Synthesis of 2-Amino-2-deoxy-α-D-altrofuranoside Derivatives from 2,3-*O*-Isopropylidene-D-glyceraldehyde via Bicyclic β-Lactam Intermediates

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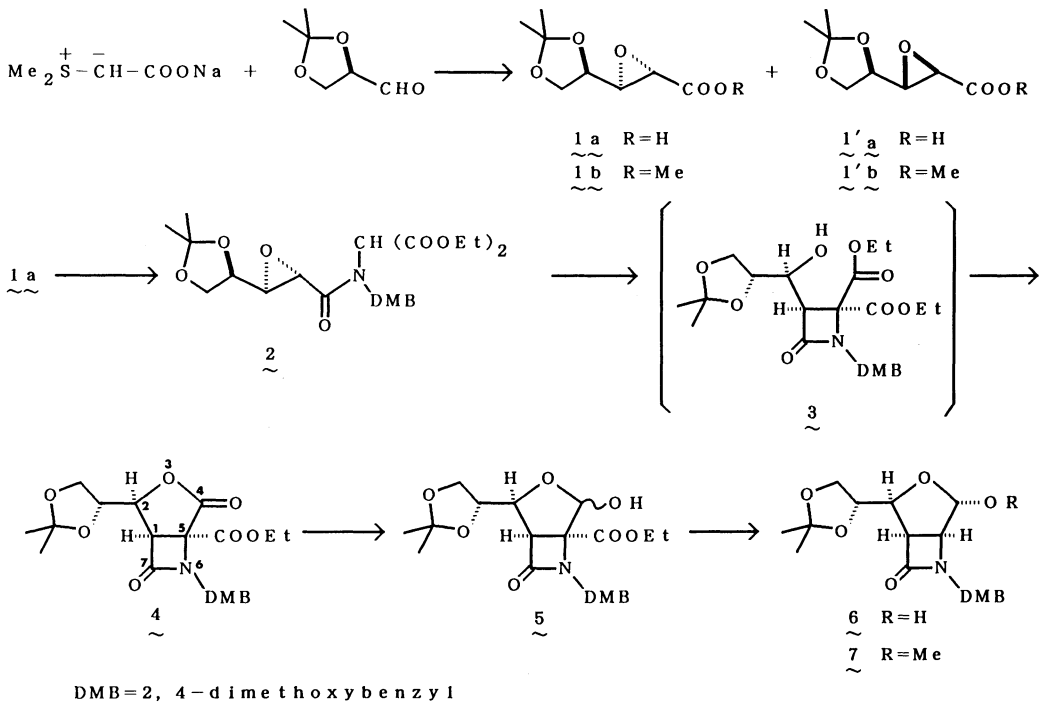
A bicyclic β-lactam (**4**), obtained from 2,3-*O*-isopropylidene-D-glyceraldehyde in 3 steps, was converted to methyl 2-benzamido-2-deoxy-5,6-*O*-isopropylidene-3-*O*-(3-chlorobenzoyl)-α-D-altrofuranoside (**24**) through an additional 8 steps by utilizing the β-lactam nitrogen via the oxidative decarboxylation of diacyl peroxide (**23**). Additionally, it was shown that the bicyclic β-lactam intermediate is a suitable precursor for 2-amino-3-(branched-chain)-2-deoxy-D-furanoside derivatives.

Many effective approaches to the synthesis of amino sugars, which are widely distributed in a variety of glycoconjugates, and which also play many important roles in living bodies, have been developed, and considerable progress has been achieved.[1] However, the synthesis of 2-amino-2-deoxy-D-altrofuranoside derivatives has not been reported, except for the conversion of D-glucose[2] or D-arabinose[3] to 2-amino-2-deoxy-D-altropyranoside analogs. We were interested in developing an alternative approach without using a sugar source, such as D-glucose or D-arabinose, for synthesizing a 2-amino-2-deoxy-D-altrofuranoside derivative. For this purpose, it has been predicted that it is suitable to use the bicyclic β-lactam previously reported[4] to introduce the 2-amino group of 2-amino-2-deoxy-D-altrofuranoside. We thus tried to synthesize a 2-amino-2-deoxy-D-altrofuranoside derivative using this approach and, as a result, could obtain that derivative from 2,3-*O*-isopropylidene-D-glyceraldehyde via bicyclic β-lactam intermediates, even though it was low in total yield. Still, this method via bicyclic 2-azetidinone offers a potential for the syntheses of various stereoisomers of amino sugars by choosing the starting epoxy carboxylic acid, such as **1a** or **1'a**. This method may also provide a route for various stereoisomers of 3-(branched-chain)-2-amino sugars in a stereo-controlled manner. We would like to describe a new procedure for 2-aminoaltrofuranoside analogs.

The treatment of 2,3-*O*-isopropylidene-D-glyceraldehyde[5] in dimethyl sulfoxide (DMSO) with dimethylthetin anion[6] under nitrogen at room temperature for 20 h gave a 2.6:1 mixture of (2*S*,3*R*,4*R*)- and (2*R*,3*S*,4*R*)-2,3-epoxy-4,5-isopropylidenedioxypen-

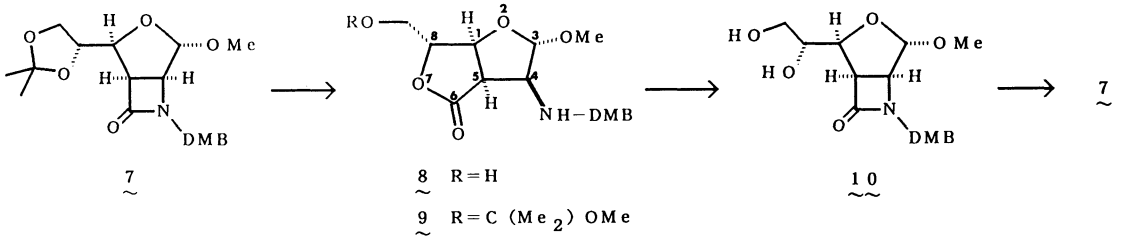


Scheme 1.

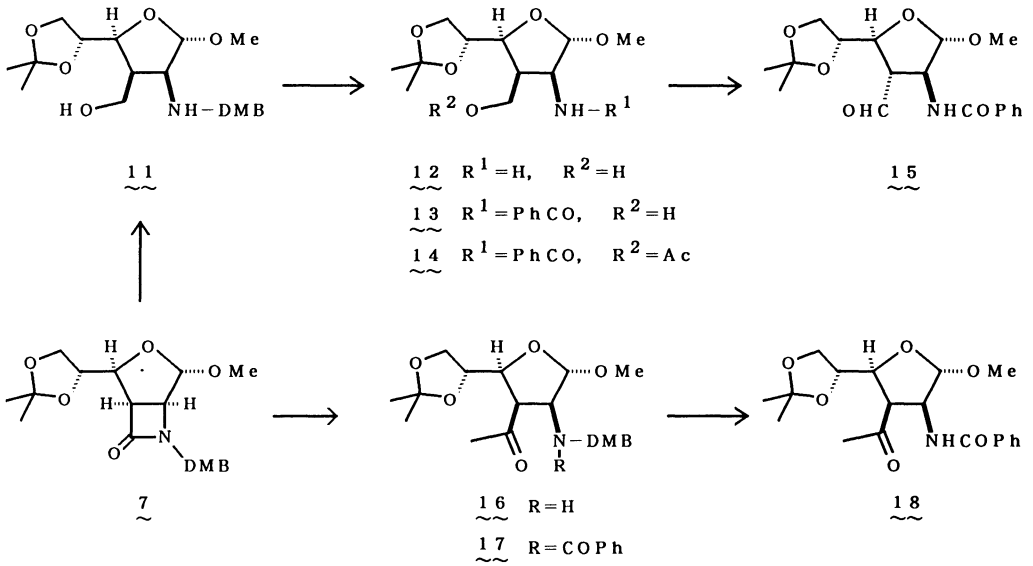
tanoic acid, **1a** and **1'a** in 77% yield (Scheme 1). The ratio of this mixture was determined from a separation of the corresponding methyl esters, **1b**[7] (42%) and **1'b** (16%). Saponification of the methyl ester (**1b**) gave acid **1a**, which was identical with an authentic sample.[8]

Treatment of the optically pure acid **1a** and diethyl 2-(*N*-2,4-dimethoxybenzylamino)malonate[9] with dicyclohexylcarbodiimide (DCC) gave the amide **2**. When a mixture of **1a** and **1'a** was used without separation, **2** was obtained in 22% yield from **1** after chromatographic purification. However, a small amount of isomer (an amide resulting from **1'a**) was an occasional contaminate.[10] Then, an azeotropic treatment of **2** in benzene with a catalytic amount of 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU) to remove the ethanol released during the reaction afforded a bicyclic β-lactam **4** via **3**. If the ethanol released was not removed, the reaction did not complete.

The reduction of **4** with sodium borohydride in methanol containing a catalytic amount of silica gel[11] gave an anomeric mixture of hemiacetal **5**. During this reaction, when the methanol solution is not treated quickly, only esterification by methanol occurs to give the corresponding methyl ester quantitatively; thus, **3** is easily obtained by allowing the ethanol solution of **4** to stand together with a catalytic amount of DBU. However, both **3** and the methyl ester are converted into **4** in good yield by an azeotropic removal of the liberated ethanol or methanol using a catalytic amount of DBU in benzene. The conversion of compound **5** to **6** was achieved by saponification of the ester and successive decarboxylation. The anomeric proton of compound **6** was almost a singlet (by D_2O addition) without only coupling with a neighboring proton on the β-lactam ring. Therefore, the configuration of the anomeric position of **6** must be the *S* configuration. This configuration was also confirmed from a series of experiments (**6**→**7**→**8**→**10**→**7**) (Scheme 2). The glycosidation of **6** with methyl iodide and silver oxide[12] in *N*,*N*-dimethylformamide (DMF) gave **7**. The treatment of crude **7** with 2 equivalents of 2 M hydrochloric acid (1 M=1 mol dm^{-3}) in methanol solution at reflux temperature gave a single product **8**. The structure of **8** was confirmed by an analysis (400 MHz ^1H NMR) of compound **9**. No coupling was observed between the anomeric proton and its neighboring proton in compound **9**. Therefore, it has been elucidated by the Karplus equation that the dihedral angle of these two protons should approach 90°, and that they exist in a trans relationship to each other. As a result, the configuration of the anomeric position of **9** is *S*. A treatment of **8** with methylmagnesium bromide[13]



Scheme 2.



Scheme 3.

gave a β-lactam **10**, which was reprotected with 2,2-dimethoxypropane in DMF containing pyridinium *p*-toluenesulphonate as a catalyst to reproduce **7**. Consequently, the configuration of **7** is (1*R*,2*S*,4*S*,5*S*).

We need to introduce an oxygen atom at the carbon 3 position for the conversion of compound **7** to an altrosamine or mannosamine derivative. At first, we attempted a Baeyer-Villiger oxidation of the C-3 formyl or C-3 acetyl groups to prepare altrosamine and mannosamine analogs.

The C_3-formyl compound **15** was prepared as follows (Scheme 3). The treatment of **7** with lithium aluminum hydride in tetrahydrofuran (THF) at 5 °C gave a C-3 hydroxymethyl compound **11**. Hydrogenolysis of **11** in ethanol by the use of 10% Pd on carbon as a catalyst gave an amino alcohol **12**, which was further converted to a benzamide **13**. Treatment of **13** with pyridinium chlorochromate (PCC)-sodium acetate gave a C_3-formyl compound **15**. The configuration of **15** was elucidated from ^{1}H NMR. Each coupling constant of $J_{1,2}$, $J_{2,3}$, and $J_{3,4}$ was almost zero. This means that the configuration of protons at C_1, C_2, C_3, and C_4 was trans to each other, and that an inversion of the formyl group occurred at C_3.

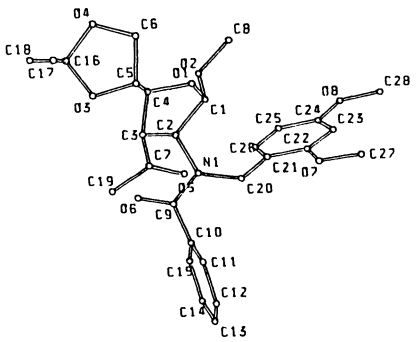
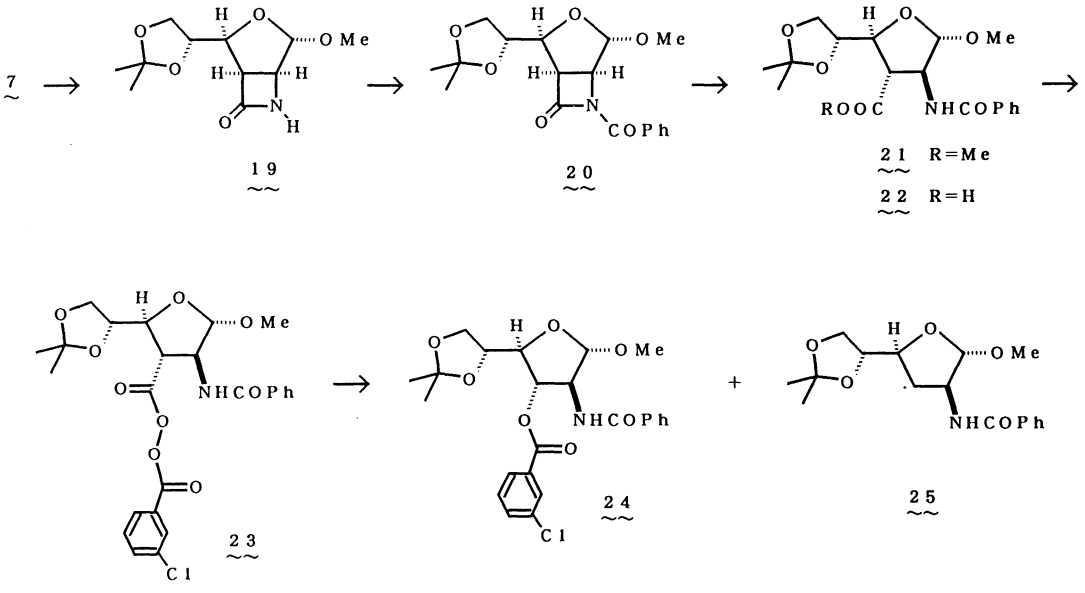


Fig. 1. Molecular structure and atomic numbering of **17**.

The C_3-acetyl compound **18** was prepared as follows. A treatment of **7** with methyllithium gave C_3-acetyl compounds **16**. This type of reaction with *N*,*N*-disubstituted amides or a single β-lactam with alkyllithium[14] is already known. However, this is the first example, as far as we know, for the reaction of β-lactam fused with a furanoside ring with alkyllithium; this reaction provides a new method for the synthesis of 2-amino-2,3-dideoxy-3-acyl-D-furanoside. Benzoylation of **16** with benzoyl chloride and triethylamine gave **17** as a main product. There was a possibility to epimerize the configuration at the C_3-acetyl group of **16** by a strong base (methyllithium) treatment. However, an X-ray crystallographic analysis of the major product **17** showed that the epimerization of the C_3-acetyl group did not occur (Fig. 1). A deprotection of the 2,4-dimethoxybenzyl group of **17** with cerium(IV) ammonium nitrate (CAN)[15] in acetone-water (1 : 1) gave **18**.

Baeyer-Villiger oxidation of both **15** and **18** with 3-chloroperbenzoic acid in chloroform failed to yield altrosamine and mannosamine analogs, respectively. We therefore tried another route to synthesize an altrosamine analog (Scheme 4). Deprotection of the 2,4-dimethoxybenzyl group of **7** with potassium persulphate-potassium hydrogenphosphate[16] in acetonitrile-water at 78 °C under argon afforded **19**. Benzoylation of **19** yielded **20**. Treatment of **20** in methanol containing DBU as a catalyst at reflux temperature gave **21**. The coupling constant between C_2-H and C_3-H of **21** changed to almost zero. This reveals that epimerization occurred at the C_3 position. This ester **21** was saponified with 1 M NaOH in methanol to give **22**, and X-ray crystallographic analysis further con-



Scheme 4.

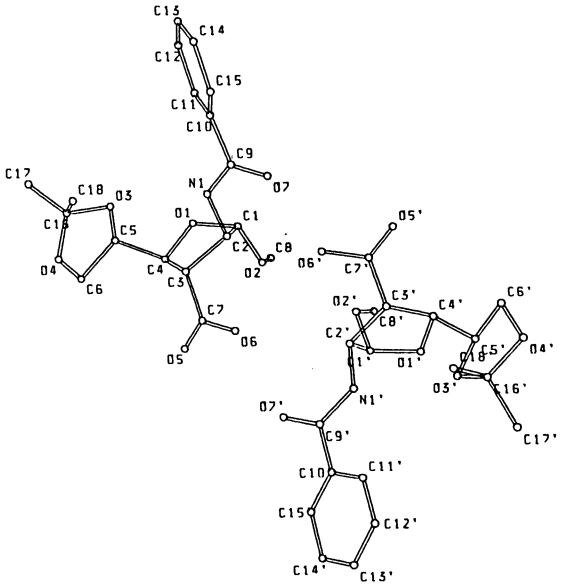


Fig. 2. Molecular structures of the two crystallographically independent molecules in the asymmetric unit, together with the numbering scheme of **22**.

firmed the epimerization (Fig. 2). The reaction of **22** with 3-chloroperbenzoic acid by using DCC as a condensing reagent gave a diacyl peroxide **23**, which was a surprisingly stable compound at room temperature. The obtained **23** was refluxed in octane to give rise to a rearrangent.[17] As a result, an altrosamine analog **24** and a decarboxylated compound **25** were obtained in 32 and 35% yield, respectively. This reaction did not occur in carbon tetrachloride at reflux temperature. The C_3-H chemical shift of **24** shows δ 5.38 shifted from 3.21 of **23**, 3.01 of **22** and 2.91 of **21**, and the coupling constants, $J_{1,2}$, $J_{2,3}$, and $J_{3,4}$, of compound **24** were 0, 0, and 2.2 Hz, respectively. This reveals that an oxygen atom attached directly to the C_3 carbon, and four substituted groups on the tetrahydrofuran ring of **24**, were alternately arranged in a trans relationship.[18] Thus, we could obtain stereoselectively an altrosamine analog **24** from 2,3-*O*-isopropylidene-D-glyceraldehyde via an bicyclic β-lactam intermediate **7** in 12 steps.

Experimental

Melting points were determined on a Yanagimoto micromelting point apparatus and were uncorrected. Optical rotations were obtained by the use of a Perkin-Elmer 241 polarimeter. ^{1}H NMR spectra were recorded using the following spectrometers: at 60 MHz with a Varian T-60, at 270 MHz with a JEOL JNN-270, and at 400 MHz with a JEOL JNN-GX 400. Tetramethylsilane was used as an internal standard (δ value). The IR absorption spectra were determined on a Jasco IR A-2 spectrophotometer. Mass spectra were obtained on a JMS-01SG mass spectrometer. Preparative TLC was performed on silica-gel plates (Merck 60 PF_{245}), and column chromatography was carried out on columns packed with Merck silica-gel 60 (230—400 mesh ASTM) using a slightly increased pressure (1.2 atm) for elution. Elemental analyses were performed by the Analytical Center of the Analytical and Metabolic Research Laboratories, Sankyo Co., Ltd.

A Mixture of (2*S*,3*R*,4*R*)- and (2*R*,3*S*,4*R*)-2,3-Epoxy-4,5-isopropylidenedioxypentanoic Acid, 1a and 1'a. To a solution of dimethylthetin bromide (4.02 g, 20 mmol) in DMSO (20 ml) was added NaH (55% mineral oil dispersion, 2.58 g, 60 mmol) with stirring under nitrogen at 15 °C. The reaction mixture was stirred for 1.5 h at room temperature to produce a suspension of the dimethylthetin anion. To this suspension was added a 2 : 1 mixture of (*R*)-2,2-dimethyl-1,3-dioxolane-4-carbaldehyde and acetic acid (2.14 g, aldehyde=40/3 mmol, acetic acid=20/3 mmol)[5] in DMSO (2 ml) with stirring at ice-cooling temperature. Then, the mixture was stirred for 20 h at room temperature, and poured into ice water (200 ml) with stirring. The mixture was washed twice with ether, and the aqueous layer was acidified with 1 M HCl (50 ml). The whole was then extracted with EtOAc. The organic layer was washed with water and brine, dried over $MgSO_4$, and concentrated in vacuo to give an oily mixture (1.88 g, 77% from the dioxolane) of acids.

Determination of the Ratio, 1a and 1'a. The mixture obtained above was esterified with diazomethane, and the oily mixture was separated to **1b** (42%) and **1'b** (16%) by silica-gel column (**1b**:**1'b**=2.6:1). ^{1}H NMR of **1b**: (60 MHz, $CDCl_3$) δ=1.35 (3H, s), 1.44 (3H, s), 3.20—3.35 (1H, m, C_3-H), 3.41 (1H, d, J=2 Hz, C_2-H), 3.79 (3H, s), 3.8—4.3 (3H, m, C_4-H, C_5-H_2). ^{1}H NMR of **1'b**: ($CDCl_3$) δ=1.35 (3H, s), 1.40 (3H, s), 3.20—3.35 (1H, m, C_3-H), 3.47 (1H, d, J=2 Hz, C_2-H), 3.79 (3H, s), 3.8—4.3 (3H, m, C_4-H, C_5-H_2).

(2*S*,3*R*,4*R*)- 2,3-Epoxy-4,5-isopropylidenedioxypentanoic Acid (1a). To a solution of methyl ester **1b** (72 mg, 0.356 mmol) in EtOH (1 ml) was added 0.5 ml of 1 M NaOH. The mixture was allowed to stand at room temperature overnight, diluted with water, and washed with ether. The aqueous layer was acidified with 1 M HCl (0.5 ml), extracted with EtOAc, washed with water and brine, and dried over $MgSO_4$. The concentration of EtOAc gave 57 mg (91%) of **1a**. IR (film): ν_{max} 3600—2500, 1735 cm^{-1}. 60 MHz ^{1}H NMR ($CDCl_3$) δ=1.37 (3H, s), 1.46 (3H, s), 3.31 (1H, m, C_3-H), 3.43 (1H, d, J=1.5 Hz, C_2-H), 3.8—4.3 (3H, m), 8.0 (1H, bs).

Diethyl 2-[*N*-(2,4-Dimethoxybenzyl)-2,3-epoxy-4,5-isopropylidenedioxypentanamido]malonate (2). To a solution of compound **1a** (42 mg, 0.223 mmol) and *N*-bis(ethoxycarbonyl)methyl-*N*-2,4-dimethoxybenzylamine (80 mg, 0.246 mmol) in CH_2Cl_2 (1 ml) was added DCC (50 mg, 0.242 mmol) at room temperature with stirring. After 30 min, the reaction mixture was filtered to remove a precipitate which was washed with a small volume of CH_2Cl_2. The filtrate was purified on a preparative silica-gel TLC plate. Development with cyclohexane: EtOAc (1 : 1) gave 50 mg (45%) of **2** at the R_f=0.36. IR (film): ν_{max} 1750 (shoulder), 1740, 1668, 1610, 1587 cm^{-1}. 60 MHz ^{1}H NMR ($CDCl_3$) δ=1.18 (3H, t, J=7 Hz), 1.20 (3H, t, J=7 Hz), 1.31 (6H, bs, CH_3×2), 3.27 (1H, m, C_3-H), 3.7—4.4 (14H, m, containing two 3H singlets at δ 3.79 and 3.81, respectively), 4.73 (2H, bs, benzyl), 5.17 (1H, s, NCH), 6.37—6.57 (2H, m), 7.13—7.30 (1H, m). MS m/z 495 (M^+), 449, 434, 394, 364, 348, 292, 166, 151, 121, 101. Found: C, 57.89; H, 6.80; N, 2.91%. Calcd for $C_{24}H_{33}NO_{10}$: C, 58.17; H, 6.71; N, 2.83%.

Ethyl (1*R*,2*S*,5*R*)-6-(2,4-Dimethoxybenzyl)-4,7-dioxo-2-[(1*R*)-1,2-isopropylidenedioxyethyl]-3-oxa-6-azabicyclo-[3.2.0]heptane-5-carboxylate (4). a) Benzene (10 ml) was distilled azeotropically to remove H_2O from a solution of **2** (496 mg, 1 mmol) in benzene (50 ml); then, DBU (40 mg) was added to this solution, and the distillation was continued gradually until the end of the liberation of ethanol. After cooling the reaction mixture was diluted with EtOAc, washed with dil. HCl, H_2O, aq. $NaHCO_3$, and brine, dried over $MgSO_4$, filtered, and concentrated in vacuo to give an oily mixture. A chromatographic analysis of the mixture was quickly performed using a silica-gel (20 g) column. Elution with EtOAc-cyclohexane (1 : 1) gave **4** (235 mg, 52%) as a gum, a by-product (58 mg), and **3** (44 mg, 10%). b) The same treatment of **3** as described above gave **4** quantitatively. IR (film): ν_{max} 1770, 1740 (shoulder), 1613, 1590 cm^{-1}. 60 MHz ^1H NMR ($CDCl_3$) δ=1.25 (3H, t, J=7 Hz), 1.36 (3H, s), 1.43 (3H, s), 3.80 (6H, s), 3.9—4.6 (9H, m), 6.3—6.5 (2H, m), 7.15 (1H, d, J=9 Hz). MS m/z 450, 449 (M^+), 434, 348, 217, 193, 192, 151, 121, 101, 91, 43. Found: m/z 449.16834. Calcd for $C_{22}H_{27}NO_9$: M, 449.16854. c) A mixture of **1a** and **1'a**, treated successively as described above, gave a mixture of **4** (23% overall yield) and **i** (cf. Scheme 5),[10] which was separated by silica-gel column.

Diethyl 3-[(1*S*,2*R*)-1-Hydroxy-2,3-isopropylidenedioxypropyl]-2-oxoazetidine-4,4-dicarboxylate (3). A solution of **4** (100 mg) in EtOH (10 ml) containing DBU (2 mg) was stirred at 0 °C for 5 min. The concentration and silica-gel column chromatography as described above gave **3**, quantitatively. IR (film): ν_{max} 3440, 1750, 1613, 1588, 1510 cm^{-1}. 60 MHz ^1H NMR ($CDCl_3$) δ=1.09 (3H, t, J=7 Hz), 1.27 (3H, t, J=7 Hz), 1.39 (3H, s), 1.41 (3H, s), 2.5 (1H, broad, OH), 3.6—4.7 (17H, m, containing 6H singlet at δ 3.78), 6.3—6.5 (2H, m), 7.11 (1H, d, J=9 Hz). Found: C, 58.26; H, 6.50; N, 2.72%. Calcd for $C_{24}H_{33}NO_{10}$: C, 58.17; H, 6.71; N, 2.83%. MS m/z 495 (M^+), 449, 434, 394, 364, 348, 151. Found: m/z 495.20805. Calcd for $C_{24}H_{33}NO_{10}$: M, 495.21035.

A Mixture of Ethyl (1*R*,2*S*,4*R*,5*R*)- and (1*R*,2*S*,4*S*,5*R*)-6-(2,4-Dimethoxybenzyl)-4-hydroxy-2-[(1*R*)-1,2-isopropylidenedioxyethyl]-3-oxa-7-oxo-6-azabicyclo[3.2.0]heptane-5-carboxylate (5). To a solution of compound **4** (3.58 g) in MeOH (80 ml) was added a silica gel powder (50 mg)[10] and then $NaBH_4$ (650 mg) at −40 °C under nitrogen with stirring. After 15 min, the excess $NaBH_4$ was gradually quenched with AcOH (2.5 ml). The reaction mixture was diluted with EtOAc, washed with aq. $NaHCO_3$ and brine, dried over $MgSO_4$, filtered, and concentrated to give a hemiacetal **5**. Purification of crude **5** by silica-gel column chromatography (developed with cyclohexane : EtOAc=1 : 1) gave pure **5** (3.51 g, 98%) as a gummy anomeric mixture. IR (film): ν_{max} 3380, 1760 (shoulder), 1750—1730, 1610, 1588 cm^{-1}. 60 MHz ^1H NMR ($CDCl_3$) δ=1.50 (3H, t, J=7 Hz), 1.37 (3H, s), 1.40 (3H, s), 1.8 (1H, broad, OH), 3.6—4.6 (15H, m, containing 6H singlet at δ 3.80), 5.00 (1H, d, J=3.5 Hz, changed to a singlet on addition of D_2O), 6.3—6.6 (2H, m), 7.15 (1H, d, J=9 Hz). Found: C, 58.95; H, 6.74; N, 3.28%. Calcd for $C_{22}H_{29}NO_9$: C, 58.53; H, 6.47; N, 3.10%. In this reaction, the corresponding methyl ester of **3** was obtained quantitatively on occasion. However, the same treatment of this compound, as described above in the formation of **4** from **3**, regenerated **4** (94%).

(1*R*,2*S*,4*S*,5*S*)-6-(2,4-Dimethoxybenzyl)-4-hydroxy-2-[(1*R*)-1,2-isopropylidenedioxyethyl]-3-oxa-6-azabicyclo-[3.2.0]heptan-7-one (6). A solution of compound **5** (3.87 g) in pyridine (40 ml), water (2 ml) and DBU (400 mg) was refluxed for 45 min, and concentrated in vacuo to give a crude oily mixture for chromatography by silica-gel column. Elution with cyclohexane : EtOAc (1 : 2) gave **6** (2.59 g, 79%), mp 172—173 °C (needles from EtOAc); IR (Nujol): ν_{max} 3320, 1715, 1612, 1590 cm^{-1}. 60 MHz ^1H NMR ($CDCl_3$) δ=1.36 (3H, s), 1.42 (3H, s), 3.10 (1H, d, J=2 Hz, OH, D_2O exchangeable), 3.4—4.6 (14H, m, containing two 3H singlets at δ 3.80 and 3.82), 5.17 (1H, d, J=2 Hz, changed to a singlet on addition of D_2O), 6.3—6.6 (2H, m), 7.12 (1H, d, J=9 Hz). $[\alpha]_D^{24}$ −10.5° (c 1.61, $CHCl_3$). MS m/z 379 (M^+), 364, 321, 279, 250, 193, 166, 151, 121, 101. Found: C, 59.86; H, 6.56; N, 3.72%. Calcd for $C_{19}H_{25}NO_7$: C, 60.14; H, 6.64; N, 3.69%.

(1*R*,2*S*,4*S*,5*S*)-6-(2,4-Dimethoxybenzyl)-2-[(1*R*)-1,2-isopropylidenedioxyethyl]-4-methoxy-3-oxa-6-azabicyclo-[3.2.0]heptan-7-one (7). To a solution of compound **6** (379.4 mg, 1.0 mmol) in DMF (5 ml) and methyl iodide (5 ml) was added Ag_2O (700 mg) with stirring at room temperature. After stirring for 4 h the reaction mixture was diluted with EtOAc, and filtered. The filtrate was washed with water and brine, dried over $MgSO_4$, and concentrated in vacuo to give a crude mixture for chromatography by silica-gel column. Elution with cyclohexane : EtOAc (1 : 1) gave a gummy **7** (340 mg, 86%). MS m/z 393 (M^+), 378 (M^+−15), 362, 335, 264, 193, 151, 121, 101, 43. IR (film): ν_{max} 1748, 1610, 1588 cm^{-1}. 60 MHz ^1H NMR ($CDCl_3$) δ=1.38 (3H, s), 1.43 (3H, s), 3.29 (3H, s), 3.6—4.6 (14H, m, containing 6H singlet at δ 3.83), 4.69 (1H, s, C_1-H), 6.35—6.60 (2H, m), 7.15 (1H, d, J=8.5 Hz).

(1*S*,3*S*,4*S*,5*R*,8*R*)-4-(2,4-Dimethoxybenzylamino)-8-hydroxymethyl-3-methoxy-2,7-dioxabicyclo[3.3.0]octan-6-one (8). A solution of **7** (67 mg) in MeOH (2 ml) and 1 ml of 2 M HCl solution in MeOH was refluxed for 1.5 h and concentrated in vacuo. The residue was dissolved in CH_2Cl_2 (4 ml). $NaHCO_3$ (0.2 g) was added and the mixture was stirred for 30 min. After filtration, the solution was concentrated and the residue was subjected to chromatography by silica-gel column. Elution with EtOAc gave **8** (47 mg, 78%) as a thick oil and an unknown solid (5 mg) having a lower R_f value. IR (film): ν_{max} 3500—3200, 1760 (broad), 1612, 1588 cm^{-1}. 60 MHz ^1H NMR ($CDCl_3$) δ=2.8 (2H, broad, OH and NH, D_2O exchangeable), 3.2—3.6 (5H, m, containing a 3H singlet at δ 3.33), 3.70—3.85 (10H, m), 4.4—4.9 (3H, m, containing a 1H singlet at δ 4.87), 6.3—6.5 (2H, m), 7.11 (1H, d, J=9 Hz). MS m/z 354 (M^++1), 353, 352, 322, 293, 262, 218, 166, 151, 121.

(1*S*,3*S*,4*S*,5*R*,8*R*)-4-(2,4-Dimethoxybenzylamino)-3-methoxy-8-(1-methoxy-1-methylethoxy)methyl-2,7-dioxabicyclo[3.3.0]octan-6-one (9). A solution of **8** (20 mg) in DMF (0.5 ml) and 2,2-dimethoxypropane (1 ml) containing toluene-4-sulfonic acid monohydrate (5 mg) was refluxed for 1.5 h. Concentration and preparative chromatography on a silica-gel plate (developed with cyclohexane-EtOAc=1 : 1) gave 15 mg of **9** (63%) as a gum. IR (film): ν_{max} 1763, 1612, 1588 cm^{-1}. MS m/z 426 (M^++1), 394, 352, 323, 293, 275, 204, 166, 151, 121, 91, 73, 43. 400 MHz ^1H NMR ($CDCl_3$) δ=1.282 (3H, s), 1.299 (3H, s), 1.920 (1H, bs, NH), 3.159 (3H, s), 3.365 (3H, s), 3.365 (1H, dd, J=8—9, 6—7 Hz, C_5-H), 3.469 (1H, dd, J=8.8, 1.0 Hz, C_4-H), 3.520 (1H, dd, J=10.7, 1.9 Hz, C_8-CH), 3.734 (1H, dd, J=10.7, 2.4 Hz, C_8-CH), 3.781 (3H, s), 3.826 (3H, s), 3.700, 3.867 (2H, AB-q, J=13.6

Hz, NCH_2Ar), 4.680 (1H, t, J=1.9—2.4 Hz, C_8-H), 4.715 (1H, d, J=6.8 Hz, C_1-H), 4.896 (1H, s, C_3-H), 6.428 (1H, dd, J=2.4, 8.3 Hz), 6.450 (1H, d, J=2.4 Hz), 7.126 (1H, d, J=8.3 Hz).

(1*R*,2*S*,4*S*,5*S*)-2-[(1*R*)-1,2-Dihydroxyethyl]-6-(2,4-dimethoxybenzyl)-4-methoxy-3-oxa-6-azabicylo[3.2.0]heptan-7-one (10). To a solution of **8** (54 mg, 0.153 mmol) in THF (4 ml) was added 0.6 ml of a 1 M solution of MeMgBr in THF with stirring under nitrogen at −78 °C and then another 1 ml of the same Grignard reagent. After 30 min the reaction mixture was quenched with 1 M HCl (1.6 ml) and extracted with EtOAc. The organic layer was washed with sat. $NaHCO_3$ and brine, dried over $MgSO_4$, and concentrated in vacuo to give an oily mixture, which was subjected to chromatography by silica-gel column. Elution with EtOAc gave recovered **8** (9 mg, 17%) and elution with 10% MeOH in EtOAc gave **10** (36 mg, 67%), which was employed for the next reaction.

(1*R*,2*S*,4*S*,5*S*)-6-(2,4-Dimethoxybenzyl)-2-[(1*R*)-(1,2-isopropylidenedioxyethyl]-4-methoxy-3-oxa-6-azabicyclo-[3.2.0]heptan-7-one (7). A solution of **10** (33 mg) and pyridinium *p*-toluenesulfonate (1 mg) in DMF (0.3 ml) and 2,2-dimethoxypropane (0.6 ml) was stirred for 18 h at room temperature. The reaction mixture was concentrated in vacuo, and subjected to chromatography by silica-gel column. Elution with cyclohexane: EtOAc (1 : 1) gave 34 mg of **7** (92%).

Methyl 2,3-Dideoxy-2-(2,4-dimethoxybenzylamino)-3-hydroxymethyl-5,6-*O*-isopropylidene-α-D-mannofuranoside (11). To a solution of β-lactam **7** (200 mg) in THF (4 ml) was added $LiAlH_4$ (60 mg) at 5 °C with stirring. The reaction mixture was quenched with acetic acid, diluted with EtOAc, washed with sat. $NaHCO_3$ and brine, and dried over $MgSO_4$. After filtration, the solvent was concentrated in vacuo, and the residual oil was subjected to chromatography by silica-gel column. Elution with cyclohexane: EtOAc (1 : 4) gave 178 mg of **11** in 88% yield. 270 MHz ^{1}H NMR ($CDCl_3$) δ=1.35 (3H, s), 1.40 (3H, s), 2.67 (1H, quintuplet, J=6.5 Hz, C_3-H), 3.31 (1H, dd, J=2.6, 6.5 Hz, C_2-H), 3.32 (3H, s, C_1-OMe), 3.72, 3.73 (2H, AB-q, J=12.8 Hz, N-CH_2Ar), 3.80 (3H, s), 3.82 (3H, s), 3.88—4.03 (4H, m), 4.11—4.24 (2H, m), 4.77 (1H, d, J=2.6 Hz, C_1-H), 6.42—6.46 (2H, m), 7.11 (1H, d, J=8.4 Hz). IR (film): ν_{max} 3500—3300, 1610, 1588 cm^{-1}. MS m/z 397 (M^+), 382, 339, 306, 236, 166, 151, 121. Found: m/z 397.20715; Calcd for $C_{20}H_{31}NO_7$: 397.20995.

Methyl 2-Amino-2,3-dideoxy-3-hydroxymethyl-5,6-*O*-isopropylidene-α-D-mannofuranoside (12). A solution of **11** (143 mg) in EtOH (8 ml) was hydrogenolyzed on 10% Pd on charcoal for 5 h with stirring under hydrogen. After filtration, the reaction mixture was concentrated and subjected to chromatography by silica-gel (1.0 g) column. Elution with cyclohexane: ethyl acetate (1 : 1) to remove 2,4-dimethoxytoluene and then with methanol: ethyl acetate (1 : 9) gave 43 mg of **12** (48.3%) as a gum. 270 MHz ^{1}H NMR ($CDCl_3$) δ=1.37 (3H, s), 1.43 (3H, s), 1.90 (3H, bs, D_2O exchangeable, OH and NH_2), 2.68 (1H, quintuplet, J=6.5 Hz, C_3-H), 3.34 (3H, s, C_1-OCH_3), 3.52 (1H, dd, J=1.7, 6.4 Hz, C_2-H), 3.91—4.00 (3H, m), 4.05 (1H, dd, J=7.3, 9.5 Hz), 4.18 (1H, dd, J=6.1, 8.6 Hz), 4.31 (1H, dt, J=9.5, 5.7 Hz), 4.66 (1H, d, J=1.8 Hz, C_1-H). IR (film): ν_{max} 3360 (broad) cm^{-1}.

Methyl 2-Benzamido-2,3-dideoxy-3-hydroxymethyl-5,6-*O*-isopropylidene-α-D-mannofuranoside (13). A mixture of **12** (37 mg), benzoyl chloride (25 mg), and triethylamine (50 mg) in THF (2 ml) was stirred for 15 min at room temperature. Preparative TLC on a silica-gel plate developed with cyclohexane: ethyl acetate (1 : 1) gave **13** (51 mg, 97%) as a gum. IR (film): ν_{max} 3350, 1640 cm^{-1}. 270 MHz ^{1}H NMR ($CDCl_3$) δ=1.37 (3H, s), 1.41 (3H, s), 2.91 (1H, m, C_3-H), 3.40 (3H, s, C_1-OCH_3), 3.51 (1H, dd, J=5.1, 8.8 Hz, D_2O exchangeable, OH), 3.91—4.03 (2H, m, C_3-CH and C_6- or C_5-H), 4.08 (1H, td, J=5.1, 12.8 Hz, changed to dd, J=5.1 and 12.8 Hz in addition of D_2O, C_3-CH), 4.14—4.27 (3H, m, C_4-H, C_6-H and C_5-H or C_6-H), 4.59 (1H, t, J=6.2 Hz, C_2-H), 4.99 (1H, s, C_1-H), 7.42—7.56 (4H, m, containing CONH), 7.78—7.82 (2H, m).

Methyl 3-Acetoxymethyl-2-benzamido-2,3-dideoxy-5,6-*O*-isopropylidene-α-D-mannofuranoside (14). A solution of **13** (29 mg) in 0.6 ml of pyridine: acetic anhydride (2 : 1) was allowed to stand overnight at room temperature. Evaporation in vacuo gave **14** (quantitatively) which was recrystallized from hexane: EtOAc (9 : 1). Mp 120—121 °C (needles). $[\alpha]_D^{24}$ +48.9° (*c* 1.13, EtOH). IR (film): ν_{max} 3360, 1737, 1640 cm^{-1}. 270 MHz ^{1}H NMR ($CDCl_3$) δ=1.37 (3H, s), 1.41 (3H, s), 2.04 (3H, s, $OCOCH_3$), 3.19 (1H, m, C_3-H), 3.38 (3H, s, OCH_3), 3.86 (1H, dd, J=6.6, 8.4 Hz, C_5-H or C_6-H), 4.13 (1H, dd, J=7.1, 8.6 Hz, C_5-H or C_6-H), 4.28 (1H, dd, J=5.5, 8.4 Hz, C_4-H), 4.34—4.42 (2H, m, C_3-CH and C_5-H or C_6-H), 4.50 (1H, dd, J=8.1, 11.7 Hz, C_3-CH), 4.79 (1H, ddd, J=1.0, 6.4, 8.8 Hz, C_2-H), 4.84 (1H, d, J=1.0 Hz, C_1-H), 7.08 (1H, d, J=8.8 Hz, NH), 7.40—7.54 (3H, m), 7.77—7.80 (2H, m). MS m/z 378 (M^+−15), 362, 345, 333, 304, 292, 232, 173. Found: C, 61.22; H, 7.13; N, 3.59%. Calcd for $C_{20}H_{27}NO_7$: C, 61.05; H, 6.92; N, 3.56%.

Methyl 2-Benzamido-2,3-dideoxy-3-formyl-5,6-*O*-isopropylidene-α-D-altrofuranoside (15). To a solution of **13** (121 mg, 0.344 mmol) in CH_2Cl_2 (10 ml) were added anhydrous CH_3COONa (280 mg) and pyridinium chlorochromate (740 mg, 3.44 mmol) with stirring at room temperature (24 °C). After 15 min, the reaction mixture was passed through a silica gel (20 g) column eluted with EtOAc (200 ml), and the eluant was washed with saturated $NaHCO_3$ and brine. The EtOAc layer was dried over $MgSO_4$ and concentrated in vacuo to give an oily residue which was subjected to chromathography by silica-gel column. Elution with cyclohexane-EtOAc (3 : 2) gave **15** in 92% yield as a gum. IR (film): ν_{max} 1665—1655, 1601, 1579 cm^{-1}. 270 MHz ^{1}H NMR ($CDCl_3$) δ=1.30 (3H, s), 1.40 (3H, s), 2.75 (1H, d, J=2.9 Hz, C_3-H), 3.61 (1H, dd, J=7.0, 8.8 Hz, C_6-H), 4.18 (1H, dd, J=7.7, 8.8 Hz, C_6-H), 4.55 (1H, dd, J=1.5—1.8, 2.9—3.3 Hz, C_4-H), 4.62 (1H, dt, J=1.5, 7.0—7.7 Hz, C_5-H), 4.91 (1H, s, C_1H), 5.13 (1H, d, J=8.8 Hz, C_2-H), 7.40—7.55 (4H, m, olefinic 3H and NH), 7.78—7.82 (2H, m), 9.87 (1H, s, CHO). MS m/z 334 (M^+−15), 328, 260, 248, 228, 213, 199, 189.

Methyl 3-Acetyl-2,3-dideoxy-2-(2,4-dimethoxybenzylamino)-5,6-*O*-isopropylidene-α-D-mannofuranoside (16). To a solution of **7** (393 mg, 1 mmol) in THF (10 ml) was added MeLi (1.5 ml of 1.4 M solution in diethyl ether) in THF (2 ml) at −78 °C under a nitrogen atmosphere with stirring. After 15 min, the reaction mixture was quenched with acetic acid, diluted with EtOAc, washed with sat. $NaHCO_3$ and brine, dried over $MgSO_4$ filtered, and concentrated in vacuo to give an gummy mixture. The mixture was subjected to chromatography by silica-gel column. Elution with cyclohexane: EtOAc (1 : 1) gave 311 mg of **16** (higher R_f value, 76% yield) and 44 mg of unknown product.

16: Found: *m/z* 409.20950. Calcd for $C_{21}H_{31}NO_7$: 409.21010.

Methyl 3-Acetyl-2,3-dideoxy-2-(*N*-2,4-dimethoxybenzylbenzamido)-5,6-*O*-isopropylidene-α-D-mannofuranoside (17). To a solution of **16** (82 mg, 0.2 mmol) in THF (2 ml) was added Et_3N (50 mg) and benzoyl chloride (30 mg, 0.213 mmol) with stirring at room temperature. Preparative TLC on a silica-gel plate (developed with cyclohexane:EtOAc=3:2) gave 76 mg (74%) of **17** as a crystalline solid. Mp 143—146 °C (from EtOAc-cyclohexane). $[\alpha]_D^{24}$ +140.0° (*c* 1.21, $CHCl_3$). IR (Nujol): ν_{max} 1705, 1625, 1607, 1588, 1205 cm^{-1}. 400 MHz ^1H NMR ($CDCl_3$) δ=1.304 (3H, s), 1.492 (3H, s), 2.369 (3H, s, $COCH_3$), 2.960 (3H, s, OCH_3), 3.671 (3H, s, 2′-OCH_3), 3.803 (3H, s, 4′-OCH_3), 3.879 (1H, td, *J*=6.5—6.8, 4.0 Hz, C_5-H), 4.090 (2H, m, C_6-H_2), 4.152 (1H, dd, *J*=5.2, 7.0 Hz, C_4-H), 4.356 (1H, broad, C_3-H), 4.507 (2H, s, N-CH_2Ar), 4.945 (1H, dd, *J*=7.5, 3.0 Hz, C_2-H), 5.052 (1H, d, *J*=3.4 Hz, C_1-H), 6.355 (1H, d, *J*=2.4 Hz, $C_{3'}$-H), 6.509 (1H, dd, *J*=8.3, 2.4 Hz, $C_{5'}$-H), 7.115 (1H, d, *J*=8.3 Hz, $C_{6'}$-H), 7.283 (4H, d, *J*=3.9 Hz), 7.300 (1H, m). MS *m/z* 513 (M^+), 495, 481, 436, 408, 350, 322, 270, 188, 151. Found: *m/z* 513.23404. Calcd for $C_{28}H_{35}NO_8$, 513.23616. Found: C, 65.15; H, 6.86; N, 2.76%. Calcd for $C_{28}H_{35}NO_8$: C, 65.48; H, 6.87; N, 2.73%.

Methyl 3-Acetyl-2-benzamido-2,3-dideoxy-5,6-*O*-isopropylidene-α-D-mannofuranoside (18). To a stirred solution of **17** (51 mg, 0.10 mmol) in acetone (1.5 ml) was added a solution of cerium(IV) ammonium nitrate (165 mg, 0.30 mmol) in H_2O (1 ml) at 25 °C. After 15 min, the reaction mixture was diluted with EtOAc and washed with aq. $NaHCO_3$, dried over $MgSO_4$, and concentrated to give a residue which was subjected to chromatography by silica-gel column. Elution with cyclohexane-EtOAc (3:2) gave **18** (12 mg, 33%) as a solid. 270 MHz ^1H NMR ($CDCl_3$) δ=1.33 (3H, s), 1.43 (3H, s), 2.35 (3H, s), 3.39 (3H, s), 3.94—3.99 (2H, m), 4.04—4.15 (2H, m), 4.28 (1H, dd, *J*=7.7, 9.2 Hz), 4.69 (1H, dt, *J*=2.2, 6.9 Hz, C_2-H), 5.08 (1H, d, *J*=2.2 Hz, C_1-H), 7.41—7.81 (6H, aromatic 5H and NH). MS *m/z*, 362 (M^+−1), 348 (M^+−15), 332, 227, 199, 167, 122, 105.

(1*R*,2*S*,4*S*,5*S*)-2-[(1*R*)-(1,2-*O*-Isopropylideneethyl]-4-methoxy-3-oxa-6-azabicyclo[3.2.0]heptan-7-one (19). To a solution of **7** (1.3 g, 3.3 mmol) in CH_3CN (70 ml) and H_2O (70 ml), was added $K_2S_2O_8$ (10 g) and K_2HPO_4 (5 g). The mixture was heated at 78 °C for 30 min under an argon atmosphere with stirring. The reaction mixture was concentrated in vacuo, and the residue was extracted with EtOAc. The organic layer was washed with aq. $NaHCO_3$ and brine, dried over $MgSO_4$, and then concentrated to give a residue. The crude material was subjected to chromatography by silica-gel column to give **19** (642 mg, 80%) as a crystalline solid. Mp 166—167 °C. IR (Nujol): ν_{max} 3310, 1750 cm^{-1}; 270 MHz ^1H NMR ($CDCl_3$) δ=1.38 (3H, s), 1.45 (3H, s), 3.36 (3H, s), 3.80—4.08 (4H, m), 4.15 (1H, dd, *J*=6.2, 8.8 Hz), 4.41 (1H, m), 4.89 (1H, s), 5.89 (1H, bs, NH). MS *m/z* 228 (M^+−15), 212, 155, 125, 101.

(1*R*,2*S*,4*S*,5*S*)-6-Benzoyl-2-[(1*R*)-(1,2-*O*-isopropyridene-ethyl]-4-methoxy-3-oxa-6-azabicyclo[3.2.0]heptan-7-one (20). To a solution of **19** (390 mg, 1.6 mmol), Et_3N (1.6 ml), DMAP (30 mg) in CH_2Cl_2 (10 ml) was added a solution of PhCOCl (340 mg, 1.5 equiv, 2.4 mmol) in CH_2Cl_2 (2 ml) with stirring at room temperature. After 1 h, the reaction mixture was diluted with EtOAc, washed with aq. $NaHCO_3$ and brine, dried over $MgSO_4$, and concentrated in vacuo to give a residue which was subjected to chromatography by silica-gel column. Elution with cyclohexane-EtOAc (2:1) gave 512 mg of **20** (92%). IR (film): ν_{max} 1795, 1732, 1672, 1601, 1581 cm^{-1}. 60 MHz ^1H NMR ($CDCl_3$) δ=1.38 (3H, s), 1.46 (3H, s), 3.40 (3H, s), 3.7—4.5 (5H, m), 4.57 (1H, d, *J*=4.5 Hz), 5.27 (1H, s), 7.3—7.6 (3H, m), 7.9—8.1 (2H, m). MS *m/z*, 348 (M^++1), 334, 333, 332 (M^+−15), 316.

Methyl 2-Benzamido-2,3-dideoxy-5,6-*O*-isopropylidene-3-methoxycarbonyl-α-D-altrofuranoside (21). A solution of **20** (150 mg) in MeOH containing 10 mg of DBU was refluxed for 30 min. The mixture was concentrated in vacuo to give a residue which was subjected to chromatography by silica-gel column. Elution with cyclohexane-EtOAc (1:1) gave 150 mg (90%) of **21** as a viscous gum. IR (film): ν_{max} 3360, 1732, 1662, 1643 cm^{-1}. 270 MHz ^1H NMR ($CDCl_3$) δ=1.32 (3H, s), 1.41 (3H, s), 2.91 (1H, d, *J*=3.7 Hz, C_3-H), 3.32 (3H, s, C_1-OCH_3), 3.70 (1H, dd, *J*=7.0, 8.8 Hz, C_6-H), 3.79 (3H, s, C_3-$COOCH_3$), 4.17 (1H, dd, *J*=7.3, 8.8 Hz, C_6-H), 4.61 (1H, dt, *J*=1.6, 7.3 Hz, C_5-H), 4.75 (1H, dd, *J*=1.7, 3.7 Hz, C_4-H), 4.86 (1H, s, C_1-H), 5.17 (1H, d, *J*=8.8 Hz, C_2-H), 7.33 (1H, d, *J*=8.8 Hz, NH), 7.39—7.51 (3H, m), 7.78—7.82 (2H, m). MS *m/z* 380 (M^++1), 364, 348, 290, 278, 258, 219.

Methyl 2-Benzamido-3-carboxy-2,3-dideoxy-5,6-*O*-isopropylidene-α-D-altrofuranoside (22). A solution of **21** (326 mg, 0.859 mmol) in MeOH (2.6 ml), and aqueous 1 M NaOH (1.03 ml, 1.03 mmol, 1.2 equiv) was refluxed for 30 min. The whole was concentrated in vacuo, acidified with 1 M HCl (1.1 ml), and extracted with EtOAc. The organic layer was washed with H_2O and brine, dried over $MgSO_4$, and concentrated to give 310 mg of an acid **22** (99%) as a crystalline solid. Mp 145—146.5 °C (from EtOAc-hexane). 270 MHz ^1H NMR ($CDCl_3$) δ=1.29 (3H, s), 1.38 (3H, s), 3.01 (1H, dd, *J*=1.3, 4.6 Hz, C_3-H), 3.36 (3H, s, C_1-OCH_3), 3.75 (1H, dd, *J*=7.1, 9.3 Hz, C_6-H), 4.15 (1H, dd, *J*=7.1, 9.3 Hz, C_6-H), 4.58 (1H, dt, *J*=2.1, 7.1 Hz, C_5-H), 4.74 (1H, dd, *J*=2.1, 4.6 Hz, C_4-H), 4.95 (1H, dd, *J*=1.3, 8.1 Hz, C_2-H), 4.97 (1H, s, C_1-H), 7.34 (1H, d, *J*=8.1 Hz, C_2-NH), 7.41—7.57 (3H, m), 7.79—7.82 (2H, m), 9.50 (1H, bs, COOH). $[\alpha]_D^{24}$ −60.0° (*c* 1.06, $CHCl_3$). Found: C, 59.06; H, 6.26; N, 3.74%. Calcd for $C_{18}H_{23}NO_7$: C, 59.17; H, 6.35; N, 3.83%.

Methyl 2-Benzamido-3-(3-chlorobenzoyldioxycarbonyl)-2,3-dideoxy-5,6-*O*-isopropylidene-α-D-altrofuranoside (23). To a solution of **22** (121.8 mg, 1/3 mmol) and 3-chloroperbenzoic acid (80—90%, 75 mg) in CH_2Cl_2 (3 ml) was added DCC (83 mg, 1.2 equiv) at room temperature with stirring. After 15 min, the precipitate was filtered off. The filtrate was concentrated and subjected to chromatography by silica-gel column. Elution with cyclohexane-EtOAc (3:2) gave 146 mg of **23** (84%) as a powder. IR (Nujol): ν_{max} 3330, 1800, 1768, 1640, 1602 cm^{-1}. 270 MHz ^1H NMR ($CDCl_3$) δ=1.37 (3H, s), 1.42 (3H, s), 3.21 (1H, dd, *J*=1.1, 4.1 Hz, C_3-H), 3.40 (3H, s), 3.76 (1H, dd, *J*=7.0, 8.8 Hz, C_6-H), 4.20 (1H, dd, *J*=7.3, 8.8 Hz, C_6-H), 4.64 (1H, ddd, *J*=1.8, 4.0, 7.3 Hz, C_5-H), 4.79 (1H, dd, *J*=1.8, 4.0 Hz, C_4-H), 4.98 (1H, s, C_1-H), 5.20 (1H, dd, *J*=1.1, 8.8 Hz, C_2-H), 7.27 (1H, d, *J*=8.8 Hz, C_2-NH), 7.4—8.02 (9H, m). Found: C, 57.47; H, 5.04; N, 2.60; Cl, 7.08%. Calcd for $C_{25}H_{26}NO_9Cl$: C, 57.75; H, 5.04; N, 2.69; Cl, 6.82%.

Methyl 2-Benzamido-3-*O*-(3-chlorobenzoyl)-2-deoxy-5,6-*O*-isopropylidene-α-D-altrofuranoside (24) and Methyl 2-Benzamido-2,3-dideoxy-5,6-*O*-isopropylidene-α-D-altrofuranoside (25) The peroxyester **23** (91 mg) in octane (5 ml) was refluxed for 1 h with stirring. Concentration of the

reaction mixture and preparative TLC on a silica-gel plate (developed with cyclohexane-EtOAc=3 : 2) gave 27 mg of **24** (32%) as a gum and 20 mg of **25** (36%) as a gum. Physical data of **24**: IR (film): ν_{max} 3350, 1723, 1646 cm^{-1}. 270 MHz ^{1}H NMR ($CDCl_3$) δ=1.40 (3H, s), 1.44 (3H, s), 3.47 (3H, s), 4.04 (1H, t, J=8.1—8.8 Hz, C_6-H), 4.16 (1 H dd, J=6.6, 8.8 Hz, C_6-H), 4.38 (1H, dd, J=1.5, 2.2 Hz, C_4-H), 4.51 (1H, dt, J=1.5, 6.6—8.1 Hz, C_5-H), 4.81 (1H, d, J=8.4 Hz, coupling with NH, C_2-H), 5.04 (1H, s, C_1-H), 5.39 (1H, d, J=2.2 Hz, C_3-H), 7.38 (1H, d, J=8.4 Hz, NH), 7.38—7.58 (5H, m), 7.80—8.04 (4H, m). Found: C, 60.52; H, 5.78; N, 2.96; Cl, 7.64%. Calcd for $C_{24}H_{26}NO_7Cl$: C, 60.58; H, 5.51; N, 2.94; Cl, 7.45%. Found: m/z (M^++1) 476.14390. Calcd for $C_{24}H_{26}NO_7Cl$ (Cl=34.96885): 476.14750. Physical data of **25**: IR (film): ν_{max} 3360, 1650 cm^{-1}. 270 MHz ^{1}H NMR ($CDCl_3$) δ=1.35 (3H, s), 1.43 (3H, s), 1.82 (1H, dd, J=2.9, 13.6 Hz, C_3-βH), 2.52 (1H, ddd, J=8.1, 9.5, 13.6 Hz, C_3-αH), 3.37 (3H, s), 3.52 (1H, t, J=8.4 Hz, C_6-H), 4.14 (1H, dd, J=7.3, 8.4 Hz, C_6-H), 4.32 (1H, ddd, J=1.9, 2.9, 9.5 Hz, C_4-H), 4.54 (1H, dt, J=1.9, 7.3—8.4 Hz, C_5-H), 4.61 (1H, dd, J=8.1, 8.4 Hz, C_2-H), 4.88 (1H, s, C_1-H), 7.38—7.49 (4H, m, aromatic 3H and NH), 7.52—7.80 (2H, m). Found: C, 63.28; H, 7.01; N, 4.07%. Calcd for $C_{17}H_{23}NO_5$: C, 63.53; H, 7.21; N, 4.36%. Found: m/z (M^++1) 322.16809. Calcd for $C_{17}H_{24}NO_5$: 322.16549.

X-Ray Crystallography of 17, 22, and vi. Crystals of dimensions 0.7×0.4×0.4 mm for **17**, 0.5×0.4×0.4 mm for **22**, and 0.4×0.3×0.2 mm for **vi** were used for X-ray crystallography. Lattice constants were determined by least-squares fit of angular settings of 20 reflections within the range $15<\theta<30°$. Intensity data were obtained on a Rigaku AFC-5R diffractometer equipped with graphite-monochromatized Cu $K\alpha$ radiation and using θ-2θ scan technique ($2\theta<128°$). During data collection five standards, measured before every 200 reflections, indicated no systematic variation of intensity with time. Of 2591, 3270, and 1904 independent reflections measured, only 2411, 2689, and 1750 for **17**, **22**, and **vi**, respectively, were considered as observed on the basis of the criterion $F_o>2\sigma(F_o)$. All intensities were corrected for Lorentz and polarization effects, but not for absorption.

Crystal data: **17**, $C_{28}H_{35}NO_8$, M_r=513.4. Orthorhombic, space group $P2_12_12_1$, a=22.449(6), b=16.662(5), c=7.219(2) Å, U=2700.4 Å^3, Z=4, D_c=1.26 g cm^{-3}, μ(Cu $K\alpha$)=8 cm^{-1}.

22, $C_{18}H_{23}NO_7$, M_r=365.4. Monoclinic, space group $P2_1$, a=16.380(3), b=7.438(1), c=15.738(5) Å, β=109.51(2)°, U=1807.3 Å^3, D_c=1.34 g cm^{-3}, μ(Cu $K\alpha$)=9 cm^{-1}.

vi, $C_{19}H_{25}NO_7$, M_r=379.4. Orthorhombic, space group $P2_12_12_1$, a=19.719(5), b=9.682(2), c=10.382(2) Å, U=1982.2 Å^3, D_c=1.27 g cm^{-3}, μ(Cu $K\alpha$)=8 cm^{-1}.

The structures of **17**, **22**, and **vi** were solved by MULTAN84,[19] and refined by the block-diagonal least-squares methods. The positions of the hydrogen atoms were estimated using standard geometry. The final refinements with anisotropic temperature factors for the nonhydrogen atoms and isotropic temperature factors for the hydrogen atoms were lowered R values to 0.080 (R_w=0.069, $w=1/\sigma^2(F_o)$), 0.070 (R_w=0.057, $w=1/\sigma^2(F_o)$), and 0.072 (R_w=0.057, $w=1/\sigma^2(F_o)$) for **17**, **22**, and **vi**, respectively.

The complete F_o—F_c data are deposited as Document No. 8900 at the Office of the Editor of Bull. Chem. Soc. Jpn

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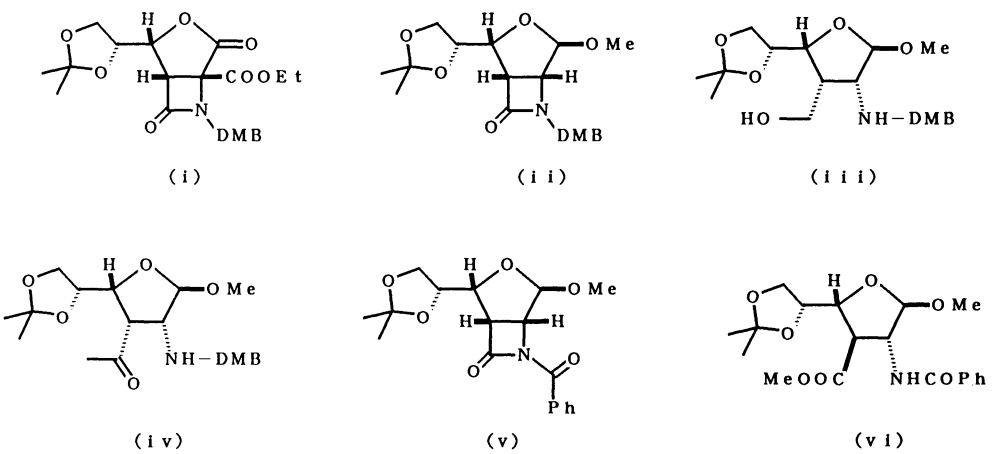
10) The stereochemical assignments of compounds, ano-



(i) (ii) (iii) (iv) (v) (vi)

Scheme 5.

mer of **7**, that of **11** and also that of **16** described in "*Chem. Lett.*, **1987**, 1403"[4] must be corrected as **ii**, **iii**, and **iv**, respectively. The chromatographic separation of the mixed fractions should be repeated. If the separation was not sufficient, a small amount of **i** derived from **1'a** contaminates, causing the contamination of **iii**, **iv**, or **v** in latter stages, although fortunately separable by chromatography. (Scheme 5).

iii: 270 MHz ^{1}H NMR, ($CDCl_3$) δ=1.35 (3H, s), 1.40 (3H, s), 2.63—2.68 (1H, m, C_3-H), 3.7—4.2 (15H, m, containing two 3H singlets at δ 3.80 and 3.81), 4.85 (1H, d, J=1.8 Hz, C_1-H), 6.41—6.45 (2H, m), 7.13 (1H, d, J=8.1 Hz). IR (film): ν_{max} 3500—3300, 1612, 1590 cm^{-1}. MS m/z 397 (M^+), 392, 366, 339, 322, 306, 296, 279, 264, 248, 236, 166, 151, 121. Found: m/z 397.20979. Calcd for $C_{20}H_{31}NO_7$: 397.20995.

iv: High resolution MS: Observed, 409.21010. Calcd for $C_{21}H_{31}NO_7$: 409.21010. 270 MHz ^{1}H NMR ($CDCl_3$) δ=1.33 (3H, s), 1.37 (3H, s), 1.73 (1H, broad, NH), 2.25 (3H, s), 2.89 (1H, dd, J=3.8, 6.4 Hz, C_3-H), 3.28 (3H, s), 3.47 (1H, d, J=3.7 Hz, C_2-H), 3.77 (2H, s), 3.80 (3H, s), 3.81 (3H, s), 3.7—3.9 (1H, m), 4.09 (1H, dd, J=6.8, 7.6 Hz), 4.25 (1H, dd, J=5.7, 12.3 Hz), 4.40 (1H, t, J=6.0 Hz), 4.82 (1H, s, C_1-H), 6.42—6.47 (2H, m), 7.19 (1H, d, J=9.2 Hz).

v: 60 MHz ^{1}H NMR ($CDCl_3$) δ=1.39 (3H, s), 1.46 (3H, s), 3.44 (3H, s), 3.5—4.5 (5H, m), 4.56 (1H, d, J=4.5 Hz, C_1-H), 5.31 (1H, s), 7.3—7.6 (3H, m), 7.8—8.1 (2H, m). IR (film): ν_{max} 1795, 1713, 1672, 1601, 1581 cm^{-1}. MS m/z 348 (M^++1), 332 (M^+−15), 316, 125, 105, 101.

vi: Mp 109—111 °C (from cyclohexane). $[\alpha]_D^{24}$ −59.8° (c 0.94, $CHCl_3$). IR (Nujol): ν_{max} 3400, 1732, 1635 cm^{-1}. 270 MHz ^{1}H NMR ($CDCl_3$) δ=1.25 (3H, s), 1.43 (3H, s), 3.02 (1H, d, J=3.6 Hz, C_3-H), 3.32 (3H, s), 3.79 (3H, s), 4.05 (1H, dd, J=8.1, 8.4 Hz, C_6-H), 4.14 (1H, dd, J=6.6, 8.4 Hz, C_6-H), 4.29 (1H, ddd, J=1.3, 6.6, 8.1 Hz, C_5-H), 4.72 (1H, dd, J=1.3, 3.6 Hz, C_4-H), 4.88 (1H, s, C_1-H), 5.10 (1H, d, J=9.2 Hz, C_2-H, coupling with NH), 7.40—7.55 (4H, m, aromatic 3H and NH), 7.77—7.81 (2H, m). Found: C, 60.02; H, 6.60; N, 3.77%. Calcd for $C_{19}H_{25}NO_7$: C, 60.15; H, 6.64; N, 3.67%.

The structure of **vi** derived from **v** was confirmed by X-Ray crystallographic analysis. (Fig. 3).

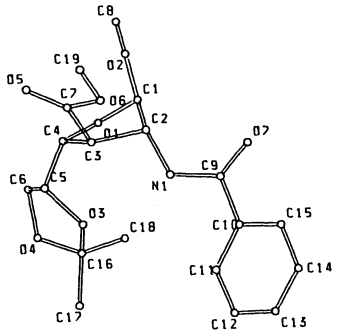


Fig. 3. Molecular structure and atomic numbering of **vi**.

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