9-Deazapurine Nucleosides. The Synthesis of Certain *N*-5-β-D-Ribofuranosylpyrrolo[3,2-*d*]pyrimidines

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Several *N*-5 ribofuranosyl-2,4-disubstituted pyrrolo[3,2-*d*]pyrimidine (9-deazapurine) nucleosides were prepared by the single phase sodium salt glycosylation of 2,4-dichloro-5*H*-pyrrolo[3,2-*d*]pyrimidine (**3**) using 1-chloro-2,3-*O*-isopropylidene-5-*O*-(*t*-butyl)dimethylsilyl-α-D-ribofuranose (**2**). Use of **2** for the glycosylation avoided the formation of "orthoamide" products **1** and provided an excellent yield of the β nucleoside, 2,4-dichloro-5-[2,3-*O*-isopropylidene-5-*O*-(*t*-butyl)dimethylsilyl-β-D-ribofuranosyl]-5*H*-pyrrolo[3,2-*d*]pyrimidine (**4**), along with a small amount of the corresponding α anomer, **5**. Compound **4** served as the versatile intermediate from which the *N*-7 ribofuranosyl analogs of the naturally-occurring purine nucleosides adenosine, inosine and guanosine were synthesized. Thus, controlled amination of **4** followed by sugar deprotection and dehalogenation yielded the adenosine analog, 4-amino-5-β-D-ribofuranosyl-5*H*-pyrrolo[3,2-*d*]pyrimidine (**8**) as the hydrochloride salt. Base hydrolysis of **4** followed by deprotection gave the 2-chloroinosine analog, **10**, and subsequent dehalogenation provided the inosine analog, 5-β-D-ribofuranosyl-5*H*-pyrrolo[3,2-*d*]-pyrimidin-4(3*H*)-one (**11**). Amination of **10** furnished the guanosine analog, 2-amino-5-β-D-ribofuranosyl-5*H*-pyrrolo[3,2-*d*]pyrimidin-4(3*H*)-one (**12**). Finally, the α anomer in the guanosine series, **16**, was prepared from **5** by the same procedure as that used to prepare **12**. The structural assignments were made on the basis of ultraviolet and proton nmr spectroscopy. In particular, the isopropylidene intermediates **9** and **14** were used to assign the proper configuration as β and α, respectively, according to Imbach's rule.

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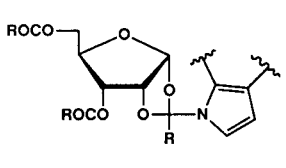
As part of our ongoing program in the design and synthesis of novel nucleosides as immune modulating agents, we recently described [1] the use of the single phase sodium salt glycosylation procedure for the preparation of 2'-deoxyribofuranosyl and arabinofuranosylnucleosides of the pyrrolo[3,2-*d*]pyrimidine (9-deazapurine) ring system. Since the carbohydrate moiety in both cases is attached to the pyrrole nitrogen of this ring system, these nucleosides are isosteric with 7-glycosylpurines. In the present work, we report the extension of this glycosylation procedure to now include the synthesis of the corresponding β-D-ribofuranosylnucleosides in this 9-deazapurine system. Thus, the analogous *N*-7 glycosyl derivatives of the naturally occurring purine nucleosides adenosine, inosine and guanosine were prepared.

The successful attachment of a ribofuranose moiety to a pyrrole or fused pyrrole ring system using the sodium salt glycosylation procedure requires that one avoid the use of the usual ester-blocked sugars since the neighboring group effect (provided by participation of the 2-*O*-acyl group) always facilitates the formation of a stabilized acyloxonium intermediate. Condensation of the sodium salt of the pyrrole derivative with this type of intermediate has been observed by us [2] and others [3] to result in bond formation at the carbonyl carbon of the participating group instead of at the *C*-1 carbon of the glycon, thus forming an "orthoamide" product **1**. We have observed exceptions to this generalization in cases where the fused pyrroles contain an electron-withdrawing group (relative to hydrogen in terms of field effects) such as a cyano or chloro substituent [4,5] adjacent to the pyrrole ring nitrogen. In these cases, the glycosylation proceeds normally to yield the *N* to *C*-1 bonded glycosides. For the studies reported here, however, we elected to use a recently reported ribofuranose derivative which would avoid the neighboring group participation problem, namely 1-chloro-2,3-*O*-isopropylidene-5-*O*-(*t*-butyl)dimethylsilyl-α-D-ribofuranose [6] (**2**). The versatile heterocycle 2,4-dichloro-5*H*-pyrrolo[3,2-*d*]pyrimidine (**3**) [1,7] was used as the aglycon for the glycosylation studies. Treatment of the sodium salt of **3** with the α-chlorosugar **2** at room temperature in acetonitrile provided the key intermediate 2,4-dichloro-5-[2,3-*O*-isopropylidene-5-*O*-(*t*-butyl)dimethylsilyl-β-D-ribofuranosyl]-5*H*-pyrrolo[3,2-*d*]pyrimidine (**4**) in 62% yield, along with a small amount (13%) of the corresponding α anomer **5** (Scheme I). This α anomer was most likely formed as a result of slow anomerization of the starting α-chlorosugar to the corresponding β anomer (which is more thermodynamically stable) followed by nucleophilic attack of the fused pyrrole anion. Indeed, Rosemeyer and Seela [8] recently described the versatility of the halogenose **2** for the stereoselective preparation of



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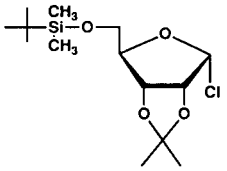

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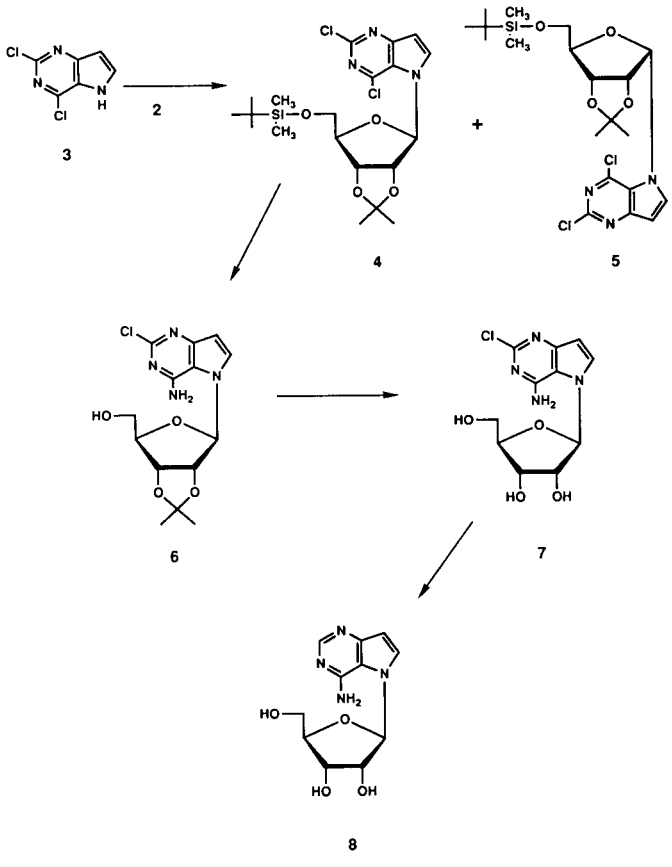
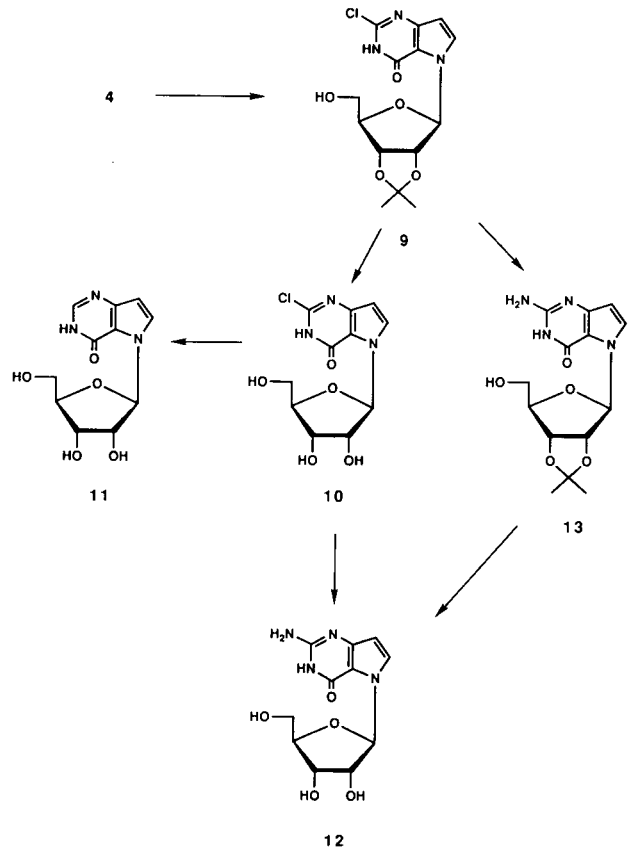
both α and β nucleosides in the 7-deazapurine (pyrrolo[2,3-*d*]pyrimidine) ring system and showed that simple "aging" at room temperature of the reaction mixture of the α-halogenose preparation resulted in significant α to β anomerization.

Scheme I



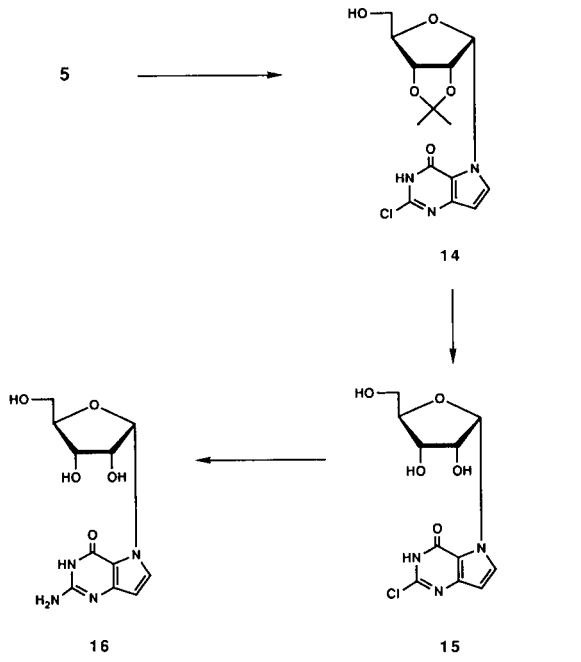
Reaction of **4** with methanolic ammonia at 110° for 12 hours provided 4-amino-2-chloro-5-[2,3-*O*-isopropylidene-5-(*t*-butyl)dimethylsilyl-β-D-ribofuranosyl]-5*H*-pyrrolo-[3,2-*d*]pyrimidine (**6**) in 81% yield. Deprotection of the glycon of **6** was accomplished by treatment with 80% aqueous trifluoroacetic acid at room temperature for 3 hours to yield 4-amino-2-chloro-5-β-D-ribofuranosyl-5*H*-pyrrolo[3,2-*d*]pyrimidine (**7**). Dehalogenation of **7** using palladium on carbon in a hydrogen atmosphere furnished the 7-β-D-ribofuranosyl-9-deaza analog of adenosine, 4-amino-5-β-D-ribofuranosyl-5*H*-pyrrolo[3,2-*d*]pyrimidine as the hydrochloride salt (**8**). Treatment of **4** with boiling aqueous sodium hydroxide in dioxane resulted in displacement of the 4-chloro group with concomitant desilylation to provide 2-chloro-5-(2,3-*O*-isopropylidene-β-D-ribofuranosyl)-5*H*-pyrrolo[3,2-*d*]pyrimidin-4(3*H*)-one (**9**) in 77% yield (Scheme II). Removal of the isopropylidene group with aqueous trifluoroacetic acid gave 2-chloro-5-β-D-ribofuranosyl-5*H*-pyrrolo[3,2-*d*]pyrimidin-4(3*H*)-one (**10**) in 86% yield. Dehalogenation of **10** using palladium on carbon in a hydrogen atmosphere furnished the 7-β-D-ribofuranosyl-9-deazainosine analog, 5-β-D-ribofuranosyl-5*H*-pyrrolo[3,2-*d*]pyrimidin-4-(3*H*)-one (**11**), while treatment of **10** with methanolic ammonia at 140° for 12 hours provided the corresponding guanosine analog, 2-amino-5-β-D-ribofuranosyl-5*H*-pyrrolo[3,2-*d*]pyrimidin-4(3*H*)-one (**12**). Compound **12** was also obtained by treatment of **9** with methanolic ammonia at 140° for 12 hours to yield 2-amino-5-(2,3-*O*-isopropylidene-β-D-ribofuranosyl)-5-*H*-pyrrolo[3,2-*d*]-pyrimidin-4(3*H*)-one (**13**) followed by deprotection of the ribose moiety with aqueous trifluoroacetic acid.

Scheme II



The α anomer in the guanosine series was prepared in three steps from the dichloro intermediate **5** in exactly the same manner as was described for the preparation of nucleoside **12** (Scheme III). Thus, treatment of **5** with boiling aqueous sodium hydroxide in dioxane provided 2-chloro-5-(2,3-*O*-isopropylidene-α-D-ribofuranosyl)-5*H*-pyrrolo[3,2-*d*]pyrimidin-4(3*H*)-one (**14**). Deprotection of **14** using aqueous trifluoroacetic acid yielded the 2-chloro-α-nucleoside, **15**, which was then treated with methanolic ammonia at 140° for 12 hours to furnish 2-amino-5-α-D-ribofuranosyl-5*H*-pyrrolo[3,2-*d*]pyrimidin-4(3*H*)-one (**16**).

Scheme III



The assignment of the site of glycosylation as *N*-5 for all nucleosides was based on examination of the ultraviolet absorption spectra in which the spectra of the final target nucleosides were compared to those of their respective heterocyclic bases [7] and to those of their respective arabinofuranosyl and 2'-deoxyribofuranosylnucleosides, whose structures have been previously established [1]. The anomeric configurations were assigned primarily on the basis of proton nmr spectra observed for the isopropylidene derivatives **9** and **14**. The chemical shift difference between the two methyl signals of the isopropylidene group has proven to be a characteristic indicator of the anomeric configuration of *N*-nucleosides [9,10]. A difference of < 0.15 ppm indicates that the nucleoside has the α configuration, while a value > 0.15 ppm is characteristic of nucleosides having the β configuration. The difference values for **9** and **14** were found to be 0.225 and 0.056 ppm, respectively, and thus each was easily assigned as β and α, respectively. Furthermore, the assignment of configuration for the precursors of **9** and **14** (**4** and **5**, respectively) as well as all the nucleosides derived from them, would be expected to have the corresponding β and α configurations, respectively.

The isopropylidene-blocked α-chlorosugar **2** appears to be a useful carbohydrate derivative for obtaining β nucleoside products in the sodium salt glycosylation procedure, particularly when applied to pyrroles and fused pyrroles in which no electron-withdrawing substituent adjacent to the pyrrole nitrogen is present, such as was demonstrated here in the 9-deazapurine ring system.

EXPERIMENTAL

Melting points were taken on a Thomas-Hoover capillary melting point apparatus or on a Haake-Buchler digital melting point apparatus and are uncorrected. Nuclear magnetic resonance (^{1}H nmr) spectra were determined at 300.1 MHz with an IBM NR300AF spectrometer. The chemical shifts are expressed in δ values (parts per million) relative to tetramethylsilane as internal standard (br = broad singlet). Ultraviolet spectra were recorded on a Beckman DU-50 spectrophotometer. Elemental analyses were preformed by Robertson Laboratory, Madison, NJ. Evaporations were carried out under reduced pressure with the bath temperature below 40°. Thin layer chromatography (tlc) was run on silica gel 60 F-254 plates (EM reagents). E. Merck silica gel (230-400 mesh) was used for flash column chromatography. The hplc purity determinations were done using a Waters 600 solvent delivery system equipped with a Waters 990 photodiode array detector and a Beckman ultrasphere 5 μm C-18 reversed phase column (4.6 x 250 mm).

2,4-Dichloro-5-[2,3-*O*-isopropylidene-5-*O*-(*t*-butyl)dimethylsilyl-β-D-ribofuranosyl]-5*H*-pyrrolo[3,2-*d*]pyrimidine (**4**) and the Corresponding α anomer **5**.

To a solution of 2,4-dichloro-5*H*-pyrrolo[3,2-*d*]pyrimidine (**3**, 3.8 g, 20 mmoles) [1,7] in dry acetonitrile (250 ml) was added sodium hydride (0.88 g, 22 mmoles, 60% in oil) and the mixture was stirred at room temperature for 30 minutes. 1-Chloro-2,3-*O*-isopropylidene-5-(*t*-butyl)dimethylsilyl-α-D-ribofuranose (**2**, 22 mmoles, prepared from the corresponding 1-hydroxy derivative by the procedure of Wilcox and Otoski [6]) in dry tetrahydrofuran (50 ml) was added to the mixture in one lot and the whole was stirred at room temperature for 24 hours. The mixture was then filtered through a celite pad and the filtrate was evaporated to dryness to yield an oily residue which was purified by flash silica gel column chromatography using toluene-ethyl acetate (9:1, v/v). The β anomer eluted from the column first to provide 6.0 g (63%) of **4** as a colorless foam; ^{1}H mnr (dimethyl sulfoxide-d_6): δ 8.36 (d, J = 3.43 Hz, 1H, C_6H), 6.87 (d, J = 3.43 Hz, 1H, C_7H), 6.69 (d, J = 1.89 Hz, 1H, $C_{1'}H$), 1.54 and 1.33 (2s, 3H each, methyls of isopropylidene).

Anal. Calcd. for $C_{20}H_{29}Cl_2N_3O_4Si$: C, 50.63; H, 6.16; Cl, 14.94; N, 8.86. Found: C, 50.88; H, 6.25; Cl, 14.80; N, 8.55.

The α anomer eluted next from the column to provide 1.3 g (13%) of **5** as a colorless foam. ^{1}H nmr (dimethylsulfoxide-d_6) δ 8.19 (d, J = 3.46 Hz, 1H, C_6H), 6.80 (d, J = 3.46 Hz, 2H, C_7H and $C_{1'}H$).

Anal. Calcd. for $C_{20}H_{29}Cl_2N_3O_4Si$: C, 50.63; H, 6.16; Cl, 14.94; N, 8.86. Found: 50.91; H, 6.26; Cl, 14.60; N, 8.49.

4-Amino-2-chloro-5-[2,3-*O*-isopropylidene-5-*O*-(*t*-butyl)dimethylsilyl-β-D-ribofuranosyl]-5*H*-pyrrolo[3,2-*d*]pyrimidine (**6**).

A solution of **4** (4.6 g, 10 mmoles) in methanolic ammonia (75 ml, saturated at 0°) was heated in a steel reaction vessel at 110° for 12 hours. After cooling, the ammonia was allowed to evaporate and the solid which formed was collected by filtration and recrystallized from ethanol to give 3.4 g (81%) of **6**, mp 179-180°; ^{1}H nmr (dimethyl sulfoxide-d_6): δ 7.83 (d, J = 3.23 Hz, 1H, C_6H), 7.11 (s, 2H, NH_2, exchangeable), 6.42 (d, J = 3.23 Hz, 1H, C_7H), 6.24 (d, J = 2.48 Hz, 1H, $C_{1'}H$).

Anal. Calcd. for $C_{20}H_{31}ClN_4O_4Si$: C, 52.79; H, 6.87; Cl, 7.79; N, 12.31. Found: C, 52.74; H, 6.92; Cl, 8.00; N, 12.33.

4-Amino-2-chloro-5-β-D-ribofuranosyl-5*H*-pyrrolo[3,2-*d*]pyrimidine (**7**).

A solution of **6** (2.1 g, 5 mmoles) in 80% aqueous trifluoroacetic acid (50 ml) was stirred at room temperature for 3 hours. The reaction mixture was evaporated to dryness under reduced pressure and the residue was co-evaporated with methanol (3 x 25 ml). The resulting solid was crystallized from acetone to give 1.4 g (93%) of **7**, mp 213-214°; ^{1}H nmr (dimethyl sulfoxide-d_6): δ 7.80 (d, J = 3.20 Hz, 1H, C_6H), 7.18 (s, 2H, NH_2, exchangeable), 6.38 (d, J = 3.20 Hz, 1H, C_7H), 5.74 (d, J = 5.75 Hz, 1H, $C_{1'}H$).

Anal. Calcd. for $C_{11}H_{13}ClN_4O_4$: C, 43.94; H, 4.36; Cl, 11.79; N, 18.63. Found: C, 43.95; N, 4.44; Cl, 11.58; N, 18.47.

4-Amino-5-β-D-ribofuranosyl-5*H*-pyrrolo[3,2-*d*]pyrimidine Hydrochloride (**8**).

A mixture containing **7** (0.9 g, 3.0 mmoles) and palladium on carbon (0.25 g, 5%) was hydrogenated at 20 psi for 6 hours at room temperature. The mixture was filtered through a celite pad and the filtrate was evaporated to dryness *in vacuo* and then co-evaporated once with ethanol (25 ml). The solid residue was crystallized from ethanol to furnish 0.65 g (72%) of **8** as colorless crystals, mp 213-214°; ^{1}H nmr (dimethyl sulfoxide-d_6): δ 14.85 (br, 1H, HCl), 8.59 (s, 1H, C_2H), 8.55 (s, 2H, NH_2), exchangeable), 8.13 (d, J = 3.38 Hz, 1H, C_6H), 6.64 (d, J = 3.38 Hz, 1H, C_7H), 5.95 (d, J = 6.02 Hz, 1H, $C_{1'}H$).

Anal. Calcd. for $C_{11}H_{14}N_4O_4 \cdot HCl \cdot \frac{1}{4}H_2O$: C, 43.01; H, 5.09; N, 18.24; Cl, 11.54. Found: C, 42.88; H, 5.09; N, 17.93; Cl, 11.20.

2-Chloro-5-(2,3-*O*-isopropylidene-β-D-ribofuranosyl)-5*H*-pyrrolo-[3,2-*d*]pyrimidin-4(3*H*)-one (**9**).

A solution of **4** (4.66 g, 10 mmoles) in dioxane (75 ml) was added dropwise over 20 minutes to boiling aqueous sodium hydroxide (75 ml, 2*N*). After addition, the mixture was refluxed an additional 60 minutes and then cooled and neutralized by passing through a column of Dowex-50 H^+ form resin. The eluent was evaporated to dryness and the residue was purified by flash silica gel column chromatography using dichloromethane-methanol (10:1, v/v) to give 2.6 g (77%) of **9**, mp 192-193°; ^{1}H nmr (dimethyl sulfoxide-d_6); δ 13.00 (br, 1H, NH, exchangeable), 7.81 (d, J = 3.10 Hz, 1H, C_6H), 6.61 (d, J = 3.39 Hz, 1H, $C_{1'}H$), 6.46 (d, J = 3.10 Hz, 1H, C_7H), 1.52 and 1.30 (2s, 3H each, methyls of isopropylidene).

Anal. Calcd. for $C_{14}H_{16}ClN_3O_5$: C, 49.20; H, 4.72; Cl, 10.37; N, 12.30. Found: C, 49.20; H, 4.71; Cl, 10.27; N, 12.03.

2-Chloro-5-β-D-ribofuranosyl-5*H*-pyrrolo[3,2-*d*]pyrimidin-4(3*H*)-one (**10**).

Compound **9** (1.7 g, 5 mmoles) was treated for 1 hour with aqueous trifluoroacetic acid as described for the preparation of **7**. The solid obtained was crystallized from ethanol to give 1.3 g (86%) of **10**, mp 239-239.5°; ^{1}H nmr (dimethyl sulfoxide-d_6): δ 13.00 (s, 1H, NH, exchangeable), 7.86 (d, J = 3.10 Hz, 1H, C_6H), 6.47 (d, J = 5.55 Hz, 1H, $C_{1'}H$), 6.44 (d, J = 3.10 Hz, 1H, C_7H).

Anal. Calcd. for $C_{11}H_{12}ClN_3O_5$: C, 43.79; H, 4.01; Cl, 11.75; N, 13.93. Found: C, 43.94; H, 4.13; Cl, 11.70; N, 13.82.

5-β-D-Ribofuranosyl-5*H*-pyrrolo[3,2-*d*]pyrimidin-4(3*H*)-one (**11**).

A solution of **10** (0.6 g, 2 mmoles) in aqueous ethanol (50%, 75 ml) was hydrogenated as described for the preparation of **8**. The solid residue obtained was crystallized from ethanol to give 0.42 g (80%), mp 165-166°; ^{1}H nmr (dimethyl sulfoxide-d_6): δ 8.62 (s, 1H, C_2H), 8.01 (d, J = 3.20 Hz, 1H, C_6H), 6.57 (d, J = 3.20 Hz, 1H, C_7H), 6.48 (d, J = 5.36 Hz, 1H, $C_{1'}H$).

Anal. Calcd. for $C_{11}H_{13}N_3O_5 \cdot 1.5H_2O$: C, 44.90; H, 5.48; N, 14.28. Found: C, 44.83; H, 4.95; N, 14.18.

2-Amino-5-(2,3-*O*-isopropylidene-β-D-ribofuranosyl)-5*H*-pyrrolo-[3,2-*d*]pyrimidin-4(3*H*)-one (**13**).

Reaction of **9** (1.7 g, 5 mmoles) in methanolic ammonia (50 ml, saturated at 0°) in a steel reaction vessel at 140° for 12 hours furnished a residue after evaporation which was crystallized from ethanol to give 1.4 g (86%) of **13**, mp 174-175°; ^{1}H nmr (dimethyl sulfoxide-d_6): δ 10.65 (br, 1H, NH, exchangeable), 7.52 (d, J = 3.10 Hz, 1H, C_6H), 6.46 (d, J = 3.63 Hz, 1H, $C_{1'}H$), 6.04 (d, J = 3.10 Hz, 1H, C_7N), 5.94 (s, 2H, NH_2, exchangeable).

Anal. Calcd. for $C_{14}H_{18}N_4O_5$: C, 52.17; H, 5.63; N, 17.38. Found: C, 52.21; H, 5.65; N, 17.03.

2-Amino-5-β-D-ribofuranosyl-5*H*-pyrrolo[3,2-*d*]pyrimidin-4(3*H*)-one (**12**).

From **10**.

A solution of **10** (0.6 g, 2 mmoles) in methanolic ammonia (25 ml, saturated at 0°) was treated as described above for **13**. The resulting solid residue after evaporation was crystallized from ethanol to yield 0.42 g (75%), mp 194-196; ^{1}H nmr (dimethyl sulfoxide-d_6): δ 10.65 (s, 1H, NH, exchangeable), 7.55 (d, J = 2.96 Hz, 1H, C_6H), 6.33 (d, J = 5.55 Hz, 1H, $C_{1'}H$), 6.02 (d, J = 2.96 Hz, 1H, C_7H), 5.92 (s, 2H, NH_2), exchangeable).

Anal. Calcd. for $C_{11}H_{14}N_4O_5 \cdot H_2O$: C, 44.00; H, 5.37; N, 18.66. Found: C, 43.86; H, 4.94; N, 18.04.

From **13**.

An aqueous trifluoroacetic acid solution of **13** (0.65 g, 2 mmoles in 20 ml of 80%) was stirred at room temperature for 1 hour and then worked up as described for the preparation of **7**. The residue was crystallized from ethanol to provide 0.4 g (72%) of **12**. All physicochemical characteristics of the sample prepared by this route were found to be identical to those of the sample prepared from **10**, including mp, mixed mp, and nmr.

2-Chloro-5-(2,3-*O*-isopropylidene-α-D-ribofuranosyl)-5*H*-pyrrolo-[3,2-*d*]pyrimidin-4(3*H*)-one (**14**).

A solution of **5** (2.33 g, 5 mmoles) in dioxane (40 ml) was added dropwise over 15 minutes to a refluxing aqueous sodium hydroxide solution (40 ml, 2*N*) and the mixture was heated at reflux for 2 hours. The solution was then cooled and the *p*H was adjusted to **6** with glacial acetic acid and then evaporated to dryness *in vacuo*. The residual solid was purified by silica gel flash column chromatography using dichloromethane-methanol (10:1, v/v) as eluent to give 1.3 g (75%) of **14**, mp 106-108°; ^{1}H nmr (dimethyl sulfoxide-d_6): δ 12.90 (br, 1H, NH, exchangeable), 7.53 (d, J = 3.08 Hz, 1H, C_6H), 6.81 (d, J = 3.53 Hz, 1H, $C_{1'}H$), 6.37 (d, J = 3.08 Hz, 1H, C_7H), 1.20 and 1.17 (2s, 3H each, methyls of isopropylidene).

Anal. Calcd. for $C_{14}H_{16}ClN_3O_5$: C, 49.20; H, 4.72; Cl, 10.37; N, 12.30. Found: C, 49.13; H, 4.82; Cl, 10.47; N, 12.02.

2-Chloro-5-α-D-ribofuranosyl-5*H*-pyrrolo[3,2-*d*]pyrimidin-4(3*H*)-one (**15**).

Compound **14** (1.7 g, 5 mmoles) was treated with aqueous trifluoroacetic acid (50 ml) exactly as described for the preparation

of **9**. The solid obtained was crystallized from ethanol to provide 1.2 g (77%) of **15**, mp 182-183°; ^{1}H nmr (dimethyl sulfoxide-d_6): δ 12.95 (br, 1H, NH, exchangeable), 7.71 (d, J = 3.0 Hz, 1H, C_6H), 6.79 (d, J = 4.77 Hz, 1H, $C_{1'}H$), 6.34 (d, J = 3.0 Hz, 1H, C_7H).

Anal. Calcd. for $C_{11}H_{12}ClN_3O_5$: C, 43.79; H, 4.01; Cl, 11.75; N, 13.93. Found: C, 43.77; H, 4.05; Cl, 12.02; N, 13.73.

2-Amino-5-α-D-ribofuranosyl-5*H*-pyrrolo[3,2-*d*]pyrimidin-4(3*H*)-one (**16**).

Nucleoside **15** (0.6 g, 2 mmoles) was treated with methanolic ammonia (25 ml) exactly as described for the preparation of **12**. The residual solid obtained was purified by flash silica gel column chromatography using dichloromethane-methanol (9:1, v/v) to give 0.41 g (74%) of **16**, mp 200-202°; ^{1}H nmr (dimethyl sulfoxide-d_6): δ 13.00 (br, 1H, NH, exchangeable), 7.71 (d, J = 3.10 Hz, 1H, C_6H), 6.78 (d, J = 4.75, 1H, $C_{1'}H$), 6.35 (d, J = 3.10 Hz, 1H, C_7H), 5.21 (s, 2H, NH_2, exchangeable).

Anal. Calcd. for $C_{11}H_{14}N_4O_5$: C, 46.81; H, 5.00; N, 19.85. Found: C, 46.77; H, 4.84; N, 19.72.

REFERENCES AND NOTES

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[1] N. S. Girgis, H. B. Cottam, S. B. Larson and R. K. Robins, *J. Heterocyclic Chem.*, **24**, 821 (1987).

[2] K. Ramasamy, R. K. Robins and G. R. Revankar, *J. Heterocyclic Chem.*, **24**, 863 (1987).

[3] F. Seela, U. Lüpke and D. Hasselman, *Chem. Ber.*, **113**, 2808 (1980).

[4] Z. Kazimierczuk, G. R. Revankar and R. K. Robins, *Nucleic Acids Res.*, **12**, 1179 (1984).

[5] J. D. Anderson, R. J. Bontems, S. Geary, H. B. Cottam, S. B. Larson, S. S. Matsumoto, D. F. Smee and R. K. Robins, *Nucleosides Nucleotides*, **8**, 1201 (1989).

[6] C. S. Wilcox and R. M. Otoski, *Tetrahedron Letters*, **27**, 1011 (1986).

[7] K. Imai, *Chem. Pharm. Bull.*, **12**, 1030 (1964).

[8] H. Rosemeyer and F. Seela, *Helv. Chim. Acta*, **71**, 1573 (1988).

[9] B. Rayner, C. Tapiero and J-L. Imbach, *J. Heterocyclic Chem.*, **10**, 417 (1973).

[10] J-L. Imbach, J. L. Barascut, B. L. Kam and C. Tapiero, *Tetrahedron Letters*, 129 (1974).