Anomeric Equilibria in Derivatives of Amino Sugars. Some 2-Amino-2-deoxy-D-hexose Derivatives[1-3]

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Equilibria between anomers, in deuterium oxide solution, for the 2-acetamido-2-deoxy and 2-amino-2-deoxy (hydrochloride) derivatives of D-galactose, D-glucose, and D-mannose, were studied by nmr spectroscopy. It is shown that, relative to a 2-hydroxyl group, an acetamido or ammonium group at C-2 exerts a stabilizing effect on a *cis*-related hydroxyl group at C-1. The chemical shifts of the H-1 signals of the anomeric pyranose forms of the sugars are compared as a function of the nature of the C-2 substituent.

In the first paper of this series[4] it was shown that 2-amino-2-deoxy-D-mannose hydrochloride exists in aqueous solution as a mixture of the α-D- and β-D-pyranose anomers. The present report describes measurements on the anomeric equilibria of several related 2-amino-2-deoxyhexose derivatives.

For each sugar studied, the interconversion of tautomeric forms in solution was observed by nmr spectroscopy, with deuterium oxide as the solvent. This method,[5,6] as employed in the current investigation, does not give anomeric compositions to the degree of accuracy that careful polarimetric measurements can furnish. Accurate compositions by polarimetry, however, require that both pure pyranose anomers be available, and the mixture at equilibrium must not contain appreciable proportions of furanose or acyclic forms. Advantages of the nmr method are that it can give approximate tautomeric compositions even when no crystalline form of the sugar is available and it can indicate whether a crystalline sugar is a single, tautomeric form or a cocrystallized mixture of forms.[4,6]

The procedure involves observation of the nmr signal for H-1 of each separate tautomer in solution, and determination of the relative proportions of the tautomers by integration of the spectrum. Chemical shifts and first-order $J_{1,2}$ coupling constants have been reported for the H-1 signals of the pyranose anomers of a number of simple aldoses,[5,7] and also for the corresponding signals of 2-amino-2-deoxy-D-glucose and -D-galactose hydrochlorides.[7] Details of the nmr measurements made in the present work are recorded in Table I and in the Experimental Section. The observed anomeric compositions, for 20–35% solutions of the sugars at equilibrium in deuterium oxide, are recorded in Table II. Also listed are anomeric compositions calculated from optical rotatory data recorded in the literature,[8-14] for aqueous solutions at lower concentration. The latter compositions are calculated on the assumption that only the pyranose forms are involved at equilibrium; the values for D-galactose, D-glucose, and D-mannose are in reasonable agreement with those determined by bromine oxidation[14] and by calculations[15] based on estimates of the interaction energies between substituent groups on the pyranose ring. It is recognized that a small proportion of furanose form[16] may be present at equilibrium in aqueous solutions of D-galactose.

TABLE I

CHEMICAL SHIFTS OF H-1 SIGNALS OF HEXOPYRANOSES, 2-ACETAMIDO-2-DEOXYHEXOPYRANOSES, AND 2-AMINO-2-DEOXYHEXOPYRANOSE HYDROCHLORIDES, IN DEUTERIUM OXIDE

		Chemical shifts (τ scale), ppm		
Parent hexopyranose	Disposition of H-1 in favored conformation	Free sugar[a]	2-Acetamido-2-deoxy derivative	2-Amino-2-deoxy (hydrochloride) derivative
α-D-Galactose	Equatorial	4.71 (4.66)	4.72	4.52
β-D-Galactose	Axial	5.37 (5.32)	5.31	5.11
α-D-Glucose	Equatorial	4.72 (4.68)	4.82	4.54
β-D-Glucose	Axial	5.30 (5.26)	5.30	5.03
α-D-Mannose	Equatorial	4.80 (4.75)	4.89	4.60[b]
β-D-Mannose	Axial	5.08 (5.03)	4.99	4.78[b]

[a] Data in parentheses are taken from ref 5, and are relative to an external standard of tetramethylsilane. [b] Data from ref 4.

In the case of the 2-acetamido-2-deoxy derivatives of D-galactose and D-mannose, where only one crystalline anomer has been described in each instance, the specific rotations of the uncrystallized anomers were estimated on the basis of Hudson's rules,[17] and anomeric compositions were calculated from these values. The molecular rotatory contribution of C-1 (2*A* value) was taken as +17,640° in the D-galactose series and +8340° in the D-mannose series.[18] It is known that, at least in the D-glucose series, the 2*A* value is not substantially affected when the 2-hydroxyl group is replaced by an acetamido group[19] or by an ammonium group.[20] Furthermore, the present work indicates that crystalline 2-acetamido-2-deoxy-α-D-galactose and 2-aceta-

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(3) Funds for purchase of the nmr spectrometer were provided by the National Science Foundation, Washington, D. C.

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TABLE II

ANOMERIC COMPOSITIONS AT EQUILIBRIUM IN WATER

Sugar	Specific rotations, deg: α anomer	β anomer	Final	Ref	Per cent pyranose anomers: From optical rotatory data[a]: α anomer	β anomer	From nmr data[b]: α anomer	β anomer
2-Acetamido-2-deoxy-D-galactose	+115	*c*	+86	8	~64[d]	~36[d]	65	35
2-Acetamido-2-deoxy-D-glucose	+64	−21.5	+40.6	9, 10	72.6	27.4	68	32
2-Acetamido-2-deoxy-D-mannose	*c*	−9.4[e]	+9.7[e]	11	~55[f]	~45[f]	57	43
2-Amino-2-deoxy-D-galactose hydrochloride	+121	+44.5	+80	12	46.4	53.6	47	53
2-Amino-2-deoxy-D-glucose hydrochloride	+100	+25	+72.5	13	63.3	36.7	63	37
2-Amino-2-deoxy-D-mannose hydrochloride			−3.7	4			43[g]	57[g]
D-Galactose	+150	+52.8	+80.1	14	29.6	70.4	27[h]	73[h]
D-Glucose	+112.2	+18.7	+52.7	14	36.2	63.8	36[h]	64[h]
D-Mannose	+29.3	−17.0	+14.2	14	68.8	31.2	67[h]	33[h]

[a] Assuming a simple equilibrium between pyranose anomers. [b] By integration of the H-1 signals of the pyranose anomers, accuracy of integration measurements ±3%. [c] Not known. [d] Calculated by assuming that the β-D anomer has a specific rotation of +35°. [e] For the monohydrate. [f] Calculated by assuming that the α-D anomer (as monohydrate) has a specific rotation of +25°. [g] See ref 4. [h] See ref 5.

mido-2-deoxy-β-D-mannose monohydrate are anomerically pure, and that little anomerization had taken place at the times of the initial rotation measurements recorded in Table II.

2-Acetamido-2-deoxy-D-hexoses.—Polarimetric data[9,10] on the anomeric 2-acetamido-2-deoxy-D-glucoses (Table II) clearly indicate that both pyranose forms are present at equilibrium in water, although it has been stated[7] on the basis of nmr data that there is no indication of the presence of the β-D anomer. In the present study, it was found that an equilibrated solution of 2-acetamido-2-deoxy-D-glucose in deuterium oxide showed a narrow doublet, τ 4.82 and $J_{1,2}$ = 2.8 cps, assigned[7] to the equatorial H-1 of the α-D-pyranose form (**1**), and a wide doublet, τ 5.30 and $J_{1,2}$ = 7.4 cps, assigned to the axial H-1 of the β-D-pyranose form (**2**). In order to observe the H-1 signal of **2** it was necessary to heat the solution[5] so that the interfering HOD signal was shifted upfield. Integration of the spectrum showed that **1** and **2** were present in approximately 7:3 proportion. It was not possible to determine directly whether any of the β-D anomer **2** was present in the crystalline acetamido sugar, but the data strongly support the view that the crystalline, downward-mutarotating 2-acetamido-2-deoxy-D-glucose is exclusively the α-D anomer (**1**).

The nmr spectrum of 2-acetamido-2-deoxy-D-galactose, measured immediately after dissolution of crystalline material[8] in deuterium oxide, showed a one-proton doublet, τ 4.72 and $J_{1,2}$ = 3.7 cps, indicating that the crystalline substance is the pure α-D-pyranose form. At equilibrium, a second doublet, τ 5.31 and $J_{1,2}$ = 7.0 cps, assigned to H-1 of the β-D-pyranose form, was observed when the sample was heated.

Crystalline 2-acetamido-2-deoxy-D-mannose monohydrate[11] exhibits upward mutarotation,[11,21-23] indicating that it has the β-D configuration, and the fact that it exhibits no absorption near 12.0 μ in the infrared spectrum indicates[24] that no detectable proportion of the α-D-pyranose form (**3**) is present. The nmr spectrum of the substance, measured 2.5 min after dissolution in deuterium oxide, showed at low field a one-proton doublet, τ 4.99 and $J_{1,2}$ = 1.4 cps, assigned to the (axial) H-1 of the β-D-pyranose form (**4**), demonstrating that the crystalline substance is the pure β-D-pyranose form. Subsequent scans showed the progressive appearance of a second, low-field signal at the expense of the first; the second signal, τ 4.89 and $J_{1,2}$ = 1.5 cps, was assigned to the (equatorial) H-1 of the α-D-pyranose form (**3**). At equilibrium, the anomers **3** and **4** were present in 57:43 proportion.

2-Amino-2-deoxy-D-hexose Hydrochlorides.—The nmr spectrum of a freshly prepared solution of 2-amino-2-deoxy-D-glucose hydrochloride showed the α-D-pyranose form (**5**) as the only detected tautomer 2 min after dissolution. Appearance of the β-D-pyranose anomer (**6**) was revealed in subsequent scans, and the H-1 signal of **6** was clearly observed when the sample was heated.

2-Amino-2-deoxy-D-galactose hydrochloride,[12] mp 176–190° dec, was observed to be exclusively the β-D-pyranose form (**8**) when first dissolved in deuterium oxide. At equilibrium, the α-D-pyranose form (**7**) was present in almost equal proportion with **8**. It is noteworthy that the H-5 signal, observed at τ 6.82 in **8**, is shifted about 0.4 ppm downfield in **7**, where H-5 and the 1-hydroxyl group are in a *syn*-diaxial relationship.[25]

The behavior of 2-amino-2-deoxy-D-mannose hydrochloride in aqueous solution has already been discussed.[4] Measurements on D-galactose, D-glucose, and D-mannose in this laboratory gave data concordant with those recently reported by Lemieux and Stevens,[5] and the data of the latter authors are also given in Tables I and II. The chemical shifts, measured relative to an internal standard of sodium 4,4-dimethyl-4-silapentane-1-sulfonate, are observed to be approximately 0.05 ppm to higher field than those reported[5] relative to an external standard of tetramethylsilane.

Equilibrium Composition.—Within the limits of accuracy of the integration measurements (±3%), there is good correlation (Table II) between the compositions as determined by nmr, and those determined by polarimetry. The accuracy of the nmr method could be further improved, if desired, with use of a computer of averaged transients.

The data in Table II reveal that, in the D-*gluco* and D-*galacto* series, replacement of the (equatorial) C-2 hydroxyl group by an acetamido or ammonium group leads

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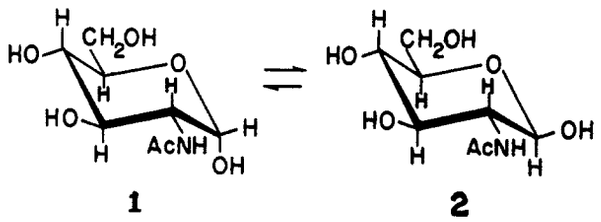
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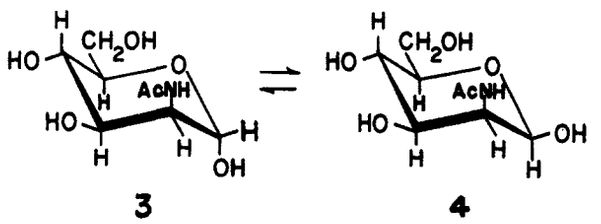
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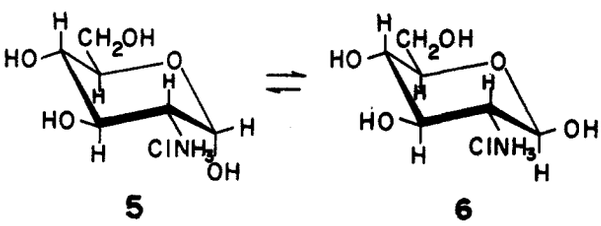
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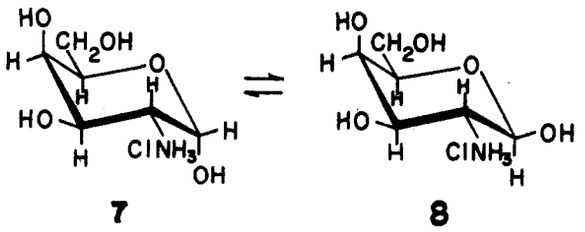
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to a greater stabilization of the α-D-pyranose form (C-1 hydroxyl group axial) in the equilibrium mixture. In contrast, in the D-*manno* series, replacement of the (axial) C-2 hydroxyl group by an acetamido or ammonium group leads to a greater stabilization of the β-D-pyranose form (C-1 hydroxyl group equatorial). It is evident that an acetamido or ammonium group at C-2 exerts a stabilizing effect, relative to a C-2 hydroxyl group, on a *cis*-hydroxyl group at C-1. The magnitude of this effect appears to be greater for the acetamido group than for the ammonium group when the C-2 substituent is equatorial, but when the latter is axial the ammonium group has a greater stabilizing effect than the acetamido group. It is probable that hydrogen bonding between the C-1 and C-2 substituents, to give a five-membered fused ring (a seven-membered ring is also possible with the acetamido group) accounts for these observations. A five-membered ring, fused *cis* to a six-membered ring, is known[26] to be a much more stable structure than the corresponding *trans*-fused (diequatorial) system. Other factors cannot, however, be excluded entirely. A detailed discussion of the quantitative free-energy differences between the 2-hydroxy, 2-acetamido, and 2-ammonium derivatives, as a function of configuration, is reserved until data on other configurations have all been determined.

Chemical Shifts.—The anomeric 2-acetamido-2-deoxy-D-mannopyranoses **3** and **4** gave separate signals, at τ 7.92 and 7.97, for the methyl protons of the (axial) acetamido group. The corresponding signals for the (equatorial) acetamido group in the anomers of 2-acetamido-2-deoxy-D-glucose and -D-galactose were not so resolved.

The data in Table I indicate that the chemical shift of the H-1 signal is not greatly affected when a 2-hydroxyl group is replaced by a 2-acetamido group. Replacement of a C-2 hydroxyl group (axial or equatorial) by an ammonium group causes a small downfield shift of the H-1 signal, about 0.2 ppm for an equatorial proton and about 0.25–0.3 ppm for an axial proton.

Experimental Section[27]

Measurements of Anomeric Equilibria. A. 2-Acetamido-2-deoxy-D-glucose.—A 30% solution of 2-acetamido-2-deoxy-α-D-glucopyranose[9,28] in deuterium oxide was allowed to reach mutarotational equilbrium, and the nmr spectrum was recorded at 70°, giving the following data: τ 4.82 (doublet, $J_{1,2}$ = 2.8 cps, H-1 of 1) (lit.[7] τ 4.81, $J_{1,2}$ = 2.7 cps) and 5.30 (doublet, $J_{1,2}$ = 7.4 cps, H-1 of 2) in relative proportion 68:32 and total integral of one proton, 5.65 (HOD), 6.05–6.35, and 6.35–6.70 (multiplets, six protons, H-2, -3, -4, -5, -6, -6′), 7.96 (singlet, three protons, NAc). At 40° the HOD signal was observed at τ 5.32.

B. 2-Acetamido-2-deoxy-D-galactose.—A 28% solution of 2-acetamido-2-deoxy-α-D-galactopyranose[8,29] in deuterium oxide showed, 2 min after dissolution, a one-proton doublet τ 4.72 ($J_{1,2}$ = 3.7 cps, H-1 of α-D-pyranose anomer). At mutarotational equilibrium and at 90° the spectrum showed two doublets, total integral of one proton, at τ 4.78 and at 5.31 ($J_{1,2}$ = 7.0 cps, H-1 of β-D-pyranose anomer), in relative proportion 62:38, τ 5.50 (HOD), 5.78–6.31 (multiplets, six protons, H-2, -3, -4, -5, -6, -6′), τ 7.93 (singlet, three protons, NAc).

C. 2-Acetamido-2-deoxy-D-mannose.—Crystalline 2-acetamido-2-deoxy-β-D-mannopyranose hydrate,[11,29] mp 125–126°, free from its 2-epimer (papergram, 5:5:1:3 pyridine–ethyl acetate–acetic acid–water), had λ_{max}^{Nujol} 6.05, 6.34 (HNAc), 11.28 μ and no peaks between 11.5 and 12.5 μ (axial H-1 in pyranoid ring);[23] X-ray powder diffraction data 7.03 vw, 5.94 vs (1), 5.21 w, 4.86 m, 4.03 s (2), 3.78 w, 3.56 m, 3.45 s (3), 3.24 w, 3.11 w, 2.99 w, 2.90 w, 2.77 w, 2.69 w, 2.56 w. The nmr spectrum of a 32% solution of the substance in deuterium oxide, measured 2.5 min after dissolution, showed at τ 4.99 a one-proton doublet, $J_{1,2}$ = 1.4 cps (axial H-1 of **4**), a very weak signal at 4.89 (equatorial H-1 of **3**), a three-proton singlet, 7.92, (NAc of **4**). The intensity of the signal at τ 4.89 ($J_{1,2}$ = 1.5 cps) increased with time at the expense of the signal at τ 4.99, and the signals were of approximately equal intensity after 17 min. At equilibrium (2 hr), integration indicated that **3** and **4** were present in 57:43 proportion. Two singlets, τ 7.96 and 7.92,

(26) Reference 15, p 360.

(27) Melting points were determined with a Thomas–Hoover "Unimelt" apparatus (Arthur H. Thomas Co., Philadelphia, Pa.). Infrared spectra were measured with a Perkin-Elmer Infracord infrared spectrometer. Nmr spectra were measured with a Varian A-60 spectrometer equipped with a Varian V-6040 variable-temperature probe. All spectra were measured in deuterium oxide, with sodium 4,4-dimethyl-4-silapentane-1-sulfonate (τ 10.00) as the internal standard. Unless otherwise stated, the spectra were measured at about 40°. The recorded first-order coupling constants are the measured peak spacings, and are considered accurate to ±0.5 cps; in many cases expanded-scale spectra were also used and give J values of greater accuracy than this. Integrated peak intensities are the mean of several integration curves, determined in both directions at a sweep width of 100 cps, and were also determined with the use of a planimeter. Each experiment was repeated a number of times, and concordant spectral data were recorded. Integration data are considered accurate within ±3%. X-Ray powder diffraction data give interplanar spacings (A) for Cu Kα radiation. Camera diameter was 114.59 mm. Relative intensities were estimated visually: s, strong; m, moderate; w, weak; v, very. The strongest lines are numbered (1, strongest); double numbers indicate approximately equal intensities.

(28) D. Horton, *Biochem. Prep.*, **11**, 1 (1966).

(29) Pfanstiehl Laboratories, Inc., Waukegan, Ill.

total integral three protons, present in similar proportion, were assigned to the NAc group of **3** and **4**, respectively. Multiplets, total integral six protons, in the range τ 5.42–6.63, were assigned to H-2, -3, -4, -5, -6, and -6′.

D. 2-Amino-2-deoxy-D-glucose Hydrochloride.—Crystalline 2-amino-2-deoxy-α-D-glucopyranose hydrochloride[29] was dissolved in deuterium oxide to give a 30% solution. The nmr spectrum, measured 2 min after dissolution, showed a one-proton doublet at τ 4.54, $J_{1,2}$ = 3.5 cps (equatorial H-1 of **5**) (lit.[7] τ 4.54, $J_{1,2}$ = 3.8 cps). After 10 min a doublet was detectable at τ 5.03, $J_{1,2}$ = 8.3 cps (axial H-1 of **6**) (lit.[7] τ 5.04, $J_{1,2}$ = 8.5 cps); it increased in intensity with time at the expense of the lower field signal, and at equilibrium the integrated peak intensities (measured at 70°) indicated that **5** and **6** were present in 63:37 proportion. The spectrum showed the HOD signal at τ 5.25 (τ 5.46 at 70°), and a six-proton multiplet, τ 5.9–7.2 (H-2, -3, -4, -5, -6, and -6′).

E. 2-Amino-2-deoxy-D-galactose Hydrochloride.—The crystalline substance[29] had mp 176–190°, λ_{max}^{Nujol} 11.45 with no absorption 11.6–12.6 μ (axial H at C-1), X-ray powder diffraction data 6.78 s (2), 5.45 vw, 4.93 m, 4.71 m, 4.26 m, 3.97 vs (1), 3.64 m, 3.56 m, 3.41 m, 3.21 m, 3.10 w, 2.97 w, 2.93 w, 2.79 vw, 2.72 vw, 2.60 w, 2.52 vw, 2.45 w, 2.36 w, 2.32 vw, 2.21 w, 2.15 w, 2.07 w. The nmr spectrum of a 34% solution in deuterium oxide, measured 5 min after dissolution, showed a one-proton doublet, τ 5.11 ($J_{1,2}$ = 8.3 cps, axial H-1 of **8**) (lit.[7] τ 5.12, $J_{1,2}$ = 8.3 cps) and a one-proton multiplet, 6.82 (width 22 cps, H-5 of **8**). A very weak doublet, observed at τ 4.52 ($J_{1,2}$ = 3.4 cps, equatorial H-1 of **7**) (lit.[7] τ 4.53, $J_{1,2}$ = 3.8 cps), increased in intensity with time at the expense of the signal at τ 5.11, and simultaneously a multiplet at 6.42 (H-5 of **7**) appeared at the expense of the signal at 6.82. At equilibrium, the H-1 signals for **7** and **8** were in the relative proportions 47:53; the spectrum was measured at 70° for integration so that the HOD signal did not interfere with the signal for the axial H-1. Signals for H-2, -3, -4, -6, and -6′ were observed in the region τ 5.7–6.35.

F. D-Galactose, D-Glucose, and D-Mannose.—Solutions (25–30%) of the aldoses in deuterium oxide were allowed to reach mutarotational equilibrium, and spectra were measured at 80–100°. The chemical shifts observed for the H-1 signals are listed in Table I, together with shifts reported[5] relative to an external standard of tetramethylsilane. Anomeric compositions determined by integration were in good agreement with the reported[5] values given in Table II.

Pyrrolidine Sugars. Synthesis of 4′-Acetamidoadenosine and Other Derivatives of 4-Amino-4-deoxy-D-ribose[1]

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Derivatives of 4-amino-4-deoxy-D-ribose have been prepared starting from methyl 2-*O*-benzoyl-3,4-di-*O*-(*p*-tolylsulfonyl)-β-L-arabinopyranoside (**1**). Thus, selective displacement of the 4-tosylate of **1** by azide gave methyl 4-azido-2-*O*-benzoyl-4-deoxy-3-*O*-(*p*-tolylsulfonyl)-α-D-xylopyranoside (**2**). Conversion of **2** to the 4-acetamide followed by intramolecular displacement of the 3-tosylate gave after deacylation methyl 4-acetamido-4-deoxy-α-D-ribopyranoside (**7**). Acetolysis of **7** effected a ring contraction to 4-acetamido-1,2,3,5-tetra-*O*-acetyl-4-deoxy-D-ribofuranose (**10**). An alternative synthesis of **10** from methyl 2,3-*O*-isopropylidene-4-*O*-(*p*-tolylsulfonyl)-α-L-lyxopyranoside was also described. Conversion of **10** to methyl 4-acetamido-4-deoxy-D-ribofuranoside (**16**) and its tri(*p*-nitrobenzoate) (**17**) was described. Compound **16** exhibited hindered internal rotation about the C–N bond in the nmr spectrum. Benzoylation of **7** gave methyl 4-acetamido-2,3-di-*O*-benzoyl-4-deoxy-α-D-ribopyranoside (**20**) as well as methyl 4-acetamido-2,3-di-*O*-benzoyl-4-*N*-benzoyl-4-deoxy-α-D-ribopyranoside (**21**). Acetolysis of **20** again gave ring contraction to give 4-acetamido-1,5-di-*O*-acetyl-2,3-di-*O*-benzoyl-4-deoxy-D-ribofuranose (**22**) which was converted to 4′-acetamidoadenosine (**23**). The nucleoside **23**, also exhibited hindered internal rotation in the nmr, a phenomenon which is observed in the nmr of amido sugars with nitrogen in the ring when the spectrum is run in D_2O.

Nucleoside analogs of the natural nucleic acid components frequently show striking differences, both qualitative and quantitative, as compared to the natural nucleosides, as substrates for important enzymes such as adenosine deaminase or nucleoside phosphorylase. The adenosine analogs, 9-(β-D-arabinofuranosyl)-adenine and 9-(β-D-xylofuranosyl)adenine, for example are not cleaved by nucleoside phosphorylase.[2]

Substitution of the sugar ring oxygen of a nucleoside by another atom represents another type of structural change which could have effects of biological significance. The synthesis of 4′-thioadenosine[3] represents one example of this type of alteration; this manuscript describes the synthesis of an adenosine analog in which the sugar heteroatom is nitrogen.

Azide displacement of a C-4 sulfonate ester was the most attractive entrée to a 4-amino sugar. Methyl 2-*O*-benzoyl-3,4-di-*O*-(*p*-tolylsulfonyl)-β-L-arabinopyranoside (**1**)[4] could be expected to yield selectively the 4-azido derivative (**2**) on the basis of several considerations. First, there is considerable documentation that C-4 sulfonates of hexopyranosides are readily displaced by sodium benzoate in N,N-dimethylformamide (DMF)[5] even if the sulfonate has the equatorial configuration. Secondly, Dick and Jones[6] have described the reaction of a number of methyl 2,3,4-tri-*O*-methylsulfonylpentopyranosides with sodium azide in DMF in which the C-4 sulfonate was more readily displaced than either the C-2 or C-3 sulfonate, *e.g*, reaction of methyl 2,3,4-tri-*O*-methylsulfonyl-β-L-arabinopyranoside yielded methyl 4-azido-4-deoxy-2,3-di-*O*-methylsulfonyl-α-D-xylopyranoside.

Treatment of the di-*p*-toluenesulfonate (**1**) with sodium azide in DMF afforded a crystalline monoazide that could be converted to methyl 2,3-anhydro-4-azido-4-deoxy-α-D-ribopyranoside (**5**) by treatment with

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