A New Approach to 3′-Amino-3′-deoxynucleosides. Synthesis of 9-(3-Amino-3-deoxy-α-L-ribofuranosyl)adenine[1]

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Methyl 2,3,4-tri-*O*-acetyl-6-deoxy-6-nitro-α-D-glucopyranoside (**1**) was acetolyzed to give 1,2,3,4-tetra-*O*-acetyl-6-deoxy-6-nitro-α-D-glucopyranose (**2**). Compound **2** (or alternatively, 6-deoxy-1,2-*O*-isopropylidene-6-nitro-α-D-glucofuranose **4**) was converted into 2,3,4-tri-*O*-acetyl-6-deoxy-6-nitro-α-D-glucopyranosyl bromide (**3**) which was condensed with chloromercuri 6-benzamidopurine. De-*O*-acetylation of the condensation product **5** afforded 6-benzamido-9-(6-deoxy-6-nitro-β-D-glucopyranosyl)purine (**6**) which could be hydrogenated to the corresponding 6′-amino nucleoside **7**. Periodate oxidation of **6** followed by internal Henry cyclization and borohydride reduction gave 6-benzamido-9-(3-deoxy-3-nitro-α-L-ribofuranosyl)purine (**10**) which upon catalytic hydrogenation and subsequent de-*N*-benzoylation produced the title compound, **12**. The sensitivity of certain nitro intermediates towards alkali is commented upon.

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Amino nucleosides command great interest especially because of the biological activity of such natural products as puromycin, 3′-amino-3′-deoxyadenosine, and gougerotin (1–3), and because of the potential usefulness of synthetic analogs in biochemical and medicinal research. Among other methods for the synthesis of 3′-amino-3′-deoxy-hexopyranosyl nucleosides, the cyclization of sugar dialdehydes with nitromethane (4) has been applied (5, 6) with much success, and the related principle of adding nitromethane to oxo sugars (7–9) has been used in the synthesis of nucleosides that contain branched-chain amino sugars (9, 10). In our laboratory was recently accomplished (11) a novel furanoside synthesis which involves the conversion of methyl 6-deoxy-6-nitro-α-D-glucopyranoside into methyl 3-deoxy-3-nitro-β-L-ribo- and -arabinofuranosides and the corresponding amino sugars, and we now report an application of this reaction to a nucleoside. The work opens a new avenue into the hitherto comparatively little-investigated class of ribonucleosides having the L-configuration (12).

As key starting compound, a nucleoside bearing a nitro group at the terminal carbon of the sugar moiety was required. We attempted to prepare 5′-deoxy-5′-nitro-inosine and -uridine from the corresponding 2′,3′-*O*-isopropylidene-6-iodo derivatives (or 6-tosylates) by displacement with sodium nitrite, using a wide variety of solvents and reaction conditions. However, the desired nitro compounds could not be obtained. We therefore resorted to a nucleoside synthesis departing from a nitro sugar and a purine base. It was decided to prepare in this fashion 6-benzamido-9-(6-deoxy-6-nitro-β-D-glucopyranosyl)-purine (**6**) which would then serve as an intermediate for the synthesis of 9-(3-amino-3-deoxy-α-L-ribofuranosyl)purine (**12**) whose β-D isomer (3′-amino-3′-deoxyadenosine) has been reported to possess antitumor activity (13).

Acetolysis of known (11, 14) methyl 2,3,4-tri-*O*-acetyl-6-deoxy-6-nitro-α-D-glucopyranoside (**1**) afforded 1,2,3,4-tetra-*O*-acetyl-6-deoxy-6-nitro-α-D-glucopyranose (**2**) in 92% yield. The tetraacetate was then converted into 2,3,4-tri-*O*-acetyl-6-deoxy-6-nitro-α-D-glucopyranosyl bromide (**3**). Although one of the standard procedures for such a bromination, namely the use of hydrogen bromide in glacial acetic acid, was successfully applied (15) to the 3-nitro isomer of **2**, it did not prove satisfactory in this instance.[3] However, the modification of Scheurer and Smith (16) readily gave the desired bromide in 77% yield. Alternatively, the known (17) 6-deoxy-1,2-*O*-isopropylidene-6-nitro-α-D-glucofuranose (**4**) was deacetonated with 80% acetic acid and then brominated by the same method (16), giving **3** in about 50% yield. Analytical, spectral, and optical rotation data of **2** and **3** were in accord with the structures. Employing the general method of Davoll and Lowy (18) we then pro-

[1]Part XVIII in a series on the reactions of nitro sugars. For Part XVII see ref. 15.

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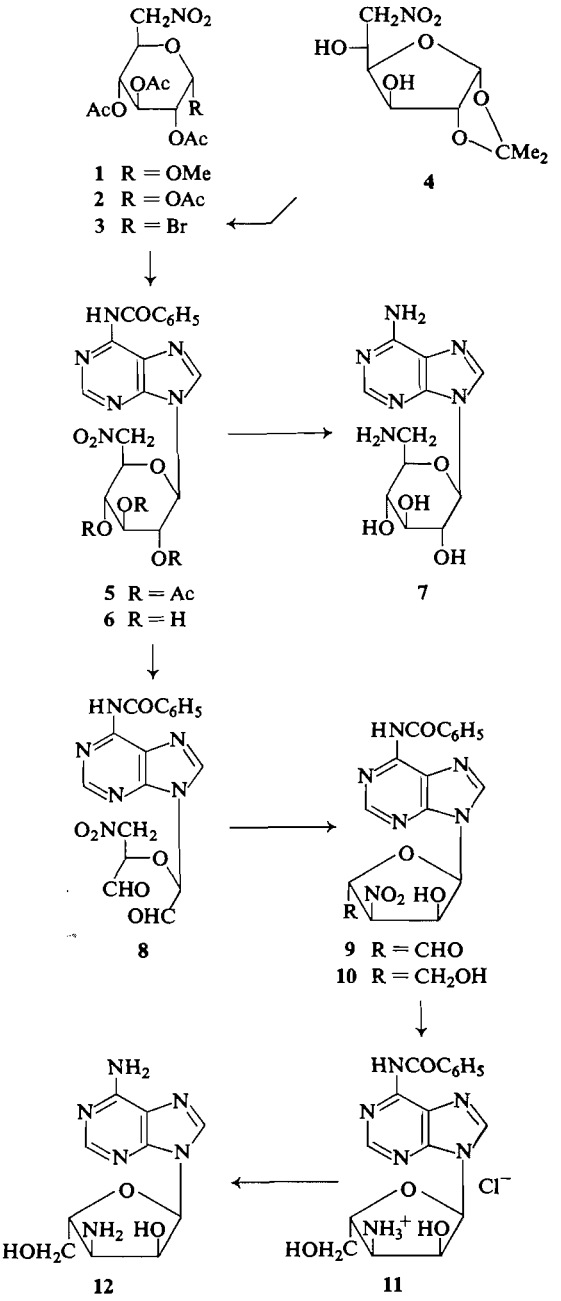
[3]Only unchanged **2** could be isolated even after prolonged reaction times.

ceeded to couple **3** with chloromercuri 6-benzamidopurine (19) in refluxing toluene. A 36% yield of crystalline 6-benzamido-9-(2,3,4-tri-*O*-acetyl-6-deoxy-6-nitro-β-D-glucopyranosyl)-purine (**5**) was obtained. The β-D configuration was indicated by its levorotation ($[\alpha]_D$ −26° in $CHCl_3$), and definitely established by a large splitting observed in the n.m.r. signal assignable to H-1′ (doublet at τ 3.92, $J_{1',2}$ = 8.7 Hz, in $CDCl_3$). The t.l.c. of the mother liquor revealed the presence of unreacted **3**, 6-benzamidopurine, an unidentified sugar derivative,[4] and a second nucleoside. The latter possibly was the α-anomer of **5**; however, it could not be isolated.[5]

Next, removal of the acetyl blocking groups in **5** was necessary. Since the nucleosidic bond in this nitro derivative is extremely prone to cleavage in alkaline media as will be outlined further below, we first tried methanolytic deacetylation catalyzed by *p*-toluenesulfonic acid, which had served satisfactorily (11) in the de-*O*-acetylation of **1**. Unfortunately, in the present case, debenzoylation and salt formation at N-6 predominated, and deacetylation was extremely slow, remaining incomplete even after a reaction time of 2 weeks. However, the acetyl groups were selectively removed by cautious treatment of **5** with sodium methoxide in chloroform at −19°, which produced 6-benzamido-9-(6-deoxy-6-nitro-β-D-glucopyranosyl)purine (**6**) in yields of 72–90%. In order to buttress the structure of the product at this stage, a sample was converted by catalytic hydrogenation and subsequent debenzoylation into the known (21) 6′-amino-6′-deoxy-β-D-glucopyranosyladenine (**7**). The potential usefulness of nitro sugar bromides in conjunction with the chloromercuri procedure for the synthesis of amino nucleosides was thereby demonstrated.

Periodate oxidation of the nitro nucleoside **6** was carried out in aqueous suspension and, although proceeding sluggishly, it afforded the dialdehyde **8** in good yield. Without characterization other than by t.l.c., **8** was then cyclized in methanolic solution by the addition of sodium methoxide at −19°, and the 5′-aldo derivative **9** that arose was immediately reduced with sodium borohydride, at low temperature, to give crystalline 6-benzamido-9-(3-deoxy-3-nitro-α-L-ribofuranosyl)purine (**10**) in a yield of 50% (based on **8**). Catalytic hydrogenation in the presence of 1 equiv of hydrochloric acid converted **10** into the corresponding 3′-amino ribonucleoside hydrochloride (**11**) which, although crystalline



[4]Compare the formation of an unsaturated sugar in a similar nucleoside synthesis (19).

[5]Attempted separation of the mother liquor components by column or preparative t.l.c. resulted in extensive decomposition. Equally discouraging were pilot experiments to synthesize the α-anomer by the boron trichloride method recently described by Furukawa *et al.* (20).

and chromatographically homogeneous, was difficult to handle due to considerable hygroscopicity and was, therefore, not analyzed. Treatment of **11** with picric acid removed the *N*-benzoyl group and gave a crystalline dipicrate from which the title compound **12** was liberated, by anion exchange, in a yield of 37% based on **10**. The L-*ribo* configuration was proved by hydrochloric acid hydrolysis producing the known 3-amino-3-deoxy-L-ribose hydrochloride (22, 23). The anomeric center must possess the same absolute configuration as that of the precursor **6** and consequently receives the α designation. In agreement herewith, physical constants found for **12** are different from those expected[6] for the β-L anomer. The reaction sequence **6** → **8** → **9** → **10** is therefore seen to have taken a stereochemical course that was predictable on the basis of our previous work (11). That is to say, an α-L-ribofuranosyl derivative was generated from a β-D-glucopyranosyl derivative, in full harmony with the analogous, earlier synthesis of a β-L-ribofuranoside.[7]

The mother liquor of the nitro ribonucleoside **10** contained a small proportion of a compound that moved slightly faster in t.l.c. and was presumed to be an isomeric nucleoside. Complete separation from remnant **10** could not be effected, but a sample enriched in this by-product was hydrogenated and hydrolyzed with hydrochloric acid for inspection by paper chromatography. The major, ninhydrin-positive spot had the same mobility as an authentic sample of 3-amino-3-deoxy-L-arabinose hydrochloride (25), and a minor spot corresponded to the L-*ribo* isomer. Assignment of the α-L-arabinofuranosyl structure to the by-product must remain tentative but would be in line with previous results (11).

The nitro nucleosides **5**, **6**, and **10**, as well as the intermediates **8** and **9**, possess an acetal linkage activated by a nitro group in β-position, and such linkages are known to be prone to eliminative cleavage by alkali (4). For example, the primary nitro compound **5** suffered complete loss of the aglycon in a 1:1 mixture of acetone and 0.1 *M* sodium bicarbonate within 5 min at room temperature, and **6** was cleaved to about 50% after 35 min. The secondary nitro compound **10** was stable under these conditions but was cleaved to about 50% by *N* alcoholic potassium hydroxide within 50 min at room temperature. It was largely cleaved by 0.1 *N* aqueous sodium hydroxide within a few minutes at 98°. Further examples are given in the Experimental. It is obvious that, with compounds of this type, synthetic work in which alkaline reagents are indispensable must be conducted under most carefully controlled conditions.

[6]Compare the data published for the β-D enantiomer (24*a*, *b*). The α-D antipode of **12** has been encountered (24*a*), but no physical constants were given.

[7]These configurational inversions result from the interchange of positions, relative to each other in the sugar chain, that is incurred by C-4 and -6 of the pyranose structure when these carbon atoms become C-5 and -3, respectively, in the furanose structure. No chemical epimerization takes place at the configurationally determinant carbon atom, at least not as far as the products isolated under the reaction conditions are concerned (11).

Experimental

General Techniques

Melting points were determined in capillaries in an electric aluminum block apparatus equipped with a calibrated thermometer. Optical rotations were measured at about 25° in a Perkin–Elmer 141 automatic polarimeter. The i.r. spectra were obtained from Nujol mulls on Beckman IR-8 or IR-20 instruments, and significant bands only are reported as ν_{max} values. The u.v. data reported were obtained with a Jasco ORD/UV-5 spectrophotometer, whereas a Perkin–Elmer 202 instrument was used for routine monitoring. The n.m.r. spectra (100 MHz) were recorded on a Varian HA-100 spectrometer. The t.l.c. was performed on silica gel HT-254 according to Stahl, with the following solvent systems (v/v): *a*, chloroform–ether (2:1); *b*, chloroform–methanol (9:1); *c*, chloroform–methanol (4:1); *d*, 2-propanol – water (7:3); *e*, ethyl acetate – methanol (9:1). The t.l.c. plates were viewed under u.v. light and (or) sprayed with ceric sulfate – sulfuric acid and heated. For paper chromatography, the following systems were used: *f*, 1-propanol – water (8.5:1.5); *g*, ethyl acetate – pyridine – water – acetic acid (5:5:3:1); *h*, 1-butanol – ethanol – water (10:5:7). The spots were indicated by ammoniacal silver nitrate or ninhydrin.

1,2,3,4-Tetra-O-acetyl-6-deoxy-6-nitro-α-D-glucopyranose (2)

The nitro glucoside triacetate **1** (11) (26 g) was dissolved in a mixture of acetic acid (260 ml) and acetic anhydride (260 ml), and the solution was cooled to 0°. Concentrated sulfuric acid (26 ml) was added dropwise and with stirring which was maintained for 2 h at 0° and 5 days at room temperature, during which time some of the product crystallized. The reaction mixture was poured into ice–water (2.5 l) and the solid was collected and washed successively with water, ethanol, and ether. The dried product (23.5 g, 92%) consisted of white needles, m.p. 241°, which gave a single spot on t.l.c. (system *a*) and could be used without further purification. Samples were recrystallized from ethanol–chloroform, acetone, acetic acid, or dioxane: m.p. to 245°; $[\alpha]_D$ +99.3° (*c*, 0.5 in dimethylformamide); ν_{max} 1740 (acetyl C=O), 1545 (NO_2), 1230 with shoulder at 1260 cm^{-1} (acetyl C—O); n.m.r. data ($CDCl_3$), τ 3.70 (doublet, H-1, with $J_{1,2}$ = 4

Hz), 7.79 (singlet, axial acetyl), 7.93, 7.97, 7.98 (singlets, 3 equatorial acetyls); in DMSO-d_6, τ 3.89 (doublet, H-1, with $J_{1,2}$ = 4 Hz), 7.82 (singlet, axial acetyl), 8.00–8.02 (singlets, 3 equatorial acetyls).

Anal. Calcd. for $C_{14}H_{19}NO_{11}$ (377.3): C, 44.56; H, 5.08; N, 3.71. Found: C, 44.72; H, 5.20; H, 3.84.

2,3,4-Tri-O-acetyl-6-deoxy-6-nitro-α-D-glucopyranosyl Bromide (3)

(a) From 2

Bromine (48 ml) was added dropwise to a chilled suspension of red phosphorus (24 g) in glacial acetic acid (240 ml). When all the bromine had reacted, the mixture was filtered through glass wool and the filtrate was stored at 0° if it was not to be used immediately. The tetraacetate **2** (22 g) was introduced, and the mixture was stirred for 2 h at 60–70° (bath temperature) and then kept at room temperature overnight. The crystalline product **3** (16 g) was collected on a fritted funnel and washed thoroughly with ether. Additional **3** (2 g) was obtained from the mother liquor by aeration with nitrogen under diminished pressure; total yield, 77%. The product, which is only sparingly soluble in most common solvents except dimethylformamide (DMF) and dimethyl sulfoxide (DMSO), was recrystallized by dissolution in a large volume of boiling acetone and concentration of the solution at reduced pressure. It forms white needles that decompose at 212–215° and show $[\alpha]_D$ +148° (*c*, 1.6 in DMF). The mobility in t.l.c. (system *a*) is slightly greater that that of **2**. The i.r. data, ν_{max} 1740 (C=O), 1555 (NO_2), and 1220 with shoulder at 1250 cm^{-1} (C—O); n.m.r. data ($CDCl_3$), τ 3.48 (doublet, H-1, with $J_{1,2}$ = 4 Hz), 7.90, 7.92, 7.97 (singlets, 3 equatorial acetyls); in DMSO-d_6 the corresponding signals were at τ 3.17, 7.96, 7.99, and 8.01.

Anal. Calcd. for $C_{12}H_{16}NO_9Br$ (398.2): C, 36.19; H, 4.05; Br, 20.07. Found: C, 36.19; H, 3.96; Br, 19.97.

(b) From 4

The monoisopropylidene derivative **4** (14.3 g) (17) was hydrolyzed in 80% acetic acid (300 ml) for 6 h at 100–105°, with the progress of deacetonation being monitored by t.l.c. (system *d*). Evaporation followed by one co-evaporation with toluene gave a syrup which was treated with the brominating reagent (300 ml) as described in section (*a*). The product (11.5 g, 50%) was identical with **3** in every respect.

6-Benzamido-9-(2,3,4-tri-O-acetyl-6-deoxy-6-nitro-β-D-glucopyranosyl)purine (5)

A suspension of chloromercuri 6-benzamidopurine (6 g) (19) and Celite (8.5 g) in toluene (500 ml) was dried azeotropically by distilling off about 150 ml of the solvent. The bromide **3** (5 g) in dry toluene (100 ml) was added at about 70° and the bath temperature was then raised slowly to 130–135°. Reflux and vigorous stirring were maintained for 3 h. The reaction mixture was then filtered and the filtrate evaporated to dryness. The residue as well as the filter cake were extracted by stirring each with 150 ml of chloroform for 30 min. The filtered and combined extracts were washed successively with 30% aqueous potassium iodide solution (2 × 50 ml), and water (3 × 50 ml), dried over magnesium sulfate, and evaporated to give a partly oily residue (*ca.* 6 g). The material crystallized from 99% ethanol (60 ml) upon scratching of the flask. Recrystallization from ethanol furnished **5** (2.5 g, 36%) as colorless needles, m.p. 203° (dec.); $[\alpha]_D$ −26° (*c*, 1.4 in chloroform); homogeneous in t.l.c. (system *b*); ν_{max} 3650 (NH), 1755 (acetyl C=O), 1700 (*N*-benzoyl C=O), 1615, 1585 (purine C=N and C=C), 1555 (NO_2), 1255–1215 cm^{-1} (C—O); λ_{max} 277 nm (ε 20 900) and λ_{min} 242 nm (in methanol). The n.m.r. data ($CDCl_3$), τ 1.17, 1.78 (singlets, H-2 and -8), 1.94 and 2.40 (2- and 3-proton multiplets of benzoyl), 3.92 (doublet, H-1′, with $J_{1',2'}$ = 8.7 Hz), 4.24, 4.43, 4.74 (three triplets with spacings of 9–10 Hz assigned to H-2′, -3′, and -4′, but not necessarily in that order), 5.4 region (overlapping signals of H-5′, -6*a*′, -6*e*′), 7.89, 7.96, 8.24 (singlets, 3 acetyls). The high value τ 8.24 is noteworthy; it presumably represents the C-2′ acetoxy group which is strongly shielded by the purine ring.

Anal. Calcd. for $C_{24}H_{24}N_6O_{10}$ (556.5): C, 51.80; H, 4.35; N, 15.10. Found: C, 51.62; H, 4.46; N, 14.95.

In the above condensation, deviations from the 3-h reaction time on either side, or use of xylene as the solvent, were found to decrease the yield. Even though substantial quantities of unreacted **3** remained after 3 h, employment of a large excess of the purine component was of little effect, and yields generally ranged from 15–30%. Equimolar proportions of **3** and the chloromercuri derivative in DMF solution reacted at room temperature (4 days), but the isolation of **5** was difficult (yield, <20%).

Column chromatography of the mother liquor of **5** on silica gel or acid-washed alumina (Brockmann, activity grade 1) with chloroform and chloroform containing 5–10% of methanol resulted in extensive decomposition of the nucleoside components to give yellow substances that could not be eluted.

6-Benzamido-9-(6-deoxy-6-nitro-β-D-glucopyranosyl)-purine (6)

High-purity anhydrous solvents stored over molecular sieves were used, and moisture was excluded during the reaction. To a magnetically stirred solution of the acetate **5** (3.6 g) in chloroform (18 ml), which was kept at −19°, was added dropwise from a syringe a solution of sodium (360 mg) in methanol (18 ml). Stirring at −19° was continued for 1 h after which time the mixture was stirred for 5–10 min with added water (18 ml) and then acidified to p*H* 4–5 with methanolic hydrochloric acid under continued cooling. Removal of most of the organic solvents *in vacuo* (bath temperature 35°) caused sudden crystallization of white needles from the concentrated, largely aqueous solution. The product was collected at once, washed with water, and air-dried. Recrystallization from methanol gave **6** (2.0 g, 72%) showing a single spot in t.l.c. (system *c*) and decomposing at 194° (with gradual darkening above 175°). Yields up to 90% were obtained in smaller-scale runs. The compound exhibited $[\alpha]_D$ +4° (*c*, 1.2 in DMF), λ_{max} 278 nm (ε 21 800) and λ_{min} 242 nm (in methanol), ν_{max} 3600–3100 (broad, NH, OH), 1690 (*N*-benzoyl C=O), 1610, 1585 (C=C, C=N), 1550 cm^{-1} (NO_2).

Anal. Calcd. for $C_{18}H_{18}N_6O_7$ (430.4): C, 50.24; H, 4.22; N, 19.53. Found: C, 50.04; H, 4.12; N, 19.24.

9-(6-Amino-6-deoxy-β-D-glucopyranosyl)adenine (7)

A solution of the nitro nucleoside **6** (100 mg) in 95%

ethanol (15 ml) was hydrogenated using 10% palladium-on-charcoal (200 mg) at ordinary temperature and pressure (3 days). Paper chromatography (system *h*) then revealed a single ninhydrin-positive spot, R_f about 0.6. The filtered solution was concentrated to a small volume (*ca.* 1 ml), a solution of picric acid (140 mg) in ethanol (3 ml) and water (1 ml) was added, and the mixture was refluxed on a steam bath for 1 h. The crystalline picrate that separated on cooling was recrystallized once from water; decomposition point 217° (with sintering at 160–170°); lit. (21), dec. 215° with sintering from 168°. It was dissolved in a sufficiently large amount of water, and the solution was stirred with Dowex 1-X2 (carbonate form) until it was colorless. The ion exchange resin was filtered off and washed well with water. Evaporation of the combined filtrate and washing water gave a residue which by trituration with ethanol yielded **7** as a white powder that showed a single spot ($R_{adenine}$ 0.36) in paper chromatography (system *h*), decomposed at 210°, and exhibited λ_{max} 259 nm (in water), in agreement with the reported data (21).

*6-Benzamido-9-(3-deoxy-3-nitro-α-L-ribofuranosyl)-purine (**10**)*

A suspension of finely powdered nitro nucleoside **6** (1.5 g) in a solution of sodium metaperiodate (3 g) in water (60 ml) was stirred in the dark for 3 days. The t.l.c. of the reaction mixture (system *c*) indicated the conversion, in heterogeneous phase, of **6** into fast-moving dialdehyde **8** which was the only major reaction product that exhibited u.v. absorption. The product was collected by filtration, washed thoroughly with water, dried in a vacuum desiccator over P_2O_5, and stored below 0°. The yield was 1.0 g (72%).

A solution of **8** (500 mg) in absolute methanol (25 ml) was cooled to −19° in an ice–salt bath, and a chilled, 0.1 *N* sodium methoxide solution (15 ml) was added dropwise with magnetic stirring. The mixture was kept at −19° for 1 h after which time almost complete conversion of **8** into a slightly slower-migrating product **9** was indicated by t.l.c. (system *b*). With continued cooling, sodium borohydride (200 mg) suspended in chilled ethanol (10 ml) was added immediately, and the mixture was then allowed to stand at −15° for 24 h. Although the 5′-aldo nucleoside **9** and its reduction product **10** had identical R_f values in several t.l.c. and paper chromatographic systems tested, the course of the reduction could be conveniently monitored on short paper strips (ascending technique in system *f*), unreacted **9** being detectable by spraying with Tollens reagent. The reaction mixture was then acidified with acetic acid – methanol (1:1) and evaporated to dryness. Three portions of methanol were successively evaporated from the oily residue which was then triturated twice with small amounts of cold water to remove sodium acetate. The remaining, water-insoluble gum was dissolved in ethanol or methanol from which colorless crystals of **10** were deposited overnight at −15°. Recrystallization from methanol yielded **10** (250 mg, 50% based on **8**); m.p. 172°; $[\alpha]_D$ −61° (*c*, 1 in DMF); λ_{max} 277 nm (ε 20 300) and λ_{min} 245 nm (in methanol); ν_{max} 3600–3100 (broad, NH, OH), 1690 (*N*-benzoyl C=O), 1610, 1580 (C=N, C=C), and 1550 cm^{-1} (NO_2).

Anal. Calcd. for $C_{17}H_{16}N_6O_6$ (400.4): C, 51.00; H, 4.03; N, 20.99. Found: C, 50.90; H, 4.03; N, 20.98.

The mother liquor from which **10** had crystallized was shown by t.l.c. (system *e*) to contain, besides a large amount of additional **10**, a minor component of slightly greater mobility. Preparative t.l.c. (system *e*) provided a material in which this by-product was enriched but which contained some **10** (see Discussion).

*6-Benzamido-9-(3-amino-3-deoxy-α-L-ribofuranosyl)-purine Hydrochloride (**11**)*

Platinum dioxide catalyst (150 mg) was prehydrogenated in 36 ml of 0.01 *N* hydrochloric acid. The solid nitro nucleoside **10** (150 mg) was added, and it went slowly into solution as its hydrogenation proceeded. About 3 h of vigorous shaking under hydrogen at ordinary temperature and pressure was needed. The filtered solution was then concentrated to a volume of about 5 ml. A small sample was withdrawn and evaporated to dryness with several additions of absolute ethanol. Trituration of the residue with ethyl acetate gave hygroscopic needles of the hydrochloride **11** which decomposed above 160° and showed a single spot in paper chromatography (system *g*, ninhydrin spray).

*9-(3-Amino-3-deoxy-α-L-ribofuranosyl)adenine (**12**)*

The major part of the concentrated aqueous solution from the hydrogenation just described (estimated to contain about 130 mg of **11**) was mixed with a solution of picric acid (74 mg) in ethanol (2 ml). The mixture was refluxed on a steam bath for 1 h, and for another 30 min following the addition of a second, identical portion of alcoholic picric acid. The debenzoylation could be monitored by paper chromatography (system *g*). On cooling of the reaction mixture, the picrate of **12** (m.p. 185°) crystallized in part but was redissolved by dilution with ethanol. The solution was stirred with 20 ml of Dowex 1-X2 (OH^-), 50–100 mesh, and then applied to a column (2 × 15 cm) of the same ion exchange resin. The column was eluted with water, 15-ml fractions being collected and checked for u.v. absorption at 257 nm which appeared in fractions 17–65. These fractions were pooled and evaporated to dryness, with several portions of ethanol finally being evaporated from the residue which was then dried in a high vacuum. Compound **12** was thus obtained as a white powder (32 mg, 37% based on **10**), m.p. 162° with sintering from 150°, $[\alpha]_D$ +18° (*c*, 0.4 in water), λ_{max} 257 nm (ε 13 600) and λ_{min} 225 nm (in 0.1 *N* HCl). It appeared homogeneous in paper chromatography (system *g*) and t.l.c. (system *d*).

Anal. Calcd. for $C_{10}H_{14}N_6O_3$ (266.3): C, 45.11; H, 5.30; N, 31.57. Found: C, 44.88; H, 5.17; N, 31.32.

A sample of **12** (5.00 mg) was hydrolyzed in 3 *N* hydrochloric acid (1.00 ml) for 2 h at 98°. The hydrolysate had a rotation of α_D +0.067° (1 dm tube, 25 °C), corresponding to a specific rotation of $[\alpha]_D$ +19° calculated for the aminodeoxypentose hydrochloride produced. Reported for 3-amino-3-deoxy-L-ribose hydrochloride: +18.9° (11), +23° (23). The hydrolysate was evaporated with several additions of water, and paper chromatography (system *g*) of the residue indicated complete cleavage of **12** into adenine and a single amino sugar whose spot was indistinguishable from that of an authentic sample of 3-amino-3-deoxy-L-ribose hydrochloride.

Alkaline Degradations

The behavior of the nitro compounds **5**, **6**, **8**, **9**, and **10** in alkaline media was examined by t.l.c. Samples taken at intervals were acidified with dilute acetic acid before application. The chromatograms were viewed under u.v. light and spot intensities were estimated visually, with 6-benzamidopurine and adenine used as controls. The aglycons were readily distinguished from the nucleosides not only by the mobilities but also by spraying the plates with ceric sulfate – sulfuric acid followed by heating, dark spots being produced from carbohydrate-containing substances only.

(*a*) To compound **5** (2 mg) in acetone (0.4 ml) was added aqueous, 0.1 *M* sodium bicarbonate buffer (0.4 ml, p*H* 8.4). After 5 min at room temperature, 6-benzamidopurine was the only spot visible in the u.v., indicating complete cleavage of the nucleoside (system *b*).

(*b*) A similar experiment with compound **6** revealed 50% cleavage in 35 min (system *c*).

(*c*) A solution of the dialdehyde **8** (100 mg) in methanol (5 ml) was adjusted to p*H* 7.5 with alcoholic potassium hydroxide, at room temperature, and 50% cleavage was observed after 30 min (system *e*).

(*d*) To an ice-cooled solution of **8** (100 mg) in methanol (5 ml) was added 3 ml (1.2 equiv) of a 0.1 *N* sodium methoxide solution. After 1 h at 0°, about 30% of the aglycon was liberated (system *e*).

(*e*) When the sodium borohydride reduction of intermediate **9** (for the preparation of **10** as described above) was carried out at room temperature rather than at −19 to −15°, the *N*-glycosidic bond was cleaved to the extent of 30–50% depending on the amount of $NaBH_4$ employed (system *e*).

(*f*) A few milligrams of compound **10** were tested in 1 ml of each of the following media: *i*, 0.1 *M* sodium bicarbonate – acetone (1:1) at 25°; *ii*, 0.01 *N* sodium hydroxide – acetone (1:1) at 25°; *iii*, *N* potassium hydroxide, ethanolic, at 25°; *iv*, 0.1 *N* sodium hydroxide, aqueous, at 98°. Compound **10** appeared to be stable overnight in *i* and *ii*, but was 50% cleaved within 50 min in *iii* and still more extensively within 3 min in *iv* (system *e*).

Attempted Displacements with Nitrite

5′-Deoxy-5′-iodo-2′,3′-*O*-isopropylideneinosine (26) was treated with sodium nitrite (1–3 equiv) according to the general procedure of Kornblum (27). Solvents tried were DMF, DMSO, mixtures of the same, and hexamethylphosphoric triamide. Reaction times and temperatures ranged from 2–4 days and 5 to 25° respectively. Trials were made with and without addition of phloroglucinol or urea. The t.l.c. (system *b*) revealed the formation of several reaction products, but the desired 5′-nitro derivative could not be isolated.

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