Carbohydrate Research, 79 (1980) 63–77

SYNTHESIS OF AN ANALOG OF THE NUCLEOSIDE MOIETY OF THE POLYOXINS*

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(Received December 5th, 1978; accepted for publication in revised form, March 10th, 1979)

ABSTRACT

Addition of methyl nitroacetate to 1,2:5,6-di-*O*-isopropylidene-α-D-*ribo*-hexofuranos-3-ulose in the presence of ammonium acetate in anhydrous *N*,*N*-dimethylformamide afforded 1,2:5,6-di-*O*-isopropylidene-3-*C*-(*R*,*S*)nitro(methoxycarbonyl)methyl-α-D-allofuranose (**2**). Reduction of the nitro acetate **3** over palladium-on-charcoal gave the oxime **4**, whereas reduction of **3** over Raney nickel afforded methyl L (and D)-2-(3-*O*-acetyl-1,2:5,6-di-*O*-isopropylidene-α-D-allofuranos-3-yl)-glycinates (**5** and **6**), in 67 and 8% yields, respectively. Saponification of **5** and **6** afforded the glycos-3-yl-α-amino acids **11** and **12**. Conversion of the allofuranos-3-yl adduct **2** into the glucofuranos-3-yl reduction-products **13** and **14** was achieved by treatment of **2** with methanol and acetic anhydride in the presence of palladium-on-charcoal. The *N*-trifluoracetyl derivative (**10**) of **5**, underwent selective hydrolysis by 66% acetic acid to afford a diol that was acetylated to afford the *allo* tri-acetate **15**. The 5,6-glycol was selectively degraded by standard reactions to yield methyl *N*-acetyl-L-2-(5-*O*-acetyl-1,2-*O*-isopropylidene-α-D-ribofuranos-3-yl)glycinate (**19**). Application of the triflate-alkylation synthesis of nucleosides to the allo trifluoroacetyl amino acid **15** and silylated thymine yielded 1-[2,3,5,6-tetra-*O*-acetyl-[3-*C*-(methyl *N*-trifluoroacetyl-L-2-glycinate)]-β-D-allofuranosyl]thymine (**23**) in 93% yield. Deprotection of **23** to yield the nucleoside amino acid **25** was not successful.

DISCUSSION

Polyoxins A-L, found in 1965, are antifungal agents produced by *Streptoamyces cacavi* var. *asoensis* and are useful as an agricultural fungicide[1].

The structures of the polyoxins, established by degradative chemical studies[1,2], was confirmed by chemical synthesis[3–5]. Their principal structural features include the following: (*i*) possession of 5-amino-5-deoxy-D-allofuranosyluronic acid as the sugar component[2], and (*ii*) a unique L-amino acid constituent attached by a C–C linkage to C-4 of the erythrofuranose ring.

*Branched-chain Glycosyl α-Amino Acids. Part VII.

As the introduction of branching at C-3′ of naturally occurring nucleosides has elicited interesting changes in biological activity of the nucleosides[6], it was of interest to synthesize structural analogs of the nucleoside moiety of the polyoxins in which the amino acid moiety would be attached to C-3′, rather than C-4′, of the nucleoside.

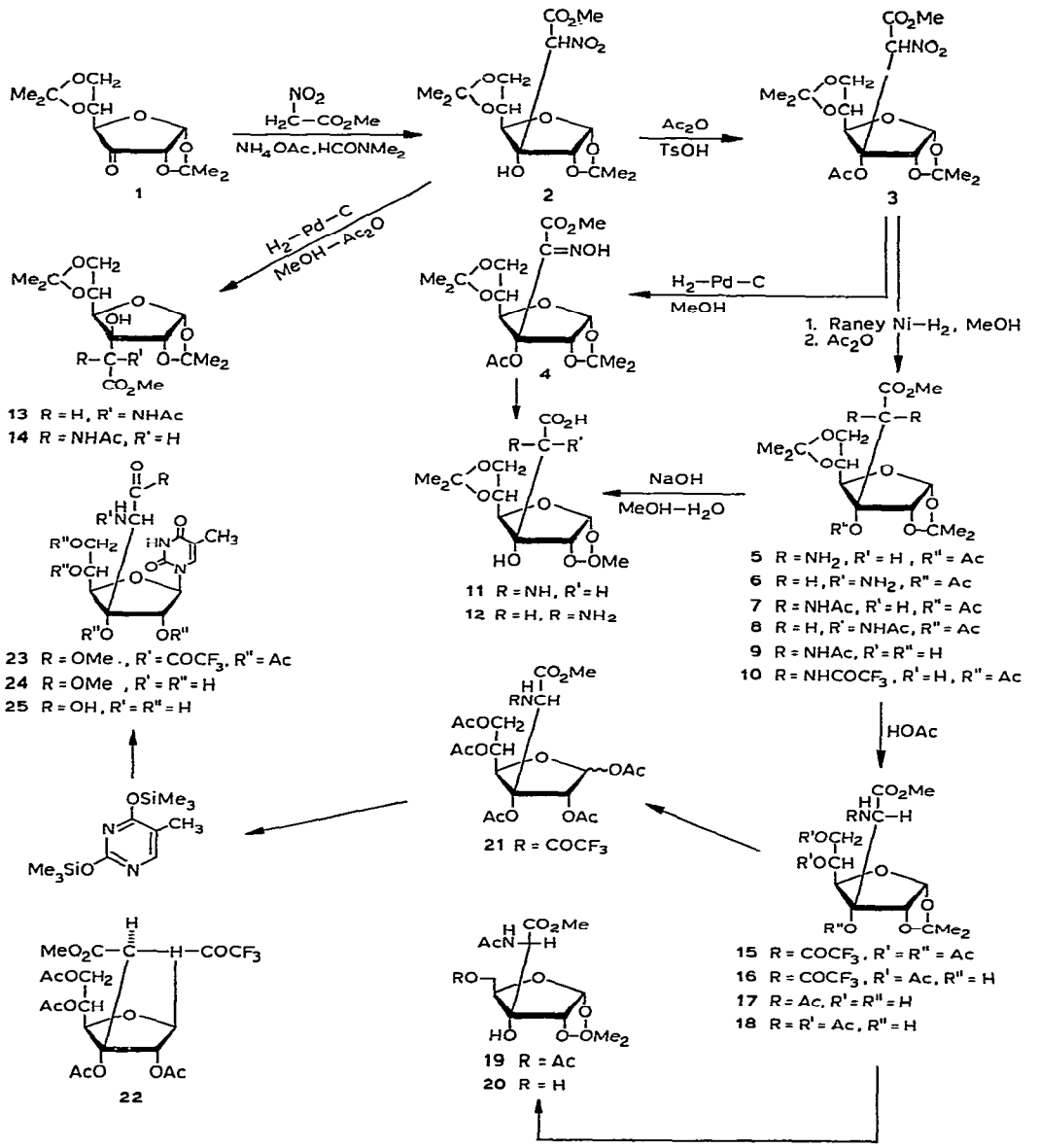
The first approach utilized here for the synthesis of 3-deoxyglycos-3-yl glycine derivatives involved stereospecific hydroxylation of 3-deoxy-1,2:5,6-di-*O*-isopropylidene-3-*C*-*trans*-(methoxycarbonylmethylene)-α-D-*ribo*-hexofuranose with osmium tetraoxide, followed by known conversions of the secondary hydroxyl function to give L- and D-2-(3-deoxy-1,2:5,6-di-*O*-isopropylidene-α-D-allofuranos-3-yl)glycine[7,8]. The L- and D-2(α-D-glucofuranos-3-yl)glycine derivatives have also been synthesized by the same approach[9]. A more-direct approach for introduction of the α-amino acid functionality at C-3 of the sugar was achieved by condensation of 1,2:5,6-di-*O*-isopropylidene-α-D-*ribo*-hexofuranos-3-ulose with ethyl isocyanoacetate[10,11]. The final product, however, contained the (*R*)-α-amino acid functionality attached by a carbon–carbon linkage to C-3′ of the nucleoside. Recently, a facile synthesis of both the *S*- and *R*-2-glycine derivatives has been achieved by reaction of a 3-ketose with methyl nitroacetate followed by reduction of the nitro ester adduct[12]. In this communication, we present complete details for synthesis of L- and D-2(1,2:5,6-di-*O*-isopropylidene-α-D-allofuranos-3-yl)glycine, and in addition, describe the utilization of branched-chain sugar amino acids in the synthesis of a branched-chain sugar nucleoside-α-L-amino acid, which is an analog of the nucleoside moiety of the polyoxins.

Condensation of 1,2:5,6-di-*O*-isopropylidene-α-D-*ribo*-hexofuranos-3-ulose (**1**) with methyl nitroacetate in the presence of ammonium acetate in anhydrous *N*,*N*-dimethylformamide afforded 1,2:5,6-di-*O*-isopropylidene-3-*C*-(*R*,*S*)-nitro(methoxycarbonyl)methyl]-α-D-allofuranose (**2**), which could not be freed completely from unreacted methyl nitroacetate. As a consequence, the partially purified product **2** was acetylated with acetic anhydride and *p*-toluenesulfonic acid monohydrate to afford, after column chromatography on silica gel with 4:1 benzene–ethyl acetate as developer, the crystalline 3-acetate **3** in 82% yield.

Reduction of the nitro ester **3** with palladium-on-charcoal as a catalyst gave only the oxime **4** in 94% yield. Catalytic, stereospecific reduction of compound **3** or the oxime **4** over freshly activated Raney nickel, followed by chromatographic separation on silica gel with 9:1 ethyl acetate–ether as developer afforded methyl L-2-(3-*O*-acetyl-1,2:5,6-di-*O*-isopropylidene-α-D-allofuranos-3-yl)glycinate (**5**) and the D-2 diastereoisomer **6**, in 67 and 8% yields, respectively.

Acetylation of the L-amino acid ester **5** in methanol with acetic anhydride gave the (L)-*N*-acetylglycinate **7** in quantitative yield. Similar acetylation of the D-amino acid ester **6** afforded the (D)-*N*-acetylglycinate **8** in 100% yield. Trifluoroacetylation of **5** with trifluoroacetic anhydride in the presence of dichloromethane and pyridine gave the L-2-(D-allofuranos-3-yl)-*N*-trifluoroacetylglycinate **10** in 85% yield.

Treatment of the L-amino acid ester **5** with 1.25% aqueous sodium hydroxide afforded L-2-(1,2:5,6-di-*O*-isopropylidene-α-D-allofuranos-3-yl)glycine (**11**) in 82%



yield. Similar saponification of the D-amino acid ester **6** gave the D-diastereomer **12** in 85% yield.

The nitro ester adduct **2**, surprisingly, gave two new amino acid esters **13** and **14**, together with some ketose **1**, when **2** was hydrogenated with palladium-on-charcoal catalyst in a mixture of methanol and acetic anhydride. It thus appears that the addition between the ketose **1** and methyl nitroacetate is reversible. The two new, branched-chain glycosyl amino acid esters (**13** and **14**), and unidentified minor components, were separated chromatographically. Direct comparison of the *N*-acetyl

amino esters **13** and **14** with the *N*-acetyl derivatives of the previously characterized methyl L- and D-2-(1,2:5,6-di-*O*-isopropylidene-α-D-glucofuranos-3-yl)glycinates[9] (i.r., n.m.r., and optical rotation) showed that the respective compounds were identical. Therefore, compound **2** must have been formed by the addition of methyl nitroacetate to the less hindered side of the ketose **1**. As reduction of the nitro ester **3** afforded the two remaining diastereomers **5** and **6**, proof of their structures, by physical methods, appeared to suffice. Saponification of the methyl glycinates **5** and **6** afforded the respective glycosyl α-amino acids **11** and **12**. The α-amino acid **11** was assigned the L-configuration on the basis of its intensely positive Cotton-effect[13], whereas the α-amino acid **12**, which exhibited a strongly negative Cotton-effect, was assigned the D configuration.

Selective hydrolysis of the 1,2:5,6-di-*O*-isopropylideneallofuranos-3-yl *N*-trifluoroacetylamino acid **10** with 66% acetic acid removed the 5,6-substituent to afford a diol (not characterized) that was immediately acetylated with acetic anhydride and *p*-toluenesulfonic acid to yield the 3,5,6-triacetate **15** in 79% yield. Acetylation of the triol intermediate with acetic anhydride and pyridine yielded the 5,6-diacetate **16** and the 3,5,6-triacetate **15** in 65 and 29% yields, respectively.

O-Deacetylation of methyl *N*-acetyl-L-2-(3-*O*-acetyl-1,2:5,6-di-*O*-isopropylidene-α-D-allofuranos-3-yl)glycinate (**7**) with sodium methoxide afforded the partially protected amino acid ester **9** in 91% yield. Selective hydrolysis of **9** with 66% acetic acid yielded the triol **17** in quantitative yield. Acetylation of the triol **17** with acetic anhydride and pyridine gave the 5,6-diacetate **18** in 96% yield.

Conversion of the hexofuranose triol **17** into a pentofuranose diol (**19**) was accomplished in fair yield. Thus, cleavage of the 5,6-diol of **17** with sodium metaperiodate, followed by reduction of the dialdose derivative with sodium borohydride afforded a diol that was immediately acetylated with acetic anhydride and pyridine; the resulting product was separated by column chromatography. Surprisingly, the desired acetate, namely, methyl *N*-acetyl-L-2-(5-*O*-acetyl-1,2-*O*-isopropylidene-α-D-ribofuranos-3-yl)glycinate (**19**) was obtained in 13% yield, whereas the unacetylated diol **20** was recovered in 26% yield. The low yields of pentose led us to abandon this procedure.

The following part of the discussion deals with the utilization of the trifluoroacetylated sugar amino acid derivative **15** in the synthesis of an analog of the nucleoside component of the polyoxins. Acetolysis of **15** with acetic acid, acetic anhydride, and *p*-toluenesulfonic acid yielded (after column chromatography) methyl L-(2-1,2,3,5,6-penta-*O*-acetyl-α,β-D-allofuranos-3-yl)-*N*-trifluoroacetylglycinate (**21**) in 47% yield as an anomeric mixture. Treatment of the furanosyl acetates **21** with hydrogen bromide–dichloromethane afforded a glycosyl bromide that was immediately allowed to condense with N^6-benzoyl-N^6,9-bis(trimethylsilyl)adenine according to a fusion procedure previously described[14]. Surprisingly, the product isolated by column chromatography consisted of unreacted starting compound **21** and an anhydro, bicyclic carbohydrate **22**, obtained in 52% yield. No nucleoside was formed in the reaction. On the basis of n.m.r., mass spectrometry, and elemental analysis,

compound **22** was assigned the structure 2,3,5,6-tetra-*O*-acetyl-1,1[1]-anhydro-3-*C*-(*R*)-(methoxycarbonyl)methyl-1-(*R*), 1[1](*S*)-*N*-trifluoroacetoepimino-β-D-allofuranose. Presumably, the *N*-trifluoroacetamido group participated intramolecularly with expulsion of bromide to yield the bicyclic structure **22**. Attempted fusion[15] of the pentaacetate **21** with N^6-benzoyl-N^6,9-bis(trimethylsilyl)adenine or with 2,6-dichloropurine for 20 min at 160° afforded no nucleoside. The reaction of **21** with 2,4-bis(trimethylsilyl)thymine in acetonitrile and tin tetrachloride[16] at room temperature for 2.5 h yielded no nucleoside.

Application of the novel triflate-alkylation synthesis of nucleosides[17,18] to the pentaacetate **21** was successful. Thus, direct conversion of **21** into the triflate, followed by addition of bis(trimethylsilyl)thymine in anhydrous dichloromethane, gave 1-[2,3,5,6-tetra-*O*-acetyl-[3-*C*-(methyl *N*-trifluoroacetyl-L-2-glycinate)]-β-D-allofuranosyl]thymine (**23**) in 93% yield (based on the pentaacetate **21** consumed. Unreacted **21** was readily recovered from **23** by chromatography. Because large $J_{1',2'}$ values of furanosyl nucleosides cannot be used with certainty[19] to assign the anomeric configuration of the nucleoside **23**, we used the chemical shift of H-1′ of **23** (δ 6.05) in comparison to the chemical shift of H-1 of the precursor β-acetate **21** (δ 6.04) to support a tentative assignment of the β configuration[19]. Research in our laboratory dealing with α and β nucleosides of C-3′ branched-chain sugars has clearly shown that H-1′ of α-nucleosides resonates at lower field than H-1′ of their β-counterparts[20–22]. Mechanistic considerations indicate **23** to be a β-nucleoside, because the triflate-nucleoside synthesis has been shown to yield β-nucleosides[17] exclusively. The *trans* rule[23] also supports the formation of a β-nucleoside from a furanosyl peracetate having the 2-acyloxy group below the plane of the furanose ring. Finally, Cushley and co-workers[24], and Montgomery[25], have observed the anisotropic effect of the 5,6-double bond of the pyrimidine ring on the 2′-OAc signal of acetylated pyrimidine furanosyl nucleosides; for *cis*-nucleosides, this effect causes an upfield shift of the shielded methyl group. Because the chemical shift of 2′-OAc of **23** and 2-OAc of **21** remained practically the same, it may be assumed that nucleoside **23** is trans. This assumption was fully supported by the c.d. spectrum of **23**, which exhibited a positive Cotton-effect characteristic of the β-D configuration of glycofuranosylpyrimidines[26]. Thus, compound **23** is assigned the structure 1-[2,3,5,6-tetra-*O*-acetyl-[3-*C*-(methyl *N*-trifluoroacetyl-L-2-glycinate)]-β-D-allofuranosyl)thymine.

Unfortunately, it was not possible to remove the protecting groups from **23** without leading to intractable mixtures of compounds. Thus, attempted deprotection of the nucleoside **23** with sodium methoxide in methanol gave a mixture of six components that could not be separated pure by paper chromatography. Attempted separation of the product mixture on Bio-Rex 70 (H^+) resin was unsuccessful. Treatment of **23** with methanolic ammonia[27] for 14 days gave an intractable mixture of products. Attempted deprotection of **23** with hydrogen chloride in methanol[28] was also unsuccessful. Finally, the triethylamine–methanol and triethylamine–methanol–water[29] procedures previously used for the deacetylation of *O*-acetyl nucleosides and polysaccharides failed to remove the acetyl groups completely.

EXPERIMENTAL

General methods. — ^{1}H-N.m.r. spectra were determined in chloroform-*d* solution with tetramethylsilane as the internal standard ($\delta = 0$) by using a Varian XL-100 spectrometer. Optical rotations were measured at room temperature with a Perkin–Elmer Model 141 automatic polarimeter. The c.d. measurements were performed with a Jasco J-20 and a J-5 automatic recording spectropolarimeter at room temperature, and i.r. spectra were recorded with a Perkin–Elmer 337 spectrometer. Mass spectra were performed with a HMS-9 spectrometer. Column chromatography was performed on t.l.c.-grade silica gel, without binder, under a pressure of 4–8 lb.in^{-2} and flow rates of 70–140 mL.h^{-1}; t.l.c. on silica gel G was used to monitor all reactions. Melting points were determined on a Leitz microscope heating-stage, model 350, and are corrected. Evaporations were performed under diminished pressure. Chemical analyses were preformed by Mr. P. Borda, Microanalytical Laboratory, University of British Columbia.

*1,2:5,6-Di-*O*-isopropylidene-3-*C*-[(*R,S*)-nitro(methoxycarbonyl)methyl]-α-*D*-allofuranose* (**2**). — To a mixture of 1,2:5,6-di-*O*-isopropylidene-α-D-ribohexofuranos-3-ulose (**1**, 1.0 g, 1 equiv.), ammonium acetate (0.3 g, 1 equiv.), and anhydrous *N,N*-dimethylformamide (4 mL), was added dropwise with stirring methyl nitroacetate (0.9 g, 1.95 equiv.). The mixture was stirred for 5 h at room temperature, water (4 mL) was added, and the mixture was then extracted with chloroform (3 × 10 mL). The combined organic extracts were dried (magnesium sulfate), and evaporated to yield an orange syrup (1.4 g). The product was chromatographed under a pressure of 8 lb.in^{-2} on a column of t.l.c.-grade silica gel (17 × 5 cm), with 1:1 benzene–ethyl acetate as developer, to afford starting material **1** (R_F 0.44), and a 1:5 mixture (1 g, R_F 0.58) of methyl nitroacetate and product **2**; ν_{max}^{film} 3450 (OH), 1755 (C=O), and 1570 cm^{-1} (NO_2); n.m.r. ($CDCl_3$): δ 5.90 (d, 1, $J_{1,2}$ 4 Hz, H-1), 5.83 (s, 1, H′), 5.18 (s, CH_2 of methyl nitroacetate), 4.77 (d, 1, H-2), 3.88 (s, OCH_3 of methyl nitroacetate), 3.83 (s, 3, OCH_3), 3.47 (s, 1, OH, exchanges in D_2O), 1.46, 1.37, and 1.33 (s, 12, CH_3).

*3-*O*-Acetyl-1,2:5,6-di-*O*-isopropylidene-3-*C*-(*R,S*)-nitro(methoxycarbonyl)-α-*D*-allofuranose* (**3**). — The crude product (not chromatographed) obtained from 5.7 g of ketose **1** was acetylated with acetic anhydride (40 mL) and *p*-toluenesulfonic acid monohydrate (0.8 g) for 5 h at 80–90°. The mixture was then evaporated to ~10 mL and azeotropically dried with toluene (3 × 30 mL) to yield a dark-brown syrup (9.0 g) that was chromatographed on silica gel (24 × 5 cm) with 4:1 benzene–ethyl acetate as developer to afford pure **3** (7.5 g, 82%). Recrystallized from ether–hexane, compound **3** had m.p. 136–137°, $[\alpha]_D^{24}$ +71.2° (*c* 5.3, chloroform); $\nu_{max}^{CHCl_3}$ 1740 (C=O), and 1570 cm^{-1} (NO_2); n.m.r. ($CDCl_3$): 5.93 (d, 1, $J_{1,2}$ 3.5 Hz, H-1), 5.90 (s, 1, H-1′), 4.90 (d, 1, H-2), 4.87 (s, 1), 4.34 (s, 3), 3.80 (s, 3, OCH_3), 2.08 (s, 3, OAc), 1.50, 1.43, 1.37, and 1.33 (4s, 12, CH_3).

Anal. Calc. for $C_{17}H_{25}NO_{11}$: C, 48.69; H, 6.01; N, 3.34. Found: C, 48.86; H, 6.08; N, 3.10.

3-O-Acetyl-1,2:5,6-di-O-isopropylidene-3-C-(methoxydicarbonyl)-α-D-allofuranose oxime (**4**). — Compound **3** (0.165 g) in methanol (20 mL) was hydrogenated with 5% palladium-on charcoal (0.150 g) as catalyst for 48 h at atmospheric pressure and room temperature. The catalyst was removed by filtration and the filtrate evaporated to yield the oxime **4** (0.148 g, 94%). The product was sublimed at 110°/0.075 torr; $[\alpha]_D^{23}$ +10.7° (*c* 1.19, chloroform); $\nu_{max}^{CHCl_3}$ 3600 (OH) and 1740 cm^{-1} (C=O).

Anal. Calc. for $C_{17}H_{25}NO_{10}$: C, 50.62; H, 6.25; N, 3.47. Found: C, 50.49; H, 6.58; N, 3.23.

Methyl L-*2-(3-O-acetyl-1,2:5,6-di-O-isopropylidene-α-D-allofuranos-3-yl)glycinate* (**5**) *and methyl* D-*2-(3-O-acetyl-1,2:5,6-di-O-isopropylidene-α-D-allofuranos-3-yl)glycinate* (**6**). — Compound **3** (200 mg) in methanol (12 mL) was hydrogenated over freshly activated Raney nickel (0.4 mL) as catalyst for 24 h at atmospheric pressure and room temperature. The catalyst was removed by filtration and the filtrate evaporated to yield a syrup (150 mg, 81%). The product was chromatographed on silica gel (22 × 2.3 cm) with 9:1 ethyl acetate–ether as developer to afford compound **5** (124 mg, 67%) and compound **6** (15 mg, 8%). Compound **5** was distilled at 110°/0.05 mm; $[\alpha]_D^{24}$ +38.4° (*c* 0.90, dichloromethane); n.m.r. ($CDCl_3$): δ 5.81 (d, 1, $J_{1,2}$ 3.5 Hz, H-1), 4.70–4.14 (overlapping signals, 5), 4.41 (d, H-2), 4.11 (broad s, 1, H-1′, collapses to sharp s on addition of D_2O), 3.66 (s, 3, OCH_3), 2.0 (s, 3, OAc), 1.83 (broad s, 2, NH_2, exchanges with D_2O), 1.48 (s, 9, Me), and 1.34 (s, 3, Me).

Anal. Calc. for $C_{17}H_{27}NO_9$: C, 52.44; H, 6.99; N, 3.60. Found: C, 52.73; H, 6.87; N, 3.46.

Compound **6** was distilled at 120°/0.2 mm; $[\alpha]_D^{23}$ +16.6° (*c* 1.7, dichloromethane); n.m.r. ($CDCl_3$): δ 5.88 (d, 1, $J_{1,2}$ 4 Hz, H-i), 4.68 (d, 1, *J* 2 Hz), 4.58 (d, 1, H-2), 4.28 (s, 3), 4.02 (broad s, 1, H-1′, collapses to sharp s on addition of D_2O), 3.76 (s, 3, OCH_3), 2.08 (s, 5, OAc and NH_2, collapses to 3-proton s on addition of D_2O), 1.53 (s, 3, Me), 1.44 (s, 6, Me), and 1.34 (s, 3, Me).

Anal. Calc. for $C_{17}H_{27}NO_9$: C, 52.44; H, 6.99; N, 3.60. Found: C, 52.39; H, 7.10; N, 3.49.

Methyl N-*acetyl*-L-*2-(3-O-acetyl-1,2:5,6-di-O-isopropylidene-α-D-allofuranos-3-yl)glycinate* (**7**) *and methyl* N-*acetyl*-D-*2-(3-O-acetyl-1,2:5,6-di-O-isopropylidene-α-D-allofuranos-3-yl)glycinate* (**8**). — To a solution of the amino ester **5** (519 mg) in methanol (10 mL) was added acetic anhydride (3 mL) and the resulting solution was stirred for 21 h at room temperature. Volatile components were evaporated off, and toluene (3 × 5 mL) was added and evaporated off to afford **7** as an amorphous solid (579 mg, 100%). An analytical sample of **7** was obtained by distillation at 140°/0.2 mm; m.p. 56–59°, $[\alpha]_D^{25}$ +18.1° (*c* 3.3, dichloromethane); n.m.r. ($CDCl_3$): δ 6.68 (d, 1, $J_{NH,H-1}$ 9.5 Hz, exchanges in D_2O, NH), 5.93 (d, 1, $J_{1,2}$ 4 Hz, H-1), 5.45 (d, 1, collapses to singlet on addition of D_2O, H-1′), 4.51 (d, 1, H-2), 4.46–4.0 (overlapping signals, 4, H-4,5, and 6), 3.76 (s, 3, OCH_3), 2.14 and 2.10 (2s, 6, CH_3CO), 1.50, 1.48, 1.42, and 1.37 (4s, 12, CH_3).

Anal. Calc. for $C_{19}H_{29}NO_{10}$: C, 52.89; H, 6.78; N, 3.25. Found: C, 52.68; H, 6.90; N, 3.27.

Similar treatment of amino ester **6** (50 mg) yielded compound **8** (56 mg, 100%) as a clear, colorless syrup that was distilled at 120°/0.2 mm; $[\alpha]_D^{25}$ +30.8° (*c* 3.58, chloroform); n.m.r. ($CDCl_3$): δ 7.00 (d, 1, $J_{NH,H'}$ 10 Hz, exchanges in D_2O, NH), 5.91 (d, 1, $J_{1',2}$ 3.75 Hz, H-1), 5.27 (d, 1, collapses to singlet after addition of D_2O, H-1'), 4.59 (d, 1, H-2), 4.42–4.12 (overlapping signals, 4, H-5 and H-6), 3.78 (s, 3, OCH_3); 2.06 and 2.01 (2s, 6, OAc), 1.58, 1.50, 1.47, and 1.38 (4s, 12, CH_3).

Anal. Calc. for $C_{19}H_{29}NO_{10}$: C, 52.89; H, 6.78; N, 3.25. Found: C, 52.65; H, 6.81; N, 3.15.

Methyl L-*2-(3-*O*-acetyl-1,2:5,6-di-*O*-isopropylidene-α-*D*-allofuranos-3-yl-*N*-trifluoroacetylglycinate* (**10**). — To a solution of compound **5** (7.94 g) in dichloromethane (120 mL) and pyridine (10 mL) at −10° was added trifluoroacetic anhydride (10 mL), and the mixture was stirred for 0.5 h at −10°. To this mixture water (50 mL) was added and vigorous stirring maintained until the solution attained room temperature. The aqueous layer was separated and extracted with chloroform (2 × 40 mL), and the combined extracts were dried over sodium sulfate and evaporated to afford a pale-amber syrup. Column chromatography of the crude product on silica gel (450 g, 6 × 40 cm), with 3:2 benzene–ethyl acetate as developer, afforded the title compound **10** as a clear, colorless syrup (8.41 g, 85%). An analytical sample of **10** was obtained by distillation at 120–140° and 0.005 torr; $[\alpha]_D^{22}$ +5.7° (*c* 4.6, chloroform); n.m.r. ($CDCl_3$): δ 8.24 (br d, 1, $J_{1',NH}$ 9 Hz, N*H*), 6.16 (d, 1, $J_{1,2}$ 3.8 Hz, H-1), 5.88 (d, 1, H-1'), 4.75 (d, 1, H-2), 5.0–4.5 (overlapping signals, 4, H-4,5, and 6), 3.70 (s, 3, CO_2CH_3), 2.07 (s, 3, OAc), 1.77, 1.73, 1.66, and 1.51 (4s, 12, CH_3).

Anal. Calc. for $C_{19}H_{26}F_3NO_{10}$: C, 47.01; H, 5.40; N, 2.89. Found: C, 47.21; H, 5.43; N, 3.10.

L-*2-(1,2:5,6-Di-*O*-isopropylidene-α-*D*-allofuranos-3-yl)glycine* (**11**) *and* D-*2-(1,2:5,6-di-*O*-isopropylidene-α-*D*-allofuranos-3-yl)glycine* (**12**). — A solution of the α-amino ester **5** (50 mg) in 1.25% aqueous methanolic sodium hydroxide (2 mL of 1:1 solution) was stirred for 4 h, then passed through 15 mL of Rexyn-51 (H^+) (polystyrene carboxylic-acid type resin) that had been prewashed with 1% acetic acid and then water until the effluent was neutral. The column was eluted with water and the fractions giving positive ninhydrin tests were combined and evaporated to yield the amino acid **11** (35 mg, 82%) as a pale-yellow glass. Recrystallization of **11** from ethanol–ethyl acetate yielded tan crystals; m.p. 189–191°, $[\alpha]_D^{25}$ +89.2° (*c* 1.06, water); c.d. (*c* 0.68, 0.5M hydrogen chloride in methanol) $\Delta\varepsilon_{209}$ +0.97; n.m.r. (D_2O): δ 6.08 (d, 1, $J_{1,2}$ 3.5 Hz, H-1), 5.07 (d, 1, $J_{4,5}$ 3 Hz), 4.68 (DOH), 4.57 (d, 1, H-2), 4.37–3.73 (overlapping signals, 4), 1.48, and 1.30 (2s, 12, Me).

Anal. Calc. for $C_{14}H_{23}NO_8 \cdot 0.25H_2O$: C, 49.77; H, 7.01; N, 4.15. Found: C, 49.74; H, 7.10; N, 4.04.

Identical treatment of the α-amino ester **6** (55 mg) yielded amino acid **12** (40 mg, 85%) as a crystalline solid. Recrystallization of **12** from ethanol–ether yielded a white, crystalline solid; m.p. 157–159°, $[\alpha]_D^{25}$ +25° (*c* 0.7, water); c.d. (*c* 0.5, 0.5M hydrogen chloride in methanol) $\Delta\varepsilon_{209}^{MeOH}$ −0.93; n.m.r. (D_2O): δ 6.07

(d, 1, $J_{1,2}$ 3.5 Hz, H-1), 4.70 (DOH), 4.37–3.60 (overlapping signals, 5), 1.57, 1.53, and 1.38 (3s, 12, Me).

Anal. Calc. for $C_{14}H_{23}NO_8 \cdot 0.5H_2O$: C, 49.12; H, 7.07; N, 4.09. Found: C, 49.03; H, 7.15; N, 4.10.

Methyl N-*acetyl*-L-*2-(1,2:5,6-di*-O-*isopropylidene*-α-D-*glucofuranos-3-yl)glycinate* (**13**) *and methyl* N-*acetyl*-D-*2-(1,2:5,6-di*-O-*isopropylidene*-α-D-*glucofuranos-3-yl)glycinate* (**14**). — To a prehydrogenated mixture of palladium-on-charcoal (0.95 g) in methanol (100 mL) was added a solution of **2** (2.3 g) in the minimum amount of methanol, followed by acetic anhydride (6 mL). The mixture was hydrogenated for 18 h, filtered, made neutral with aqueous sodium hydrogencarbonate, and extracted with chloroform (5 × 100 mL) to yield a pale-yellow syrup (1.7 g). Column chromatography of the product on silica gel (300 g), packed and eluted with 10:5:1 benzene–ether–ethanol afforded **13** (0.27 g) and **14** (0.20 g) as pale-yellow syrups, together with ketose **1** and two unidentified compounds (0.22 g and 0.24 g).

Compound **13** was rechromatographed on silica gel (37 g, 1.8 × 30 cm, 4:1 ethyl acetate–ethanol) to yield a clear, colorless syrup (0.17 g) that was distilled at 130°/0.2 mm to yield a hard glass; m.p. 52–62°, $[\alpha]_D^{25}$ +71° (*c* 1.5, dichloromethane); n.m.r. ($CDCl_3$): δ 6.92 (broad d, 1, $J_{NH,1'}$ 6.5 Hz, NH), 5.83 (d, 1, $J_{1,2}$ 3.5 Hz, H-1), 4.97 (d, 1, H-1'), 4.35 (d, 1, H-2), 4.30 (s, 1, OH, exchanges in D_2O), 3.78 (s, 3, OCH_3), and 2.04 (s, 3, OAc).

Anal. Calc. for $C_{17}H_{27}NO_9$: C, 52.43; H, 6.99; N, 3.60. Found: C, 52.17; H, 7.10; N, 3.58. Mol. wt. by mass spectrometry 374.1430; $C_{16}H_{24}NO_9$ ($M^+ - CH_3$) requires 374.1449.

Compound **14** (0.20 g) was rechromatographed on silica gel (40 g, 1.8 × 38 cm) with 4:1 ethyl acetate–ethanol to yield a clear, colorless syrup (0.12 g). An analytical sample of **14** was prepared by preparative t.l.c. on silica-gel plates by using 1:1 benzene–ethyl acetate as developer followed by sublimation of **14** at 110°/0.1 mm to afford a hard glass, m.p. 54–56°, $[\alpha]_D^{20}$ +49.5° (*c* 0.2, dichloromethane); n.m.r. ($CDCl_3$): δ 6.90 (broad d, 1, $J_{NH,H\text{-}1'}$ 10 Hz, NH), 5.89 (d, 1, $J_{1,2}$ 4 Hz, H-1), 5.18 (d, 1, H-1'), 4.48 (d, 1, H-2), 4.28 (s, 1, OH, exchanges in D_2O), 3.80 (s, 3, OCH_3), and 2.00 (s, 1, OAc). Mol. wt. by mass spectrometry 374.1469; $C_{16}H_{24}NO_9$ ($M^+ - CH_3$) requires 374.1449.

Anal. Calc. for $C_{17}H_{27}NO_9$: C, 52.43; H, 6.99; N, 3.60. Found: C, 52.18; H, 7.07; N, 3.39.

Compounds **13** and **14** were compared directly (m.p. n.m.r., $[\alpha]_D$) with the *N*-acetyl derivatives of the previously reported[9] methyl L-(and D)-2-(1,2:5,6-di-*O*-isopropylidene-α-D-glucofuranos-3-yl)glycinate and shown to be identical.

Chromatographic investigations of the two unidentified fractions from the initial chromatography showed that the first (0.22 g) was a mixture of at least six components and the second (0.24 g) was a mixture of three components, all of which remain unidentified.

Methyl L-*2-(3,5,6-tri*-O-*acetyl-1,2*-O-*isopropylidene*-α-D-*allofuranos-3-yl)*-N-*trifluoroacetylglycinate* (**15**). — Compound **10** (716 mg) was dissolved in 66% acetic

acid (20 mL) and stirred for 48 h at room temperature. The mixture was processed conventionally to yield a pale-yellow syrup. This syrup was dissolved in a solution of acetic anhydride (20 mL) and *p*-toluenesulfonic acid monohydrate (100 mg) and stirred for 3 h at 85° and then for an additional 5.5 h at 110°. Standard isolation gave an amber syrup that was chromatographed on a column of silica gel (40 g, 2 × 32 cm), with 1:1 benzene–ethyl acetate as developer, to afford compound **15** as a clear syrup (616 mg, 79%). An analytical sample of **15** was obtained by distillation at 130° and 0.01 torr; $[\alpha]_D^{22}$ +77.3° (*c* 2.0, chloroform); n.m.r. ($CDCl_3$): δ 7.64 (br d, 1, $J_{1',NH}$ 10.0 Hz, exchanges with D_2O, NH), 6.05 (d, 1, $J_{1,2}$ 3.8 Hz, H-1), 5.83 (d, 1, collapses to singlet upon addition of D_2O, H-1'), 5.40 (oct, 1, $J_{4,5}$ 7.5 Hz, $J_{5,6b}$ 5.5 Hz, $J_{5,6a}$ 2.5 Hz, H-5), 5.12 (d, 1, H-2), 4.61 (d, 1, H-4), 4.58 (q, 1, $J_{6a,6b}$ 12.5 Hz, H-6a), 4.08 (q, 1, H-6b), 3.78 (s, 3, CO_2CH_3), 2.10, 2.06 and 2.03 (3s, 9, OAc), 1.56, 1.38, and 1.27 (3s, 6, CH_3).

Anal. Calc. for $C_{20}H_{26}F_3NO_{12}$: C, 45.37; H, 4.95; N, 2.65. Found: C, 45.17; H, 4.82; N, 2.50.

Methyl L-*2-(5,6-*O*-acetyl-1,2-*O*-isopropylidene-α-*D*-allofuranos-3-yl)-*N*-trifluoroacetylglycinate* (**16**). — Compound **10** (157 mg) was dissolved in 66% acetic acid (12 mL) and the mixture was kept for 5 h at 22° and then for 4h at 40°. The crude product obtained by conventional isolation was dissolved in acetic anhydride (1 mL) and pyridine (4 mL) and kept for 13 h at room temperature. The reagents were evaporated off to afford a pale-yellow syrup that was chromatographed on a column of silica gel (15 g, 1.5 × 22 cm) with 3:2 benzene–ethyl acetate as developer to yield the starting compound **10** (2 mg), the triacetate **15** (49 mg, 29%), and the diacetate **16** (101 mg, 65%). Compound **16** was recrystallized from ether–hexane; m.p. 141–142°, $[\alpha]_D^{22}$ +54.4° (*c* 1.1, chloroform); n.m.r. ($CDCl_3$): δ 7.54 (br d, 1, $J_{1'NH}$ 9.0 Hz, exchanges in D_2O, NH), 5.94 (d, 1, $J_{1,2}$ 3.8 Hz, H-1), 5.33 (sept, 1, $J_{5,6b}$ 7.0 Hz, $J_{4,5}$ 4.5 Hz, $J_{5,6a}$ 2.2 Hz, H-5), 5.09 (d, 1, collapses to s upon addition of D_2O, H-1'), 4.69 (q, 1, $J_{6a,6b}$ 12.5 Hz, H-6a), 4.51 (d, 2, H-2 and 4), 4.20 (q, 1, H-6b), 3.93 (s, 1, OH, exchanges in D_2O), 3.83 (s, 3, CO_2CH_3), 2.13 and 2.06 (2s, 6, OAc), 1.48, and 1.32 (2s, 6, CH_3).

Anal. Calc. for $C_{18}H_{24}F_3NO_{11}$: C, 44.36; H, 4.96; N, 2.87. Found: C, 44.57; H, 4.86; N, 2.70.

Methyl N-*acetyl*-L-*2-(1,2:5,6-di-*O*-isopropylidene-α-*D*-allofuranos-3-yl)glycinate* (**9**). — To a solution of compound **7** (500 mg) in anhydrous methanol (5 mL) was added a catalytic amount of sodium methoxide (1.5 mL of a 0.5% solution) and the solution was kept for 25 min. The solution was decationized with Amberlite IRC-50 (H^+) resin and evaporated to yield a pale-yellow glass (499 mg). The product was chromatographed on silica gel (50 g, 2 × 39 cm), with 9:1 benzene–ethyl acetate as the developer, to afford the starting material **7** (R_F 0.31, 16 mg) and compound **9** (R_F 0.30, 396 mg, 91% based on starting material consumed). Compound **9** was recrystallized from benzene–hexane; m.p. 141–142°, $[\alpha]_D^{24}$ +27.4° (*c* 1.7, chloroform); n.m.r. ($CDCl_3$): δ 6.83 (d, 1, $J_{1'-NH}$ 9.5 Hz, NHAc, exchanges with D_2O), 5.86 (d, 1, $J_{1,2}$ 4.0 Hz, H-1), 5.22 (d, 1, H-1', collapses to a singlet upon addition of D_2O),

4.44 (d, 1, H-2), 4.35 (d, 1, $J_{4,5}$ 3.0 Hz, H-4), 4.09 (s, 1, $J_{5,6a}$ 6.0 Hz, $J_{5,6b}$ 6.5 Hz, H-5), 3.83 (q, 1, $J_{6a,6b}$ 14 Hz, H-6a), 3.72 (q, 1, H-6b), 3.69 (s, 3, CO_2CH_3), 3.09 (broad s, 1, OH, exchanges with D_2O), 2.05 (s, 3, NAc), 1.46 (s, 6, CH_3), 1.39, and 1.32 (2s, 6, CH_3).

Anal. Calc. for $C_{17}H_{27}NO_9$: C, 52.43; H, 6.99; N, 3.60. Found: C, 52.08; H, 6.96; N, 3.42.

Methyl N-*acetyl*-L-*2*-(*1,2*-O-*isopropylidene*-α-D-*allofuranos-3-yl*)*glycinate* (**17**). — Compound **9** (200 mg) was dissolved in 66% acetic acid (10 mL) and kept for 28 h at room temperature. Evaporation of the solution gave a pale-yellow glass, which was then dissolved in methanol (10 mL). This solution was decolorized with activated charcoal and evaporated to give a clear, colorless glass in quantitative yield; n.m.r. (Me_2SO-d_6): δ 8.52 (d, 1, $J_{NH,1'}$ 8.5 Hz, NHAc, exchanges with D_2O), 5.85 (d, 1, $J_{1,2}$ 3.5 Hz, H-1), 5.70 (br s, 1, OH, exchanges with D_2O), 5.13 (d, 1, H-1′, collapses to s upon addition of D_2O), 5.09 (br s, 1, OH, exchanges with D_2O), 4.92 (br s, 1, OH, exchanges in D_2O), 4.52 (d, 1, H-2), 4.30 (d, 1, $J_{4,5}$ 6 Hz, H-4), 4.00–3.10 (m, 3, H-5,6), 3.69 (s, 3, CO_2CH_3), 2.00 (s, 3, Ac), 1.47, and 1.36 (2s, 6, CH_3).

Compound **17** was acetylated with acetic anhydride and pyridine to yield the previously prepared methyl *N*-acetyl-L-2-(5,6-di-*O*-acetyl-1,2-*O*-isopropylidene-α-D-allofuranos-3-yl)glycinate (**18**), 214 mg (96%).

Methyl N-*acetyl*-L-*2*-(*5,6-di*-O-*acetyl*-*1,2*-O-*isopropylidene*-α-D-*allofuranos-3-yl*)*glycinate* (**18**). — Compound **17** (110 mg) in anhydrous pyridine (2 mL) and acetic anhydride (1 mL) was stirred for 24 h at 22°. Conventional isolation yielded compound **18** (117 mg, 96%) as a clear syrup. An analytical sample of **18** was obtained by distillation at 160–170° and 0.3 torr; $[\alpha]_D^{23}$ +72.5° (*c* 0.8, chloroform); $\nu_{max}^{CHCl_3}$ 3450 (OH, NH), 1740 (C=O), and 1690 cm^{-1} (amide I); n.m.r. ($CDCl_3$): δ 6.82 (d, 1, $J_{NH,H-1'}$ 8.5 Hz, N*H*, exchanges in D_2O), 5.90 (d, 1, $J_{1,2}$ 3.8 Hz, H-1), 5.49 (oct, 1, $J_{4,5}$ 3.5 Hz, $J_{5,6a}$ 2.5 Hz, $J_{5,6b}$ 7.8 Hz, H-5), 5.08 (d, 1, H-1′, collapsed to singlet upon addition of D_2O), 4.74 (q, 1, $J_{6a,6b}$ 12.5 Hz, H-6a), 4.46 (d, 1, H-4), 4.45 (s, 1, OH, exchanges in D_2O), 4.44 (d, 1, H-2), 4.13 (q, 1, H-6b), 3.79 (s, 3, CO_2CH_3), 2.09 (s, 3, OAc), 2.03 (s, 3, OAc), 1.48, and 1.31 (2s, 6, CH_3).

Anal. Calc. for $C_{18}H_{27}NO_{11}$: C, 49.88; H, 6.28; N, 3.23. Found: C, 49.66; H, 6.33; N, 3.20.

Methyl N-*acetyl*-L-*2*-(*5*-O-*acetyl*-*1,2*-O-*isopropylidene*-α-D-*ribofuranos-3-yl*)*glycinate* (**19**) *and methyl* N-*acetyl*-L-*2*-(*1,2*-O-*isopropylidene*-α-D-*ribofuranos-3-yl*)*glycinate* (**20**). — To a solution of crude compound **17** in water (10 mL) and methanol (5 mL) was added a solution of sodium metaperiodate (109 mg) in water (4 mL) over a period of 15 min. Ethylene glycol (2 drops) was then added to consume the unreacted sodium metaperiodate, and after 5 min, sodium borohydride (10 mg) was added to the solution. The resulting solution was stirred for 15 min at room temperature and then acetone (1 mL) was added. After a further 15 min, the solution was evaporated and ethanol (5 mL) was added to the resulting, white solid. The mixture was cooled to 0°, filtered through sintered glass, and the filtrate evaporated to yield

a colorless glass. The crude product was dissolved in acetic anhydride (1 mL) and pyridine (2 mL) and stirred for 24 h at room temperature. The mixture was processed conventionally to yield a tan-coloured solid that was chromatographed on a column of silica gel (20 g) with 4:1 benzene–ethanol as the developer, to afford compounds **19** (21 mg, 13%) and **20** (38 mg, 26%). An analytical sample of compound **19** was obtained by distillation at 150° and 0.02 torr; $[\alpha]_D^{24}$ +57° (*c* 0.4, chloroform); n.m.r. ($CDCl_3$): δ 6.79 (broad d, 1, $J_{NH,1'}$ 8.5 Hz, exchanges in D_2O, N-H), 5.95 (d, 1, $J_{1,2}$ 3.8 Hz, H-1), 5.07 (d, 1, H-1'), 4.47 (d, 1, H-2), 4.6–4.2 (overlapping signals, 4, addition of D_2O reduces integration to 3 protons, H-4, H-5, and OH), 3.80 (s, 3, CO_2CH_3), 2.12 and 2.08 (2s, 6, Ac), 1.50, and 1.32 (2s, 6, CH_3).

Anal. Calc. for $C_{15}H_{23}NO_9$: C, 49.86; H, 6.41; N, 3.88. Found: C, 49.47; H, 6.40; N, 3.83. Mol. wt. by mass spectrometry 361.1349; $C_{15}H_{23}NO_9$ requires 361.1372; ($M^+ - CH_3$) 346.1136; required = 346.1138.

An analytical sample of compound **20** was obtained by distillation at 150° and 0.02 torr; $[\alpha]_D^{24}$ +44° (*c* 1.0, chloroform); n.m.r. ($CDCl_3$): δ 6.95 (broad d, 1, $J_{NH-1'}$ 9.0 Hz, exchanges in D_2O, NH), 5.95 (d, 1, $J_{1,2}$ 3.7 Hz, H-1), 5.57 (broad s, 1, exchanges in D_2O, OH), 5.20 (d, 1, collapses to singlet upon addition of D_2O, H-1'), 4.60–3.95 (overlapping signals, 5, addition of D_2O decreases integral to 4 protons, H-2, 4, 5, and OH), 3.80 (s, 3, CO_2CH_3) 2.10 (s, 3, Ac), 1.52 and 1.34 (2s, 6, CH_3).

Anal. Calc. for $C_{13}H_{21}NO_8$: C, 48.89; H, 6.63; N, 4.39. Found: C, 48.51; H, 6.46; N, 4.35. Mol. wt. by mass spectrometry 304.1013; $C_{12}H_{18}NO_8$ ($M^+ - CH_3$) requires 304.1032.

Methyl L-*2-(1,2,3,5,6-penta*-O-*acetyl-α,β*-D-*allofuranos-3-yl)*-N-*trifluoroacetyl-glycinate* (**21**). — To a solution of compound **15** (3.9 g) in acetic acid (78 mL) and acetic anhydride (78 mL) was added *p*-toluenesulfonic acid monohydrate (1.9 g), and the resulting solution was stirred for 2 h at 110°. Chloroform (300 mL) was added and the solution was washed with water (2 × 100 mL) and saturated sodium hydrogencarbonate solution (2 × 125 mL), dried over sodium sulfate, and evaporated to yield a dark-amber syrup. This syrup was chromatographed on silica gel (400 g), with 3:2 benzene–ethyl acetate as the developer, to yield compound **21** (2.0 g, 47%) as a bright-yellow foam. An analytical sample of compound **21** was obtained by distillation at 150° and 0.01 torr; $[\alpha]_D^{22}$ +59.7° (*c* 1.9, chloroform); n.m.r. ($CDCl_3$): δ 7.56 (br d, 1, $J_{NH,1'}$ 9.6 Hz, exchanges in D_2O; NH), 6.42 (d, 1/3, $J_{1,2}$ 5.1 Hz, H-1α), 6.04 (s, 2/3, H-1β), 6.01 (s, 2/3, H-2b), 5.64 (d, 1/3, H-2α), 5.56, (1, H-1'), 5.34 (0, 2/3, $J_{4,5}$ 7.2 Hz, $J_{5,6a}$ 2.6 Hz, $J_{5,6b}$ 6.1 Hz, H-5β), 5.28 (0, 1/3, $J_{5,6a}$ 2.4 Hz, $J_{4,5}$ 5.6 Hz, $J_{5,6b}$ 6.4 Hz, H-5a), 4.68 (d, 2/3, H-4b), 4.63, (2, 2/3, $J_{6a,6b}$ 12.1 Hz, H-6a,b), 4.61 (q, 1/3, $J_{6a,6b}$ 12.5 Hz, H-6a), 4.51 (2s, 3, CO_2CH_3), 2.14, 2.12, 2.10, 2.08, 2.07, 2.06, 2.06, 2.03, and 2.01 (8s, 15, OAc).

Anal. Calc. for $C_{21}H_{26}F_3NO_{14}$: C, 43.99; H, 4.57; N, 2.44. Found: C, 43.74; H, 4.31; N, 2.33.

Attempted synthesis of adenine nucleoside from pentaacetate **21**: *synthesis of 2,3,5,6-tetra*-O-*acetyl-1,1*^{1}-*anhydro-3*-C-(R)-(*methoxycarbonyl)methyl-1*-(R), *1*^{1}(S)-

N-trifluoroacetoepimino-β-D-allofuranose (**22**). — To a solution of compound **21** (52 mg) in dichloromethane (6 mL) kept at 0° was added a slow stream of anhydrous hydrogen bromide for 2.5 h. The solvent and the residual acidic components were removed by repeated evaporation of toluene (3 × 3 mL) at <35° and 15 torr. To the resulting syrup was added a solution of N^6-benzoyl-N^6, 9-bis(trimethylsilyl)adenine in dichloromethane (3 mL) and, after removal of the solvent, the resulting syrup was fused for 20 min at 160° and 15 torr.

The mixture was cooled to give a dark glass, to which was added ethanol (10 mL) saturated with sodium hydrogencarbonate. The mixture was filtered and the solvent evaporated to yield 65 mg of a dark-brown, amorphous solid. The crude product was chromatographed on a column of silica gel (17 g, 1.5 × 25 cm) with 3:2 benzene–ethyl acetate as developer to yield the starting material **21** (19 mg) and the title compound **22** (15 mg, 52% based on starting material consumed). An analytical sample of compound **22** was obtained by distillation at ~150° and 0.02 torr; $[\alpha]_D^{22}$ +117° (*c* 1.8, chloroform); n.m.r. ($CDCl_3$): δ 5.59 [s (with two shoulders), 1, H-1], 5.39 [s (with shoulders) 1, H-1'], 5.30 (sex, 1, $J_{4,5}$ 6.5 Hz, $J_{5,6a}$ 3.9 Hz, $J_{5,6b}$ 6.2 Hz, H-5), 5.00 (d, 1, H-4), 4.76 (s, 1, H-2), 4.44 (q, 1, $J_{6a,6b}$ 12.0 Hz, H-6a), 4.01 (q, 1, H-6b), 3.76 (s, 3, CO_2CH_3), 2.10, 2.06, 2.01 and 2.00 (4s, 12, OAc).

Anal. Calc. for $C_{19}H_{22}F_3NO_{12}$: C, 44.45; H, 4.32; N, 2.73. Found: C, 44.40; H, 4.25; N, 2.79. Mol. wt. by mass spectrometry 514.1194; $C_{19}H_{23}F_3NO_{12}$ requires 514.1173; ($M^+ - OCH_3$) 482.0897; required 482.0910.

Fusion of compound **21** with 2,6-dichloropurine or with N^6-benzoyl-$N^{6,9}$-bis(trimethylsilyl)adenine for 20 min at 160° afforded no nucleoside. The reaction[16] of **21** with 2,4-bis(trimethylsilyl)thymine in acetonitrile and tin tetrachloride for 2.5 h at room temperature yielded no nucleoside.

1-[2,3,5,6-Tetra-O-acetyl-[3-C-(methyl N-trifluoroacetyl-L-2-glycinate)]-β-D-allofuranosyl]thymine (**23**). — An α,β mixture of compound **21** (500 mg) was dissolved in anhydrous dichloromethane (30 mL) and the solution was cooled to 0°. A slow stream of anhydrous hydrogen bromide was passed through the cooled solution for 2 h. The solution was evaporated to dryness and toluene (2 × 5 mL) was evaporated from the mixture to remove traces of acetic acid. The resulting syrup was dissolved in anhydrous dichloromethane (2.6 mL) and added to a cooled (−70°) mixture of silver triflate (112 mg, 0.5 equiv) in anhydrous dichloromethane (0.6 mL) and to the resulting mixture was added a solution of bis(trimethylsilyl)thymine (259 mg, 1.0 equiv) in anhydrous dichloromethane (1.4 mL)[17,18]. The mixture was maintained for 2 h at −70° and then allowed to attain room temperature. After 18 h, the solution was cooled to 0° and a saturated solution of sodium hydrogencarbonate (2 mL) added with vigorous stirring. The mixture was filtered and the precipitate washed with water (5 mL) and dichloromethane (10 mL). The dichloromethane layer was then separated, dried over sodium sulfate, and evaporated to afford a yellow syrup. Column chromatography of the crude product on silica gel (60 g, 2.8 × 26 cm) with 10:5:1 benzene–ether–ethanol as developer yielded the starting material **21** (267 mg, 54%) and the

title compound **23** (242 mg, 93% based on starting material consumed) as a glass; m.p. 91–96°, $[\alpha]_D^{22}$ +51.8° (*c* 1.5, dichloromethane); n.m.r. ($CDCl_3$): δ 9.55 (s, 1, NH), 7.63 (d, 1, $J_{NH,1''}$, 10.0 Hz, $NHCOCF_3$), 7.24 (s, 1, H-6), 6.05 (d, 1, $J_{1',2'}$ 7.2 Hz, H-1′), 5.78 (d, 1, H-2′), 5.61 (d, 1, H-1″), 5.42 (sept, 1, $J_{4',5'}$ 7.5 Hz, $J_{5',6'a}$ 2.2 Hz, $J_{5',6'b}$ 6.0 Hz, H-5′), 4.88 (d, 1, H-4′), 4.60 (q, 1, $J_{6'a,6'b}$ 12.2 Hz, H-6′a), 4.03 (q, 1, H-6′b), 3.84 (s, 3, CO_2CH_3), 2.10, 2.07 and 2.04 (3s, 12, OAc), and 1.93 (s, 3, CH_3); c.d. (*c* 0.001, methanol) $[\theta]_{268}$ +3600 (peak).

Anal. Calc. for $C_{24}H_{28}F_3N_3O_{14}$: C, 45.08; H, 4.41; N, 6.57. Found: C, 45.77; H, 4.57; N, 6.56.

Attempted deprotection of nucleoside **23** *to yield* **24** *and* **25**. — *(A) With sodium methoxide in methanol.* To a solution of nucleoside **23** (44 mg) in anhydrous methanol (5 mL) was added a methanolic solution of sodium methoxide (0.1 mL, 0.1 equiv.) and the solution was kept for 24 h at room temperature. The mixture was deionized with IRC-50 (H^+) cation-exchange resin and the filtrate then evaporated to yield a solid (30 mg). Paper chromatography of the product with 10:4:3 ethyl acetate–pyridine–water as developer showed the presence of six compounds. The ^{1}H-n.m.r. spectrum of the major component (3 mg) showed it to be a mixture.

Attempted column chromatography of the crude product on Bio-Rex 70 (H^+) resin using water or 4:1 methanol–water as developer failed to separate the products.

B. With methanolic ammonia. The nucleoside **23** (30 mg) was allowed to react[27] with a saturated solution of ammonia in methanol for 5 days at 0°. The mixture of products could not be separated by paper chromatography with 10:4:3 ethyl acetate–pyridine–water.

C. With hydrogen chloride–methanol. The nucleoside **23** was allowed to react with anhydrous hydrogen chloride in methanol for 18 h at room temperature. Conventional isolation of the product[28] gave partially deprotected nucleoside.

D. With triethylamine–methanol or triethylamine–methanol–water[2]. Application of these procedures to nucleoside **23** failed to *O*-deacetylate the nucleoside fully.

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