mg) was then treated with lithium chloride in *N*,*N*-dimethylformamide as described for **8** (100°, 20 min) to give **9** as a solid, 20 mg (44%), $[\alpha]_D^{22}$ +28° (*c* 1, chloroform); ^{1}H-n.m.r. ($CDCl_3$): δ 3.41 (s, 3 H, OCH_3), 3.97 (t, 1 H, H-3), 4.40 (dt, 1 H, H-2), 4.71 (d, 1 H, H-1), and 6.50 (slightly br d, 1 H, NH); $J_{1,2}$ 3.5, $J_{2,3}$ = $J_{2,NH}$ = $J_{3,4}$ 10 Hz.

Anal. Calc. for $C_{15}H_{21}ClF_3NO_5$: C, 46.46; H, 5.46; Cl, 9.14; F, 14.70; N, 3.61; Found: C, 46.74; H, 5.92; Cl, 9.00; F, 14.87; N, 3.48.

*Methyl 3-O-benzoyl-4,6-O-cyclohexylidene-2-deoxy-2-trifluoroacetamido-α-*D*-allopyranoside* (**15**). — A mixture of **13** (124 mg) and benzoic anhydride (230 mg) in dry pyridine (2.5 mL) was heated for 30 h at 100°. Conventional processing gave a crude mixture that was chromatographed on a column of silica gel with 20:1 benzene–ethyl acetate to give **15**, 121 mg (75%) and **13**, 27.4 mg (22%), both recovered as solids.

Compound **15** had $[\alpha]_D^{22}$ +3° (*c* 1, methanol); ^{1}H-n.m.r. ($CDCl_3$): δ 3.48 (s, 3 H, OCH_3), 3.82 (t, 1 H, H-6), 3.90 (dd, 1 H, H-4), 3.95 (dd, 1 H, H-6′), 4.19 (dt, 1 H, H-5), 4.47 (apparent quintet, 1 H, H-2), 4.76 (d, 1 H, H-1), 5.74 (t, 1 H, H-3), and 6.70 (d, 1 H, NH); $J_{1,2}$ 4.5, $J_{2,NH}$ 9, $J_{2,3}$ = $J_{3,4}$ ~3, $J_{4,5}$ 10, $J_{5,6}$ = $J_{6,6'}$ 10.5, and $J_{5,6'}$ 5.5 Hz.

Anal. Calc. for $C_{22}H_{26}F_3NO_7$: C, 55.81, H, 5.54; F, 12.04; N, 2.96. Found: C, 56.09; H, 5.78; F, 12.04; N, 3.22.

*Methyl 3-O-benzoyl-4,6-O-cyclohexylidene-2-deoxy-2-trifluoroacetamido-α-*D*-glucopyranoside* (**7**) *and methyl 2-O-benzoyl-4,6-O-cyclohexylidene-3-deoxy-3-trifluoroacetamido-α-*D*-altropyranoside* (**17**). — A mixture of **6** (345 mg) and sodium benzoate (119 mg) in *N,N*-dimethylformamide (7 mL) was heated for 3 h at 60°. Additional sodium benzoate (50 mg) was added and the reaction was continued for 1 h. T.l.c. with 10:1 benzene–ethyl acetate showed spots of R_F 0.6 (major, **17**), 0.45 (slight, **15**), 0.4 (**7**), 0.15 and 0. Evaporation gave a residue that was extracted with chloroform. The chloroform-soluble products were column chromatographed (silica gel) with 20:1 → 10:1 benzene–ethyl acetate to give solids of **17**, 204 mg (62%), **15**, 12 mg (4%), and **7**, 55 mg (17%).

Compound **7** had $[\alpha]_D^{22}$ +43° (*c* 1, methanol); ^{1}H-n.m.r. ($CDCl_3$): δ 3.42 (s, 3 H, OCH_3), 3.8–4.0 (m, 4 H, H-4,5,6,6′), 4.43 (dt, 1 H, H-2), 4.82 (d, 1 H, H-1), 5.47 (dd, 1 H, H-3), and 6.98 (d, 1 H, NH); $J_{1,2}$ 3.5, $J_{2,3}$ 10, $J_{2,NH}$ 9, and $J_{3,4}$ 9 Hz.

Anal. Calc. for $C_{22}H_{26}F_3NO_7$: C, 55.81; H, 5.54; F, 12.04; N, 2.96. Found: C, 56.26; H, 5.76; F, 11.34; N, 2.69.

Compound **17** had $[\alpha]_D^{21}$ −15° (*c* 1, methanol); ^{1}H-n.m.r. ($CDCl_3$): δ 3.50 (s, 3 H, OCH_3), 3.78–3.96 (m, 3 H, H-5,6,6′), 4.22 (dd, 1 H, H-4), 4.64 (slightly br dt, 1 H, H-3), 4.82 (apparent t, 1 H, H-1), and 5.16 (dd, 1 H, H-2); $J_{1,2}$ ~1.7, $J_{1,3}$ ~1, $J_{2,3}$ 3, $J_{3,NH}$ 9, $J_{3,4}$ ~4, and $J_{4,5}$ ~9 Hz.

Anal. Calc. for $C_{22}H_{26}F_3NO_7$: C, 55.81; H, 5.54; F, 12.04; N, 2.96. Found: C, 56.08; H, 5.79; F, 12.13; N, 2.81.

(1S,3S,4R,5R,6R)-3,6-Dimethoxy-4-trifluoroacetamido-2,7-dioxabicyclo-[3.3.0]octane (**18**). — A solution of **6** (303 mg) in dry methanol (6.0 mL) was heated in a sealed tube for 6 min at 100°. T.l.c. with 2:1 benzene–ethyl acetate of the resulting acidic solution showed spots at R_F 0.65 (**18**) and 0, no starting material (R_F 0.8) being observed. Isolation of the product as described for **19** gave, after column chromatography on silica gel with 7:1 benzene–ethyl acetate, **18** as a solid, 124 mg (72%), $[\alpha]_D^{23}$ 0° (*c* 1, chloroform); ^{1}H-n.m.r. ($CDCl_3$): δ 2.62 (t, 1 H, H-5); 3.32 and 3.42 (each s. 3 H, two OCH_3); 3.86 (dd, 1 H, H-8B), 3.95 (d, 1 H, H-8A), 4.22 (dt, 1 H, H-4), 4.84 (dd, 1 H, H-1), 4.95 (d, 1 H, H-3), 5.25 (s, 1 H, H-6), and 6.85 (br, 1 H, NH); $J_{1,5} = J_{4,5}$ 7, $J_{3,4}$ 4.5, $J_{5,6}$ 0, $J_{1,8A}$ 0, $J_{1,8B}$ 4, $J_{8A,8B}$ 10.5, and $J_{4,NH}$ ~7 Hz; ^{13}C-n.m.r. ($CDCl_3$): δ 54.56 and 54.66 (each q, two OCH_3); 55.85 and 56.01 (each d, C-4 and 5), 70.67 (t, C-8), 82.14 (d, C-1), 103.04 (d, C-3), 108.11 (d, C-6), 115.75 (q, $^1J_{C,F}$ 288 Hz, $COCF_3$), 157.13 (q, $^2J_{C,F}$ 37 Hz, $COCF_3$); the chemical shifts of C-3 and -6 were determined by selective proton irradiations at H-3, and -6, respectively.

Anal. Calc. for $C_{10}H_{14}F_3NO_5$: C, 42.11; H, 4.95; F, 19.98; N, 4.91. Found: C, 42.17; H, 4.95; F, 20.33; N, 4.81.

(1S,3S,4R,5R,6R)-6-Hydroxy-3-methoxy-4-trifluoroacetamido-2,7-dioxabicyclo[3.3.0]octane (**19**). — To a solution of **6** (2.58 g) in commercial methanol (52 mL) was added dry cesium fluoride (720 mg), and the solution was heated for 40

h at 50°. T.l.c. with 40:1 chloroform–ethanol showed a major spot at R_F 0.22 (**19**) and trace spots (R_F 0.38, 0.28, 0.26, 0.12); no starting material (R_F 0.41) was observed. After addition of triethylamine (0.5 mL), the solution was evaporated, and the residue extracted with chloroform. The chloroform-soluble products were subjected to column chromatography with 3:1 benzene–ethyl acetate to give **19** as a solid, 865 mg (62%), $[\alpha]_D^{23}$ +31° (*c* 1, chloroform); ν_{max}^{KBr} 1710, 1560, 1190 cm^{-1}; ^{1}H-n.m.r. ($CDCl_3$): δ 2.60 (d, 1 H, OH), 2.68 (t, 1 H, H-5), 3.43 (s, 3 H, OCH_3), 4.00 (d, 1 H, H-8A), 4.10 (dd, H-8B), 4.22 (dt, 1 H, H-4), 4.90 (dd, 1 H, H-1), 4.96 (d, 1 H, H-3), 5.80 (d, 1 H, H-6), and 6.88 (br, 1 H, NH); $J_{1,5} = J_{4,5}$ 7, $J_{3,4}$ 4.5, $J_{5,6}$ 0, $J_{6,OH}$ 2, $J_{1,8A}$ 0, $J_{1,8A}$ 4, $J_{8A,8B}$ 10.5, and $J_{4,NH}$ ~7 Hz; ^{13}C-n.m.r. ($CDCl_3$): δ 54.67 (q, OCH_3), 56.11 and 56.47 (each d, C-4 and 5), 71.07 (t, C-8), 82.17 (d, C-1), 101.97 (d, C-6), 103.04 (d, C-3); the chemical shifts of C-3 and -6 were determined by selective proton irradiations at H-3 and -6, respectively.

Anal. Calc. for $C_9H_{12}F_3NO_5$: C, 39.86; H, 4.46; F, 21.02; N, 5.16. Found: C, 39.98; H, 4.63; F, 20.98; N, 5.27.

*(1S,3S,4*R*,5*R*,6S)-6-Acetoxy-3-methoxy-4-trifluoroacetamido-2,7-dioxabicyclo[3.3.0]octane* (**20**). — Compound **19** (140 mg) was treated conventionally with acetic anhydride in pyridine. The resulting solid (161 mg, 100%) was recrystallized from benzene–hexane to give needles, m.p. 130.5–131.5°, $[\alpha]_D^{22}$ −3° (*c* 1, chloroform); ν_{max}^{KBr} 1730, 1705, 1560, 1185, 1160 cm^{-1}; ^{1}H-n.m.r. ($CDCl_3$): δ 2.05 (s, 3 H, Ac), 2.80 (t, 1 H, *J* 7 Hz, H-5), 3.48 (s, 3 H, OCH_3), 4.30 (dt, 1 H, *J* 4.5, 7 and 7 Hz, H-4), 4.92 (dd, 1 H, H-1), and 5.03 (d, 1 H, $J_{3,4}$ 4.5 Hz, H-3).

Anal. Calc. for $C_{11}H_{14}F_3NO_6$: C, 42.18; H, 4.51; F, 18.20; N, 4.47. Found: C, 42.22; H, 4.64; F, 18.66; N, 4.49.

*Methyl 2,3-dideoxy-3-*C*-hydroxymethyl-2-trifluoroacetamido-α-*D*-xylofuranoside* (**21**). — To an ice-cold solution of **19** (37 mg) in methanol (0.8 mL) was added sodium borohydride (4 mg), and the solution was kept for 30 min at room temperature. After addition of Dowex 50 W X2 (H^+ form) resin followed by filtration, the organic solution was concentrated, and the methanol solution of the residue was repeatedly evaporated with additions of methanol to remove boric acid. The residue was further purified by column chromatography on silica gel with 1:1 benzene–ethyl acetate to give a solid, 34 mg (91%); recrystallization from benzene–hexane gave granular crystals, m.p. 80.5–81°, $[\alpha]_D^{22}$ +79° (*c* 1, chloroform); ^{1}H-n.m.r. ($CDCl_3$-D_2O): δ 2.48 (dddd, 1 H, H-3), 3.47 (s, 3 H, OCH_3), 3.76 (d, 2 H, H-5,5′), *ABX* centered at 3.84 (2 H, H-3a,3a′), 4.28 (dt, 1 H, H-4), 4.50 (dd, 1 H, H-2), and 5.04 (d, 1 H, H-1); $J_{1,2}$ 5, $J_{2,3}$ 10.5, $J_{3,4}$ 9, $J_{4,5} = J_{4,5'}$ 3, $J_{3,3a}$ 5, $J_{3,3a'}$ 3, and $J_{3a,3a'}$ 13 Hz.

Anal. Calc. for $C_9H_{14}F_3NO_5$: C, 39.57; H, 5.17; F, 20.86; N, 5.13. Found: C, 39.70; H, 5.37; F, 21.36; N, 5.22;

*Methyl 3-*C*-acetoxymethyl-5-*O*-acetyl-2,3-dideoxy-2-trifluoroacetamido-α-*D*-xylofuranoside* (**22**). — Compound **21** (21.6 mg) was acetylated with acetic anhydride in pyridine to give a syrup (26.3 mg, 93%), $[\alpha]_D^{22}$ +85° (*c* 1, chloroform); ^{1}H-n.m.r. ($CDCl_3$): δ 2.04 and 2.12 (each s, 3 H, two Ac), 2.73 (m, 1 H, H-3), 3.45

(s, 3 H, OCH_3), 4.05 (dd, 1 H, H-5), *ABX* centered at 4.25 (2 H, H-3a,3a′), 4.37 (dd, 1 H, H-5′), ~4.47 (m, 1 H, H-4), 4.48 (dt, 1 H, H-2), 4.96 (d, 1 H, H-1), and 6.79 (d, 1 H, NH); $J_{1,2}$ 5, $J_{2,3} = J_{2,NH}$ 8.5, $J_{3,4}$ ~8, $J_{3,3a} = J_{3,3a'}$ 7, $J_{3a,3a'}$ 11.5, $J_{4,5}$ 5, $J_{4,5'}$ 4, and $J_{5,5}$ 12 Hz.

Anal. Calc. for $C_{13}H_{18}F_3NO_7$: C, 43.70; H, 5.08; F, 15.95; N, 3.92. Found: C, 43.42; H, 5.03; F, 16.14; N, 3.79.

*Methyl 2-amino-6-benzyloxycarbonylamino-2,6-dideoxy-α-*D*-glucopyranoside* (**24**). — To a solution of **23** (753 mg as the base) in aqueous *N,N*-dimethylformamide (1:1, 17 mL) was added a solution of *N*-(benzyloxycarbonyloxy)succinimide[14] (983 mg) in *N,N*-dimethylformamide (9 mL) gradually (~1 h) at 0 to 5°, and the solution was kept at that temperature for 1 h. T.l.c. with 5:7:5 chloroform–methanol–20% acetic acid (lower layer) showed spots at R_F 0.9 [slight, bis(benzyloxycarbonyl) isomer], 0.4 (major, **24**), 0.15 (slight, **23**), and several other trace spots. The crude mixture obtained by conventional processing was then chromatographed on a column of Dowex 50W X2 resin (NH_4^+ form) with 0 → 0.5M aqueous ammonia to give **24** as a solid, 810 mg (62% as the 0.25 hydrate), $[\alpha]_D^{21}$ +93° (*c* 1, methanol); ^{1}H-n.m.r. (10:1 pyridine-d_5–D_2O): δ 2.99 (dd, 1 H, H-2), 3.28 (s, 3 H, OCH_3), 3.96 (t, 1 H, H-3), and 5.00 (d, 1 H, H-1); $J_{1,2}$ 3.5, $J_{2,3}$ 10, and $J_{3,4}$ 9 Hz.

Anal. Calc. for $C_{15}H_{22}N_2O_6 \cdot 0.25\ H_2O$: C, 54.45; H, 6.85; N, 8.47. Found: C, 54.54; H, 6.66; N, 8.73.

*Methyl 6-benzyloxycarbonylamino-2,6-dideoxy-2-trifluoroacetamido-α-*D*-glucopyranoside* (**25**). — To a solution of **24** (744 mg) in pyridine (16 mL) was added ethyl trifluoroacetate (0.8 mL) and the solution was kept for 1 h at room temperature. The syrup obtained by evaporation was chromatographed (silica gel) with 20:1 chloroform–ethanol to give **25** as a solid, 728 mg (75%), $[\alpha]_D^{22}$ +93° (*c* 1, methanol); ^{1}H-n.m.r. (10:1 pyridine-d_5–D_2O): δ 3.24 (s, 3 H, OCH_3), 3.73 (dd, 1 H, H-6), 3.90 (dd, 1 H, H-4), 4.13 (ddd, 1 H, H-5), 4.27 (dd, 1 H, H-6′), 4.50 (dd, 1 H, H-3), 4.68 (dd, 1 H, H-2), and 5.11 (d, 1 H, H-1); $J_{1,2}$ 3.5, $J_{2,3}$ 10.5, $J_{3,4}$ 8.5, $J_{4,5}$ 9.5, $J_{5,6}$ 7, $J_{5,6'}$ 2.5, and $J_{6,6'}$ 13.5 Hz.

Anal. Calc. for $C_{17}H_{21}F_3N_2O_7 \cdot 0.5\ H_2O$: C, 47.33; H, 5.14; F, 13.21; N, 6.49. Found: C, 47.51; H, 5.14: F, 13.35; N, 6.72.

*(1*S*,3*S*,4*R*,5*R*,6*S*)-7-*N*-Benzyloxycarbonyl-3,6-dimethoxy-4-trifluoroacetamido-7-aza-2-oxabicyclo[3.3.0]octane* (**27**). — To a cold (−20°) solution of **25** (700 mg) in pyridine (14 mL) was added trifluoromethanesulfonic anhydride (0.56 mL), and the solution was kept for 10 min at that temperature and then for 30 min at 0°. Processing as described for **6** gave an unstable solid containing **26**, 758 mg. T.l.c. with 20:1 chloroform–ethanol showed spots at R_F 0.36 (slight, di-*O*-sulfonyl isomer?), 0.33 (major, **26**), 0.3 (slight 4-*O*-sulfonyl isomer?), 0.13 (trace, **25**), 0.05 (trace) and 0; ^{1}H-n.m.r. of the mixture (5:1 pyridine-d_5–D_2O) (only major signals are reported): δ 3.20 (s, OCH_3), 3.94 (t, H-4), 4.86 (dd, H-2), 4.98 (d, H-1), and 5.55 (dd, H-3); $J_{1,2}$ 3.5, $J_{2,3}$ 10.5, $J_{3,4} = J_{4,5}$ 8.5 Hz.

A solution of the product mixture (700 mg) in dry methanol (14 mL) was heated in a sealed tube for 25 min at 100°. T.l.c. with 20:1 chloroform–ethanol of the acidic solution showed spots at R_F 0.43 (major, **27**), 0.32 (slight, **26**), 0.05, and 0. Evaporation gave a syrup that was extracted with 6:1 benzene–ethyl acetate. The extracted products were chromatographed on a column of silica gel with 6:1 benzene-ethyl acetate to give **27** as a syrup, 220 mg (34% based on **25**), $[\alpha]_D^{20}$ +79° (c 1, chloroform); m/z 418 (M^+); ^{1}H-n.m.r. (CDCl$_3$–D$_2$O at 20°) (the data in brackets are those at 50°): δ 2.65 (narrow m, 1 H, H-5) [sharp t]; 3.20 and 3.36 (each s, the intensity ratio being ~4:3, 3 H in total, 6-OCH$_3$) [each br s, the height being 1/5 of that at 20°], 3.42 (s, 3 H, 3-OCH$_3$) [unchanged], 3.47 (m, 1 H, H-8A) [slightly br dd], 3.90 (apparent t, 1 H, H-8B) [br d], 4.12 and 4.18 (each dd, the intensity ratio being ~4:3, 1 H in total, H-4; the pattern was complex when measured in near CDCl$_3$) [br s], 4.81 (dd, 1 H, H-1) [unchanged], 4.92 (deformed t, 1 H, H-3) [sharp d]; AB q centered at 5.21 (~1.2 H, $J_{A,B}$ 12 Hz) and two s at 5.15 and 5.16 (~0.8 H in total) (CO$_2$CH_2Ph) [deformed s centered at 5.18]; 5.56 and 5.62 (each s, the intensity ratio ~4:3, 1 H in total, H-6) [5.57, br s]; $J_{1,5}$ = $J_{4,5}$ 7, $J_{3,4}$ 4.5, $J_{5,6}$ 0, $J_{1,8A}$ 5, $J_{1,8B}$ 0, and $J_{8A,8B}$ 13 Hz.

Anal. Calc. for $C_{18}H_{21}F_3N_2O_6 \cdot H_2O$: C, 49.54; H, 5.31; F, 13.06; N, 6.42. Found: C, 50.22; H, 5.13; F, 13.38; N, 6.66.

(1S,3S,4R,5R)-3-Methoxy-4-trifluoroacetamido-7-aza-2-oxabicyclo[3.3.0]-octane (**28**). — A solution of **27** (130 mg) in a mixture of 1,4-dioxane–acetic acid–water (7:2:1, 6.6 mL) was hydrogenated in the presence of palladium black under atmospheric pressure of hydrogen for 20 min at room temperature. T.l.c. with 3:1 chloroform–ethanol showed two spots at R_F 0.45 (major, reaction intermediate) and 0.15 (trace, **28**) (*cf.* **27**: 0.95). After a further 20 min of reaction, however, the spot (R_F 0.45) disappeared. Both spots were ninhydrin negative. Filtration followed by evaporation of the mixture gave a syrup, 90 mg (93% as the acetic acid salt), $[\alpha]_D^{22}$ +142° (c 1, methanol); ν_{max}^{KBr} 1715, 1550 cm^{-1}; m/z 254 (M^+); ^{1}H-n.m.r. (5:1 pyridine-d_5–D$_2$O): δ 2.78 (dd, 1 H, H-8A), 2.91 (dd, 1 H, H-6A), 3.02 (q, 1 H, H-5), 3.30 (s, 3 H, OCH$_3$), 3.32 (d, 1 H, H-8B), 3.37 (d, 1 H, H-6B), 4.63 (dd, 1 H, H-4), 4.71 (dd, 1 H, H-1), and 5.22 (d, 1 H, H-3); $J_{1,5}$ = $J_{4,5}$ 7, $J_{3,4}$ 4.5, $J_{1,8A}$ 5, $J_{1,8B}$ 0, $J_{8A,8B}$ 12.5, $J_{5,6A}$ 7, $J_{5,6B}$ 0, and $J_{6A,6B}$ 11.5 Hz; ^{13}C-n.m.r. (5:1 pyridine-d_5–D$_2$O): δ 46.63 (d, C-5), 50.78 and 51.63 (each t, C-6,8), 54.62 (q, OCH$_3$), 59.34 (d, C-4), 81.11 (d, C-1), and 103.61 (d, C-3).

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