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TRIFLUOROACETYL AS AN *N*-PROTECTIVE GROUP IN THE SYNTHESIS OF PURINE NUCLEOSIDES OF 2-AMINO-2-DEOXY SACCHARIDES

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ABSTRACT

Selective *N*-(trifluoroacetyl)ation of 2-amino-2-deoxy-D-glucose, followed by *O*-acetylation, gave the anomeric 1,3,4,6-tetra-*O*-acetyl-2-deoxy-2-(trifluoroacetamido)-α(and β)-D-glucopyranoses (**3** and **4**). Conversion of **3** and **4** into the bromide, followed by condensation with 6-benzamido-9-(chloromercuri)-9*H*-purine, produced 6-benzamido-9-[3,4,6-tri-*O*-acetyl-2-deoxy-2-(trifluoroacetamido)-α-D-glucopyranosyl]-9*H*-purine and the corresponding β-D anomer. Removal of substituent groups was achieved by means of methanolic ammonia, giving the anomeric, crystalline 9-(2-amino-2-deoxy-α(and β)-D-glucopyranosyl)adenines. Application of this procedure to 2-amino-2-deoxy-D-galactose gave, as the final products, 9-(2-amino-2-deoxy-α-D-galactopyranosyl)adenine and the corresponding β-D anomer, characterized as their crystalline dihydrochlorides.

INTRODUCTION

In the synthesis of nucleosides of 2-amino-2-deoxy saccharides, considerable difficulty has been experienced in the selection of an *N*-protective group which can be conveniently introduced and easily removed. The synthesis of purine nucleosides of this type presents special problems, since purine nucleosides, in contrast to pyrimidine nucleosides, are unstable to acid[1]. Thus, the *N*-protective group employed must be removable under basic or neutral conditions. The *N*-acetyl protective group was employed by Baker and co-workers[2] for the synthesis of 9-(2-amino-2-deoxy-β-D-allopyranosyl)-6-(dimethylamino)-9*H*-purine. The removal of the *N*-acetyl group was effected by refluxing with aqueous barium hydroxide, but this procedure failed when applied to nucleoside derivatives wherein the 3-hydroxyl group bore a *trans* relationship to the 2-amino group. Stevens and co-workers[3] also employed the *N*-acetyl protective group for the synthesis of pyrimidine nucleosides, where the stability of these nucleosides to acids allowed the removal of this protective group. The *N*-(benzyloxycarbonyl) and *N*-(methoxycarbonyl) protective groups were also employed by Stevens and co-workers for synthesis of pyrimidine nucleosides. The *N*-bis(phenoxy)phosphinyl[4] and the *N*-(2,4-dinitrophenyl)[5,6] groups have been successfully employed in the synthesis of purine nucleosides of 2-amino-2-deoxy sugars. In all cases, the

N-(2,4-dinitrophenyl) group gave both anomeric nucleosides, since it shows no tendency to participate at C-1. The *N*-bis(phenoxy)phosphinyl[4] and *N*-(2,4-dinitrophenyl)[7] groups have also been employed in the synthesis of pyrimidine nucleosides of 2-amino-2-deoxy saccharides.

We report herein the use of the trifluoroacetyl group as an *N*-protecting group in the synthesis of both anomers of 9-(2-amino-2-deoxy-D-glucopyranosyl)adenine[5] (**6c** and **7c**) and of 9-(2-amino-2-deoxy-D-galactopyranosyl)adenine (**13c** and **14c**). We have previously reported the use of this group in the synthesis of a pyrimidine nucleoside[8].

RESULTS AND DISCUSSION

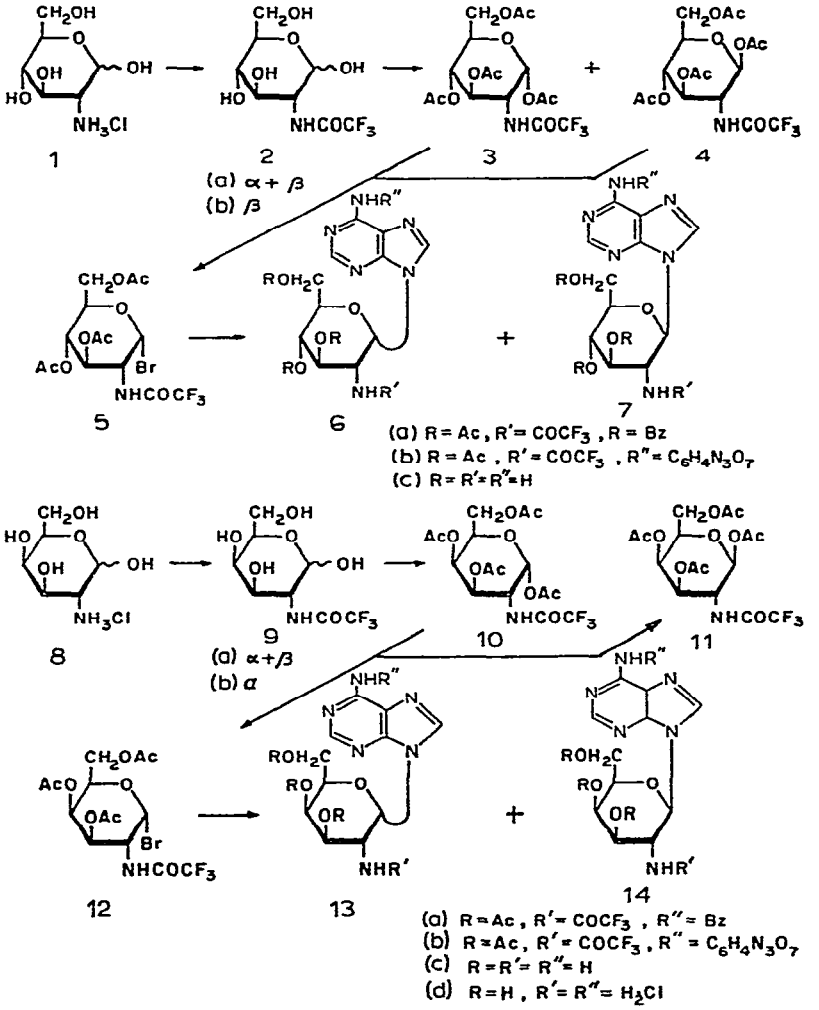
In the present work, direct introduction of the *N*-(trifluoroacetyl) group into the unsubstituted saccharide was accomplished by selective acylation of the amino group with *S*-ethyl trifluorothioacetate. This reagent has been employed for the introduction of the *N*-(trifluoroacetyl) group into amino acids, for peptide synthesis[9]. Previous methods for the introduction of the *N*-(trifluoroacetyl) group in the sugar series[8,10] required prior selective acetylation of the hydroxyl groups.

Treatment of a solution of 2-amino-2-deoxy-D-glucose in methanol with *S*-ethyl trifluorothioacetate produced 2-deoxy-2-(trifluoroacetamido)-D-glucose (**2a**). By repeated recrystallization, the β-D anomer (**2b**) was obtained. Similar treatment of a solution of 2-amino-2-deoxy-D-galactose in methanol produced 2-deoxy-2-(trifluoroacetamido)-D-galactose (**9a**). In this case, the α-D anomer (**9b**) was isolated by repeated recrystallization.

By acetylating **2a** with pyridine–acetic anhydride, crystalline 1,3,4,6-tetra-*O*-acetyl-2-deoxy-2-(trifluoroacetamido)-α-D-glucopyranose (**3**) and the corresponding crystalline β-D anomer (**4**) were obtained in yields of 40 and 45%, respectively. The latter compound was identical with authentic **4** previously prepared in this laboratory[8] from 1,3,4,6-tetra-*O*-acetyl-2-amino-2-deoxy-β-D-glucopyranose hydrochloride[11]. The α-D anomer (**3**) was found to be more dextrorotatory than **4**, indicating qualitative agreement with the Hudson rules of rotation[12]. Anomeric assignments for **2b**, **9b**, **10**, and **11** were thus made on the basis of optical rotation. Acetylation of **9a** produced crystalline 1,3,4,6-tetra-*O*-acetyl-2-deoxy-2-(trifluoroacetamido)-α-D-galactopyranose (**10**) and the corresponding crystalline β-D anomer (**11**) in yields of 46 and 37%, respectively. Treatment of **3** with hydrogen bromide in acetic acid produced the crystalline 3,4,6-tri-*O*-acetyl-2-deoxy-2-(trifluoroacetamido)-α-D-glucopyranosyl bromide (**5**) previously reported[8,10]. Compound **5** was also prepared from a mixture of **3** and **4**, thus avoiding the isolation of the individual anomeric acetates. Similarly, treatment of **10** or **11**, or a mixture of the two, produced syrupy 3,4,6-tri-*O*-acetyl-2-deoxy-2-(trifluoroacetamido)-α-D-galactopyranosyl bromide (**12**).

Condensation of **5** with 6-benzamido-9-(chloromercuri)-2*H*-purine by the general procedure of Davoll and Lowy[13] produced an anomeric mixture of fully substituted nucleoside derivatives which was separable, by preparative t.l.c., into

crystalline 6-benzamido-9-[3,4,6-tri-*O*-acetyl-2-deoxy-2-(trifluoroacetamido)-α-D-glucopyranosyl]purine (**6a**) and the corresponding, amorphous β-D anomer (**7a**) in yields of 6.6 and 26%, respectively. Both **6a** and **7a** formed well defined, crystalline picrates (**6b** and **7b**) on de-*N*-benzoylation with picric acid in isopropyl alcohol–methanol. Complete removal of all of the substituent groups from 6-benzamido-9-[3,4,6-tri-*O*-acetyl-2-deoxy-2-(trifluoroacetamido)-α(and β)-D-glucopyranosyl]purine (**6a** and **7a**) was achieved by treatment with methanolic ammonia at room temperature for 7 days, to give crystalline 9-(2-amino-2-deoxy-α-D-glucopyranosyl)adenine (**6c**) and the crystalline β-D anomer (**7c**), in yields of 89 and 86%, respectively. Both products exhibited physical constants identifiable with those for the compounds previously prepared in this laboratory[5]. For each anomeric pair (**6a**, **7a**; **6b**, **7b**; and **6c**, **7c**), the α-D anomer was the more dextrorotatory.



Condensation of 3,4,6-tri-*O*-acetyl-2-deoxy-2-(trifluoroacetamido)-α-D-galactopyranosyl bromide (**12**) with 6-benzamido-9-(chloromercuri)purine, by the procedure used for the corresponding 2-amino-2-deoxy-D-glucosyl bromide (**5**), produced an anomeric mixture of nucleoside derivatives. Separation by preparative t.l.c. gave crystalline 6-benzamido-9-[3,4,6-tri-*O*-acetyl-2-deoxy-(2-trifluoroacetamido)-α-D-galactopyranosyl]adenine (**13a**) and the corresponding amorphous β-D anomer (**14a**) in yields of 9.3 and 30%, respectively. Both products gave crystalline picrates (**13b** and **14b**) on de-*N*-benzoylation with picric acid in isopropyl alcohol–methanol. Deacylation of **13a** and **14a** with methanolic ammonia yielded 9-(2-amino-2-deoxy-α-D-galactopyranosyl)adenine (**13c**) and the corresponding β-D anomer (**14c**) in yields of 83 and 81%, respectively. Both **13c** and **14c** were amorphous but formed crystalline dihydrochlorides (**13d** and **14d**) on treatment with dilute hydrochloric acid in methanol. Since a qualitative agreement with Hudson's rules of rotation was shown by the nucleoside derivatives of 2-amino-2-deoxy-D-glucose (**6a–c** and **7a–c**), it was assumed that the corresponding derivatives of 2-amino-2-deoxy-D-galactose would show similar agreement. The anomeric assignments of the preceding nucleoside derivatives of 2-amino-2-deoxy-D-galactose were thus made on the basis of optical rotation, **13a–d** being the more dextrorotatory of the respective anomeric pairs.

The *N*-trifluoroacetyl group has thus proved to be a suitable *N*-protective group in synthesis of purine nucleosides of 2-amino-2-deoxy-D-glucopyranose and 2-amino-2-deoxy-D-galactopyranose. As the *N*-trifluoroacetyl group could be directly introduced, without the need for prior selective substitution of the hydroxyl groups, and as it could be removed simultaneously with the *O*-acetyl groups, only five steps were needed to synthesize the nucleoside from the free amino saccharide. The overall yields of 9-(2-amino-2-deoxy-α-D-glucopyranosyl)adenine (**6c**) and the corresponding β-D anomer (**7c**) were 5.9 and 22%, respectively, based on the glycosyl bromide (**5**), or 3.5 and 13%, respectively, based on 2-amino-2-deoxy-D-glucose hydrochloride (**1**). The overall yields of 9-(2-amino-2-deoxy-α-D-galactopyranosyl)adenine (**13c**) and the corresponding β-D anomer (**14c**) were 7.7 and 24%, respectively, based on the bromide (**12**), or 4.5 and 14%, respectively, based on 2-amino-2-deoxy-D-galactose hydrochloride (**8**). The overall yields of **6c** and **7c**, obtained by previous procedures, were 4.0 and 5.2%, respectively[5], and 9.3% for[4] **7c**, based on the particular *N*-protected 2-amino-2-deoxy-D-glucosyl bromides used.

The fact that both anomers of the nucleoside derivatives of 2-amino-2-deoxy-D-glucose and 2-amino-2-deoxy-D-galactose were obtained indicates that the *N*-trifluoroacetyl group does not participate strongly at C-1. The use of such a strongly participating group as *N*-acetyl[14,15] has been found to give only the β-D anomers of purine nucleoside derivatives of 2-amino-2-deoxy-D-glucose. The α:β ratio was 26:100 for the *N*-(trifluoroacetyl)-protected, anomeric nucleoside derivatives of 2-amino-2-deoxy-D-glucose (**6a** and **7a**), and 31:100 for the corresponding derivatives of 2-amino-2-deoxy-D-galactose (**13a** and **14a**). These results indicate that the *N*-(trifluoroacetyl) group probably participates to a slight extent at C-1. Steric factors

might also account for the preponderance of the β-D anomer. However, use of the completely nonparticipating *N*-(2,4-dinitrophenyl) group gave a much higher α:β ratio. Thus, condensation of 3,4,6-tri-*O*-acetyl-2-deoxy-2-(2,4-dinitroanilino)-α-D-glucopyranosyl bromide with 6-acetamido-9-(chloromercuri)purine gave[5] the anomeric nucleoside derivatives in the α:β ratio of 60:100. In view of this result, a much higher α:β ratio for **6a**:**7a** and **13a**:**14a** would be expected were the *N*-(trifluoroacetyl) group completely nonparticipating at C-1.

EXPERIMENTAL

General methods. — Melting points were determined with a Thomas–Hoover apparatus. Specific rotations were determined in a 2-dm polarimeter tube. Infrared spectra were recorded with a Perkin–Elmer Infracord spectrometer. Ultraviolet spectra were recorded with a Bausch and Lomb Spectronic 505 spectrometer. X-Ray powder diffraction data (interplanar spacing, Å; Cu Kα radiation; λ 1.539 Å; Ni filter; camera diameter 114.6 mm; photographic recording) are expressed as relative intensities, estimated visually: m, moderate; s, strong; v, very; w, weak. Parenthetical numbers indicate the order of the most intense lines; 1, most intense; multiple numbers indicate approximately equal intensities. T.l.c. was performed with Desaga equipment, by use of Silica Gel G (E. Merck, Darmstadt, Germany), activated at 110°. Unless otherwise noted, indication was by sulfuric acid; amounts of developers are by volume. Microanalyses were performed by W. N. Rond. Unless otherwise indicated, evaporations were performed under diminished pressure (water aspirator).

2-Deoxy-2-(trifluoroacetamido)-D-glucose (**2**). — A suspension of 2-amino-2-deoxy-D-glucose hydrochloride (**1**, 10 g) in anhydrous methanol (50 ml) was treated with an equivalent amount of sodium methoxide in methanol (1.06 g of sodium dissolved in 10 ml of methanol), and the mixture was swirled until only a small residue (sodium chloride) remained. *S*-Ethyl trifluorothioacetate (10 g) was added, the mixture was kept for 24 h at room temperature, and the solution was evaporated to a solid residue which was extracted with hot acetone (300 ml), the insoluble material being discarded. After the acetone extract had been cooled to room temperature, ether (200 ml) was added, and the mixture was refrigerated overnight. The white, crystalline solid which formed was recrystallized from acetone–ether, giving 9.3 g (73%) of 2-deoxy-2-(trifluoroacetamido)-D-glucose (**2a**): m.p. 193–195° (dec.), $[\alpha]_D^{22}$ +12 ±1 (initial, extrapolated) → +15 ±1° (final; *c* 2.5, water).

Anal. Calc. for $C_8H_{12}F_3NO_6$: C, 34.92; H, 4.40; N, 5.09. Found: C, 35.04; H, 4.70; N, 5.37.

Four additional recrystallizations from acetone gave the β-D anomer (**2b**): m.p. 196–197° (dec.), $[\alpha]_D^{22}$ −28 ±2 (initial, extrapolated) → +15 ±1° (final; *c* 1.5, water); λ_{max}^{KBr} 2.9–3.1 (OH, NH), 5.85 (*N*-trifluoroacetyl carbonyl), 6.4 (NH), 8.6 (CF), 7.35, 7.6, 7.8, 8.23, 8.45, 9.08, 9.28, 9.6, 9.82, 10.1, 11.1, 11.32, 11.44, and 13.64 μm; X-ray powder diffraction data: 10.72 m, 9.41 vw, 6.81 m, 5.32 vs (2), 5.00 m, 4.60 vs (3), 4.23 s, 3.95 vs (1), 3.75 w, 3.68 s, 3.49 vs, 3.19 m, 3.08 w, 2.93 w, 2.84 vs, 2.64 s, 2.50 m, 2.37 m, 2.31 vs, 2.21 w, 2.08 s, 1.99 w, 1.93 w, 1.86 vw,

1.77 w, and 1.66 w. The physical constants of this compound were unchanged by-further recrystallization.

Anal. Calc. for $C_8H_{12}F_3NO_6$: C, 34.92; H, 4.40; N, 5.09. Found: C, 34.55; H, 4.29; N, 5.13.

2-Deoxy-2-(trifluoroacetamido)-D-galactose (**9**). — A suspension of 2-amino; 2-deoxy-D-galactose hydrochloride (**8**, 5 g) in methanol (25 ml) was treated with sodium (0.53 g) in methanol (10 ml) and *S*-ethyl trifluorothioacetate (5 g) by the procedure described in the preceding experiment. The yield, after recrystallization from acetone–ether, was 4.8 g (76%) of 2-deoxy-2-(trifluoroacetamido)-D-galactose (**9a**): m.p. 184–186° (dec.), $[\alpha]_D^{21}$ +68 ±2 (initial, extrapolated) → +59 ±1° (final; *c* 2.9, water).

Anal. Calc. for $C_8H_{12}F_3NO_6$: C, 34.92; H, 4.40; N, 5.09. Found: C, 34.88; H, 4.65; N, 4.88.

Four additional recrystallizations from acetone gave the α-D anomer (**9b**): m.p. 192–193° (dec.), $[\alpha]_D^{22}$ +108 ±2 (initial extrapolated) → +60 ±1.5° (final; *c* 2.0, water); λ_{max}^{KBr} 3.0–3.1 (NH, OH), 5.9 (*N*-trifluoroacetyl carbonyl), 6.42 (NH), 8.62 (CF), 7.42, 7.68, 7.9, 8.28, 8.35, 8.8, 9.03, 9.18, 9.44, 9.56, 9.7, 9.98, 10.28, 10.6, 11.06, 11.42, 11.75, 12.43, and 13.7 μm; X-ray powder diffraction data: 11.26 vw, 9.88 vw, 8.85 vw, 6.63 m, 5.56 s, 5.10 s (2), 4.77 w, 4.50 s (1), 4.31 s (3), 3.96 s, 3.70 s (2), 3.50 m, 3.31 m, 3.16 m, 3.01 m, 2.84 m, 2.68 w, 2.49 w, 2.39 vw, 2.30 m, 2.22 w, and 2.06 w. The physical constants of this compound were unchanged by further recrystallization.

Anal. Calc. for $C_8H_{12}F_3NO_6$: C. 34.92; H, 4.40; N, 5.09. Found: C, 34.79; H, 4.69; N, 4.78.

1,3,4,6-Tetra-O-acetyl-2-deoxy-2-(trifluoroacetamido)-α(and β)-D-glucopyranose (**3** *and* **4**). — 2-Deoxy-2-(trifluoroacetamido)-D-glucose (**2a**, 2.0 g) was dissolved in a pre-cooled (0°) mixture of pyridine (16 ml) and acetic anhydride (9 ml); the solution was kept overnight at room temperature, and then poured into iced water (30 ml), and the mixture extracted with dichloromethane (80 ml). The extract was washed successively with N hydrochloric acid (until the acid was no longer neutralized), 15% aqueous sodium hydrogen carbonate solution, and water, and dried (sodium sulfate). Evaporation of the solvent yielded a clear syrup which, by t.l.c. with ether as the developer, showed two major components (R_F 0.47 and 0.57). The crude product was crystallized and recrystallized from methanol–water, to give 1.0 g (31%) of 1,3,4,6-tetra-*O*-acetyl-2-deoxy-2-(trifluoroacetamido)-β-D-glucopyranose (**4**) as a white, crystalline solid: m.p., and m.m.p. with authentic material[8], 166–167.5°; $[\alpha]_D^{25}$ −12 ±1° (*c* 3.4, chloroform); lit.[8] m.p. 167°, $[\alpha]_D^{22}$ −13° (*c* 2.4, chloroform). The X-ray powder diffraction data were identical with those for this compound previously prepared in this laboratory[8]. The compound was homogeneous by t.l.c., with ether as the developer, and corresponded to the faster-moving component of the crude product (R_F 0.57).

The mother liquors from the two recrystallizations of **4** were evaporated to yield a clear, syrupy residue which, by t.l.c. with ether as the developer, showed a major component (R_F 0.48) and a minor component (R_F 0.56). These two components

were isolated by resolution on 24 chromatoplates (200 × 200 × 1.25 mm), with ether as the developer and indication by iodine vapor. The two zones were removed, and extracted with acetone. Each acetone extract was evaporated, and the residues were dissolved in dichloromethane. The resulting solutions were successively washed with 15% aqueous potassium iodide and water, dried (sodium sulfate), and evaporated. The residue from the faster-moving zone (R_F 0.56) was crystallized from methanol–water, to yield an additional 0.45 g (14%) of **4**: m.p. and m.m.p. 166–167.5°; $[\alpha]_D^{23}$ −11.5 ±2° (*c* 1.5, chloroform).

The material from the slower-moving zone (R_F 0.48) was crystallized from ether–hexane to give 1.3 g (40%) of 1,3,4,6-tetra-*O*-acetyl-2-deoxy-2-(trifluoroacetamido)-α-D-glucopyranose (**3**): m.p. 124.5–126°; $[\alpha]_D^{21}$ +70 ±1° (*c* 4.7, chloroform); λ_{max}^{KBr} 3.0 (NH), 5.7 (*O*-acetyl carbonyl), 5.83 (*N*-trifluoroacetyl carbonyl), 6.4 (NH), 8.1–8.25 (ester), 8.55 (CF), 6.9, 7.0, 7.3, 8.9, 9.4, 9.76, 10.4, 10.62, 10.8, 11.1–11.2, 11.5, 12.95, and 13.7 μm; X-ray powder diffraction data: 16.37 vw, 10.53 s, 9.46 vs (1), 8.21 s, 7.06 m, 6.08 m, 5.49 w, 5.19 s, 4.82 vs (3), 4.66 m, 4.44 w, 4.29 vs (3), 4.03 w, 3.78 vs (2), 3.52 s, 3.45 s, 3.25 vw, 3.02 vw, 2.92 m, 2.79 w, 2.64 w, 2.52 m, 2.34 w, 2.22 vw, 2.17 w, 2.07 w, and 1.90 vw. This compound was homogeneous by t.l.c., with ether as the developer.

Anal. Calc. for $C_{16}H_{20}F_3NO_{10}$: C, 43.35; H, 4.55; N, 3.16. Found: C, 43.19; H, 4.52; N, 3.49.

*1,3,4,6-Tetra-*O*-acetyl-2-deoxy-2-(trifluoroacetamido)-α(and β)-D-galactopyranose* (**10** and **11**). — 2-Deoxy-2-(trifluoroacetamido)-D-galactose (**9a**, 2.0 g) was acetylated with pyridine (16 ml) and acetic anhydride (9 ml) by the procedure described in the preceding experiment. The crude, syrupy product showed two principal components (R_F 0.43 and 0.56) by t.l.c. with ether as the developer. Three recrystallizations from methanol–water gave 1,3,4,6-tetra-*O*-acetyl-2-deoxy-2-(trifluoroacetamido)-α-D-galactopyranose (**10**) as a white, crystalline solid, yield 0.97 g (30%): m.p. 155–156.5°; $[\alpha]_D^{23}$ +84 ±1° (*c* 2.1, chloroform); λ_{max}^{KBr} 3.05 (NH), 5.7 (*O*-acetyl carbonyl), 5.85 (*N*-trifluoroacetyl carbonyl), 6.4 (NH), 8.1–8.3 (ester), 8.68 (CF), 7.32, 9.15, 9.34, 9.6, 9.9, 10.7, 11.1, 11.64, 12.2, 13.1, and 13.8 μm; X-ray powder diffraction data: 7.54 vs (1), 6.33 s, 5.85 m, 5.45 s, 5.01 s, 4.63 m, 4.32 vs (2), 4.10 s, 3.96 s, 3.79 w, 3.66 w, 3.51 s (3), 3.41 vw, 3.34 vw, 3.05 m, 2.91 w, 2.84 m, 2.77 vw, 2.59 vw, 2.51 m, 2.45 vw, 2.31 w, 2.23 vw, 2.17 m, and 2.11 w. This compound was homogeneous by t.l.c. with ether as the developer, and corresponded to the slower-moving component of the crude product (R_F 0.43).

Anal. Calc. for $C_{16}H_{20}F_3NO_{10}$: C, 43.35; H, 4.55; N, 3.16. Found: C, 43.29; H, 4.40; N, 2.95.

The mother liquors from the three recrystallizations of **10** were evaporated to yield a syrupy residue which, on t.l.c. with ether as the developer, showed a major component (R_F 0.57) and a minor component (R_F 0.41). These two components were isolated by resolution on 24 chromatoplates (200 × 200 × 1.25 mm) with ether as the developer, by the procedure described in the preceding experiment. Crystallization of the material obtained from the slower-moving zone (R_F 0.41) from methanol–

water yielded an additional 0.52 g (16%) of **10**: m.p. and m.m.p. 155–156.5°, $[\alpha]_D^{22}$ +84 ±1° (*c* 2.1, chloroform).

The material obtained from the faster-moving zone (R_F 0.57) was crystallized from ether–hexane to give 1.2 g (37%) of 1,3,4,6-tetra-*O*-acetyl-2-deoxy-2-(trifluoroacetamido)-β-D-galactopyranose (**11**): m.p. 130–131°; $[\alpha]_D^{21}$ +11 ±1° (*c* 3.1, chloroform); λ_{max}^{KBr} 3.06 (NH), 5.7 (*O*-acetyl carbonyl), 5.8 (*N*-trifluoroacetyl carbonyl), 6.36 (NH), 8.1–8.3 (ester), 8.65 (CF), 7.33, 8.45, 9.18, 9.66, 10.46, 11.2, 11.7, 13.52, and 13.9 μm; X-ray powder diffraction data: 13.05 m, 7.90 vs (1), 6.25 s, 5.71 s, 5.40 w, 5.17 s (3), 4.80 s, 4.54 m, 4.10 vs (2), 3.83 m, 3.70 m, 3.60 m, 3.43 m, 3.28 s, 3.10 s, 2.98 w, 2.90 m, 2.80 w, 2.70 m, 2.59 m, 2.50 w, 2.44 m, 2.29 m, 2.24 m, 2.18 vw, and 2.08 m. This compound was homogeneous by t.l.c. with ether as the developer.

Anal. Calc. for $C_{16}H_{20}F_3NO_{10}$: C, 43.35; H, 4.55; N, 3.16. Found: C, 43.52; H, 4.58; N, 3.57.

3,4,6-Tri-O-acetyl-2-deoxy-2-(trifluoroacetamido)-α-D-glucopyranosyl bromide[8,10] (**5**). — *Method* (*A*). 1,3,4,6-Tetra-*O*-acetyl-2-deoxy-2-(trifluoroacetamido)-α-D-glucopyranose (**3**, 2.0 g) was moistened with chloroform (1.0 ml), and acetic acid (20 ml) almost saturated at 0° with hydrogen bromide was added. The mixture was kept for 2 h at room temperature in a glass-stoppered flask, and was then dissolved in dichloromethane (30 ml). The solution was successively washed with cold, 20% aqueous sodium acetate solution and water, and dried (magnesium sulfate). Evaporation of the solvent gave a syrupy residue which was crystallized from ether–hexane, yield 2.0 g (96%), m.p. 96–97°, $[\alpha]_D^{20}$ +125 ±1° (*c* 2.7, chloroform); lit.[10] m.p. 95–97°; lit.[8] m.p. 96°, $[\alpha]_D^{21}$ +126° (*c* 2.92, chloroform).

Method (*B*). 2-Deoxy-2-(trifluoroacetamido)-D-glucose (**2a**, 0.8 g) was acetylated with a mixture of pyridine (6.5 ml) and acetic anhydride (3.5 ml) by the procedure described for the preparation of **3** and **4**. The crude, syrupy product was crystallized from ether–hexane, giving a white, crystalline material; yield 1.1 g (85%); m.p. 116–121°. T.l.c. of the product with ether as the developer showed two components (R_F 0.45 and 0.56) which, presumably, were 1,3,4,6-tetra-*O*-acetyl-2-deoxy-2-(trifluoroacetamido)-α-D-glucopyranose (**3**) and its β-D anomer (**4**), the anomers having co-crystallized.

The material was treated with acetic acid (1.1 ml) almost saturated at 0° with hydrogen bromide, according to the procedure used in the preceding experiment. Crystallization of the crude product from ether–hexane gave **5**; yield 1.08 g (94%): m.p. and m.m.p. 96–97°; $[\alpha]_D^{21}$ +127 ±2° (*c* 1.4, chloroform).

3,4,6-Tri-O-acetyl-2-deoxy-2-(trifluoroacetamido)-D-galactopyranosyl bromide (**12**). — *Method* (*A*). 1,3,4,6-Tetra-*O*-acetyl-2-deoxy-2-(trifluoroacetamido)-α-D-galactopyranose (**10**, 1.0 g) was treated with acetic acid almost saturated at 0° with hydrogen bromide, according to the procedure used in the preceding experiment for the preparation of **5**. A clear, syrupy product was obtained which formed a solid foam on removal of the last traces of solvent under diminished pressure in a vacuum desiccator, yield 1.02 g (97%): m.p. 60–62°; $[\alpha]_D^{22}$ +146 ±1° (*c* 1.5, chloroform); λ_{max}^{KBr} 3.05 (NH), 5.7–5.8 (*O*-acetyl and *N*-trifluoroacetyl carbonyl), 6.45 (NH),

8.1–8.3 (ester), 8.65 (CF), 7.3, 9.2, 10.55, 11.1, 11.8, 12.9, and 13.7 μm. This compound was homogeneous by t.l.c. with 2:1 ether–petroleum ether as the developer. Attempts to crystallize the product were unsuccessful.

Anal. Calc. for $C_{14}H_{17}BrF_3NO_8$: C, 36.22; H, 3.69; N, 3.02. Found: C, 36.22; H, 3.90; N, 2.97.

Method (B). 1,3,4,6-Tetra-*O*-acetyl-2-deoxy-2-(trifluoroacetamido)-β-D-galactopyranose (**11**, 0.50 g) was treated with acetic acid (0.50 ml) almost saturated at 0° with hydrogen bromide, according to the procedure used in the preceding experiment; yield 0.49 g (94%) of **12**: m.p. 60–63°; $[\alpha]_D^{20}$ +144 ±2° (*c* 1.1, chloroform).

Method (C). 2-Deoxy-2-(trifluoroacetamido)-D-galactose (**9a**, 0.60 g) was acetylated with a mixture of pyridine (4.5 ml) and acetic anhydride (3.0 ml) by the procedure described for the preparation of **2** and **3**. The crude, syrupy product was dissolved in methanol (20 ml), water (30 ml) was added, and the solution was concentrated to half volume. After refrigeration overnight, a white, crystalline material formed; yield 0.58 g (60%): m.p. 126–130°. Further concentration of the mother liquor to about 15 ml, followed by refrigeration overnight, produced a second crop of crystalline material; yield 0.20 g (21%), m.p. 121–126°. Treatment of the combined material (0.78 g) with acetic acid (0.8 ml) almost saturated at 0° with hydrogen bromide, according to the procedure used in the preceding experiment, produced amorphous **12**, yield 0.76 g (93%), m.p. 59–62°, $[\alpha]_D^{22}$ +143 ±2° (*c* 1.0, chloroform).

6-Benzamido-9-[3,4,6-tri-O-acetyl-2-deoxy-2-(trifluoroacetamido)-α(andβ)-D-glucopyranosyl]-9H-purine (**6a** *and* **7a**). — A mixture of 6-benzamido-9-(chloromercuri)-9*H*-purine[13] (8.0 g), cadmium carbonate (2.0 g), and Celite (2.5 g) in toluene (75 ml) was azeotropically dried by distillation of approximately one third of the solvent. To the hot suspension was added, with stirring, 3,4,6-tri-*O*-acetyl-2-deoxy-2-(trifluoroacetamido)-α-D-glucopyranosyl bromide (**5**, 2.6 g), and the mixture was refluxed for 8 h with stirring, and then kept overnight at room temperature. The mixture was poured into cold (0°) petroleum ether (b.p. 30–60°, 100 ml), and the precipitate that formed was collected by filtration, and extracted with chloroform (300 ml, total). The extract was successively washed with 30% aqueous potassium iodide solution and water, and dried (sodium sulfate). The solution was evaporated to a pale-amber glass (1.65 g) which, on t.l.c. with 5:2 chloroform–acetone as developer, showed a major component (R_F 0.35) and two minor components (R_F 0.6 and 0.8). The crude product was resolved by preparative t.l.c. on 24 chromatoplates (200 × 200 × 1.25 mm), with 5:2 chloroform–acetone as the developer and indication by u.v. light. The two slower-moving zones (R_F 0.35 and 0.6) were excised, and extracted with acetone. Evaporation of the extract from the faster-moving zone (R_F 0.6) gave a clear glass (0.25 g), which was crystallized from chloroform–isopropyl ether to give a gelatinous mixture that yielded 6-benzamido-9-[3,4,6-tri-*O*-acetyl-2-deoxy-2-(trifluoroacetamido)-α-D-glucopyranosyl]-9*H*-purine (**6a**) as a white, crystalline solid, yield 0.23 g (6.6%): m.p. 169–172°, $[\alpha]_D^{22}$ +105 ±2.5° (*c* 0.7, chloroform); λ_{max}^{KBr} 3.1 (NH), 5.75 (*O*-acetyl, and *N*-trifluoroacetyl carbonyl), 6.2, 6.35, 6.65, 6.9 (aryl C=C, purine, NH), 8.1–8.3 (ester), 8.6 (CF), 14.1 (substituted benzene), 7.36,

7.55, 9.15, 9.6, 10.3, 11.2, 12.52, and 13.6 μm; λ_{max}^{EtOH} 211 (ε 21,000), 234 (ε 13,550), and 282 nm (ε 19,500); X-ray powder diffraction data: 13.81 s (1), 11.95 m, 10.43 s (3), 9.69 vw, 8.61 s, 7.45 m, 7.01 vw, 6.50 m, 6.05 m, 5.68 m, 5.28 w, 5.01 w, 4.82 m, 4.60 m, 4.23 w, 3.84 w, 3.60 s (2), 3.32 m, 3.05 w, 2.81 vw, and 2.64 vw. This compound was homogeneous by t.l.c. with 3:1 chloroform–acetone as the developer.

Anal. Calc. for $C_{26}H_{25}F_3N_6O_9$: C, 50.16; H, 4.05; N, 13.50. Found: C, 50.19; H, 4.14; N, 13.70.

Evaporation of the extract from the slower-moving zone (R_F 0.35) gave a clear glass (1.04 g). Attempted crystallization from chloroform–isopropyl ether gave 6-benzamido-9-[3,4,6-tri-*O*-acetyl-2-deoxy-2-(trifluoroacetamido)-β-D-glucopyranosyl]-9*H*-purine (**7a**) as a white, amorphous solid, yield 0.90 g (26%): m.p. 148–153° (softening above 133°); $[\alpha]_D^{21}$ −50 ±1° (*c* 2.6, chloroform); λ_{max}^{KBr} 3.05 (NH), 5.7 (*O*-acetyl and *N*-trifluoroacetyl carbonyl) 6.2, 6.32, 6.65, 6.75, 6.9 (aryl C=C, purine, NH), 8.1–8.3 (ester), 8.6 (CF), 14.1 (substituted benzene), 7.32, 8.7, 9.3, 10.8, 11.2, 12.2, 12.5, and 13.2 μm; λ_{max}^{EtOH} 210 (ε 21,200), 234 (ε 12,500), and 280 nm (ε 19,700). This compound was homogeneous by t.l.c. with 2:1 chloroform–acetone as the developer.

Anal. Calc. for $C_{26}H_{25}F_3N_6O_9$: C, 50.16; H, 4.05; N, 13.50. Found: C, 50.23; H, 4.03; N, 13.80.

9-[3,4,6-Tri-O-acetyl-2-deoxy-2-(trifluoroacetamido)-α-D-glucopyranosyl]adenine picrate (**6b**). — To a solution of 6-benzamido-9-[3,4,6-tri-*O*-acetyl-2-deoxy-2-(trifluoroacetamido)-α-D-glucopyranosyl]-9*H*-purine (**6a**, 60 mg) in isopropyl alcohol (10 ml) was added a solution of picric acid (25 mg) in methanol (5 ml). The solution was concentrated to about one third its volume by boiling (20 min), allowed to cool slowly to room temperature, and then refrigerated overnight. The yellow, crystalline solid which separated was filtered off, and washed with cold hexane; yield 60 mg (83%), m.p. 210–213° (dec.). Further recrystallizations from isopropyl alcohol–methanol–petroleum ether (b.p. 60–110°) afforded pure material: m.p. 216–217° (dec.), $[\alpha]_D^{22}$ +83 ±2° (*c* 0.6, acetone), λ_{max}^{KBr} 3.1–3.3 (NH, NH_3^+), 5.75 (*O*-acetyl and *N*-trifluoroacetyl carbonyl), 5.92, 6.2, 6.4, 6.75, 7.05 (aryl C=C, purine, NH, NH^+), 6.5, 7.6 (NO_2), 8.1–8.25 (ester), 8.6 (CF), 14.0–14.3 (substituted benzene), 7.35, 9.6, 10.96, 12.66, and 13.4 μm; X-ray powder diffraction data: 11.63 s, 10.34 w, 8.23 vs (1), 6.94 m, 6.28 m, 5.79 w, 5.45 m, 5.25 m, 4.81 m, 4.49 m, 4.32 m, 3.99 s (2), 3.81 w, 3.64 w, 3.47 m, 3.35 s (3), 3.20 vw, and 3.02 m.

Anal. Calc. for $C_{25}H_{24}F_3N_9O_{15}$: C, 40.17; H, 3.24; N, 16.86. Found: C, 40.39; H, 3.52; N, 16.68.

9-[3,4,6-Tri-O-acetyl-2-deoxy-2-(trifluoroacetamido)-β-D-glucopyranosyl]adenine picrate (**7b**). — A solution of 6-benzamido-9-[3,4,6-tri-*O*-acetyl-2-deoxy-2-(trifluoroacetamido)-β-D-glucopyranosyl]-9*H*-purine (**7a**, 0.20 g) in isopropyl alcohol (15 ml) was treated with picric acid (0.08 g) in methanol (8 ml) by the procedure described in the preceding experiment, yield 0.22 g (92%); m.p. 207–210° (dec.). Recrystallization from isopropyl alcohol afforded pure material, m.p. 212–214° (dec.), $[\alpha]_D^{21}$ −39 ±1° (*c* 1.9, acetone); λ_{max}^{KBr} 3.0–3.25 (NH, NH_3^+) 5.72 (*O*-acetyl and *N*-trifluoroacetyl

carbonyl), 5.92, 6.2, 6.35, 6.68, 7.04 (aryl C=C, purine, NH, NH^+), 6.5, 7.6 (NO_2), 8.1–8.3 (ester), 8.6 (CF), 14.1 (substituted benzene), 7.35, 9.25, 9.6, 11.0, 12.25, 12.65, and 13.45 μm; X-ray powder diffraction data: 12.63 s (1), 10.28 m, 9.07 m, 7.05 m, 6.44 m, 6.01 vw, 5.47 s (3), 5.00 s, 4.50 s, 4.22 s (2), 4.01 w, 3.83 w, 3.69 vw, 3.52 s, 3.36 m, 3.25 w, 3.16 w, and 3.10 vw.

Anal. Calc. for $C_{25}H_{24}F_3N_9O_{15}$: C, 40.17; H, 3.24; N, 16.86. Found: C, 40.13; H, 3.16; N, 16.79.

9-(2-Amino-2-deoxy-α-D-glucopyranosyl)adenine (**6c**). — 6-Benzamido-9-[3,4,6-tri-*O*-acetyl-2-deoxy-2-(trifluoroacetamido)-α-D-glucopyranosyl]-9*H*-purine (**6a**, 0.20 g) was dissolved in 40 ml of methanol almost saturated at 0° with ammonia. The solution was kept for 7 days at room temperature, after which it was concentrated to 5 ml and an excess of ether (50 ml) was added. The resultant, white, flocculent precipitate was filtered off, washed with ether, and recrystallized from methanol–ethanol; yield 0.085 g (89%): m.p. and m.m.p. with authentic material[5] 242–244° (dec.), $[\alpha]_D^{21}$ +84 ±2° (*c* 1.5, water); lit.[5] m.p. 242–244° (dec.), $[\alpha]_D^{22}$ +83 ±6° (*c* 0.2, water).

9-(2-Amino-2-deoxy-β-D-glucopyranosyl)adenine (**7c**). — 6-Benzamido-9-[3,4,6-tri-*O*-acetyl-2-deoxy-2-(trifluoroacetamido)-β-D-glucopyranosyl]-9*H*-purine (**7a**, 0.50 g) was deacylated with methanol (80 ml) almost saturated at 0° with ammonia, as described in the preceding experiment. The yield, after recrystallization from ethanol, was 0.205 g (86%): m.p. and m.m.p. with authentic material[5] 185–188° (dec.), $[\alpha]_D^{22}$ −17 ±1° (*c* 2.3, water); lit.[5] m.p. 186–188° (dec.), $[\alpha]_D^{23}$ −17 ±2° (*c* 0.2, water).

6-Benzamido-9-[3,4,6-tri-O-acetyl-2-deoxy-2-(trifluoroacetamido)-α(and β)-D-galactopyranosyl]-9H-purine (**13a** *and* **14a**). — 3,4,6-Tri-*O*-acetyl-2-deoxy-2-(trifluoroacetamido)-D-galactosyl bromide (**12**, 2.0 g) was condensed with 6-benzamido-9-(chloromercuri)-9*H*-purine (6.0 g) in refluxing toluene (50 ml) in the presence of cadmium carbonate (2.0 g) and Celite (2.0 g) by the procedure described for the preparation of **6a** and **7a**. A pale-amber glass (1.6 g) was obtained which, by t.l.c. with 5:2 chloroform–acetone as the developer, showed a major component (R_F 0.33) and two minor components (R_F 0.6 and 0.8). The crude product was resolved on 24 chromatoplates (200 × 200 × 1.25 mm), with 5:2 chloroform–acetone as the developer and indication by u.v. light. The two slower-moving zones (R_F 0.33 and 0.6) were removed, and extracted with acetone. Evaporation of the extract from the faster-moving zone gave a clear glass (0.31 g) which was crystallized from chloroform–isopropyl ether to give a gelatinous mixture that yielded 6-benzamido-9-[3,4,6-tri-*O*-acetyl-2-deoxy-2-(trifluoroacetamido)-α-D-galactopyranosyl]-9*H*-purine (**13a**) as a white, crystalline solid upon suction filtration; yield 0.25 g (93%), m.p. 140–144° (softening above 130°), $[\alpha]_D^{22}$ +120 ±3° (*c* 1.0, chloroform); λ_{max}^{KBr} 3.1 (NH), 5.75 (*O*-acetyl and *N*-trifluoroacetyl carbonyl), 6.2, 6.35, 6.65, 6.76, 6.9 (aryl C=C, purine, NH), 8.1–8.3 (ester), 8.65 (CF), 14.1 (substituted benzene), 7.32, 7.55, 9.2, 10.55, 11.1, 11.7, and 12.52 μm; λ_{max}^{EtOH} 210 (ε 22,300), 234 (ε 13,300), and 282 nm (ε 19,500); X-ray powder diffraction data: 13.50 w, 9.98 s (1), 5.17 m, 4.42 m, 3.87 s (2),

3.55 w, and 3.33 s (3). This compound was homogeneous by t.l.c. with 3:1 chloroform–acetone as the developer.

Anal. Calc. for $C_{26}H_{25}F_3N_6O_9$: C, 50.16; H, 4.05; N, 13.50. Found: C, 50.21; H, 4.42; N, 13.42.

Evaporation of the extract from the slower-moving zone (R_F 0.33) gave a clear glass (0.94 g). Attempted crystallization from chloroform–isopropyl ether yielded 6-benzamido-9-[3,4,6-tri-*O*-acetyl-2-deoxy-2-(trifluoroacetamido)-β-D-galactopyranosyl]-9*H*-purine (**14a**) as an amorphous, white solid, yield 0.80 g (30%); m.p. 150–155° (softening above 135°), $[\alpha]_D^{19}$ −34 ±1° (*c* 2.7, chloroform); λ_{max}^{KBr} 3,05, 5.7 (*O*-acetyl and *N*-trifluoroacetyl carbonyl), 6.2, 6.32, 6.65, 6.75, 6.9 (aryl C=C, purine, NH), 8.1–8.3 (ester), 8.65 (CF), 14.1 (substituted benzene), 9.2, 10.5, 10.85, 12.55, and 13.2 μm; λ_{max}^{EtOH} 211 (ε 20,900), 234 (ε 12,600), and 280 nm (ε 19,900). This compound was homogeneous by t.l.c. with 2:1 chloroform–acetone as the developer.

Anal. Calc. for $C_{26}H_{25}F_3N_6O_9$: C, 50.16; H, 4.05; N, 13.50. Found: C, 50.21; H, 4.36; N, 13.56.

*9-[3,4,6-Tri-*O*-acetyl-2-deoxy-2-(trifluoroacetamido)-α-D-galactopyranosyl]adenine picrate* (**13b**). — A solution of 6-benzamido-9-[3,4,6-tri-*O*-acetyl-2-deoxy-2-(trifluoroacetamido)-α-D-galactopyranosyl]-9*H*-purine (**13a**, 50 mg) in isopropyl alcohol (8 ml) was treated with picric acid (20 mg) in methanol (4 ml) as described for the preparation of **6b**. The yield of crude product was 50 mg (83%); m.p. 177–182°. Further recrystallizations from isopropyl alcohol–methanol–petroleum ether (b.p. 60–110°) afforded pure material; m.p. 181–185°, $[\alpha]_D^{22}$ +108 ±4° (*c* 0.3, acetone); λ_{max}^{KBr} 3.1–3.3 (NH, NH_3^+), 5.76 (*O*-acetyl and *N*-trifluoroacetyl carbonyl), 5.92, 6.2, 6.4, 6.7, 7.05 (aryl C=C, purine, NH, NH_3^+), 6.5, 7.6 (NO_2), 8.1–8.3 (ester), 8.65 (CF), 14.1–14.2 (substituted benzene), 7.36, 9.5, 11.0, 12.7, and 13.5 μm; X-ray powder diffraction data: 10.72 w, 9.51 s (2), 7.53 w, 6.73 w, 5.28 w, 4.63 m, 4.34 m, 3.93 s (1), and 3.50 s (3).

Anal. Calc. for $C_{25}H_{24}F_3N_9O_{15}$: C, 40.17; H, 3.24; N, 16.86. Found: C, 40.01; H, 3.35; N, 16.64.

*9-[3,4,6-Tri-*O*-acetyl-2-deoxy-2-(trifluoroacetamido)-β-D-galactopyranosyl]adenine picrate* (**14b**). — A solution of 6-benzamido-9-[3,4,6-tri-*O*-acetyl-2-deoxy-2-(trifluoroacetamido)-β-D-galactopyranosyl]-9*H*-purine (**14b**, 0.18 g) in isopropyl alcohol (12 ml) was treated with picric acid (0.075 g) in methanol (7 ml) as described for the preparation of **6b**. The yield of crude product was 0.19 g (88%); m.p. 203–205° (dec.). Recrystallization from isopropyl alcohol afforded pure material: m.p. 205–207° (dec.), $[\alpha]_D^{19}$ −37 ±1.5° (*c* 1.3, acetone); λ_{max}^{KBr} 3.05–3.3 (NH, NH_3^+), 5.75 (*O*-acetyl and *N*-trifluoroacetyl carbonyl), 5.92, 6.2, 6.4, 6.75, 7.05 (aryl C=C, purine, NH, NH_3^+), 6.5, 7.6 (NO_2), 8.2 (ester), 8.6 (CF), 13.9–14.05 (substituted benzene), 7.36, 9.25, 9.55, 10.85, 12.7, and 13.5 μm; X-ray powder diffraction data: 11.05 w, 8.93 s (1), 7.85 vw, 7.28 s (3), 6.51 m, 5.88 w, 5.44 m, 5.05 m, 4.81 w, 4.59 w, 4.47 s, 4.36 w, 4.19 w, 3.99 vw, 3.74 vw, 3.60 m, 3.40 s (2), 3.28 m, 3.21 vw, 3.09 w, 2.91 vw, 2.83 vw, and 2.73 w.

Anal. Calc. for $C_{25}H_{24}F_3N_9O_{15}$: C, 40.17; H, 3.24; N, 16.86. Found: C, 39.98; H, 3.36; N, 16.79.

9-(2-Amino-2-deoxy-α-D-galactopyranosyl)adenine (**13c**). — 6-Benzamido-9-[3,4,6-tri-*O*-acetyl-2-deoxy-2-(trifluoroacetamido)-α-D-galactopyranosyl]-9*H*-purine (**13a**, 170 mg) was deacylated with methanol (40 ml) almost saturated at 0° with ammonia, as described for the preparation of **6c**. Attempted crystallization of the crude product from methanol–ether gave a white, amorphous solid, yield 67 mg (83%); m.p. 198–208° (softening and swelling above 160°), $[\alpha]_D^{21}$ +134 ±3° (*c* 0.6, water); λ_{max}^{KBr} 2.95–3.1 (OH, NH_2), 6.08, 6.25, 6.35, 6.8 (purine, NH), 7.1, 7.52, 7.7, 8.1, 8.22, 9.2, 11.38, 12.55, 13.55, and 13.95 μm; $\lambda_{max}^{H_2O}$ 210 (ε 18,900) and 262 nm (ε 14,500). This compound was homogeneous by t.l.c. with methanol as the developer.

Anal. Calc. for $C_{11}H_{16}N_6O_5$: C, 44.59; H, 5.44; N, 28.37. Found: C, 44.39; H, 5.48; N, 28.04.

9-(2-Amino-2-deoxy-β-D-galactopyranosyl)adenine (**14c**). — 6-Benzamido-9-[3,4,6-tri-*O*-acetyl-2-deoxy-2-(trifluoroacetamido)-β-D-galactopyranosyl]-9*H*-purine (**14a**, 0.40 g) was deacylated with methanol (80 ml) almost saturated at 0° with ammonia, as described for the preparation of **6c**. Attempted crystallization of the crude product from methanol–ether gave a white, amorphous solid, yield 0.155 g (81%): m.p. 211–220° (softening and swelling above 155°), $[\alpha]_D^{21}$ +19 ±1.5° (*c* 0.12, water); λ_{max}^{KBr} 2.95–3.1 (NH_2, OH), 6.08, 6.25, 6.35, 6.8 (NH, purine), 7.08, 7.3, 7.53, 7.7, 8.0, 8.3, 9.22, 9.86, 11.3, 12.2, 12.55, and 13.75 μm; $\lambda_{max}^{H_2O}$ 210 (ε 19,300) and 261 nm (ε 14,800). This compound was homogeneous by t.l.c. with methanol as the developer.

Anal. Calc. for $C_{11}H_{16}N_6O_5$: C, 44.59; H, 5.44; N, 28.37. Found: C, 44.29; H, 5.58; N, 28.54.

9-(2-Amino-2-deoxy-α-D-galactopyranosyl)adenine dihydrochloride (**13d**). — To a solution of 9-(2-amino-2-deoxy-α-D-galactopyranosyl)adenine (**13c**, 40 mg) in methanol (30 ml) was added 0.40 ml of *N* hydrochloric acid. Several evaporations with methanol (to a volume of 5 ml) were made, to remove the excess of hydrogen chloride. The solution was concentrated to 5 ml, and warmed to about 60°. Isopropyl ether (5 ml) was then slowly added, and the mixture was allowed to cool slowly to room temperature, and then refrigerated overnight. The white, crystalline material that formed was recrystallized from methanol–ethanol, yield 44 mg (88%); dec. at 208–209° (with some charring above 190°), $[\alpha]_D^{22}$ +112 ±3° (*c* 0.6, water); λ_{max}^{KBr} 3.0–3.35 (NH_3^+, OH), 5.78, 5.95, 6.18, 6.3, 6.5, 6.7, 6.85 (purine, NH_3^+), 7.05, 7.38, 7.46, 7.68, 8.2, 8.5, 8.7, 8.85, 9.1, 9.4, 9.62, 9.88, 10.22, 11.43, 12.0, 12.5, and 13.64 μm; $\lambda_{max}^{H_2O}$ 210 (ε 17,800) and 261 nm (ε 14,200); X-ray powder diffraction data: 13.92 s, 9.31 m, 8.41 vw, 7.25 s (1), 6.63 w, 6.33 w, 4.43 s, 4.22 s, 3.89 s (3), 3.60 s, 3.36 m, 3.20 s (2), 3.09 vw, 2.89 vw, 2.78 w, 2.69 vw, 2.55 m, 2.37 m, 2.23 vw, 2.14 w, and 2.01 w.

Anal. Calc. for $C_{11}H_{18}Cl_2N_6O_4$: C, 35.78; H, 4.91; Cl, 19.21; N, 22.76. Found: 35.70; H, 5.18; Cl, 19.27; N, 22.63.

9-(2-Amino-2-deoxy-β-D-galactopyranosyl)adenine dihydrochloride (**14d**). — A

solution of 9-(2-amino-2-deoxy-β-D-galactopyranosyl)adenine (**14c**, 0.10 g) in methanol (35 ml) was treated with M hydrochloric acid (1.0 ml) as described in the preceding experiment. The yield, after recrystallization from methanol–ethanol, was 0.115 g (92%); dec. at 190–192° (with some charring above 180°), $[\alpha]_D^{22}$ +38 ±2° (*c* 0.7, water); λ_{max}^{KBr} 2.95–3.4 (OH, NH_3^+), 5.9, 6.0, 6.28, 6.66, 6.9 (purine, NH_3^+), 7.05, 7.38, 7.54, 7.78, 8.14, 8.75, 8.9, 9.1, 9.45, 9.8, 10.45, 10.66, 11.3, 11.8, 12.3, 12.8, 13.12, and 13.8 μm; $\lambda_{max}^{H_2O}$ 210 (ε 18,500) and 260 nm (ε 14,000); X-ray powder diffraction data: 6.89 vs (1), 6.35 w, 5.93 m, 5.52 w, 5.14 s, 4.81 m, 4.51 s, 4.28 m, 3.72 s, 3.59 s, 3.43 s, 3.25 s (2), 3.13 s (3), 3.00 m, 2.93 vw, 2.77 m, 2.67 vs, 2.52 w, 2.43 m, 3.21 w, 2.26 vw, 2.13 w, 2.02 w, 1.90 vw, 1.84 w, and 1.76 w.

Anal. Calc. for $C_{11}H_{18}Cl_2N_6O_4$: C, 35.78; H, 4.91; Cl, 19.21; N, 22.76. Found: C, 36.02; H, 5.08; Cl, 19.39; N, 22.56.

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REFERENCES

1 R. S. TIPSON, *Advan. Carbohyd. Chem.*, 1 (1945) 193.
2 F. J. MCEVOY, M. J. WEISS, AND B. R. BAKER, *J. Amer. Chem. Soc.*, 82 (1960) 205.
3 C. L. STEVENS AND K. NAGARAJAN, *J. Med. Pharm. Chem.*, 5 (1962) 1124.
4 M. L. WOLFROM, P. J. CONIGLIARO, AND E. J. SOLTES, *J. Org. Chem.*, 32 (1967) 653.
5 M. L. WOLFROM, H. G. GARG, AND D. HORTON, *Chem. Ind.* (London), (1964) 930; *J. Org. Chem.*, 30 (1965) 1556.
6 M. L. WOLFROM AND M. W. WINKLEY, *Chem. Commun.*, (1966) 533; *J. Org. Chem.*, 32 (1967) 1823; M. L. WOLFROM, M. W. WINKLEY, and S. INOUYE, *Carbohyd. Res.*, 10 (1969) 97.
7 M. L. WOLFROM AND H. B. BHAT, *J. Org. Chem.*, 32 (1967) 2757.
8 M. L. WOLFROM AND H. B. BHAT, *Chem. Commun.*, (1966) 146; *J. Org. Chem.*, 32 (1967) 1821.
9 E. E. SCHALLENBERG AND M. CALVIN, *J. Amer. Chem. Soc.*, 77 (1955) 2779.
10 R. G. STRACHAN, W. V. RUYLE, T. Y. SHEN, AND R. HIRSCHMANN, *J. Org. Chem.*, 31 (1966) 507.
11 M. BERGMANN AND L. ZERVAS, *Ber.*, 64 (1931) 975; D. HORTON, *J. Org. Chem.*, 29 (1964) 1776.
12 C. S. HUDSON, *J. Amer. Chem. Soc.*, 31 (1909) 66; *Advan. Carbohyd. Chem.*, 3 (1948) 15.
13 J. DAVOLL AND B. A. LOWY, *J. Amer. Chem. Soc.*, 73 (1951) 1650.
14 B. R. BAKER, J. P. JOSEPH, R. E. SCHAUB, AND J. H. WILLIAMS, *J. Org. Chem.*, 19 (1954) 1786.
15 R. S. TIPSON, *J. Biol. Chem.*, 130 (1939) 55.