Synthesis and Transformations of Certain Pyridazine Cyclonucleosides

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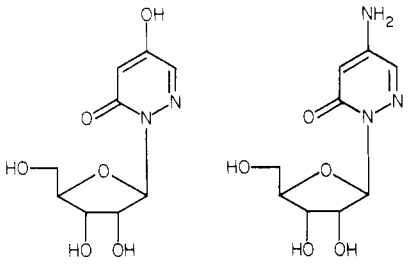
Reaction of 4-hydroxy-1-β-D-ribofuranosylpyridazin-6(1*H*)-one (**1**) with acetyl bromide has afforded the cyclonucleoside 6,2′-anhydro-6-hydroxy-1-(3,5-di-*O*-acetyl-β-D-arabinofuranosyl)pyridazin-4(1*H*)-one (**3**). Removal of the acetyl blocking groups from **3** furnished 6,2′-anhydro-6-hydroxy-1-β-D-arabinofuranosylpyridazin-4(1*H*)-one (**5**). Basic hydrolysis of the ether linkage in **5** afforded 4-hydroxy-1-β-D-arabinofuranosylpyridazin-6(1*H*)-one (**6**). Treatment of **3** with liquid ammonia furnished 6-amino-1-β-D-arabinofuranosylpyridazin-4(1*H*)-one (**4**). The nucleoside **1** was transformed into 6,5′-anhydro-6-hydroxy-1-β-D-ribofuranosylpyridazin-4(1*H*)-one (**11**) via a 4,5′-di-*O*-tosyl derivative. 4-Amino-1-β-D-ribofuranosylpyridazin-6(1*H*)-one (**2**) was reacted with α-acetoxyisobutyryl chloride to give 6,2′-anhydro-6-hydroxy-4-imino-1-β-D-arabinofuranosylpyridazine hydrochloride (**14**) which was converted into 4-amino-1-β-D-arabinofuranosylpyridazin-6(1*H*)-one (**15**). Opening of the anhydro linkage of **14** with azide yielded 4-amino-1-(2-azido-2-deoxy-β-D-ribofuranosyl)pyridazin-6(1*H*)-one (**16**), while reaction with benzyl mercaptide furnished 4-amino-1-(2-benzylthio-2-deoxy-β-D-ribofuranosyl)pyridazin-6(1*H*)-one (**17**). Desulfurization of **17** afforded 4-amino-1-(2-deoxy-β-D-*erythro*-pentofuranosyl)pyridazin-6(1*H*)-one.

Cyclonucleosides have served both as useful synthetic intermediates[1-3] for the introduction of a variety of functionalities into the heterocyclic and carbohydrate moieties of nucleosides and as chemotherapeutic prodrugs, i.e., cyclocytidine.[3] Previous studies from this laboratory[4,5] have provided synthetic routes to the pyrimidine nucleoside congeners 4-hydroxy-1-β-D-ribofuranosylpyridazin-6-(1*H*)-one (**1**, 6-aza-3-deazauridine, and 4-amino-1-β-D-ribofuranosylpyridazin-6(1*H*)-one (**2**, 6-aza-3-deazacytidine). We should now like to report our results on

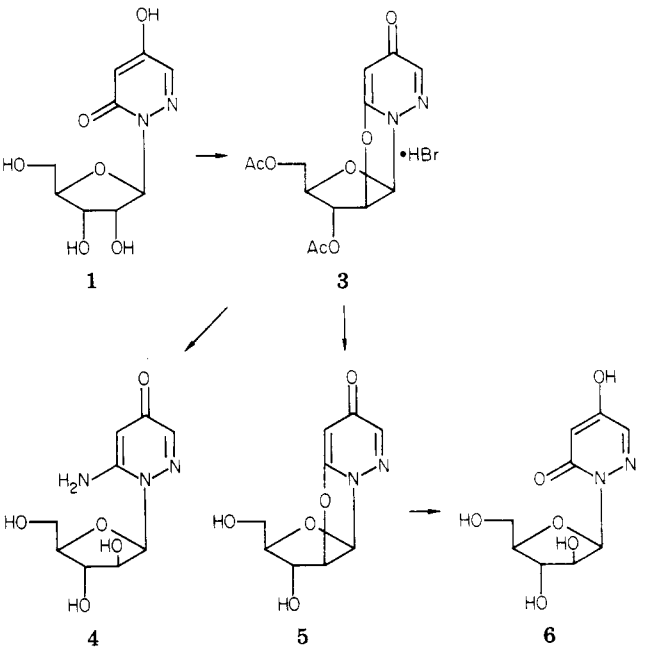


1 **2**

investigations concerning the conversion of **1** and **2** into cyclonucleosides as well as the subsequent chemical transformations of these nucleosides.

Uridine[6,7] and 6-azauridine[8] upon treatment with acetyl bromide in acetonitrile at reflux are readily converted into 2′-bromo-2′-deoxy-3′,5′-di-*O*-acetyl derivatives; through a subsequent dehalogenation of the 2′-bromo moiety, provides a high yield method for the synthesis of their respective 2′-deoxynucleosides. Since we were interested in the synthesis of the 2′-deoxypyridazine congeners of uridine and cytidine, **1** was reacted with acetyl bromide in acetonitrile and a single nucleoside product **3** was isolated. It was not, however, the expected 2′-bromo-2′-deoxy derivative. The elemental analysis of the compound was consistent with its identification as a 2′-bromo-2′-deoxy derivative of **1**, but the ultraviolet spectrum of the compound did not exhibit the expected bathochromic shift under basic conditions relative to its spectrum at pH 1, as was observed for the compounds of type **1**. In the ^1H NMR spectrum of **3**, the resonance signals of the carbohydrate moiety were remarkably similar to several reported[8] 2,2′-anhydropyrimidine nucleosides.[9] In particular, the large coupling constant between the 1′ and 2′

Scheme I



1 **3** **4** **5** **6**

protons, the relatively small coupling constant between the 2′ and 3′ protons, and the downfield chemical shift of the $H_{1'}$ proton from that in **1** support the rigid tricyclic 6,2′-anhydro-6-hydroxy-1-(3,5-di-*O*-acetyl-β-D-arabinofuranosyl)pyridazin-4(1*H*)-one structure rather than the expected 2′-bromo-2′-deoxynucleoside. This assignment was further supported by subsequent chemical transformations. The formation of a cyclonucleoside must result from the formation of an O_2–$O_{3'}$ acetoxonium intermediate

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(1) Dekker, C. A.; Goodman L. In "The Carbohydrates: Chemistry and Biochemistry"; Pigman, W.; Horton, D., Eds.; Academic Press: New York, 1970; Vol. IIA, p 28.
(2) Goodman, L. In "Basic Principles in Nucleic Acid Chemistry"; P. O. Ts'O, Ed.; Academic Press: New York, 1974; Vol. 1, p 170.
(3) Fox, J. J. *Pure Appl. Chem.* **1969**, *18*, 223.
(4) Katz, J. D.; Wise, D. S.; Townsend, L. B. *J. Heterocycl. Chem.* **1975**, *12*, 609.
(5) Katz, J. D.; Wise, D. S.; Townsend, L. B. *J. Med. Chem.*, **1982**, *25*, 813.
(6) Marumoto, R.; Honjo, M. *Chem. Pharm. Bull.* **1974**, *22*, 128.
(7) Ozaki, S.; Katakami, T.; Saneyoshi, M. *Bull. Chem. Soc. Jpn.* **1977**, *50*, 2197.
(8) Drasar, P.; Hein, L.; Beranek, J. *Collect. Czech. Chem. Commun.* **1976**, *41*, 2110.
(9) Russel, A. F.; Prystasz, M.; Hamamura, E. K.; Verheyden, J. P. H.; Moffatt, J. G. *J. Org. Chem.* **1974**, *39*, 2182.

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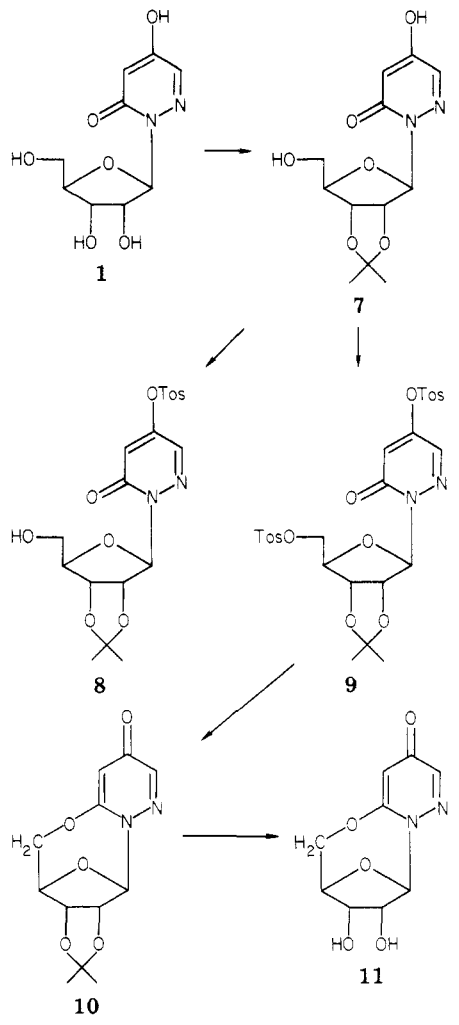
followed by participation of the 6-oxo function of the pyridazin-6-one system, even though in previous examples[5-7] the cyclonucleosides were only proposed intermediates in the formation of 2′-bromo-2′-deoxynucleosides by action with acetyl bromide. The cyclonucleoside in the pyridazine series appears to be somewhat more stable and is easily isolated as the bromide salt. The deblocked anhydronucleoside, per se, was obtained by removal of the 3′- and 5′-*O*-acetyl groups from **3** by treatment with a dilute solution of methanolic hydrogen chloride, furnishing 6,2′-anhydro-6-hydroxy-1-β-arabinofuranosylpyridazin-4-(1*H*)-one (**5**) in 89% yield (see Scheme I). The deblocked anhydronucleoside **5** exhibited the same ultraviolet spectrum as **3**, and in the ^{1}H NMR spectrum of **5** the relative values of the coupling constants between protons of the carbohydrate moiety were unchanged when compared to those of **3**, indicating that the rigid tricyclic ring system had been preserved. Cleavage of the 6,2′-anhydro linkage by basic hydrolysis of **5**, gave 4-hydroxy-1-β-D-arabinofuranosylpyridazin-6(1*H*)-one (**6**) in 81% yield. The identity of the carbohydrate in **6**, as D-arabinose was confirmed by acid hydrolysis of the nucleoside and comparison of the cleaved carbohydrate with authentic D-arabinose. ^{1}H NMR spectral data ($J_{1',2'}$ = 6 Hz) also supported the assignment of the D-arabinofuranose sugar.

When **3**, was treated with liquid ammonia at 110 °C for 34 h, a single nucleoside, **4**, was isolated in 62% yield. The ultraviolet spectrum of this compound was clearly different from the spectra of nucleosides **1** and **3**. In particular, the presence of a phenolic hydroxyl proton was not indicated by a bathochromic shift of the ultraviolet absorbance maximum under basic conditions. The elemental analysis and ^{1}H NMR spectral data for this nucleoside suggested the presence of an aromatic amino function, but the ultraviolet spectrum was different from that reported[4] for the cytidine analogue **2**. Acid hydrolysis of **4** yielded D-arabinose, indicating that D-arabinofuranose was the carbohydrate moiety of the nucleoside. This assignment of arabinofuranose to the carbohydrate was further supported by ^{1}H NMR spectral data. The coupling constant for the anomeric proton ($J_{1',2'}$ = 6 Hz) of **4** was larger than the $H_{1'}$ to $H_{2'}$ coupling constant in **1** ($J_{1',2'}$ = 3.5 Hz) or **2** ($J_{1',2'}$ = 4 Hz). This change in the coupling constant of the anomeric proton indicated a substantial change in the dihedral angle between the 1′ and 2′ protons, a change consistent with epimerization at $C_{2'}$. Therefore, it was concluded that the reaction of **3** with liquid ammonia had proceeded through nucleophilic attack on the heterocyclic ring at carbon 6 to give 6-amino-1-β-D-arabinofuranosylpyridazin-4(1*H*)-one (**4**). Similar transformations of anhydronucleosides have been previously reported in the pyrimidine[10] and 6-azapyrimidine[11] series.

An investigation was also designed to afford a 6,5′-anhydronucleoside in this series. Since sulfonate esters have been widely used as intermediates in the synthesis of anhydronucleosides,[3] a similar route was undertaken for the transformation of **1** into the desired 6,5′-anhydronucleoside. It was anticipated that the introduction of a sulfonate ester function at the $C_{5'}$ position could be followed by a base-catalyzed intramolecular cyclization to yield the desired cyclonucleoside.

The nucleoside **1** was converted to a 2′,3′-*O*-isopropylidene derivative (**7**) by using standard procedures. When **7** was treated with 1 equiv of *p*-toluenesulfonyl chloride in pyridine, a single product (**8**) was isolated in

Scheme II[a]

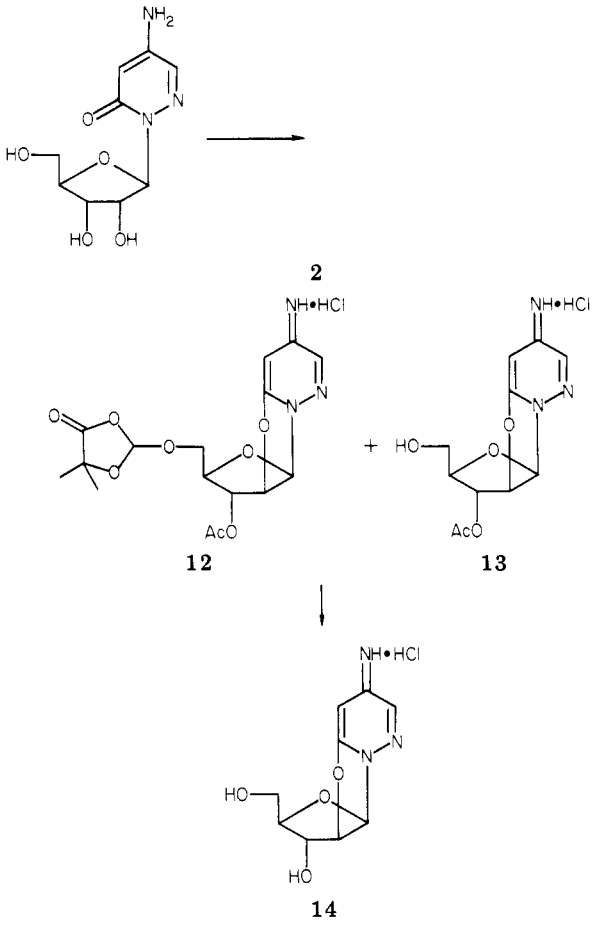


[a] Tos = *p*-toluenesulfonyl.

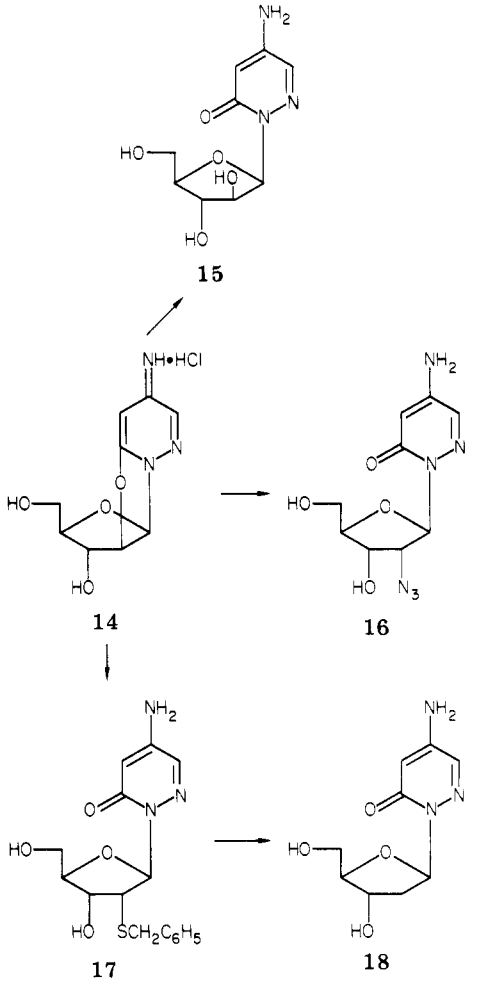
76% yield. The elemental analysis and ^{1}H NMR spectral data established the presence of one *p*-toluenesulfonate group in the molecule. However, the methylene group at the 5′ position of the ribosyl moiety did not exhibit a downfield chemical shift relative to the same protons in **7**, which would be expected if esterification at the 5′ position had taken place. The ^{1}H NMR resonance signal for H_5 of the pyridazine ring, however, exhibited a 0.32 ppm downfield chemical shift relative to the same proton in nucleoside **7**, thus establishing that esterification had taken place at the phenolic hydroxyl of the heterocyclic moiety rather than at the 5′-hydroxy group of the sugar moiety to furnish 4-*O*-*p*-toluenesulfonyl-1-(2,3-*O*-isopropylidene-β-D-ribofuranosyl)pyridazin-6(1*H*)-one (**8**). That tosylation had occurred at O_4, rather than at O_6, was established by the lack of a significant upfield chemical shift for the anomeric proton of **8** when compared to the chemical shift of the anomeric proton of **7**. An upfield chemical shift of the anomeric proton would be expected if tosylation had taken place at O_6.[12] Treatment of **7** with 2 or more equiv of *p*-toluenesulfonyl chloride resulted in esterification at both the phenolic group of the heterocyclic system and the 5-hydroxyl group of the carbohydrate moiety to yield 4,5′-di-*O*-*p*-toluenesulfonyl-1-(2,3-*O*-isopropylidene-β-D-ribofuranosyl)pyridazin-6(1*H*)-one (**9**) (see Scheme II). The structure was confirmed by elemental

(10) Doerr, I. L.; Fox, J. J. *J. Am. Chem. Soc.* **1967**, *89*, 1760.
(11) Beranek, J.; Sorm, F. *Collect. Czech. Chem. Commun.* **1968**, *33*, 913.
(12) Long, R. A.; Townsend, L. B. *J. Chem. Soc., Chem. Commun.* **1970**, 1087.

Scheme III



Scheme IV



analysis and the observation in the ^1H NMR of the expected downfield chemical shift ($\Delta\delta$ = 0.3 ppm) of the 5′-methylene protons relative to the same protons in **7** and **8**. Treatment of **9** with 2 equiv of base in aqueous acetonitrile effected an intramolecular cyclization and saponification of the 4-*O*-toluenesulfonyl group to afford 6,5′-anhydro-6-hydroxy-1-(2,3-*O*-isopropylidene-β-D-ribofuranosyl)pyridazin-4(1*H*)-one (**10**) in 66% yield. Interestingly, the ^1H NMR spectrum for **10** was almost identical with regard to the carbohydrate moiety with those reported for the corresponding derivatives of uridine[13,14] and 6-azauridine.[14] In particular, the large geminal coupling between the $C_{5'}$ methylene protons ($J_{5a',5b'}$ = 13 Hz) provides strong evidence for the rigid 6,5′-anhydro structure. The isopropylidene group was removed from **10**, with methanolic trifluoroacetic acid to give 6,5′-anhydro-6-hydroxy-1-β-D-ribofuranosylpyridazin-4(1*H*)-one (**11**) in 55% yield. The intensity of the ultraviolet absorbance of **11** and the difference between the ultraviolet spectral data for **11** and **5** are consistent with similar observations in several examples of pyrimidine[15,16] and 6-azapyrimidine[14,17] cyclonucleosides.

The reactions of nucleosides with α-(acyloxy)isobutyryl chlorides have been investigated extensively[9,18-22] as potential synthetic routes to both deoxy- and anhydronucleosides. It was found that in the case of cytidine, such reactions also provided an excellent route for the production of lipophilic "depot" forms of arabinosylcytosine.[18,22] The nucleoside **2** reacted smoothly with α-acetoxyisobutyryl chloride to yield, as demonstrated by thin-layer chromatography, a mixture of the anhydronucleoside intermediates **12** and **13**. Consistent with their anhydro structures, both **12** and **13** exhibited ultraviolet spectra identical with that of the ultimate product **14**. Without isolation, the mixture of **12** and **13** was treated with methanolic hydrogen chloride to remove the acyl blocking groups and afforded 6,2′-anhydro-6-hydroxy-1-β-D-arabinofuranosylpyridazin-4-imine hydrochloride (**14**) in an 86% overall yield from **2** (see Scheme III).

The nucleoside **14** proved to be an ideal precursor for the synthesis of pyridazin-6(1*H*)-one nucleosides modified at the $C_{2'}$ position of the sugar moiety. When **14** was treated with aqueous sodium hydroxide, 4-amino-1-β-D-arabinofuranosylpyridazin-6(1*H*)-one (**15**) was isolated in 81% yield (see Scheme IV). The structure of **15**, was

(13) Manor, P. C.; Saenger, W.; Vies, D. B. D.; Jankowski, K.; Rabczenko, A. *Biochim. Biophys. Acta* **1974**, *340*, 472.
(14) Zemlicka, J.; Sorm, F. *Collect. Czech. Chem. Commun.* **1967**, *32*, 576.
(15) Brown, D. M.; Todd, A. R.; Varadarajan, S. *J. Chem. Soc.* **1956**, 2388.
(16) Brown, D. M.; Todd, A. R.; Varadarajan, S. *J. Chem. Soc.* **1957**, 868.
(17) Farkas, J.; Beranek, J.; Sorm, F. *Collect. Czech. Chem. Commun.* **1966**, *31*, 4002.
(18) Hamamura, E. K.; Prystasz, M.; Verheyden, J. P. H.; Moffatt, J. G.; Yamaguchi, K.; Uchida, N.; Sata, K.; Nomura, A.; Shiratori, O.; Takase S.; Katagiri, K. *J. Med. Chem.* **1976**, *19*, 654, 633, 667.
(19) Russell, A. F.; Greenberg, S.; Moffatt, J. G. *J. Am. Chem. Soc.*, **1973**, *95*, 4016.
(20) Jain, T. C.; Russell, A. F.; Moffatt, J. G. *J. Org. Chem.* **1973**, *38*, 3179.
(21) Jain, T. C.; Jenkins, I. D.; Russell, A. F.; Verheyden, J. P. H.; Moffatt, J. G. *J. Org. Chem.* **1974**, *39*, 30.
(22) Moffatt, J. G.; Hamamura, E. K.; Russell, A. F.; Prystasz, M.; Verheyden, J. P. H.; Yamaguchi, K.; Uchiga, N.; Sato, K.; Nishiyama, S.; Shiratori, O.; Katagiri, K. *Cancer Chemother. Rep. Part 1.* **1974**, *54*, 451.

confirmed by acid hydrolysis to yield D-arabinofuranose and the complete similarity of its ultraviolet spectrum to that of **2**. The ^{1}H NMR spectrum of **3** also exhibited a coupling constant for the anomeric proton ($J_{1',2'}$ = 6 Hz) identical with that exhibited for the arabino nucleosides **4** and **6**. Treatment of **14** with sodium azide in dimethylformamide at reflux furnished 4-amino-1-(2-azido-2-deoxy-β-D-ribofuranosyl)pyridazin-6(1*H*)-one (**16**), isolated in 84% yield. A similar transformation has been reported for the analogous uridine cyclonucleoside.[23]

Treatment of nucleoside **14** with sodium benzylmercaptide in dimethylformamide at 70 °C yielded 4-amino-1-(2-benzylthio-2-deoxy-β-D-ribofuranosyl)-pyridazin-6(1*H*)-one (**17**). The ^{1}H NMR spectrum of compound **17** exhibited an unexpectedly large (8 Hz) coupling constant between the anomeric proton and the $C_{2'}$ proton, indicating that there had been a significant change in the configuration at the $C_{2'}$ carbon. An inspection of space-filling molecular models indicated that the sulfur atom at the $C_{2'}$ position had indeed forced the sugar into an extreme $C_{2'}$ endo conformation, resulting in a dihedral angle between the $C_{1'}$ and $C_{2'}$ protons of approximately 160°. Desulfurization of **17** with Raney nickel in ethanol gave 4-amino-1-(2-deoxy-β-D-*erythro*-pentofuranosyl)pyridazin-6(1*H*)-one (**18**), identical in all respects with the 2'-deoxyriboside synthesized previously[5] by a deoxyribosylation procedure.

In this investigation, both novel and well-established methods for the synthesis of cyclonucleosides have been applied to nucleosides in the pyridazine series. The reaction of nucleoside **1** with acetyl bromide provided a clarification of the mechanism involved in the reaction of this reagent with nucleosides. The pyridazine cyclonucleosides synthesized in this study were shown to behave chemically in a manner similar to the reported reactions of other cyclonucleosides derived from pyrimidines and pyrimidine analogues.

Experimental Section

Proton nuclear magnetic resonance (^{1}H NMR) spectra were obtained with JEOL C60H, Varian A56/60, and Varian EM-390 spectrometers (solution in dimethyl-d_6 sulfoxide or chloroform-*d* with chemical shift values reported in δ units (parts per million) relative to an internal standard (sodium 2,2-dimethyl-2-silapentane-5-sulfonate or tetramethylsilane)). Ultraviolet absorption spectra (UV) were recorded on a Beckman Acta CIII spectrophotometer. Mass spectra were recorded on an LKB 9000S spectrometer, electron impact, ionizing voltage 70 eV, filament current 60 μA; direct insertion. Melting points were determined with a Thomas-Hoover capillary apparatus and are uncorrected. Preparative thin-layer chromatography was performed on glass plates coated with silica gel (1.50 mm, SilicAR 7GF, Mallinckrodt). Analytical thin-layer chromatography was performed on glass plates coated with silica gel (0.25 mm, SilicAR 7GF, Mallinckrodt). Compounds of interest were detected by either ultraviolet lamp (Mineralight, 254 nm) or treatment with sulfuric acid followed by charring. Open-bed column chromatography was carried out on SilicAR CC7 (Mallinckrodt) using gravity flow. The columns were packed as slurries with the elution solvent. All solvent proportions are given by volume. Evaporations were performed under reduced pressure (provided by a water aspirator) or in vacuo at 40 °C with a rotary evaporator unless otherwise stated. All compounds were dried in vacuo at 80 °C for 10–15 h before submission for elemental analysis. The presence of water of crystallization in the elemental analyses were verified by ^{1}H NMR.

6,2'-Anhydro-6-hydroxy-1-(3,5-di-*O*-acetyl-β-D-arabinofuranosyl)pyridazin-4(1*H*)-one (3). 4-Hydroxy-1-β-D-ribofuranosylpyridazin-6(1*H*)-one[4] (**1**; 5 g, 19.8 mmol) was suspended in 200 mL of acetonitrile. Acetyl bromide (25 mL) was added, and the reaction mixture was stirred for 2 h at room temperature. The reaction mixture was concentrated in vacuo and the resulting syrup was coevaporated with isopropyl alcohol (2 × 100 mL). Boiling ethyl acetate (100 mL) was added to the residue and the resulting mixture was allowed to cool to room temperature. The mixture was filtered to yield **3** as a white powder: yield 7.12 g (17.4 mmol, 88%); mp 194–195 °C. Recrystallization of a small sample from isopropyl alcohol furnished an analytical sample: mp 195–196 °C; UV λ_{max} nm (ε × 10^{-3}) (MeOH) 253 (9.41), 272 (9.41); (pH 1) 254 (7.48), 274 (8.38); (pH 11) 254 (7.08), 275 (8.12); ^{1}H NMR (Me_2SO-d_6) δ 7.94 (d, 1 H, H_3, $J_{3,5}$ = 2 Hz), 6.64 (d, 1 H, $H_{1'}$, $J_{1',2'}$ = 5 Hz), 6.28 (d, 1 H, H_5, $J_{5,3}$ = 2 Hz), 5.83 (d, 1 H, $H_{2'}$, $J_{2',1'}$ = 5 Hz), 5.42 (s, 1 H, $H_{3'}$), 4.70 (m, 1 H, $H_{4'}$), 4.07 (m, 2 H, $H_{5'}$ methylene protons), 2.17 (s, 3 H, acetyl protons), 1.94 (s, 3 H, acetyl protons).

Anal. Calcd for $C_{13}H_{14}N_2O_7$·HBr·H_2O (409.2): C, 38.16; H, 4.19; N, 6.85. Found: C, 37.79; H, 4.21; N, 6.55.

6-Amino-1-β-D-arabinofuranosylpyridazin-4(1*H*)-one (4). Nucleoside **3** (1 g, 2.44 mmol) was suspended in 20 mL of liquid ammonia, and the mixture was heated in a sealed stainless steel reaction vessel at 110 °C for 34 h. After the reaction mixture was cooled to room temperature, the excess ammonia was allowed to evaporate. The remaining residue was dissolved in methanol (40 mL), and the solution was then coevaporated with 2 g of silica gel. The silica gel was applied to the top of an open-bed silica gel column (4 × 15 cm) and the column was washed with 500 mL of a methanol/chloroform (3:7) mixture. The product was then eluted from the column with an additional 500 mL of the solvent mixture. The 500 mL of eluant containing the product was evaporated to dryness under reduced pressure. The remaining residue was crystallized from methanol/ethyl acetate to yield **4** as a white powder: yield 370 mg (1.52 mmol, 62%), mp 217–218 °C. Recrystallization of a small sample from methanol yielded an analytical sample: mp 220–221 °C; UV λ_{max} nm (ε × 10^{-3}) (MeOH) 278 (6.83); (pH 1) 253 (4.33), 278 sh (2.60); (pH 11) 270 (6.57); ^{1}H NMR (Me_2SO-d_6) δ 7.40 (d, 1 H, H_3, $J_{3,5}$ = 2 Hz), 6.80 (br s, 2 H, exchanges upon addition of deuterium oxide, -NH_2), 6.01 (d, 1 H, $H_{1'}$, $J_{1',2'}$ = 6 Hz), 5.49 (d, 1 H, H_5, $J_{5,3}$ = 2 Hz).

Anal. Calcd for $C_9H_{13}N_3O_5$ (243.2): C, 44.45; H, 5.39; N, 17.28. Found: C, 44.43; H, 5.37; N, 17.12.

6,2'-Anhydro-6-hydroxy-1-β-D-arabinofuranosylpyridazin-4(1*H*)-one (5). Nucleoside **3** (3 g, 7.33 mmol) was dissolved in 150 mL of methanol. Concentrated hydrochloric acid (4 mL) was added, and the solution was then stirred for 72 h at room temperature. The mixture was concentrated under reduced pressure. Boiling ethyl acetate (500 mL) was added, and the solution was allowed to stand for 48 h at 5 °C. The nucleoside **5** was collected by filtration as white microcrystals: yield 1.6 g (6.56 mmol, 89%); mp 157–159 °C; UV λ_{max} nm (ε × 10^{-3}) (MeOH) 249 sh (6.35) 254 (6.62), 274 (6.89); (pH 1) 249 sh (7.35), 254 (7.52), 268 (7.74); (pH 11) 251 sh (6.32) 273 (7.86); ^{1}H NMR (Me_2SO-d_6) δ 8.10 (d, 1 H, H_3, $J_{3,5}$ = 2 Hz), 6.56 (d, 1 H, $H_{1'}$, $J_{1',2'}$ = 5 Hz), 6.44 (d, 1 H, H_5, $J_{5,3}$ = 2 Hz), 5.50 (d, 1 H, $H_{2'}$, $J_{2',1'}$ = 5 Hz), 4.49 (s, 1 H, $H_{3'}$), 4.21 (m, 1 H, $H_{4'}$), 3.08 (m, 2 H, $H_{5'}$ methylene H's).

Anal. Calcd for $C_9H_{10}N_2O_5$·H_2O (244.2): C, 44.30; H, 4.96; N, 11.48. Found: C, 44.00; H, 5.09; N, 11.17.

4-Hydroxy-1-β-D-arabinofuranosylpyridazin-6(1*H*)-one (6). Sodium hydroxide (10 g) was dissolved in 50 mL of distilled water and the solution was cooled to room temperature. Nucleoside **5** (500 mg, 2.05 mmol) was added, and the solution was then stirred for 17 h at room temperature. The reaction mixture was cooled to 0 °C, and concentrated hydrochloric acid (25 mL) was added dropwise while the solution temperature was maintained at 0 °C. The mixture was evaporated to dryness in vacuo at room temperature. The remaining solid was then triturated with 100 mL of ethanol for 5 h at room temperature. The mixture was filtered and the precipitated salts were washed with 50 mL of ethanol. The combined filtrates were concentrated in vacuo to an oil, which was crystallized from 15 mL of ethyl acetate/methanol/cyclohexane (1:1:1, v/v/v) to yield a white powder: yield 420 mg (1.66 mmol, 81%); mp 212–214 °C. Recrystallization of a small sample from ethyl acetate yielded an analytical sample: mp 217–218 °C; UV λ_{max} nm (ε × 10^{-3}) (MeOH) 254 (4.13), 272 sh (3.80); (pH 1) 248 (4.23), 273 sh (3.34); (pH 11) 267 (6.36), 291 sh (3.80); ^{1}H NMR (Me_2SO-d_6) δ 7.72 (d, 1 H, H_3, $J_{3,5}$ = 3 Hz),

(23) Verheyden, J. P.; Wagner, E.; Moffatt, J. G. *J. Org. Chem.* **1971**, *36*, 250.

6.45 (d, 1 H, $H_{1'}$, $J_{1',2'}$ = 6 Hz), 6.00 (d, 1 H, H_5, $J_{3,5}$ = 3 Hz).

Anal. Calcd for $C_9H_{12}N_2O_6 \cdot (0.5)H_2O$ (253.2): C, 42.69; H, 5.18; N, 11.06. Found: C, 42.29; H, 4.65; N, 10.78.

4-Hydroxy-1-(2,3-*O*-isopropylidene-β-D-ribofuranosyl)-pyridazin-6(1*H*)-one (7). A mixture of acetone (300 mL) and acetone dimethyl acetal (30 mL) was cooled to 0 °C. A few drops of perchloric acid followed by the nucleoside **1** (5 g, 19.8 mmol) was added to this solution. The solution was then stirred for 17 h at room temperature and neutralized with solid sodium bicarbonate. After filtration through Celite, the filtrate was concentrated under reduced pressure to a yellow oil. The oil was dissolved in 50 mL of methanol/chloroform (1:17), and the solution was applied to an open-bed silica gel column (5 × 3 cm). The product was eluted from the column with the same solvent system, and 20-mL fractions were collected. The fractions containing product were concentrated under reduced pressure and in vacuo to afford a homogenous foam: yield 3.9 g (13.7 mmol, 69%); ^{1}H NMR (Me_2SO-d_6) δ 7.84 (d, 1 H, H_3, $J_{3,5}$ = 2.5 Hz), 6.42 (s, 1 H, $H_{1'}$), 6.14 (d, 1 H, H_5, $J_{5,3}$ = 2.5 Hz), 5.14 (d, 1 H, $H_{2'}$, $J_{2',3'}$ = 6 Hz), 4.86 (m, 1 H, $H_{3'}$), 4.06 (m, 1 H, $H_{4'}$), 3.53 (d, 2 H, $H_{5'}$ methylene H's, $J_{4',5'}$ = 7 Hz), 1.61 (s, 3 H, ketal methyl group), 1.44 (s, 3 H, ketal methyl group); ^{1}H NMR (chloroform-*d*) δ 7.71 (d, 1 H, H_3, $J_{3,5}$ = 2.5 Hz), 6.38 (d, 1 H, $H_{1'}$, $J_{1',2'}$ = 1 Hz), 6.18 (d, 1 H, H_5, $J_{5,3}$ = 2.5 Hz), 5.06 (m, 1 H, $H_{2'}$), 4.86 (m, 1 H, $H_{3'}$), 4.31 (m, 1 H, $H_{4'}$), 3.72 (m, 2 H, $H_{5'}$ methylene H's), 1.59 (s, 3 H, ketal methyl group), 1.38 (s, 3 H, ketal methyl group); mass spectra, *m/z* 285 (M^+ + H, $C_{12}H_{17}N_2O_6$), *m/z* 113 (B + 2 H).

4-((*p*-Tolylsulfonyl)oxy)-1-(2,3-*O*-isopropylidene-β-D-ribofuranosyl)pyridazin-6(1*H*)-one (8). Nucleoside **7** (1 g, 3.52 mmol) was dissolved in pyridine (100 mL). *p*-Toluenesulfonyl chloride (670 mg, 3.52 mmol) was added, and the mixture was stirred for 40 h at room temperature. The reaction mixture was diluted with 100 mL of chloroform. The chloroform solution was washed with cold 1 N hydrochloric acid (9 × 100 mL) and then 100 mL of distilled water. The chloroform layer was dried over magnesium sulfate and filtered. The filtrate was concentrated under reduced pressure to an oil, which was crystallized from 50 mL of cyclohexane to give **8** as white needles: yield 1.17 g (2.67 mmol, 76%); mp 132–133 °C; UV λ_{max} nm (ε × 10^{-3}) (MeOH) 275 (3.77), 293 (4.03); (pH 1) 275 (5.17), 288 (4.91); (pH 11) 265 (6.31), 292 sh (3.51); ^{1}H NMR (chloroform-*d*) δ 7.76 (d, 2 H, toluenesulfonyl Ar H's), 7.63 (d, 1 H, H_3, $J_{3,5}$ = 2.5 Hz), 7.34 (d, 2 H, toluenesulfonyl Ar H's, *J* = 8 Hz), 6.51 (d, 1 H, H_5, $J_{5,3}$ = 2.5 Hz), 6.33 (d, 1 H, $H_{1'}$, $J_{1',2'}$ = 1 Hz), 4.9–5.1 (m, 2 H, $H_{2'}$ + $H_{3'}$), 4.31 (m, 1 H, $H_{4'}$), 3.71 (m, 2 H, $H_{5'}$ methylene H's), 2.48 (s, 3 H, Ar-CH_3), 1.57 (s, 3 H, ketal methyl group), 1.33 (s, 3 H, ketal methyl group).

Anal. Calcd for $C_{19}H_{22}N_2O_8S$ (438.5): C, 52.05; H, 5.06; N, 6.39. Found: C, 51.85; H, 4.96; N, 6.16.

5′-*O*-(*p*-Tolylsulfonyl)-4-((*p*-tolylsulfonyl)oxy)-1-(2,3-*O*-isopropylidene-β-D-ribofuranosyl)pyridazin-6(1*H*)-one (9). Nucleoside **7** (1 g, 3.52 mmol) was dissolved in pyridine (100 mL). *p*-Toluenesulfonyl chloride (2 g, 10.5 mmol) was added, and the mixture was stirred for 40 h at room temperature. The reaction mixture was diluted with 100 mL of chloroform. The chloroform solution was washed with cold 1 N hydrochloric acid (9 × 100 mL) and then 100 mL of distilled water. The chloroform layer was dried over magnesium sulfate and filtered. The filtrate was concentrated under reduced pressure to an oil which was then crystallized from 100 mL of cyclohexane to yield **9** as white needles: yield 1.54 g (2.60 mmol, 74%); mp 110–111 °C UV λ_{max} nm (ε × 10^{-3}) (MeOH) 266 (3.44), 273 (3.56), 294 (3.26); ^{1}H NMR (chloroform-*d*) δ 7.73 (m, 4 H, toluenesulfonyl aromatic protons), 7.53 (d, 1 H, H_3, $J_{3,5}$ = 2.5 Hz), 7.31 (m, 4 H, toluenesulfonyl aromatic protons), 6.43 (d, 1 H, H_5, $J_{5,3}$ = 2.5 Hz), 6.37 (s, 1 H, $H_{1'}$), 4.96 (d, 1 H, $H_{2'}$, $J_{2',3'}$ = 6 Hz), 4.73 (m, 1 H, $H_{3'}$), 4.29 (m, 1 H, $H_{4'}$), 4.08 (d, 2 H, $H_{5'}$, methylene H's, $J_{4',5'}$ = 6 Hz), 2.46 (s, 3 H, Ar CH_3), 2.42 (s, 3 H, Ar CH_3), 1.50 (s, 3 H, ketal methyl group), 1.30 (s, 3 H, ketal methyl group).

Anal. Calcd for $C_{26}H_{28}N_2O_{10}S_2$ (592.7): C, 52.69; H, 4.76; N, 4.73. Found: C, 52.77; H, 4.66; N, 4.50.

6,5′-Anhydro-6-hydroxy-1-(2,3-*O*-isopropylidene-β-D-ribofuranosyl)pyridazin-4(1*H*)-one (10). Nucleoside **9** (2 g, 2.37 mmol) was dissolved in a mixture of acetonitrile (100 mL) and distilled water (25 mL). To this mixture was added 1 N aqueous sodium hydroxide (6.5 mL), and the solution was diluted with a mixture of distilled water (100 mL), sodium chloride saturated distilled water (100 mL), and chloroform (100 mL). The layers were separated, and the chloroform layer was saved. The remaining aqueous layer was washed with chloroform (2 × 100 mL) to remove any remaining product. The combined chloroform extracts were dried over anhydrous magnesium sulfate and filtered. The filtrate was concentrated under reduced pressure to an oil, which was dissolved in 10 mL of methanol/chloroform (1:17) and applied to an open-bed silica gel column (4.5 × 10 cm). The column was washed with 70 mL of the solvent mixture to remove unreacted starting material and with additional solvent (60 mL) to remove the product. The eluant (60 mL) containing the product was concentrated in vacuo to a homogeneous foam: yield 590 mg (2.22 mmol, 66%); ^{1}H NMR (Me_2SO-d_6) δ 7.71 (d, 1 H, H_3, $J_{3,5}$ = 2.5 Hz), 6.09 (d, 1 H, H_5, $J_{5,3}$ = 2.5 Hz), 5.79 (s, 1 H, $H_{1'}$), 5.09 (s, 2 H, $H_{2'}$ + $H_{3'}$), 4.6–4.8 (m, 2 H, $H_{4'}$ + $H_{5a'}$), 4.13 (dd, 1 H, $H_{5b'}$, $J_{4',5b'}$ = 1 Hz, $J_{5a',5b'}$ = 13 Hz); ^{1}H NMR (chloroform-*d*) δ 7.64 (d, 1 H, H_3, $J_{3,5}$ = 2.5 Hz), 6.04 (d, 1 H, H_5, $J_{5,3}$ = 2.5 Hz), 5.90 (s, 1 H, $H_{1'}$), 4.92 (m, 2 H, $H_{2'}$ + $H_{3'}$), 4.62 (s, 1 H, $H_{4'}$), 4.51 (d, $H_{5a'}$, $J_{5a',5b'}$ = 13 Hz), 4.02 (d, $H_{5b'}$, *J* = 13 Hz), 1.52 (s, 3 H, ketal methyl group), 1.34 (s, 3 H, ketal methyl group).

6,5′-Anhydro-6-hydroxy-1-β-D-ribofuranosylpyridazin-4-(1*H*)-one (11). Nucleoside **10** (610 mg, 2.29 mmol) was dissolved in a mixture of trifluoroacetic acid (30 mL) and methanol (10 mL). The solution was stirred for 15 h at room temperature. The solution was concentrated under reduced pressure and coevaporated with portions of methanol (2 × 20 mL) under reduced pressure at 50 °C. The remaining oil was dissolved in 5 mL of methanol and applied to a preparative thick layer chromatography plate (20 × 40 cm). The plate was developed with methanol/chloroform (1:9). The band having R_f = 0.6 was removed, and the silica gel was washed with 200 mL of boiling methanol and filtered. The methanol was evaporated under reduced pressure, and the resulting solid was crystallized from methanol to give **11** as white needles: yield 280 mg (1.2 mmol, 55%); mp 178–182 °C; UV λ_{max} nm (ε × 10^{-3}) (MeOH) 267 (16.4); (pH 1) 268 (15.5); (pH 11) 265.5 (14.1); ^{1}H NMR (Me_2SO-d_6) δ 7.66 (d, 1 H, H_3, $J_{3,5}$ = 2 Hz), 6.04 (d, 1 H, H_5, $J_{5,3}$ = 2 Hz), 5.66 (s, 1 H, $H_{1'}$), 4.8–5.3 (br s, 2 H, $C_{2'}$-OH + $C_{3'}$-OH), 3.9–4.7 (m, 5 H, $H_{2'}$ + $H_{3'}$ + $H_{4'}$ + $H_{5'}$ (methylene protons)).

Anal. Calcd for $C_9H_{10}N_2O_5$ (226.2): C, 47.79; H, 4.46; N, 12.38. Found: C, 47.69; H, 4.31; N, 12.57.

6,2′-Anhydro-6-hydroxy-1-β-D-arabinofuranosyl-(1*H*)-pyridazin-4-imine Hydrochloride (14). 4-Amino-1-β-D-ribofuranosylpyridazin-6(1*H*)-one (1 g, 3.97 mmol) was suspended in 20 mL of dry acetonitrile. α-Acetoxyisobutyryl chloride[18] (2 g) was added, and the mixture was stirred under anhydrous conditions for 2 days. Ethyl ether (200 mL) was added, at which time a viscous syrup separated from the solution. The ether was decanted off, and the residue dissolved in 100 mL of methanol. Concentrated hydrochloric acid (1.5 mL) was added, and the mixture was stirred for 48 h. The reaction mixture was evaporated to dryness under reduced pressure, and the residue was crystallized from methanol/ethyl acetate to give **14** as a white powder: yield 950 mg (3.41 mmol, 86%); mp 177–179 °C. Recrystallization of a small sample from ethanol furnished an analytical sample: mp 182–183 °C; UV λ_{max} nm (ε × 10^{-3}) (MeOH) 257 sh (6.77), 263 (6.94), 283 (8.53); (pH 1) 257 sh (7.36), 262 (7.64), 282 (9.40); (pH 11) 260 sh (6.21), 280 (7.86); ^{1}H NMR (Me_2SO-d_6) δ 9.20 (br s, 2 H, exchanges upon addition of deuterium oxide, =NH·HCl), 8.42 (d, 1 H, H_3, $J_{3,5}$ = 2 Hz), 6.56–6.63 (m, 2 H, H_5 + $H_{1'}$), 5.68 (d, 1 H, $H_{2'}$, $J_{2',1'}$ = 6 Hz); $[\alpha]^{26.5}$ −55.2 (*c* 1, water).

Anal. Calcd for $C_9H_{11}N_3O_4 \cdot HCl \cdot H_2O$ (279.7): C, 38.64; H, 5.04; N, 15.02. Found: C, 38.57; H, 5.05; N, 15.37.

4-Amino-1-β-D-arabinofuranosylpyridazin-6(1*H*)-one (15). Sodium hydroxide (12 g) was dissolved in distilled water (60 mL), and the solution was cooled to room temperature. Nucleoside **14** (1 g, 3.57 mmol) was added, and the solution was then stirred for 24 h at room temperature. The reaction mixture was cooled to 0 °C, and concentrated hydrochloric acid (25 mL) was added dropwise while the solution temperature was maintained at 0 °C. The mixture was evaporated to dryness at 30 °C. The remaining solid was then triturated with ethanol (200 mL) for 24 h at room temperature. The ethanol was decanted and coevaporated with 2 g of silica gel. The silica gel was applied to an open-bed silica gel column (4.5 × 8.5 cm). The column was washed with 450 mL

of methanol/chloroform (1:4, v/v) and then with 800 mL of the same solvent mixture to remove the product. The eluant (800 mL) containing the product was concentrated under reduced pressure, and the remaining residue was crystallized from ethyl acetate to furnish **15** as white needles: yield 700 mg (2.88 mmol, 81%); mp 160–161 °C; UV λ_{max} nm ($\epsilon \times 10^{-3}$): (MeOH) 277 (8.34), 303 sh (3.94); (pH 1) 274 (8.24), 302 sh (3.79); (pH 11) 275 (7.30), 300 sh (3.33); ^{1}H NMR (Me_2SO-d_6) δ 7.43 (d, 1 H, H_3, $J_{3,5}$ = 2 Hz), 6.43 (br s, 2 H, exchanges upon addition of deuterium oxide, NH_2), 6.41 (d, 1 H, $H_{1'}$, $J_{1',2'}$ = 6 Hz), 5.43 (d, 1 H, H_5, $J_{5,3}$ = 2 Hz).

Anal. Calcd for $C_9H_{13}N_3O_5$ (243.2): C, 44.45; H, 5.39; N, 17.28. Found: C, 44.63; H, 5.47; N, 17.34.

4-Amino-1-(2-azido-2-deoxy-β-D-ribofuranosyl)pyridazin-6(1*H*)-one (16). Nucleoside **14** (250 mg, 0.89 mmol) was dissolved in dimethylformamide (25 mL). Sodium azide (500 mg) was added, and the reaction mixture was heated at reflux for 1 min. The mixture was evaporated to dryness at 50 °C, and the remaining residue was triturated with ethanol (100 mL) for 12 h at room temperature. The mixture was filtered, and the separated salts were washed with 100 mL of ethanol. The combined ethanol filtrates were coevaporated with 3 g of silica gel, and the silica gel was applied to an open-bed silica gel column (4.5 × 7.5 cm). The product was eluted from the column with methanol/chloroform (1:4), and the fractions containing product were pooled and evaporated to furnish a homogeneous foam: yield 200 mg (0.75 mmol, 84%); UV λ_{max} nm ($\epsilon \times 10^{-3}$) (MeOH) 278 (10.8), 302 sh (6.54); (pH 1) 274 (7.56), 300 sh (4.32); (pH 11) 274 (7.48), 301 sh (4.34); ^{1}H NMR (Me_2SO-d_6) δ 7.74 (d, 1 H, H_3, $J_{3,5}$ = 2 Hz), 6.88 (br s, 2 H, exchanges upon addition of deuterium oxide, NH_2), 6.25 (d, 1 H, $H_{1'}$, $J_{1',2'}$ = 4 Hz), 5.97 (d, 1 H, exchanges upon addition of deuterium oxide, $C_{3'}$-OH, $J_{3',3'OH}$ = 5 Hz), 5.61 (d, 1 H, H_5, $J_{5,3}$ = 2 Hz), 4.87 (t, 1 H, exchanges upon addition of deuterium oxide, $C_{5'}$-OH $J_{5',5'OH}$ = 5 Hz), 4.33 (m, 2 H, $H_{2'}$ + $H_{3'}$), 3.84 (m, 1 H, $H_{4'}$), 3.56 (m, 2 H, $H_{5'}$ (methylene protons)).

Anal. Calcd for $C_9H_{12}N_6O_4$ (268.2): C, 40.30; H, 4.51. Found: C, 40.50; H, 4.99.

4-Amino-1-(2-benzylthio-2-deoxy-β-D-ribofuranosyl)pyridazin-6(1*H*)-one (17). Benzyl mercaptan (1 mL, 8.52 mmol) was dissolved in dimethylformamide (70 mL). Sodium metal (250 mg, 11 mmol) was added, and the mixture was stirred for 3 h at room temperature. Nucleoside **14** (1 g, 3.57 mmol) was added, and the solution was heated at 70 °C for 1 h. The reaction mixture was evaporated to dryness in vacuo at 50 °C, and the resulting residue was triturated with ethanol (125 mL) for 2 h at room temperature. The ethanol was decanted and coevaporated with 2 g of silica gel, and the silica gel was applied to an open-bed silica gel column (5 × 20 cm). The column was washed with 300 mL of methanol/chloroform (1:17) and 250 mL of methanol/chloroform (2:23). The product was then washed from the column with 500 mL of methanol/chloroform (1:9). The eluant (500 mL) containing the product was concentrated under reduced pressure to give **17** as a homogeneous foam: yield 700 mg (2.01 mmol, 56%); UV λ_{max} nm ($\epsilon \times 10^{-3}$) (MeOH) 276 (7.13), 302 sh (4.05); (pH 1) 276 (6.67), 300 sh (4.16); (pH 11) 275 (4.51), 301 sh (3.89); ^{1}H NMR (Me_2SO-d_6) δ 7.49 (d, 1 H, H_3, $J_{3,5}$ = 2 Hz), 7.23 (br s, 5 H, bzl Ar H's), 6.59 (br s, 2 H, exchanges upon addition of deuterium oxide, NH_2), 6.41 (d, 1 H, $H_{1'}$, $J_{1',2'}$ = 8 Hz), 5.53 (d, 1 H, H_5, $J_{5,3}$ = 2 Hz), 5.49 (d, 1 H, exchanges upon addition of deuterium oxide, $C_{3'}$-OH, $J_{3',3'OH}$ = 5 Hz), 4.69 (t, 1 H, exchanges upon addition of deuterium oxide, $C_{5'}$-OH, $J_{5',5'OH}$ = 5 Hz).

Anal. Calcd for $C_{16}H_{19}N_3O_4S$ (349.4): C, 55.00; H, 5.48; N, 12.03. Found: C, 55.25; H, 5.52; N, 11.85.

4-Amino-1-(2-deoxy-β-D-*erythro*-pentofuranosyl)pyridazin-6(1*H*)-one (18). Nucleoside **17** (500 mg, 1.43 mmol) was dissolved in ethanol (50 mL), and freshly washed Raney nickel (7 g) was added. The mixture was heated at reflux for 20 h, diluted with ethanol (100 mL), boiled, and filtered through a Celite pad. The Celite pad was washed with boiling ethanol (500 mL). The combined filtrates were coevaporated with 1 g of silica gel, and the silica gel was applied to an open-bed silica gel column (4.5 × 12 cm). The column was washed with 100 mL of methanol/chloroform (1:9) and then with 200 mL of methanol/chloroform (2:8) to remove the product. The 200 mL of eluant containing the product was concentrated under reduced pressure to furnish a white powder: yield 100 mg (0.44 mmol, 31%); mp 144–146 °C; UV λ_{max} nm ($\epsilon \times 10^{-3}$) (MeOH) 275 (6.22), 302 sh (3.29); (pH 1) 274 (7.04), 297 sh (4.09); (pH 11) 274 (6.54), 295 sh (4.06). ^{1}H NMR (Me_2SO-d_6) δ 7.50 (d, 1 H, H_3, $J_{3,5}$ = 3 Hz), 6.40–6.60 (m, 3 H, $H_{1'}$ + NH_2), 6.59 (t, 1 H, $H_{1'}$, $J_{1',2'}$ = 6 Hz), 5.48 (d, 1 H, H_5, $J_{5,3}$ = 3 Hz), 5.09 (d, 1 H, exchanges upon addition of deuterium oxide, $C_{3'}$-OH, $J_{3',3'OH}$ = 5 Hz), 4.64 (t, 1 H, exchanges upon addition of deuterium oxide, $C_{5'}$OH, $J_{5',5'OH}$ = 5 Hz), 4.26 (m, 1 H, $H_{3'}$), 3.69 (m, 1 H, $H_{4'}$).

Anal. Calcd for $C_9H_{13}N_3O_4$ (227.2): C, 47.62; H, 5.77; N, 18.51. Found: C, 47.30; H, 5.84; N, 18.27.

Acid Hydrolysis of Nucleosides 4, 6, and 15. General Procedure. Samples of the nucleoside (5 mg) were dissolved in 5 mL of 1 N hydrochloric acid and heated for 1 h at 90 °C. The reaction mixture was spotted on analytical thin layer chromatography plates. The plates were developed in three solvent systems: A, propan-2-ol/1% aqueous $(NH_4)_2SO_4$ (2:1); B, butan-1-ol saturated with water; C, butan-1-ol/acetic acid/water (5:2:3). The carbohydrate component of each reaction mixture was identified by its lack of ultraviolet absorbance and its charring reaction upon heating after treatment with 10% sulfuric acid spray. In the cases of all three nucleosides (**4**, **6**, and **15**) the carbohydrate component visualized in this manner showed identical mobilities with that of D-arabinose— for D-arabinose R_f^A 0.60, R_f^B 0.17, R_f^C 0.43; for D-ribose R_v^A 0.72, R_v^B 0.37, R_v^C 0.56.

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