(KBr) 5.84 μ; $[\alpha]_{365}^{\text{dioxane, 45}}$ +118°; $[\alpha]_{578}^{\text{dioxane, 45}}$ +28° (lit.[18] $[\alpha]_{589}^{\text{CHCl}_3, 25}$ +36°; lit.[24] $[\alpha]_{589}^{\text{CHCl}_3, 25}$ +32°). This material showed one spot upon tlc on silica gel using 3:2 ether–benzene.

Preparative epimerization of **2** was also accomplished by allowing a mixture of 0.083 g (2.1×10^{-4} mol) of **1**, 3.62 g (0.051 mol) of pyrrolidine, and 6.2 ml of dioxane to stand at 45°. After 60 min (*ca.* $8 \times t_{1/2}$), the optical rotation corresponded to a mixture of 89% **2** and 11% **1**. No further change in rotation was observed for 54 hr. The mixture was evaporated to dryness *in vacuo*, affording 0.077 g (89%) of yellowish solid, mp 92–103°. Three recrystallizations from methanol afforded 0.019 g (22%) of **2**, mp 115–116.5°, which had an ir spectrum identical with that of the material prepared by acid-catalyzed epimerization.

Other Materials.—All amines except quinuclidine were purchased from the Aldrich Chemical Company and were redistilled twice from barium oxide, the last time directly before use. Purity of each amine was checked by vpc once, but not routinely. Quinuclidine was prepared by reduction of 3-quinuclidone (derived from Aldrich 3-quinuclidone hydrochloride) by the Huang-Minlon procedure,[25] with a careful work-up to avoid evaporation of the product, and was purified by sublimation at aspirator pressure at 70°. The sublimed material had mp 155–158° (sealed tube) (lit.[26] mp 158°). Matheson Coleman and Bell spectroquality reagent dioxane was used as supplied from freshly opened bottles.

Kinetic Measurements.—The conversion **1** → **2** was monitored by following the change in optical rotation of solution of **1** in dioxane on a Perkin-Elmer Model 141 automatic digital readout polarimeter. Temperature was controlled by a Haake water circulating thermostating unit at 45.0°. The polarimeter cell used was 1 decimeter in length with a volume of 0.85 ml. Polarized light of 365-mμ wavelength was chosen because the difference between the rotations of **1** and **2** is greater at this wavelength than at the other, longer wavelengths available with the polarimeter.

Solutions of **1** in dioxane at 45° showed no change in rotation on standing for several hours. In many cases, mixing of amine with the dioxane solution of **1** was done at room temperature and not on materials preheated to 45°, but the mixtures were quickly inserted into the thermostated polarimeter. Good pseudo-first-order kinetic plots were obtained in all cases, for over 80% reaction in some cases. Many of the reactions were too slow to be followed conveniently to completion, and kinetic data were obtained for as little as 20% conversion.

The linear pseudo-first-order plots of log $(\alpha_t - \alpha_\infty)$ (specific rotation at time t minus specific rotation at the completion of reaction) *vs.* time were used to determine $t_{1/2}$ for the reactions, and k_2, the specific second-order rate constants (in $\text{sec}^{-1}\ M^{-1}$) were calculated by use of the expression $k_2 = k_{\text{obsd}}/[\text{amine}] = 0.693/[t_{1/2}][\text{amine}]$. In those cases where α_∞ was not observed experimentally, it was calculated using the assumption that α_∞ would correspond to 90% conversion of **1** to **2**. This method gave linear pseudo-first-order plots. As noted in the discussion, if the α_∞ at 90% conversion corresponds to the equilibrium composition of **1** and **2** under the prevailing conditions, then the k_2's derived are equal to the sum of the forward and reverse reaction rate constants.[20]

All amines except quinuclidine and triethylamine were run at several concentrations, and gave somewhat larger rate constants at higher amine concentrations as the proportion of amine in the mixture increased.

Acknowledgment.—The authors are indebted to Professor Alex Nickon for providing details of the preparation of **1**. Considerable earlier experimentation by Mr. H. A. Budd, Jr., and Mr. E. J. L. Wasserman on the epimerization of 2β-acetoxycholestan-3-one served both to demonstrate the need for a better substrate and to familiarize us with the techniques used in the optical rotation kinetics study. We are particularly grateful to Professor K. L. Williamson and his colleagues at Mount Holyoke College, who graciously allowed us unlimited access to their polarimeter and afforded patient guidance in its use. Financial support was provided by PHS Research Grant AM11815, from the National Institute of Arthritis and Metabolic Diseases.

Registry No.—**1**, 14528-10-0; **2**, 2097-78-1.

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The Chemical Synthesis of the 1,2,4-Triazole Nucleosides Related to Uridine, 2′-Deoxyuridine, Thymidine, and Cytidine[1]

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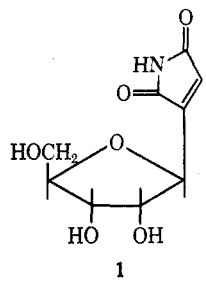
The synthesis of 1-(β-D-ribofuranosyl)urazole (**3**), 1-(2-deoxy-β-D-ribofuranosyl)urazole (**14**), and 1-(2-deoxy-β-D-ribofuranosyl)-2-methylurazole (**13**) has been accomplished *via* the trimethylsilyl derivatives of urazole and 1-methylurazole. The synthesis of the corresponding nucleoside related to cytidine, 3-amino-1-(β-D-ribofuranosyl)-1,2,4-triazolin-5-one (**26**), was accomplished in a lengthy procedure involving 3-bromo-5-nitro-1,2,4-triazole in the fusion process. Evidence in support of the site of glycosylation has been presented. The reaction mechanism involved in the various glycosylation procedures of the 1,2,4-triazole ring has been discussed.

The nucleoside antibiotic showdomycin, isolated from cultures of *Streptomyces showdoensis*,[3] has been shown by these laboratories[4] to possess structure **1**. Another antibiotic, pyrazomycin, has been shown[5] to possess the nucleoside structure **2**. It is thus quite clear that nucleoside derivatives of five-membered heterocyclic rings



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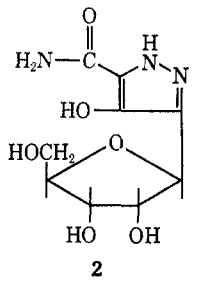

2

(1) Supported in part by a NASA Traineeship to J. T. Witkowski.
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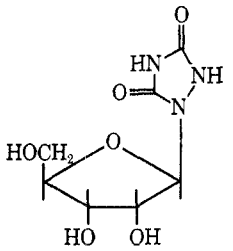
are of considerable interest as compounds of potent biological activity. The only known synthetic derivatives of this type described in the chemical literature are nucleoside derivatives of imidazoles.[6-8]

The biological activity of the antibiotic 5-azacytidine has been reviewed[9] and a new synthesis was recently reported from our laboratories.[10] Thus the insertion of an additional nitrogen atom into the pyrimidine ring in place of C_5 in the case of cytidine does indeed result in a compound with unusual biological properties.

In the present studies an –NH– has been substituted for C_5 and C_6 of the naturally occurring pyrimidine nucleosides. The fact that the five-membered ring in showdomycin results in an antibiotic which specifically inhibits uridine monophosphate kinase and uridine phosphorylase[11] is strong suggestion that these 1,2,4-triazole nucleoside analogs will resemble the natural pyrimidine nucleosides in various biochemical systems.

Another feature of compounds such as 1-(β-D-ribofuranosyl)-1,2,4-triazolidine-3,5-dione (**3**) is the fact that **3** also strongly resembles pseudouridine. Compound **3** exhibits two –NH– functions in structural similarity to pseudouridine. Pseudouridine is of current



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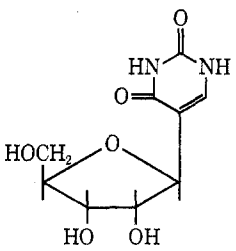
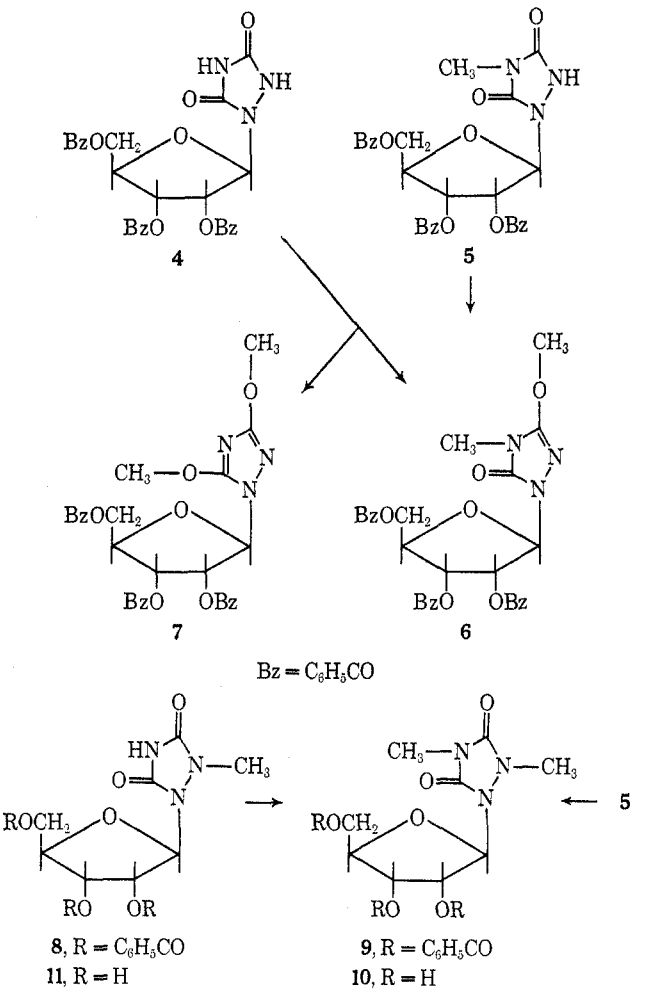


pseudouridine

interest as a minor component of various *t*-RNA's and has recently been isolated as a major product from the culture filtrates of *Streptoverticillium ladakanus*.[12]

The first goal of the presently described work was the chemical synthesis of 1-(β-D-ribofuranosyl)urazole (**3**). The trimethylsilyl derivative of urazole was prepared from urazole and hexamethyldisilazane according to the general method of Wittenburg.[13] Treatment of the trimethylsilyl derivative of urazole with 2,3,5-tri-*O*-benzoyl-D-ribofuranosyl bromide in acetonitrile at room temperature provided a single nucleoside, product **4**, in 84% yield. Elemental analysis of **4** was consistent with the structure 1-(2,3,5-tri-*O*-benzoyl-β-D-ribofuranosyl)urazole (**4**). It was possible that **4** was an N-4 ribosyl derivative or an *O*-glycoside. The assignment of the site of glycosylation in the 1,2,4-triazole ring proved to be rather difficult. Since this ring system does not exhibit an absorption maximum in the uv spectrum above 214 mμ, the typically classical procedures could not be used. The actual structure **4** was established by methylation of the blocked nucleoside **4** with diazomethane and by further comparison of the methylated product **6** with **6** prepared by an unambiguous route. For this purpose 4-methylurazole,[14] which could form only a single *N*-nucleoside, was silylated and the trimethylsilyl derivative was treated with 2,3,5-tri-*O*-benzoyl-D-ribofuranosyl bromide in acetonitrile (Scheme I). The product obtained gave correct ele-

SCHEME I



mental analysis and pmr spectrum for 4-methyl-1-(2,3,-5-tri-*O*-benzoyl-β-D-ribofuranosyl)-1,2,4-triazolidine-3,5-dione (**5**). Methylation of **5** with diazomethane provided an *O*-methyl derivative **6** as shown by elemental analysis and the pmr signal at δ 3.81, which is indicative of an *O*-methyl rather than an N-methyl group. The assignment of the signal at δ 3.81 to an *O*-methyl group is supported by comparison of the pmr spectrum of **6** with the spectra of **5** and **8**, which exhibit signals for the N-4 and N-2 methyl groups at δ 3.03 and 3.18, respectively. Since the structure of the 4-methylurazole derivative **5** was established by synthesis, the product from the methylation of **5** was 3-methoxy-4-methyl-1-(2,3,5-tri-*O*-benzoyl-β-D-ribofuranosyl-1,2,4-triazolin-5-one (**6**), which was shown to be identical with the major product from the methylation of the urazole nucleoside **4** by rigorous comparison of ir and pmr spectra and mixture melting point. A small amount of a second product **7** was isolated by column chromatography from the methylation of **4**. The pmr spectrum, which showed signals for two *O*-methyl groups at δ 3.84

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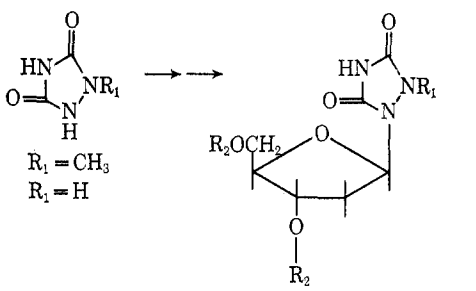
and 4.06, established this compound as 3,5-dimethoxy-1-(2,3,5-tri-*O*-benzoyl-β-D-ribofuranosyl)-1,2,4-triazole (**7**). Formation of this dimethoxy derivative conclusively demonstrated that the product **4** from the glycosylation of the trimethylsilyl derivative of urazole is not an *O*-glycoside.

The pmr spectrum of the methylated product, 3-methoxy-4-methyl-1-(2,3,5-tri-*O*-benzoyl-β-D-ribofuranosyl)-1,2,4-trizolin-5-one (**6**), exhibited a signal for the anomeric proton at δ 6.25 with a coupling constant of less than 1 Hz, which established[15] the β configuration for 1-(β-D-ribofuranosyl)urazole (**3**). Debenzoylation of **4** with methanolic ammonia provided 1-(β-D-ribofuranosyl-1,2,4-triazolidine-3,5-dione (**3**), 1-(β-D-ribofuranosyl)urazole, a structural analog of uridine.

The trimethylsilyl derivative of 1-methylurazole[16] on treatment with 2,3,5-tri-*O*-benzoyl-D-ribofuranosyl bromide in acetonitrile at room temperature provided a crystalline-blocked nucleoside in 77% yield. Elemental analysis and the pmr spectrum of the product were consistent with the structure 2-methyl-1-(2,3,5-tri-*O*-benzoyl-β-D-ribofuranosyl)urazole (**8**), but, as in the case of urazole, glycosylation at either N-1 or N-4 is possible. Methylation of **8** with methyl iodide and potassium carbonate in dimethylformamide provided **9** with two nonequivalent *N*-methyl groups as shown by the pmr spectrum. Debenzoylation of **9** with sodium methoxide in methanol afforded a crystalline compound 2,4-dimethyl-1-(β-D-ribofuranosyl)urazole (**10**). The structure of **10** was established by rigorous comparison with the same product (**10**) obtained by similar methylation of 4-methyl-1-(2,3,5-tri-*O*-benzoyl-β-D-ribofuranosyl)-1,2,4-triazolidine-3,5-dione (**5**) followed by debenzoylation with sodium methoxide in methanol. Signals for two N-methyl groups were observed in the pmr spectrum of **10** at δ 3.03 and 3.23. The nucleoside obtained by glycosylation of the trimethylsilyl derivative of 1-methylurazole is thus established as 2-methyl-1-(2,3,5-tri-*O*-benzoyl-β-D-ribofuranosyl)-1,2,4-triazolidine-3,5-dione (**8**). Debenzoylation of **8** with methanolic ammonia provided 2-methyl-1-(β-D-ribofuranosyl)-1,2,4-triazolidine-3,5-dione (**11**).

The thymidine analog **13** was obtained by fusion of the trimethylsilyl derivative of 1-methylurazole with 2-deoxy-3,5-di-*O*-*p*-toluoyl-D-*erythro*-pentosyl chloride[17] *in vacuo* at 110°. A crystalline product was obtained in 41% yield which had an elemental analysis in agreement with that required for 1-(2-deoxy-3,5-di-*O*-*p*-toluoyl-D-*erythro*-pentofuranosyl)-2-methylurazole (**12**). The blocking groups were removed from **12** with methanolic ammonia to afford a crystalline product 1-(2-deoxy-β-D-ribofuranosyl)-2-methylurazole (**13**). The pmr spectrum of **13** exhibited a pseudotriplet centered at δ 5.87 (D_2O) (one proton) with a peak width of 14.2 Hz and an apparent splitting constant of 7.1 Hz. This is in agreement with the values reported[18] for the anomeric protons of several 2′-deoxy-β-D-ribofuranosyl nucleosides (peak width of 13.0 ± 1 Hz and an apparent splitting constant of 6.5 ± 0.5 Hz) but not in agreement with the values[18] for the anomeric proton of 2′-deoxy-α-D-ribofuranosyl nucleosides (a quartet with $J_{H_{1'}}$ of 3.1 ± 0.4 Hz and 7.2 ± 0.3 Hz with a peak width of 10.4 ± 0.4 Hz). On this basis the anomeric configuration of **13** was assigned as β. The 2′-deoxyuridine analog **14** was similarly prepared from a mixture of the trimethylsilyl derivative of urazole and 2-deoxy-3,5-di-*O*-*p*-toluoyl-D-*erythro*-pentosyl chloride, which was heated *in vacuo* at 110° to give a 67% yield of the blocked nucleoside. Treatment with methanolic ammonia provided 1-(2-deoxy-β-D-ribofuranosyl)urazole or 1-(2-deoxy-β-D-*erythro*-pentofuranosyl)-1,2,4-triazolidine-3,5-dione (**14**). The pmr spectrum of **14** exhibited a poorly resolved multiplet with a peak width of 14 Hz for the anomeric proton. This peak width is consistent with the β configuration[18] for **14** and this assignment, as well as the site of glycosylation of **14**, was further confirmed by methylation of the *p*-toluoyl derivatives of **13** and **14** with methyl iodide and potassium carbonate in dimethylformamide, which in each case provided the same product, 1-(2-deoxy-3,5-di-*O*-*p*-toluoyl-β-D-*erythro*-pentofuranosyl)-2,4-dimethyl-1,2,4-triazolidine-3,5-dione.

Attempts to extend the silylation and alkylation procedure to the cytosine analog, 3-amino-1,2,4-triazolin-5-one,[19] were unsuccessful. Reaction of the trimethylsilyl derivative of 3-amino-1,2,4-triazolin-5-one with 2,3,5-tri-*O*-benzoyl-D-ribofuranosyl bromide resulted in formation of intractable products. These results appeared to be largely due to dehydrohalogenation of the blocked bromo sugar. This type of elimination reaction is often observed with nitrogen heterocycles which possess basic substituents.



12, R_2 = *p*-$CH_3C_6H_4CO$, R_1 = CH_3
13, R_2 = H, R_1 = CH_3
14, R_2 = H, R_1 = H

In an effort to study other procedures for glycosylation of the 1,2,4-triazole ring, the parent compound, 1,2,4-triazole, was employed. The trimethylsilyl derivative of 1,2,4-triazole treated in acetonitrile with 2,3,5-tri-*O*-benzoyl-D-ribofuranosyl bromide gave, after column chromatography, a 54% yield of blocked nucleoside. Deblocking with sodium methoxide gave a 90% yield of 1-(β-D-ribofuranosyl)-1,2,4-triazole (**15**). The structure of **15** was readily apparent since two singlets were observed in the pmr spectrum (δ 8.06 and 8.80). This was proof of the site of glycosylation since the pmr spectrum of the isomeric 4-(β-D-ribofuranosyl)-1,2,4-triazole[20] exhibits a singlet for the C_3 and C_5 protons due to symmetry.

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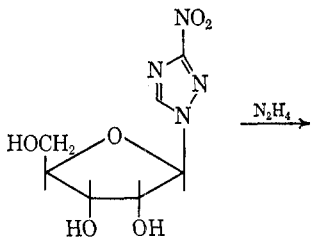
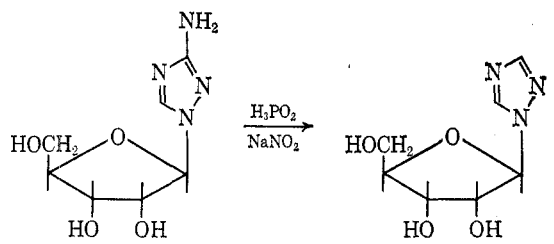
3-Nitro-1,2,4-triazole[21,22] was prepared for the present study by oxidation of 3-amino-1,2,4-triazole with pertrifluoroacetic acid.[23] 3-Nitro-1,2,4-triazole (**16**) is of interest in its own right since it may be considered an aza derivative of the antibiotic azomycin[24,25] (2-nitroimidazole). In view of the success of the fusion reaction with 2-nitroimidazole to yield 1-(β-D-ribofuranosyl)-2-nitroimidazole[7] the direct fusion of 3-nitro-1,2,4-triazole (**16**) with 1-*O*-acetyl-2,3,5-tri-*O*-benzoyl-β-D-ribofuranose was investigated. At 190° for 30 min in the absence of catalyst, an 88% yield of crystalline 3-nitro-1-(2,3,5-tri-*O*-benzoyl-β-D-ribofuranosyl)-1,2,4-triazole (**17**) was obtained. The β configuration of **17** was assigned on the basis of the coupling constant of the anomeric proton ($J_{1',2'}$ = 1.2 Hz).[15] Assignment of the site of glycosylation was next studied.

When **17** was debenzoylated with sodium methoxide in methanol and the resulting 3-nitro-1-(β-D-ribofuranosyl)-1,2,4-triazole (**18**) reduced with hydrazine,[26] an



18



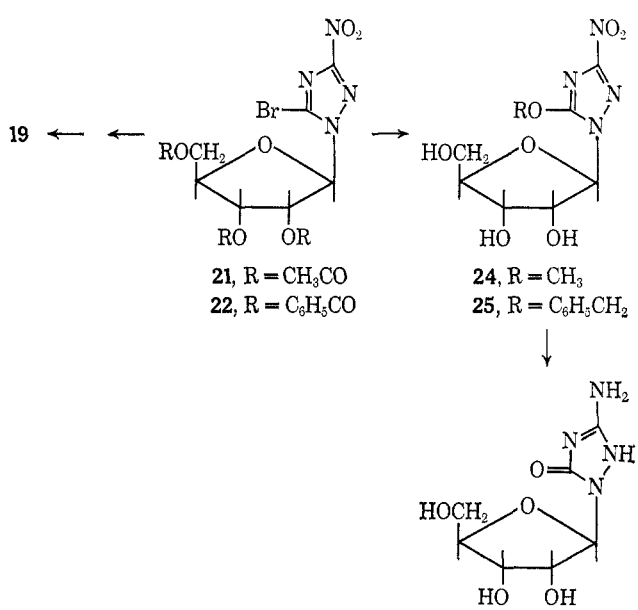
19 **15**

88% yield of 3-amino-1-(β-D-ribofuranosyl)-1,2,4-triazole (**19**) was obtained. Reductive deamination of **19** with nitrous acid in the presence of hypophosphorous acid afforded 1-(β-D-ribofuranosyl)-1,2,4-triazole (**15**).

Since the deaminated product **15** was a 1-substituted 1,2,4-triazole, the 3-amino-1,2,4-triazole nucleoside (**19**) could not be substituted at position 4. However, deamination of either 3-amino-1-(β-D-ribofuranosyl)-1,2,4-triazole or 5-amino-1-(β-D-ribofuranosyl)-1,2,4-triazole would provide 1-(β-D-ribofuranosyl)-1,2,4-triazole (**15**), since the 3 and 5 positions are equivalent in the unsubstituted 1,2,4-triazole. To distinguish between these two possible structures, the deamination of **19** was repeated in D_2O with hypophosphorous acid which had been equilibrated with D_2O.[27] This procedure is a modification of a method reported for introducing deuterium into aromatic compounds.[28] The pmr spectrum of the product obtained from deamination was identical with the spectrum of 1-(β-D-ribofuranosyl)-1,2,4-triazole (**15**) except that the intensity of the signal for the aromatic proton (3-H) at δ 8.06 (DMSO-d_6) was reduced by 73%. Exchange of the ring protons with D_2O had not occurred as shown by control experiments in which only slight exchange of the proton in the 5 position was noted after a prolonged time.

These results demonstrated that the amino group had occupied the 3 position and support the structure of **19** as 3-amino-1-(β-D-ribofuranosyl)-1,2,4-triazole. The nucleoside obtained by fusion of 3-nitro-1,2,4-triazole is therefore 3-nitro-1-(2,3,5-tri-*O*-benzoyl-β-D-ribofuranosyl)-1,2,4-triazole (**17**). The structure **19** is based on the assignment of the downfield proton in **15** at δ 8.80 as H_5, adjacent to the site of glycosylation. The electronegative effect of the sugar causes the expected deshielding of the adjacent proton approximately 0.6 ppm over that of H_5 as determined in 1-methyl-1,2,4-triazole.[29]

Bromination of 3-nitro-1,2,4-triazole in the presence of sodium hydroxide gave 3-bromo-5-nitro-1,2,4-triazole (**20**). The fusion of **20** with 1,2,3,5-tetra-*O*-acetyl-β-D-ribofuranose proved highly successful to afford 93% yield of a single crystalline product **21**. Use of 1-*O*-acetyl-2,3,5-tri-*O*-benzoyl-β-D-ribofuranose in the fusion procedure with **20** provided **22**. The site of glycosylation was established when **22** was subjected to catalytic hydrogenation with palladium on carbon. Reduction of the nitro group and simultaneous debromination occurred to yield 3-amino-1-(2,3,5-tri-*O*-benzoyl-β-D-ribofuranosyl)-1,2,4-triazole (**23**). Debenzoylation of **23** with sodium methoxide in methanol afforded 3-amino-1-(β-D-ribofuranosyl)-1,2,4-triazole (**19**) identical in all respects with **19** previously prepared *via* reduction of **18**. The structure of the nucleoside obtained by fusion of 3-bromo-5-nitro-1,2,4-tri-



21, R = CH_3CO
22, R = C_6H_5CO
24, R = CH_3
25, R = $C_6H_5CH_2$

26

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azole is thus assigned as 5-bromo-3-nitro-1-(2,3,5-tri-*O*-acetyl-β-D-ribofuranosyl)-1,2,4-triazole (**21**).

When deacetylation of **21** was attempted with sodium methoxide in methanol at room temperature, the bromo group was rapidly displaced. The product obtained in 69% yield was 5-methoxy-3-nitro-1-(β-D-ribofuranosyl)-1,2,4-triazole (**24**).

In order to obtain an oxo substituent in the 5 position of the 1,2,4-triazole nucleoside (**26**), displacement of the 5-bromo group of **21** with concomitant deacetylation was effected with sodium benzyloxide in benzyl alcohol at room temperature. After column chromatography of the crude reaction mixture to remove benzyl acetate and excess benzyl alcohol, a 40% yield of 5-benzyloxy-3-nitro-1-(β-D-ribofuranosyl)-1,2,4-triazole (**25**) was obtained. Catalytic reduction of the nitro group and simultaneous hydrogenolysis of the benzyl ether with palladium on carbon in the presence of hydrogen afforded the cytidine analog, 3-amino-1-(β-D-ribofuranosyl)-1,2,4-triazolin-5-one (**26**).

Attempts to utilize 3-nitro-1,2,4-triazolin-5-one[19] *via* trimethylsilylation and alkylation in the synthesis of **26** were unsuccessful. It would appear from these and related studies in the pyrimidine ring[30,31] that electron-withdrawing substituents hinder direct glycosylation by reducing the electron density of the pyrimidine type nitrogen to the point where alkylation by the C_1 of the sugar does not readily occur. The fusion reaction, on the other hand, is favored by electron-withdrawing substituents since it is the triazole anion which is alkylated.

Experimental Section

Detection of components on SilicAR 7 GF (Mallinckrodt) and alumina HF 254 (Brinkmann) was by ultraviolet light and by a 10% sulfuric acid in ethanol spray followed by heating under an infrared lamp. Alumina suitable for chromatographic absorption was obtained from Merck and Co.

Trimethylsilyl derivatives of the 1,2,4-triazoles were prepared by the general procedure of Wittenburg.[13] The 1,2,4-triazoles were heated under reflux in an excess of hexamethyldisilazane with a catalytic quantity of ammonium sulfate under anhydrous conditions until complete solution was achieved and evolution of ammonia ceased. The excess hexamethyldisilazane was removed by distillation under diminished pressure and the residue (oil or crystalline solid) was used directly without further purification unless otherwise specified.

1-(2,3,5-Tri-O-benzoyl-β-D-ribofuranosyl)-1,2,4-triazolidine-3,5-dione (4).—A solution of 2,3,5-tri-*O*-benzoyl-D-ribofuranosyl bromide[32] from 20.2 g (0.040 mol) of 1-*O*-acetyl-2,3,5-tri-*O*-benzoyl-β-D-ribofuranose in acetonitrile (250 ml) was added to the trimethylsilyl derivative prepared from 4.4 g (0.044 mol) of urazole[33] and the resulting solution was kept for 3 days at room temperature. After removal of the solvent, ethanol was added to the residue and the crystalline **4** separated to yield 18.3 g (84%), mp 202–204°. Recrystallization of the product from ethyl acetate–ethanol provided pure material, mp 203–205°.

Anal. Calcd for $C_{28}H_{23}N_3O_9$: C, 61.65; H, 4.25; N, 7.70. Found: C, 61.55; H, 3.95; N, 7.66.

1-(β-D-Ribofuranosyl)urazole or 1-(β-D-Ribofuranosyl)-1,2,4-triazolidine-3,5-dione (3).—A solution of **4** (5.0 g) in methanol (100 ml) saturated at 0° with ammonia was kept at room temperature for 3 days in a pressure bottle. After removal of the solvent, water (30 ml) was added and the mixture was extracted with ethyl acetate (three 25-ml portions). Dowex 50 (H) was added to the solution to pH 3, the solution was filtered, and the solvent was removed. Coevaporation of the residue with ethanol gave 1.2 g (56%) of **3** analytically pure: mp 163–165°; $[\alpha]^{30}D$ −52.6° (*c* 1.0, water); pmr (D_2O) δ 5.52 (d, 1, $J_{1',2'}$ = 5.0 Hz, 1'-H).

Anal. Calcd for $C_7H_{11}N_3O_6$: C, 36.05; H, 4.76; N, 18.02. Found: C, 36.11; H, 4.85; N, 17.80.

2-Methyl-1-(2,3,5-tri-O-benzoyl-β-D-ribofuranosyl)-1,2,4-triazolidine-3,5-dione (8).—A solution of 2,3,5-tri-*O*-benzoyl-D-ribofuranosyl bromide from 25.2 g (0.050 mol) of 1-*O*-acetyl-2,3,5-tri-*O*-benzoyl-β-D-ribofuranose in acetonitrile (250 ml) was added to the trimethylsilyl derivative prepared from 6.3 g (0.055 mol) of 1-methylurazole.[16] After 3 days at room temperature the solvent was removed, ethanol was added to the residue, and the solution was evaporated to a syrup. The syrup was dissolved in chloroform and applied to a silica gel column (4.0 × 50 cm) packed in chloroform. The column was eluted with chloroform (1.5 l.) and 100-ml fractions were taken. Fractions 8–14 were combined and evaporated to dryness. The residue was crystallized from methanol to provide 21.5 g (77%) of **8**, mp 150–152°.

Anal. Calcd for $C_{29}H_{25}N_3O_9$: C, 62.25; H, 4.50; N, 7.51. Found: C, 62.51; H, 4.52; N, 7.44.

2-Methyl-1-(β-D-ribofuranosyl)-1,2,4-triazolidine-3,5-dione (11).—A solution of **8** (11.2 g) in methanol (200 ml) saturated at 0° with ammonia was kept at room temperature for 3 days in a pressure bottle. The solvent was removed, and the product was crystallized from ethanol to give 3.5 g of **11**. The filtrate was evaporated to dryness. Water (30 ml) was added to the residue, and the mixture was extracted with ethyl acetate (three 20-ml portions). The aqueous solution was evaporated to dryness, and the residue was crystallized from ethanol to give an additional 0.9 g (total yield, 90%) of **11**: mp 180–182°; $[\alpha]^{29}D$ −12.3° (*c* 1.0, water); pmr (D_2O) δ 3.25 (s, 3, 2-CH_3), 5.47 (d, 1, $J_{1'2'}$ = 6.0 Hz, 1'-H).

Anal. Calcd for $C_8H_{13}N_3O_6$: C, 38.87; H, 5.30; N, 17.00. Found: C, 38.82; H, 5.17; N, 16.78.

4-Methyl-1-(2,3,5-tri-O-benzoyl-β-D-ribofuranosyl)-1,2,4-triazolidine-3,5-dione (5).—The preparation of **5** was accomplished as for **4** to give 46%, mp 178–181°. Recrystallization of the product from ethyl acetate–ethanol provided pure material, mp 182–184°.

Anal. Calcd for $C_{29}H_{25}N_3O_9$: C, 62.25; H, 4.50; N, 7.51. Found: C, 62.12; H, 4.52; N, 7.32.

3-Methoxy-4-methyl-1-(2,3,5-tri-O-benzoyl-β-D-ribofuranosyl)-1,2,4-triazolin-5-one (6). Method 1.—Excess diazomethane in dimethoxyethane[34] was added to a solution of **5** (1.1 g) in dimethoxyethane, and the solution was kept at room temperature for 12 hr. After removal of the solvent, the product was crystallized from methanol to give 0.6 g (53%) of **6**, mp 162–163°.

Method 2.—Methylation of **4** (3.0 g) by the procedure of method 1 above afforded 1.7 g (54%) of **6**: mp 162–163°; pmr ($CDCl_3$) δ 3.08 (s, 3, 4-CH_3), 3.81 (s, 3, 3-*O*-CH_3), 6.25 (s, 1, $J_{1',2'} < 1$ Hz, 1'-H).

Anal. Calcd for $C_{30}H_{27}N_3O_9$: C, 62.82; H, 4.75; N, 7.33. Found: C, 62.62; H, 4.65; N, 7.15.

3,5-Dimethoxy-1-(2,3,5-tri-O-benzoyl-β-D-ribofuranosyl)-1,2,4-triazole (7).—The filtrate from the methylation of **4** was evaporated to dryness, and the residue was dissolved in benzene and applied to an alumina column (2.0 × 25 cm) packed in benzene. The column was eluted with benzene (500 ml), and 50-ml fractions were taken. Fraction 4 was evaporated to dryness, and the residue was crystallized from methanol to give 0.1 g of **7**: mp 116–117°; pmr ($CDCl_3$) δ 3.84 (s, 3, 3-*O*-CH_3), 4.06 ppm (s, 3, 5-*O*-CH_3).

Anal. Calcd for $C_{30}H_{27}N_3O_9$: C, 62.82; H, 4.75; N, 7.33. Found: C, 62.89; H, 4.62; N, 7.18.

2,4-Dimethyl-1-(β-D-ribofuranosyl)-1,2,4-triazolidine-3,5-dione (10).—Methyl iodide (0.35 g, 2.5 mmol) and potassium carbonate (0.38 g, 2.8 mmol) were added to a solution of **5** (1.4 g, 2.5 mmol) in dimethylformamide (5 ml). The mixture was stirred at room temperature for 10 hr, then poured into chloroform (150 ml). The solution was filtered, and the filtrate was evaporated to dryness. Chloroform (30 ml) was added to the residue, and the mixture was extracted with water. The chloroform solution was dried over anhydrous magnesium sulfate and filtered. A small amount of **5** was removed by chromatography of this solution on an alumina column (1.5 × 35 cm) packed in chloroform. The column was eluted with chloroform (250 ml), and 25-ml

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fractions were collected. Fractions 3–7 were combined and evaporated to give 1.3 g of a homogeneous syrup. This material was debenzoylated by refluxing in methanol (25 ml) containing sodium methoxide (0.10 g) for 45 min. The solution was neutralized with Dowex 50 (H), filtered, and evaporated to dryness. The product was crystallized from ethanol–ethyl acetate to give 0.4 g (66%) of **10**, mp 115–117°.

Method 2.—Methylation of **8** (2.8 g) by the procedure of method 1 above provided 0.8 g (61%) of **10**: mp 115–117°; $[\alpha]^{28}D$ −17.1 (*c* 1.0, water); pmr (D_2O) δ 3.03 (s, 3, 4-CH_3), 3.23 (s, 3, 1-CH_3), 5.44 (d, 1, $J_{1',2'}$ = 6.0 Hz, 1′-H).

Anal. Calcd for $C_9H_{15}N_3O_6$: C, 41.38; H, 5.79; N, 16.09. Found: C, 41.18; H, 5.77; N, 16.03.

1-(2-Deoxy-3,5-di-*O*-*p*-toluoyl-β-D-*erythro*-pentofuranosyl)-2-methyl-1,2,4-triazolidine-3,5-dione (12).—A mixture of 2-deoxy-3,5-di-*O*-*p*-toluoyl-D-*erythro*-pentosyl chloride[17] (7.8 g, 0.020 mol) and the trimethylsilyl derivative prepared from 2.5 g (0.022 mol) of 1-methylurazole was heated *in vacuo* (*ca.* 14 mm) in an oil bath at 110° for 15 min. The residue was dissolved in ethyl acetate (50 ml), and the solution was washed with aqueous sodium hydrogen carbonate and water. After drying over anhydrous magnesium sulfate, the ethyl acetate solution was filtered, and the filtrate was evaporated to dryness. The product was crystallized from methanol to provide 3.8 g (41%) of **12**, mp 166–168°.

Anal. Calcd for $C_{24}H_{25}N_3O_7$: C, 61.66; H, 5.39; N, 8.99. Found: C, 61.97; H, 5.36; N, 8.77.

1-(2-Deoxy-β-D-*erythro*-pentofuranosyl)-2-methyl-1,2,4-triazolidine-3,5-dione (13).—A solution of **12** (2.6 g) was deblocked with methanolic ammonia as in the case of (**14**) to give a product which was recrystallized from ethanol to yield 0.9 g (70%) of **13**: mp 166–167°; $[\alpha]^{30}D$ +17.6 (*c* 1.0, water); pmr (D_2O); δ 3.23 (s, 3, 2-CH_3), 5.87 (t, 1, $J_{1'-2',2''}$ = 7.1 Hz, 1′-H).

Anal. Calcd for $C_8H_{13}N_3O_5$: C, 41.56; H, 5.67; N, 18.18. Found: C, 41.34; H, 5.72; N, 17.99.

1-(2-Deoxy-3,5-di-*O*-*p*-toluoyl-β-D-*erythro*-pentofuranosyl)-1,2,-4-triazolidine-3,5-dione.—A mixture of 2-deoxy-3,5-di-*O*-*p*-toluoyl-D-*erythro*-pentosyl chloride (11.7 g, 0.030 mol) and the trimethylsilyl derivative prepared from 3.3 g (0.33 mol) of urazole was heated *in vacuo* (*ca.* 14 mm) in an oil bath at 110° for 30 min. The residue was dissolved in ethyl acetate and ethanol, the solution was filtered, and the filtrate was evaporated to dryness. Crystallization of the product from ethyl acetate and ethanol provided 7.5 g of the desired product. The filtrate was evaporated to dryness, and the residue was dissolved in chloroform and applied to a silica gel column (3.0 × 55 cm) packed in chloroform. The column was eluted with chloroform (3 l.), chloroform–ethyl acetate (95:5, 1 l.), and chloroform–ethyl acetate (90:10, 5 l.); and 200-ml fractions were taken. Fractions 24–44 were combined and evaporated to dryness, and the residue was crystallized from ethyl acetate and ethanol to give an additional 1.8 g. The total yield was 67%. Recrystallization of the product from ethyl acetate and ethanol provided pure 1-(2-deoxy-3,5-di-*O*-*p*-toluoyl-β-D-*erythro*-pentofuranosyl)urazole: mp 219–221°; pmr (DMSO-d_6) δ 6.07 (t, 1, $J_{1'-2',2''}$ = 7.0 Hz, 1′-H).

Anal. Calcd for $C_{23}H_{23}N_3O_7$: C, 60.92; H, 5.11; N, 9.27. Found: C, 60.66; H, 5.14; N, 9.14.

1-(2-Deoxy-β-D-ribofuranosyl)urazole or 1-(2-Deoxy-β-D-*erythro*-pentofuranosyl)-1,2,4-triazolidine-3,5-dione (14).—A solution of the blocked nucleoside (2.0 g) in methanol (50 ml) saturated at 0° with ammonia was kept at room temperature for 3 days in a pressure bottle. After removal of the solvent, water (20 ml) was added to the residue, and the mixture was extracted with ethyl acetate (three 15-ml portions). The aqueous solution was evaporated to dryness, and the product was crystallized from ethanol to give 0.53 g (55%) of **14**: mp 208–210° dec; $[\alpha]^{27}D$ −3.3° (*c* 1.0, water); pmr (DMSO-d_6) δ 5.61 (m, 1, line width 14 Hz, 1′-H).

Anal. Calcd for $C_7H_{11}N_3O_5$: C, 38.71; H, 5.11; N, 19.35. Found: C, 38.47; H, 5.07; N, 19.38.

1-(2-Deoxy-3,5-di-*O*-*p*-toluoyl-β-D-*erythro*-pentofuranosyl)-2,4-dimethyl-1,2,4-triazolidine-3,5-dione. Method 1.—Methyl iodide (0.28 g, 2.0 mmol) and the potassium carbonate (0.30 g, 2.2 mmol) were added to a solution of 1-(2-deoxy-3,5-di-*O*-*p*-toluoyl-β-D-*erythro*-pentofuranosyl)-1,2,4-triazolidine-3,5-dione (0.45 g, 1.0 mmol) in dimethylformamide (4 ml), and the mixture was stirred at room temperature for 12 hr. The mixture was then poured into chloroform (150 ml) with stirring, the solution was filtered, and the filtrate was evaporated to dryness. Chloroform (20 ml) was added to the residue, and the mixture was extracted with water. The chloroform solution was dried over anhydrous magnesium sulfate and filtered. The filtrate was evaporated to dryness, and the product was crystallized from ether and cyclohexane to provide 0.39 g (81%), mp 98–100°.

Method 2.—Methyl iodide (0.14 g, 1.0 mmol) and potassium carbonate (0.15 g, 1.1 mmol) were added to a solution of **12** (0.47 g, 1.0 mmol) in dimethylformamide (4 ml), and the mixture was stirred at room temperature for 12 hr. The product was obtained exactly as in method 1 to give 0.41 g (85%) of product: mp 98–100°; pmr ($CDCl_3$) δ 3.05 (s, 3, 4-CH_3), 3.18 (s, 3, 2-CH_3), 5.97 (t, 1, $J_{1'-2',2''}$ = 7.0 Hz, $H_{1'}$).

Anal. Calcd for $C_{25}H_{27}N_3O_7$: C, 62.36; H, 5.65; N, 8.73. Found: C, 62.60; H, 5.62; N, 8.82.

3-Nitro-1,2,4-triazole (16).—3-Amino-1,2,4-triazole (25.2 g) was added in portions to a solution of 90% hydrogen peroxide (32.4 ml) in trifluoroacetic acid (120 ml) maintained at 0–10°. The resulting solution was gradually warmed to 70°, then maintained at 70–80° by intermittent cooling for 4 hr. The solution was kept overnight at 0°, and the crystalline product was collected to give 9.8 g of **16**. The filtrate was evaporated to an oily residue which was triturated with ethyl acetate. The resulting solid material was collected and extracted with ethyl acetate in a Soxhlet extractor. The ethyl acetate solution provided an additional 5.5 g of **16** (total yield, 45%). Recrystallization of the product from ethanol provided pure material with mp 213–215° dec. The compound exhibited uv bands at $\lambda_{max}^{pH\ 1}$ 245 mμ (ε 4610), 215 (5600); $\lambda_{max}^{pH\ 11}$ 291 mμ (ε 5870), 230 (2570).

Anal. Calcd for $C_2H_2N_4O_2$: C, 21.06; H, 1.77; N, 49.12. Found: C, 20.80; H, 1.84; N, 49.35.

3-Bromo-5-nitro-1,2,4-triazole (20).—A solution of 3-nitro-1,2,4-triazole (**16**) (5.7 g, 0.050 mol), sodium hydroxide (2.0 g, 0.050 mol), and bromine (3.0 ml) in water (25 ml) was heated at 80° until the bromination was complete (15–20 hr) as shown by tlc (SilicAR 7GF, ethyl acetate developer). The solution was cooled, acidified to pH 3 with dilute hydrochloric acid, and extracted with ethyl acetate (four 50-ml portions). The ethyl acetate solution was dried over anhydrous magnesium sulfate, filtered, and evaporated to dryness. The product was crystallized from ethyl acetate and benzene to provide 8.6 g (89%) of **20** with mp 157–159°. The compound exhibited uv bands at $\lambda_{max}^{pH\ 1}$ 262 mμ (ε 3950); $\lambda_{max}^{pH\ 11}$ 301 mμ (ε 5980), 231 (3820).

Anal. Calcd for $C_2HBrN_4O_2$: C, 12.45; H, 0.52; Br, 41.41; N, 29.03. Found: C, 12.34; H, 0.56; Br, 41.03; N, 28.84.

5-Bromo-3-nitro-1-(2,3,5-tri-*O*-acetyl-β-D-ribofuranosyl)-1,2,4-triazole (21).—3-Bromo-5-nitro-1,2,4-triazole (**20**) (5.8 g, 0.030 mol) and 1,2,3,5-tetra-*O*-acetyl-β-D-ribofuranose (9.5 g, 0.030 mol) were thoroughly mixed in a mortar, then heated *in vacuo* (*ca.* 14 mm) in an oil bath at 150° for 30 min. The residue was dissolved in ether and cyclohexane and seeded to give 12.6 g (93%) of **21** with mp 88–90°. Recrystallization of the product from ether and cyclohexane provided pure material with mp 90–92°. Seed crystals were obtained by chromatography on silica gel with benzene–ethyl acetate (9:1).

Anal. Calcd for $C_{13}H_{15}BrN_4O_9$: C, 34.60; H, 3.35; Br, 17.71; N, 12.42. Found: C, 34.36; H, 3.41; Br, 17.62; N, 12.37.

5-Methoxy-3-nitro-1-(β-D-ribofuranosyl)-1,2,4-triazole (24).—5-Bromo-3-nitro-1-(2,3,5-tri-*O*-acetyl-β-D-ribofuranosyl)-1,2,4-triazole (**21**) (9.0 g, 0.020 mol) was added to a solution of sodium (0.58 g, 0.025 mol) dissolved in methanol (50 ml), and the resulting solution was stirred at room temperature for 2.5 hr. After neutralization with Dowex 50 (H), the solution was filtered, and the filtrate was evaporated to dryness. The residue was dissolved in methanol, silica gel (20 g) was added to the solution, and the mixture was evaporated to dryness. The silica gel mixture was added to a dry-packed silica gel column (2.5 × 25 cm), and the column was eluted with chloroform (0.5 l.), ethyl acetate–chloroform (1:1, 0.5 l.), and ethyl acetate (1 l.). Fractions of 200 ml were collected, and fractions 4–7 were combined and evaporated to dryness. Crystallization of the product from ethyl acetate provided 3.8 g (69%) of **24**: mp 126–127°; $[\alpha]^{30}D$ −56.6° (*c* 1.0, water); pmr (D_2O) δ 4.17 (s, 3, *O*-CH_3), 5.80 (d, 1, $J_{1',2'}$ = 3.5 Hz, 1′-H).

Anal. Calcd for $C_8H_{12}N_4O_7$: C, 34.78; H, 4.38; N, 20.29. Found: C, 34.73; H, 4.57; N, 20.18.

5-Benzyloxy-3-nitro-1-(β-D-ribofuranosyl)-1,2,4-triazole (25).—A solution of **21** (4.5 g, 0.010 mol) in dry 1,2-dimethoxyethane (15 ml) was added to a solution of sodium (0.34 g, 0.015 mol) dissolved in benzyl alcohol (15 ml), and the mixture was stirred at room temperature for 3 hr. After neutralization with

Dowex 50 (H), the solution was filtered. Silica gel (25 g) was added to the filtrate, and the mixture was evaporated to dryness. The silica gel mixture was added to a dry-packed silica gel column (3.0 × 30 cm). The column was eluted with chloroform (1 l.) which removed benzyl alcohol and benzyl acetate, followed by chloroform–ethyl acetate (1:1, 0.5 l.) and ethyl acetate (1.5 l.); and 200-ml fractions were taken. Fractions 6–11 were combined and evaporated to dryness, and the product was crystallized from ethanol–benzene to give 1.4 g (40%) of **25** with mp 106–108°.

Anal. Calcd for $C_{14}H_{16}N_4O_7$: C, 47.73; H, 4.58; N, 15.90. Found: C, 47.85; H, 4.49; N, 15.77.

3-Amino-1-(β-D-ribofuranosyl)-1,2,4-triazolin-5-one (26).—A solution of **25** (0.50 g) in ethanol and 10% palladium-on-carbon catalyst (0.10 g) was shaken on a Parr hydrogenation apparatus at 45 psi for 3 hr at room temperature. The catalyst was removed by filtration through Celite, and the filtrate was evaporated to dryness. The residue was dissolved in methanol, and silica gel (5.0 g) was added to the solution. The mixture was evaporated to dryness, and the silica gel mixture was added to a dry-packed silica gel column (2 × 20 cm). The column was eluted with chloroform (0.2 l.), chloroform–ethyl acetate (1:1, 0.2 l.), ethyl acetate (0.2 l.), ethyl acetate–methanol (95:5, 0.5 l.), and ethyl acetate–methanol (90:10, 1 l.); 100-ml fractions were collected. Fractions 12–15 were combined and evaporated to dryness. The product was crystallized from methanol and ethanol to give 0.19 g (58%) of **26**: mp 167–169° dec; $[\alpha]^{27}D$ −91.0° (*c* 1.0, water).

Anal. Calcd for $C_7H_{12}N_4O_5$: C, 36.21; H, 5.21; N, 24.13. Found: C, 36.25; H, 5.22; N, 23.89.

3-Amino-1-(2,3,5-tri-O-benzoyl-β-D-ribofuranosyl)-1,2,4-triazole (23).—3-Bromo-5-nitro-1,2,4-triazole (**20**) (1.9 g, 0.010 mol) and 1-*O*-acetyl-2,3,5-tri-*O*-benzoyl-β-D-ribofuranose (5.0 g, 0.010 mol) were thoroughly mixed in a mortar, then heated *in vacuo* (*ca.* 14 mm) in an oil bath at 150° for 30 min. The residue was dissolved in ethyl acetate and evaporated to dryness. This syrup, crude 5-bromo-3-nitro-1-(2,3,5-tri-*O*-benozyl-β-D-ribofuranosyl)-1,2,4-triazole (**22**), was dissolved in ethyl acetate–ethanol (1:1, 50 ml). Sodium acetate (0.9 g) and 10% palladium-on-carbon catalyst (1.0 g) were added to the solution and the mixture was shaken on a Parr hydrogenation apparatus at 40 psi for 3 hr at room temperature. The catalyst was removed by filtration through Celite, and the filtrate was evaporated to dryness. Water (30 ml) was added to the residue, and the mixture was extracted with ethyl acetate (three 50-ml portions). The ethyl acetate solution was dried over anhydrous magnesium sulfate, filtered, and evaporated to dryness. Crystallization of the product from ethanol provided 3.5 g (60%) of **23**, mp 124–126°.

Anal. Calcd for $C_{28}H_{24}N_4O_7$: C, 63.63; H, 4.58; N, 10.60. Found: C, 63.82; H, 4.49; N, 10.48.

3-Nitro-1-(2,3,5-tri-O-benzoyl-β-D-ribofuranosyl)-1,2,4-triazole (17).—3-Nitro-1,2,4-triazole (**16**) (2.3 g, 0.020 mol) and 1-*O*-acetyl-2,3,5-tri-*O*-benzoyl-β-D-ribofuranose (10.1 g, 0.020 mol) were thoroughly mixed in a mortar, then heated *in vacuo* (*ca.* 14 mm) in an oil bath at 190° with magnetic stirring for 30 min. After cooling the reaction mixture, the product was crystallized from ethyl acetate and ethanol to yield 9.8 g (88%) of **17**, mp 153–155°. Recrystallization of the product from ethyl acetate and ethanol provided pure material: mp 155–156°; pmr (DMSO-d_6) δ 6.84 (d, 1, $J_{1',2'}$ = 1.2 Hz, 1'-H), 9.18 (s, 1, 5-H).

Anal. Calcd for $C_{28}H_{22}N_4O_9$: C, 60.21; H, 3.97; N, 10.03. Found: C, 60.52; H, 4.14; N, 9.96.

3-Nitro-1-(β-D-ribofuranosyl)-1,2,4-triazole (18).—A solution of **17** (11.2 g) was refluxed in methanol (50 ml) containing sodium methoxide (0.10 g) for 45 min. The solution was neutralized with Dowex 50 (H) and filtered, and the solvent was removed. The product was crystallized from 2-propanol to give 4.0 g (82%) of **18**, mp 135–137°. Recrystallization of the product from 2-propanol provided pure material: mp 138–140°; $[\alpha]^{28}D$ −24.1° (*c* 1.0, water); pmr (D_2O) δ 6.09 (d, 1, $J_{1',2'}$ = 3.0 Hz, 1'-H), 8.82 (s, 1, 5-H).

Anal. Calcd for $C_7H_{10}N_4O_6$: C, 34.15; H, 4.09; N, 22.76. Found: C, 34.00; H, 4.03; N, 22.88.

3-Amino-1-(β-D-ribofuranosyl)-1,2,4-triazole (19). Method 1.—A solution of **23** in methanol (30 ml) saturated with ammonia at 0° was kept at room temperature for 3 days in a pressure bottle. The solvent was removed, and the product was crystallized from methanol and ethyl acetate to give 0.35 g (85%) of **19** with mp 145–146°.

Method 2.—3-Nitro-1-(β-D-ribofuranosyl)-1,2,4-triazole (**18**) (1.2 g) and 85% hydrazine (5.0 ml) were heated on a steam bath until evolution of nitrogen ceased (*ca.* 20 min). The solution was evaporated to dryness, and the product was crystallized from ethanol to yield 0.95 g (88%) of **19**: mp 145–146°; $[\alpha]^{30}D$ −52.4 (*c* 0.98, water); pmr (DMSO-d_6-D_2O) δ 5.62 (d, 1, $J_{1',2'}$ = 4.0 Hz, 1'-H), 8.29 (s, 1, 5-H).

Anal. Calcd for $C_7H_{12}N_4O_4$: C, 38.89; H, 5.59; N, 25.92. Found: C, 38.75; H, 5.69; N, 25.82.

1-(2,3,5-Tri-O-benzoyl-β-D-ribofuranosyl)-1,2,4-triazole.—A solution of 1-trimethylsilyl-1,2,4-triazole[35] (3.1 g, 0.022 mol) and 2,3,5-tri-*O*-benzoyl-D-ribofuranosyl bromide prepared from 1-*O*-acetyl-2,3,5-tri-*O*-benzoyl-β-D-ribofuranose (10.1 g, 0.020 mol) in acetonitrile (50 ml) was kept for 4 days at room temperature. The solvent was removed and the residue was dissolved in chloroform (30 ml). The chloroform solution was washed with dilute aqueous sodium hydrogen carbonate and water. After drying over anhydrous magnesium sulfate, the chloroform solution was filtered, and the volume was reduced to approximately 15 ml. This solution was applied to a silica gel column (3.5 × 60 cm) packed in chloroform. The column was eluted with chloroform (2 l.), and 200-ml fractions were taken. Fractions 5–8 were combined and evaporated to dryness, and the product was crystallized from ethanol to provide 5.6 g (54%) of 1-(2,3,5-tri-*O*-benzoyl-β-D-ribofuranosyl)-1,2,4-triazole with mp 103–105°.

Anal. Calcd for $C_{28}H_{23}N_3O_7$: C, 65.49; H, 4.51; N, 8.18. Found: C, 65.54; H, 4.45; N, 8.11.

1-(β-D-Ribofuranosyl)-1,2,4-triazole (15). Method 1.—A solution of 1-(2,3,5-tri-*O*-benzoyl-β-D-ribofuranosyl)-1,2,4-triazole (5.1 g) in methanol (30 ml) containing sodium methoxide (0.10 g) was refluxed for 45 min. The solution was neutralized with Dowex 50 (H) and filtered, and the solvent was removed. The product was crystallized from methanol and ethyl acetate to give 1.8 g (90%) of **15**: mp 143–145°; $[\alpha]^{28}D$ −57.0° (*c* 1.0, water); pmr (DMSO-d_6) δ 5.85 (s, 1, $J_{1',2'}$ = 3.7 Hz, 1'-H), 8.06 (s, 1, 3-H), 8.80 (s, 1, 5-H).

Anal. Calcd for $C_7H_{11}N_3O_4$: C, 41.79; H, 5.51; N, 20.89. Found: C, 41.54; H, 5.59; N, 20.93.

Method 2.—A solution of sodium nitrite (0.15 g, 2.2 mmol) in water (3 ml) was added dropwise with stirring to a solution of 3-amino-1-(β-D-ribofuranosyl)-1,2,4-triazole (**19**) (0.43 g, 2.0 mmol) and 50% hypophosphorous acid (0.30 g) in water (5 ml) at room temperature. After 30 min the solution was evaporated to dryness. Methanol and silica gel (2.0 g) were added to the residue, and the mixture was evaporated to dryness. The silica gel mixture was added to a dry-packed silica gel column (1.5 × 20 cm), and the column was eluted with chloroform (0.1 l.), ethyl acetate–chloroform (1:1, 0.2 l.) and ethyl acetate (0.2 l.); 50-ml fractions were taken. Fractions 8 and 9 were evaporated to dryness, and the residue was crystallized from methanol and ethyl acetate to give 0.18 g (45%) of **15**.

Method 2 was repeated with 50% D_3-hypophosphorous acid in D_2O and with D_2O in place of water. The 50% D_3-hypophosphorous acid solution was prepared as follows. The water was removed from 50% hypophosphorous acid *in vacuo*, D_2O was added, and the evaporation was repeated. Sufficient D_2O was then added to make an approximately 50% D_3-hypophosphorous acid solution. The pmr spectrum of the product obtained was identical with that of **15** except that the signal for the 3-H at δ 8.06 integrated for 0.27 proton.

Registry No.—**3**, 24806-83-5; **4**, 24854-62-4; **5**, 24806-84-6; **6**, 24806-85-7; **7**, 24806-86-8; **8**, 24806-87-9; **10**, 24806-88-0; **11**, 24806-89-1; **12**, 24806-90-4; **13**, 24806-91-5; **14**, 24806-92-6; **15**, 24806-93-7; **16**, 24807-55-4; **17**, 24806-94-8; **18**, 24806-95-9; **19**, 24806-96-0; **20**, 24807-56-5; **21**, 24806-97-1; **23**, 24806-98-2; **24**, 24806-99-3; **25**, 24807-00-9; **26**, 24807-01-0; 1-(2-deoxy-3,5-di-*O*-*p*-toluoyl-β-D-*erythro*-pentofuranosyl)-1,2,4-triazolidine-3,5-dione, 24807-02-1; 1-(2-deoxy-3,5-di-*O*-*p*-toluoyl-β-D-*erythro*-pentofuranosyl)-2,4-dimethyl-1,2,4-triazolidine-3,5-dione, 24807-03-2; 1-(2,3,5-tri-*O*-benzoyl-β-D-ribofuranosyl)-1,2,4-triazole, 24807-04-3.

(35) L. Birkofer, P. Richter, and A. Ritter, *Chem. Ber.*, **93**, 2804 (1960).