with 0.1 *N* HCl (4 × 50 ml), saturated aqueous $NaHCO_3$ (4 × 50 ml), and water (2 × 50 ml). The organic phase was dried over Na_2SO_4, the Na_2SO_4 was removed by filtration and washed with $CHCl_3$ (30 ml) and the combined filtrate and wash were evaporated to dryness. The resulting syrup was dissolved in $CHCl_3$, applied to a dry packed column of SilicAR CC-7 (7 × 18 cm), and eluted with chloroform–acetone (19:1). Fractions containing the major band [R_f 0.73, chloroform–acetone (19:1), fraction no. 7–23, 20-ml fractions] were concentrated and applied to another SilicAR CC-7 (4.6 × 20 cm) column. Fractions 3–10 (20-ml fractions) from the second column contained pure **20.** These fractions were combined and evaporated to a hard foam and then triturated with ether (100 ml) to give 3.9 g of solid: mp 119–122°; ^1H NMR ($CDCl_3$) δ 8.46 (s, 1, H-2), 8.33–7.33 (m, ca. 30, $-COC_6H_5$); uv λ_{max} ($\epsilon \times 10^{-3}$) pH 1, 350 nm (14.4), sh 275 (19.5), 238 (45.3); pH 11, 350 (15.7), sh 275 (26.1), 237 (91.0).

Anal. Calcd for $C_{57}H_{43}N_3O_{15}S_2 \cdot 2H_2O$: C, 61.68; H, 4.26; N, 3.78. Found: C, 61.59; H, 4.45; N, 3.68.

Registry No.—**1,** 5082-82-6; **2,** 35867-92-6; **3,** 55520-41-7; **4,** 35867-91-5; **5,** 35867-90-4; **8,** 55520-42-8; **9,** 55520-43-9; **10,** 18903-18-9; **11,** 55520-44-0; **12,** 55520-45-1; **13,** 35867-89-1; **14,** 55520-46-2; **15,** 55520-47-3; **16,** 55520-48-4; **17,** 55520-49-5; **18,** 55520-50-8; **19,** 55520-51-9; **20,** 55520-52-0; 2,3,5-tri-*O*-benzoyl-D-ribofuranosyl bromide 22860-91-9; 1-*O*-acetyl-2,3,5-tri-*O*-benzoyl-β-D-ribofuranose, 6974-32-9.

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C-Glycosyl Nucleosides. VII.[1] Synthesis of Some 3-β-D-Ribofuranosyl-1,2,4-oxadiazoles and 3-β-D-Ribofuranosylpyrazoles

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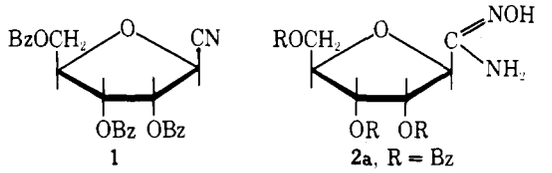
Two syntheses of 2,5-anhydro-3,4,6-tri-*O*-benzoyl-D-allonamidoxime (**2a**) are described via either addition of hydroxylamine to 2,3,5-tri-*O*-benzoyl-β-D-ribofuranosyl cyanide or chlorination and amination of 2,5-anhydro-3,4,6-tri-*O*-benzoyl-D-allose oxime. Reactions of **2a** with acetic anhydride and ethyl acetoacetate give rise to 5-substituted 3-β-D-ribofuranosyl-1,2,4-oxadiazoles, while acetaldehyde gives the related Δ^2-1,2,4-oxadiazoline. The condensation of both *O*-benzoyl and *O*-benzyl derivatives of 2,5-anhydro-D-allose with 1-chloroacetonylidenetriphenylphosphorane gives unsaturated chloro ketones that can be cyclized with hydrazine to 5-methyl-3-β-D-ribofuranosylpyrazoles. A potential route for the synthesis of pyrazoles is explored via addition of ethyl glyoxylate hydrazone to nitroolefins followed by chlorination and base-catalyzed cyclization. This has required the synthesis of a *C*-glycosyl nitroolefin via addition of nitromethane to 2,5-anhydro-3,4,6-tri-*O*-benzyl-D-allose followed by dehydration. While pyrazole synthesis was achieved in a model system, the carbohydrate derivative failed to cyclize.

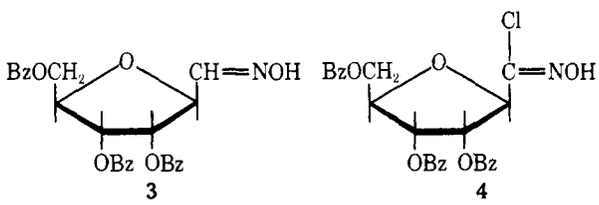
The natural occurrence of a number of *C*-glycosyl nucleosides, many of which possess antibacterial or antitumor activity,[2] has prompted considerable activity directed toward the synthesis of this type of compound.[3] Our general approach has been based upon the development of a facile synthetic route for the preparation of variously protected derivatives of 2,5-anhydro-D-allose.[4] The latter compounds, which already include the critical *C*-glycosyl carbon–carbon bond, contain a reactive aldehyde function that can be elaborated into a variety of heterocyclic systems. We have, for example, described the use of these key intermediates in syntheses of 2-β-D-ribofuranosylmaleimide (showdomycin),[5] of variously substituted 4-β-D-ribofuranosylpyrazoles,[6] and of both 3- and 5-β-D-ribofuranosylisoxazoles.[1] In the present paper we further extend those studies and describe routes for the synthesis of several 3-β-D-ribofuranosyl-1,2,4-oxadiazoles and 3-β-D-ribofuranosylpyrazoles.

The most frequently encountered route for the synthesis of substituted 1,2,4-oxadiazoles involves the acylation and subsequent cyclization of amidoximes. This procedure was originally developed by Tiemann[7] some 90 years ago and has recently been reexamined by Moussebois et al.[8] The chemistry of amidoximes has been reviewed[9] and it can be seen that the most common route for their synthesis involves the condensation of nitriles with hydroxylamine.[10] For our purposes the key intermediate would be 2,5-anhydro-3,4,6-tri-*O*-benzoyl-D-allonamidoxime (**2a**), and this compound could be obtained by the reaction of the readily available 2,3,5-tri-*O*-benzoyl-β-D-ribofuranosyl cyanide (**1**)[11,4] with hydroxylamine in methanol at 50°. Under these conditions **2a** was obtained in only 34% yield and it was necessary to effect purification by chromatography on silicic acid in order to remove several more polar by-products arising, presumably, from partial debenzoylation. While amidoximes have been prepared as substituents upon the

heterocyclic rings of several nucleosides,[12] **2a** is, to the best of our knowledge, the first example of a carbohydrate amidoxime. Debenzoylation of **2a** by treatment with methanolic ammonia gave free 2,5-anhydro-D-allonamidoxime (**2b**) in high yield. The rather low yield of **2a** obtained directly from the nitrile **1** could be much improved by use of an alternate synthetic route.[13] We have previously described the synthesis of the chloro oxime **4**, or its nitroso tautomer, via low-temperature chlorination of 2,5-anhydro-3,4,6-tri-*O*-benzoyl-D-allose oxime (**3**).[1] Without purification **4** was treated with ammonia in ether at 0° to give pure **2a** in almost quantitative yield. The entire process is extremely efficient and the overall yield of **2a** from the diphenylimidazolidine derivative of 2,5-anhydro-3,4,6-tri-*O*-benzoyl-D-allose[4] is 89% without the necessity of any chromatography.



1 **2a**, R = Bz; **b**, R = H

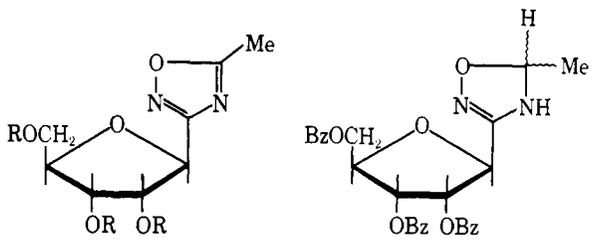


3 **4**

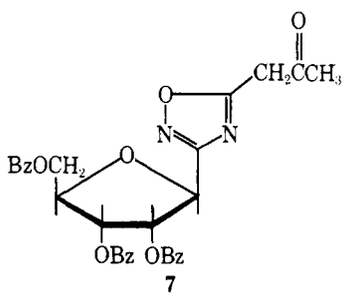
The amidoxime **2a** was then subjected to several types of ring closure reactions. First of all, it was treated with acetic anhydride under reflux, giving, presumably via the *O*-acetyl intermediate, 3-(2,3,5-tri-*O*-benzoyl-β-D-ribofuranosyl)-5-methyl-1,2,4-oxadiazole (**5a**) in 48% yield. Typical of most of the compounds in the present work, **5a** was obtained as a homogeneous foam following chromatography on silicic acid. While **5a**, and many other compounds in this series, have eluded crystallization, its purity was assured by elemental analysis and NMR spectroscopy. Debenzoylation of **5a** was readily achieved using methanolic ammonia giving 5-methyl-3-(β-D-ribofuranosyl)-1,2,4-oxadiazole (**5b**) in 70% yield. As has been seen quite frequently in other perbenzoylated *C*-glycosides that we have examined,[1,6] the NMR spectrum of **5a** shows overlapping signals for $C_2'H$ and $C_3'H$ and also for $C_4'H$ and $C_5'H_2$. The purity of the samples is nevertheless apparent from other sharp signals due to $C_1'H$, heterocyclic protons, and ring substituents. Following debenzoylation, however, there is excellent resolution of all the sugar protons, especially in spectra run in pyridine-d_5. The spectrum of **5b**, for example, is readily amenable to first-order analysis.

Amidoximes are also known to react with aldehydes giving Δ^2-1,2,4-oxadiazolines.[14] Thus a solution of **2a** and acetaldehyde in aqueous ethanol reacted slowly at room temperature over 3 days, giving a 47% yield of 3-(2,3,5-tri-*O*-benzoyl-β-D-ribofuranosyl)-5-methyl-Δ^2-1,2,4-oxadiazoline (**6**). While **6** was analytically pure, its NMR spectrum clearly showed it to be the expected mixture of diastereoisomers. Brief treatment of **6** with chlorine in carbon tetrachloride led to rapid and complete dehydrogenation giving **5a** identical with that from the acetic anhydride reaction. We have previously found chlorine to be a particularly effective reagent for the dehydrogenation of pyrazolines to pyrazoles.[6]

While amidoximes do not readily react with simple esters, they are known to condense with β-keto esters.[14a,15] In our case **2a** underwent a fairly clean condensation with ethyl acetoacetate in toluene under reflux giving 5-acetonyl-3-(2,3,5-tri-*O*-benzoyl-β-D-ribofuranosyl)-1,2,4-oxadiazole (**7**) in 61% yield. This structure is quite in accord



5a, R = Bz; **b**, R = H **6**



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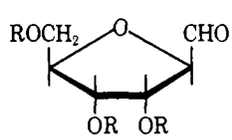
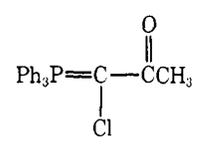
with the proposals of the early German workers[14a,15] and is confirmed by NMR spectroscopy, which shows the presence of an acetonyl function and the absence of heterocyclic protons. It should be noted that the reactions described above are basically prototypes of ones that could be used to introduce more highly functionalized substituents onto the heterocyclic ring of 1,2,4-oxadiazole-*C*-glycosides. This must, however, await further study.

In an earlier paper we have described several methods for the preparation of functionally substituted 4-(β-D-ribofuranosyl)pyrazoles.[6] It was also of interest to explore routes to 3-(β-D-ribofuranosyl)pyrazoles, especially since the antibiotic pyrazomycin fits into this class.[2] While our approaches to the synthesis of pyazomycin itself will mainly be described elsewhere,[17] we now describe some simple routes to the basic heterocyclic system. Of the various methods for the synthesis of 3,5-disubstituted pyrazoles,[18] the one best suited to the starting materials at hand appeared to be the condensation of an α-chlorovinyl ketone with hydrazine.[19] To this end 2,5-anhydro-3,4,6-tri-*O*-benzoyl-D-allose (**8a**) was freshly regenerated as previously described from its diphenylimidazolidine derivative[4] and treated with 1-chloroacetonylidenetriphenylphosphorane (**9**)[20] in methylene chloride. Following chromatography on silicic acid 5,8-anhydro-6,7,9-tri-*O*-benzoyl-3-chloro-1,3,4-



8a, R = benzoyl; **b**, R = benzyl



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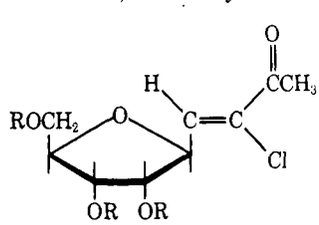
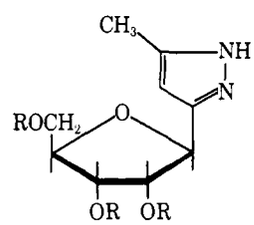


10a, R = benzoyl; **b**, R = benzyl



11a, R = benzoyl; **b**, R = H; **c**, R = benzyl

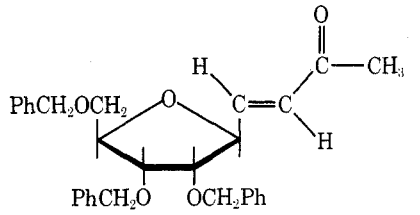
trideoxy-D-*allo*-non-3-eneulose (**10a**) was obtained as a homogeneous foam in 78% yield. The NMR spectrum of **10a** was well resolved and clearly indicated the presence of only a single geometrical isomer. In the absence of the other isomer it is difficult to make a direct assignment of configuration. As will be seen below, however, we have isolated both the *Z* and *E* isomers of the closely related benzyl ethers (**10b** and *E* isomer), which show chemical shifts for C_4H of 6.80 and 6.30 ppm, respectively. The chemical shift of C_4H (6.86 ppm) in **10a** strongly suggests that this compound has the *Z* configuration.

Treatment of **10a** with hydrazine hydrate in acetic acid under reflux led, presumably via initial hydrazone formation followed by intramolecular cyclization and dehydrohalogenation,[18] to 3-(2,3,5-tri-*O*-benzoyl-β-D-ribofuranosyl)-5-methylpyrazole (**11a**), which was isolated in 69% yield by chromatography on silicic acid. Under these conditions loss of benzoyl groups did not appear to be a serious side reaction. Attempted debenzoylation of **11a** using methanolic sodium methoxide at room temperature led to the formation of the desired triol (**11b**) as a major product accompanied by several by-products that were difficult to remove. Debenzoylation using methanolic ammonia was considerably cleaner, but even here it was necessary to use ion exchange chromatography on a column of AG-1-X2 resin with a gradient of methanol in water[21] in order to fully purify the product. In this way 5-methyl-3-(β-D-ribofuranosyl-)pyrazole (**11b**) was isolated as a spectroscopically and analytically pure amorphous solid in 30% yield.

In an effort to improve the yield of **11b** we have also examined the use of benzyl ethers as the triol protecting group. Thus 2,5-anhydro-3,4,6-tri-*O*-benzyl-D-allose (**8b**) was liberated from its diphenylimidazolidine derivative[4] and directly treated with the chloro ylide **9** at room temperature, giving a 4:1 mixture of the *Z* (**10b**) and *E* isomers of the desired unsaturated chloro ketone in a combined yield of 87%. While the mixture was entirely satisfactory for the next step, a portion of the mixture was separated by preparative TLC and the pure isomers were characterized by their NMR spectra. These assignments of configuration were based upon the expected deshielding of C_4H in the *Z* isomer (**10b**) by the C_2 carbonyl group and are supported, to a lesser degree, by a deshielding of C_5H in the *E* isomer.

Treatment of the mixture of **10b** and its *E* isomer with hydrazine in acetic acid as above for **10a** gave the desired pyrazole **11c** in 56% yield following preparative TLC. Attempted debenzylation of **11c** by catalytic hydrogenolysis in the presence of palladium catalysts seemed capricious and usually gave a mixture of products even after several changes of catalyst. The use of sodium in liquid ammonia, however, led to rapid debenzylation and gave **11b**, identical with that from the benzoate, in 83% yield. In this case only desalting with Dowex 50(H^+) resin and preparative TLC were necessary for purification of the product. Our subsequent experience with debenzylations using boron trichloride[5] suggest that this might provide a convenient alternate route.

A slightly different approach to the synthesis of **11b** was also attempted without ultimate success. Thus the condensation of **8b** with acetonylidenetriphenylphosphorane[20] led to the isolation of 5,8-anhydro-6,7,9-tri-*O*-benzyl-1,3,4-trideoxy-D-*allo*-non-3-eneulose (**12**) as a syrup in 85% yield. The formation of only a single geometrical isomer was apparent from the NMR spectrum, and the large vicinal vinyl coupling ($J_{3,4}$ = 16 Hz) allowed assignment of the *E* configuration (**12**).[22] The reaction of **12** with hydrazine hydrate in acetic acid proceeded quite rapidly and led to the isolation of a crystalline, roughly equal mixture of two diastereomeric pyrazolines in 74% yield. The NMR spectrum of this material, however, showed the presence of an extraneous three-proton singlet at 1.86 ppm. In addition, its infrared spectra showed a strong absorption at 1645 cm^{-1}, typical of a tertiary amide, and the absence of any NH stretching bands near 3300 cm^{-1}. The elemental analysis also confirmed the presence of an acetyl group and we consider this product to be *N*-acetyl-3-(2,3,5-tri-*O*-benzyl-β-D-ribofuranosyl)-5-methyl-Δ^5-pyrazoline (**13**). We can offer no convincing argument as to the mechanistic origin of the *N*-acetyl function, and the formation of this type of product does not appear to have been previously observed.[18] We have been unsuccessful in our attempts to cleave the *N*-acetyl group by treatment with methanolic ammonia, sodium methoxide, and hydrogen chloride and equally unsuccessful in various attempts to dehydrogenate **13** with chlorine, bromine, and 2,3-dichloro-5,6-dicyano-1,4-benzoquinone. In view of the successful syntheses of **11b** via the chloro ketones (**10a,b**), this route has not been explored further.



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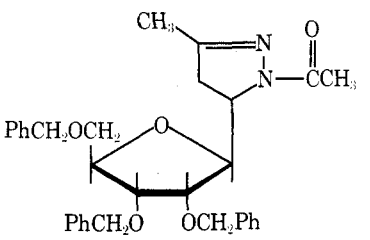

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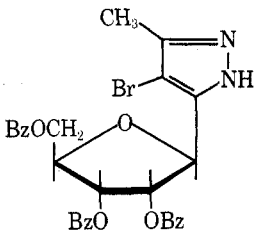
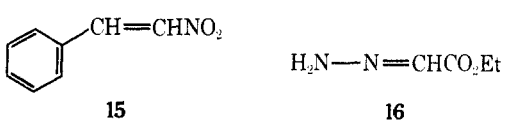


14

In an effort to introduce some reactive functionality into the pyrazole ring several approaches have been briefly explored. The reaction of **11a** with a small excess of bromine in chloroform readily gave the 4-bromo derivative **14** in 87% yield,[23] as shown by the disappearance of the resonance due to C_4H in the NMR spectrum. The nitration of **11a** under several conditions, however, led only to unreacted starting material or to the formation of nitrobenzoyl derivatives.

We have also considered an alternative route for the preparation of nitropyrazoles via cyclization of an appropriate nitroolefin. To test the concept we initially examined a model system based upon commercially available β-nitrostyrene (**15**). This nitroolefin underwent facile reaction with (*E*)-ethylglyoxylate hydrazone (**16**),[24] giving crystalline ethyl N^2-(2-nitro-1-phenylethyl)glyoxylate hydrazone (**17a**) in 39% yield. The chlorination of hydrazones has



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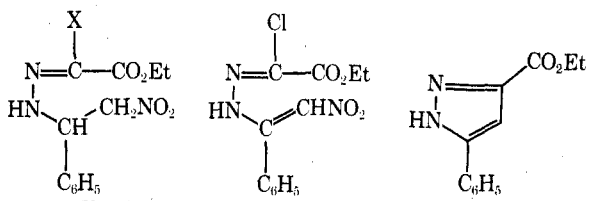


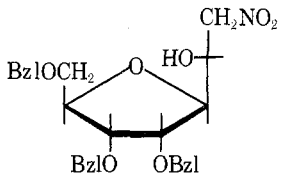
17a, X = H
b, X = Cl

18 19

been known for many years[25] and reaction of **17a** with about 5 molar equiv of chlorine at −70° gave the crystalline chlorohydrazone **17b** in 70% yield. Care had to be taken to remove the excess chlorine at a low temperature, however, and an attempted chlorination using a large excess of chlorine and allowing the reaction to warm to room temperature led to the gradual formation of a second yellow product with a TLC mobility just greater than that of **17b.** The two substances could be separated by preparative TLC and the new product, which was obtained as yellow crystals in 22% yield, was shown by NMR and mass spectra to be ethyl N^2-(2-nitro-1-phenylvinyl)-2-chloroglyoxylate hydrazone (**18**), which presumably arose by benzylic chlorination and dehydrohalogenation of **17b.**

It was hoped that generation of a nitro-stabilized carbanion from **17b** would lead to intramolecular displacement of chlorine by either a direct SN2 process or, more likely, via an intermediate nitrilimine.[26] Treatment of **17b** with triethylamine in tetrahydrofuran led to complete disappearance of the starting material and formation of several new products which were separated by preparative TLC. From the major band a crystalline product was isolated in 14% yield and shown to be the known 3-ethoxycarbonyl-5-phenylpyrazole (**19**).[27] The formation of **19** shows that the desired cyclization of **17b** to a nitropyrazoline did occur but was followed by loss of nitrous acid giving the pyrazole. Other examples of the loss of nitrous acid from nitropyrazolines are to be found in the literature.[28]

In the hope that the spontaneous loss of nitrous acid might be avoided under appropriate conditions, we reacted the sugar aldehyde **11b** with nitromethane in the presence of sodium methoxide and obtained a crystalline nitro alcohol in 74% yield. This compound gave an ORD spectrum with a positive Cotton effect centered about 284 nm and on the basis of the empirical rules developed by Satoh et al.[29] is considered to be 3,6-anhydro-4,5,7-tri-*O*-benzyl-1-deoxy-1-*nitro*-D-*glycero*-D-*altro*-heptitol (**20**). Dehydration of **20** was readily accomplished by treatment with acetic anhydride and pyridine in benzene, giving (*E*)-3,6-anhydro-4,5,7-tri-*O*-benzyl-1,2-dideoxy-1-nitro-D-*allo*-hept-1-enitol (**21**) in 84% yield. While both vinyl protons in **21** were



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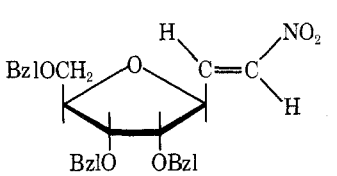

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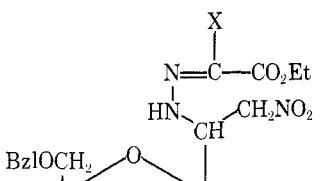
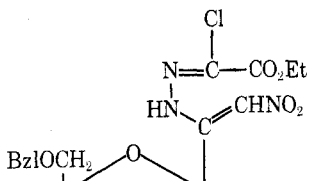


22a, X = H
b, X = Cl



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masked by the aromatic resonances, the absence of any vinyl signal near 6.0 ppm strongly suggests that the product has the *E* configuration.[30]

The nitroolefin **21** reacted readily with **16** to form a mixture of diastereomeric nitro esters (**22a**) in 59% yield. While both diastereomers are suitable for subsequent steps, the major, more polar one could be isolated in crystalline form. We are not able to assign specific stereochemistry to the crystalline isomer at this time. As was the case with the model compound **17a,** careful low-temperature chlorination of **22a** led to the chlorohydrazone **22b,** which was isolated as an analytically pure syrup by preparative TLC in 84% yield. If, however, the chlorination reaction mixture was allowed to warm up before excess chlorine was removed, the crystalline nitroolefin **23** was isolated as a major product. Unfortunately, we have been unable to effect cyclization of **22b** by treatment with triethylamine or with other tertiary bases such diisopropylethylamine and 1,5-diazabicyclo[4.3.0]non-5-ene. Using these bases in different solvents and at various temperatures **22b** either remained unchanged or underwent extensive decomposition. It would thus appear that this route is not well suited for the preparation of the desired nitropyrazole *C*-glycosides.

Forthcoming papers in this series will describe our work on totally different routes toward the synthesis of pyrazomycin[17] and of purine-related *C*-glycosides.

Experimental Section

The general analytical methods used are similar to those described previously.[5] We are particularly grateful to Dr. M. L. Maddox and Mrs. J. Nelson for their continuous help with NMR spectroscopy.

2,5-Anhydro-3,4,6-tri-*O*-benzoyl-D-allonamidoxime (2a). A. A solution of 2,3,5-tri-*O*-benzoyl-β-D-ribofuranosylcyanide (**1,** 500 mg, 1.06 mmol)[11,4] and free base hydroxylamine [from 100 mg (1.4 mmol) of the hydrochloride][31] in methanol (40 ml) was heated at 50° for 12 hr. The solvent was then evaporated and the residue was purified by preparative TLC using benzene–acetone (9:1), which separated one principal product from several more polar by-products. Elution of the major band gave 180 mg (34%) of **2a** as a TLC-homogeneous syrup: λ_{max} (MeOH) 229 nm (ε 39,600), 274 (2900), 281 (2400); $[\alpha]^{23}D$ −17.9° (*c* 0.6, $CHCl_3$); NMR (acetone-d_6) 4.70 ppm (m, 3, C_5H, C_6H_2), 4.77 (d, 1, $J_{2,3}$ = 5 Hz, C_2H), 5.20 (br s, 2, NH_2), 5.87 (dd, 1, $J_{3,4}$ = 5, $J_{4,5}$ = 10 Hz, C_4H), 6.00 (dd, 1, C_3H), 7.5 (m, 9, Ar), 8.0 (m, 6, Ar).

Anal. Calcd for $C_{27}H_{24}N_2O_8$ (504.48): C, 64.28; H, 4.80; N, 5.55. Found: C, 64.52; H, 4.89; N, 5.44.

B. A solution of **8a** [regenerated from 10.0 g (15 mmol) of the diphenylimidazolidine derivative as previously described[4]] and hydroxylamine hydrochloride (5.0 g, 75 mmol) in ethanol (125 ml) and pyridine (125 ml) was heated under reflux for 2 hr and then evaporated to dryness. The residue was dissolved in chloroform (600 ml), washed with 5% aqueous sodium bisulfate, aqueous sodium bicarbonate, and water, dried ($MgSO_4$), and evaporated, leaving 7.0 g (97%) of oxime **3** that was identical by TLC (ether–hexane, 2:1) with an authentic sample.[1] This material was dissolved in ether (100 ml), cooled to −70°, and treated with a stream of chlorine gas for 10 min. After a further 10 min at −70° the solvent was evaporated in vacuo and the residue was coevaporated with benzene. The resulting chloro oxime (**4**)[1] was dissolved in ether (200 ml) and added to a saturated solution of ammonia in ether (1 l.) at 0°. After 12 hr at 0° the solvent was evaporated and the residue was dissolved in ether, washed twice with water, dried ($MgSO_4$), and evaporated, leaving 6.74 g (92% from **3**) of **2a** that was homogeneous by TLC and NMR analysis.

2,5-Anhydro-D-allonamidoxime (2b). A solution of **2a** (1.0 g, 1.98 mmol) is saturated methanolic ammonia was stored overnight at room temperature and then evaporated to dryness. The residue was purified by chromatography on a column of silicic acid (100 g) using chloroform–methanol (7:3), giving 350 mg (92%) of homogeneous **2b** as a clear syrup. Attempted crystallization from 2-propanol gave **2b** only as an amorphous, very hygroscopic solid: $[\alpha]^{23}D$ −30.8° (*c* 0.3, MeOH); NMR (pyridine-d_5–D_2O) 4.00 (dd, 1, J_{gem} = 13, $J_{5,6a}$ = 2.5 Hz, $C_{6a}H$), 4.15 (dd, 1, $J_{5,6b}$ = 3 Hz, $C_{6b}H$), 4.43 (m, 1, C_5H), 4.74 (m, 2, C_3H and C_4H), 4.94 ppm (d, 1, $J_{2,3}$ = 3 Hz, C_2H).

Anal. Calcd for $C_6H_{12}N_2O_5$ (192.18): C, 37.50; H, 6.30; N, 14.58. Found: C, 37.78; H, 6.31; N, 13.94.

3-(2,3,5-Tri-*O*-benzoyl-β-D-ribofuranosyl)-5-methyl-1,2,4-oxadiazole (5a). A solution of **2a** (3.0 g, 5.9 mmol) in acetic anhydride (70 ml) was heated under reflux and in the dark for 12 hr in a nitrogen atmosphere. Evaporation of the solvent left a dark syrup that was coevaporated several times with dioxane and then chromatographed on a column of silicic acid using benzene–acetone

(98:2). The major product was 1.5 g (48%) of **5a**, which was obtained as a homogeneous foam: λ_{max} (MeOH) 229 nm (ε 37,500), 274 (2900), 281 (2300); $[\alpha]^{23}D$ −22.8° (*c* 0.6, $CHCl_3$); NMR ($CDCl_3$) 2.48 (s, 3, C_5Me), 4.7 (m, 3, $C_{4'}H$, $C_{5'}H_2$), 5.42 (d, 1, $J_{1',2'}$ = 3 Hz, $C_{1'}H$), 5.98 (narrow m, 2, $C_{2'}H$, $C_{3'}H$), 7.4 (m, 9, Ar), 8.0 ppm (m, 6, Ar).

Anal. Calcd for $C_{29}H_{24}N_2O_8$ (528.50); C, 65.90; H, 4.58; N, 5.30. Found: C, 65.79; H, 4.71; N, 5.29.

5-Methyl-3-(β-D-ribofuranosyl)-1,2,4-oxadiazole (5b). A solution of **5a** (280 mg, 0.53 mmol) in methanol (10 ml) was mixed with saturated methanolic ammonia (5 ml) and stored at room temperature for 48 hr. Following evaporation of the solvent the residue was chromatographed on a column of Merck silica gel G (50 g) using chloroform–methanol (19:1), giving 80 mg (70%) of **5b** as a homogeneous, clear syrup: uv (MeOH) only end absorption; $[\alpha]^{23}D$ −30.9° (*c* 0.2, MeOH); NMR (pyridine-d_5) 2.29 (s, 3, C_5Me), 4.09 (dd, 1, J_{gem} = 14, $J_{4',5'a}$ = 4 Hz, $C_{5'a}H$), 4.20 (dd, 1, $J_{4',5'b}$ = 4 Hz, $C_{5'b}H$), 4.66 (ddd, 1, $J_{3',4'}$ = 4 Hz, $C_{4'}H$), 4.81 (dd, $J_{2',3'}$ = 4 Hz, $C_{3'}H$), 4.97 (dd, 1, $J_{1',2'}$ = 5 Hz, $C_{2'}H$), 5.52 ppm (d, 1, $C_{1'}H$).

Anal. Calcd for $C_8H_{12}N_2O_5$ (216.19): C, 44.44; H, 5.60; N, 12.96. Found: C, 44.18; H, 5.63; N, 12.98.

3-(2,3,5-Tri-*O*-benzoyl-β-D-ribofuranosyl)-5-methyl-Δ²-1,2,4-oxadiazoline (6). A solution of **2a** (150 mg, 0.3 mmol) and acetaldehyde (2.5 ml) in ethanol (5 ml) and water (2.5 ml) was stored at room temperature for 3 days. The mixture was then evaporated to dryness and the residue, which still contained **2a**, was purified by preparative TLC using benzene–acetone (9:1), giving 75 mg (47%) of **6** as a syrupy, diastereomeric mixture: λ_{max} (MeOH) 230 nm (ε 31,400), 273 (3200), 281 (2500); $[\alpha]^{23}D$ −79.2° (*c* 0.4, $CHCl_3$); the NMR spectrum ($CDCl_3$) was complex owing to the presence of two diastereomers.

Anal. Calcd for $C_{29}H_{26}N_2O_8$ (530.51): C, 65.65; H, 4.94; N, 5.28. Found: C, 65.29; H, 4.92; N, 5.28.

Treatment of **6** (10 mg) with ~1 *M* chlorine in carbon tetrachloride (1 ml) in the dark for 10 min led to complete dehydrogenation, giving **5a**. Following isolation by TLC the ir and NMR spectra of the latter were identical with those of **5a** prepared using acetic anhydride as above.

5-Acetonyl-3-(2,3,5-tri-*O*-benzoyl-β-D-ribofuranosyl)-1,2,4-oxadiazole (7). A solution of **2a** (100 mg, 0.2 mmol) and ethyl acetoacetate (400 mg, 3.1 mmol) in toluene (50 ml) was heated under reflux for 48 hr. The solvent was then evaporated and the residue was purified by preparative TLC using benzene–acetone (9:1), giving 70 mg (61%) of **7** as a homogeneous syrup: λ_{max} (MeOH) 230 nm (ε 38,900), 274 (5400); $[\alpha]^{23}D$ −41.6° (*c* 0.3, $CHCl_3$); NMR ($CDCl_3$) 2.22 (s, 3, $COCH_3$), 3.91 (s, 2, CH_2CO), 4.75 (m, 3, $C_{4'}H$, $C_{5'}H_2$), 5.46 (d, 1, $J_{1',2'}$ = 3 Hz, $C_{1'}H$), 6.00 (m, 2, $C_{2'}H$, $C_{3'}H$), 7.4 (m, 9, Ar), 8.0 ppm (m, 6, Ar).

Anal. Calcd for $C_{31}H_{26}N_2O_9$ (570.54): C, 65.26; H, 4.59; N, 4.91. Found: C, 65.06; H, 4.45; N, 4.83.

(*Z*)-5,8-Anhydro-6,7,9-tri-*O*-benzoyl-3-chloro-1,3,4-trideoxy-D-*allo*-non-3-eneulose (10a). 2,5-Anhydro-3,4,6-tri-*O*-benzoyl-D-allose (**8a**) was regenerated from its diphenylimidazolidine derivative (8.25 g, 12.35 mmol) as previously described.[4] The directly obtained aldehyde was dissolved together with 1-chloroacetonylidenetriphenylphosphorane (12.0 g, 34 mmol)[20] in methylene chloride (500 ml) and stirred at room temperature for 18 hr. The solution was then washed with water, dried ($MgSO_4$), and evaporated. The residue was chromatographed on a column of silicic acid using ether–hexane (2:1), giving 5.30 g (78%) of **10a** as a foam that contained a single geometric isomer: λ_{max} (MeOH) 230 nm (ε 49,100), 274 (3300), 281 (2600); $[\alpha]^{23}D$ −36.9° (*c* 0.3, $CHCl_3$); NMR ($CDCl_3$) 2.33 (s, 3, $COCH_3$), 4.54 (dd, 1, J_{gem} = 13, $J_{8,9a}$ = 3.5 Hz, $C_{9a}H$), 4.6–4.8 (m, 2, C_8H, $C_{9b}H$), 5.30 (dd, 1, $J_{4,5}$ = 7.5, $J_{5,6}$ = 6 Hz, C_5H), 5.59 (dd, 1, $J_{6,7}$ = 6 Hz, C_6H), 5.73 (dd, 1, $J_{7,8}$ = 9 Hz, C_7H), 6.86 (d, 1, C_4H), 7.4 (m, 9, Ar), 8.0 (m, 6, Ar).

Anal. Calcd for $C_{30}H_{25}O_8Cl$ (548.96): C, 65.63; H, 4.59; Cl, 6.46. Found: C, 65.79; H, 4.74; Cl, 6.05.

5,8-Anhydro-6,7,9-tri-*O*-benzyl-3-chloro-1,3,4-trideoxy-D-*allo*-non-3-eneulose (10b). 2,5-Anhydro-3,4,6-tri-*O*-benzyl-D-allose (**8b**) was regenerated from its diphenylimidazolidine derivative (1.30 g, 2.07 mmol) as previously described.[4] The crude aldehyde was then treated with 1.5 g (4.2 mmol) of **9** in methylene chloride (100 ml) at room temperature for 14 hr. The mixture was washed with water, evaporated, and purified by chromatography on a column of silicic acid using ether–hexane (2:1), giving 910 mg (87%) of **10b** as a roughly 4:1 mixture of geometrical isomers, λ_{max} (MeOH) 244 nm (ε 10,300).

Anal. Calcd for $C_{30}H_{31}O_5Cl$ (507.01): C, 71.06; H, 6.16. Found: C, 70.96; H, 6.08.

In a separate experiment a sample of this mixture was separated into its geometric isomers by preparative TLC using ether–hexane (9:1). The NMR spectrum of the major, more polar *Z* isomer (**10b**) in $CDCl_3$ showed 2.06 (s, 3, $COCH_3$), 3.51 (dd, 1, J_{gem} = 11, $J_{8,9a}$ = 3 Hz, $C_{9a}H$), 3.70 (dd, 1, $J_{8,9b}$ = 2.5 Hz, $C_{9b}H$), 3.88 (dd, 1, $J_{5,6}$ = 3, $J_{6,7}$ = 4.5 Hz, C_6H), 4.04 (dd, 1, $J_{7,8}$ = 7 Hz, C_7H), 4.28 (m, 1, C_8H), 4.45–4.7 (m, 6, OCH_2Ar), 5.07 (dd, 1, $J_{4,5}$ = 7 Hz, C_5H), 6.80 (d, 1, C_4H), 7.3 ppm (m, 15, Ar).

The NMR spectrum of the less polar *E* isomer ($CDCl_3$) showed 3.50 (dd, 1, J_{gem} = 11, $J_{8,9a}$ = 3 Hz, $C_{9a}H$), 3.70 (dd, 1, $J_{8,9b}$ = 2.5 Hz, $C_{9b}H$, 3.81 (dd, 1, $J_{5,6}$ = 2, $J_{6,7}$ = 4.5 Hz, C_6H), 4.00 (dd, 1, $J_{7,8}$ = 8 Hz, C_7H), 4.24 (m, 1, C_8H), 4.30, 4.42, 4.49, 4.58, 4.74, and 4.91 (d, 1, J_{gem} = 12–13 Hz, CH_2Ar), 5.20 (dd, 1, $J_{4,5}$ = 8 Hz, C_5H), 6.30 (d, 1, C_4H), 7.30 ppm (m, 15, Ar).

3-(2,3,5-Tri-*O*-benzoyl-β-D-ribofuranosyl)-5-methylpyrazole (11a). A solution of **10a** (5.30 g, 9.65 mmol) and 85% hydrazine hydrate (5.0 ml, ~100 mmol) in glacial acetic acid (250 ml) was heated under reflux for 18 hr. The cooled solution was evaporated to dryness and the residue was triturated with ethyl acetate (500 ml) and filtered. The filtrate was washed with aqueous sodium bicarbonate, dried, and evaporated, leaving a residue that was purified by chromatography on a column of silicic acid using benzene–ether (2:3). Evaporation of the major product left 3.50 g (69%) of **11a** as a syrup: λ_{max} (MeOH) 229 nm (ε 41,400), 274 (3900), 279 (sh, 3100); $[\alpha]^{23}D$ −3.2° (*c* 0.2, $CHCl_3$); NMR ($CDCl_3$) 2.21 (s, 3, CH_3), 4.69 (m, 3, $C_{4'}H$, $C_{5'}H_2$), 5.36 (m, 1, virtually coupled to $C_{3'}H$, $C_{1'}H$), 5.80 (m, 2, $C_{2'}H$, $C_{3'}H$), 6.05 (s, 1, C_4H), 7.3 (m, 9, Ar), 7.9 (m, 6, Ar), 8.90 ppm (br s, 1, NH).

Anal. Calcd for $C_{30}H_{26}N_2O_7$ (526.53): C, 68.48; H, 4.98; N, 5.32. Found: C, 68.10; H, 4.96; N, 5.15.

5-Methyl-3-(β-D-ribofuranosyl)pyrazole. (11b). A. A solution of **11a** (1.0 g, 1.9 mmol) in saturated methanolic ammonia (100 ml) was kept at room temperature for 12 hr and then evaporated to dryness. The residue was partitioned between ethyl acetate and water and the aqueous phase was evaporated to a syrup. The latter was dissolved in water (3 ml) and applied to a 1 × 15 cm column of freshly regenerated Bio-Rad AG-1-X2 resin. After a water wash the column was eluted with a gradient of 10–50% methanol in water, the elution being followed by TLC using chloroform–methanol (7:3). Evaporation of the pooled major peak gave 120 mg (30%) of **11b** as an amorphous solid that was homogeneous by NMR: λ_{max} (MeOH) 216 nm (ε 5100); $[\alpha]^{23}D$ −37.7° (*c* 0.3, H_2O); ORD (MeOH) $[\Phi]_{226}$ (tr) −1300°, $[\Phi]_{200}$ 0°; NMR (pyridine-d_5) 2.22 (s, 3, CH_3), 4.12 (dd, 1, J_{gem} = 12, $J_{4',5'a}$ = 3.5 Hz, $C_{5'a}H$), 4.28 (dd, 1, $J_{4',5'b}$ = 3.5 Hz, $C_{5'b}H$), 4.63 (m, 1, $C_{4'}H$), 4.81 (m, 2, $C_{2'}H$, $C_{3'}H$), 5.55 (d, 1, $J_{1',2'}$ = 4.5 Hz, $C_{1'}H$), 6.26 ppm (s, 1, C_4H).

Anal. Calcd for $C_9H_{14}N_2O_4$ (214.22): C, 50.46; H, 6.59; N, 13.08. Found: C, 50.54; H, 6.78; N, 12.99.

B. A solution of **11c** (100 mg, 0.20 mmol) in tetrahydrofuran (3 ml) was added to liquid ammonia (50 ml) and then small pieces of freshly cut sodium were added until a blue color persisted. The mixture was kept for an additional 10 min and then solid ammonium chloride (1 g) was added. The solvent was evaporated with a stream of argon and a solution of the resulting white residue in water was passed through a column (30 ml) of Dowex 50 (H^+) resin. The resin was washed with water and then eluted with dilute ammonia, giving a material that still retained some salt. This was purified by preparative TLC using chloroform–methanol (7:3) giving 35 mg (83%) of **11b** that was homogeneous by TLC and identical with that from A above.

C. Attempted debenzoylation of **11a** using methanolic sodium methoxide at room temperature overnight led to **11b** that was contaminated with some very close-moving impurities that were difficult to remove by preparative TLC.

3-(2,3,5-Tri-*O*-benzyl-β-D-ribofuranosyl)-5-methylpyrazole (11c). A solution of **10b** (800 mg, 1.6 mmol) and 85% hydrazine hydrate (1 ml) in glacial acetic acid (50 ml) was heated under reflux for 12 hr and then worked up as above for **11a**. Preparative TLC using two developments with benzene–ether (3:2) gave 430 mg (56%) of **11c** as a syrup: λ_{max} (MeOH) 252 nm (ε 700), 259 (800), 264 (600), 268 (500); $[\alpha]^{23}D$ 9.9° (*c* 0.08, $CHCl_3$); NMR ($CDCl_3$) 2.22 (s, 3, CH_3), 3.52 (dd, 1, J_{gem} = 11, $J_{4',5'a}$ = 3 Hz, $C_{5'a}H$), 3.75 (dd, 1, $J_{4',5'b}$ = 3.5 Hz, $C_{5'b}H$), 3.96 (dd, 1, $J_{1',2'}$ = 3.5, $J_{2',3'}$ = 4.5 Hz, $C_{2'}H$), 4.08 (dd, 1, $J_{3',4'}$ = 6.5 Hz, $C_{3'}H$), 4.26 (m, 1, $C_{4'}H$), 4.38, 4.42, 4.47, 4.63 (d, 1, J_{gem} = 12 Hz, OCH_2Ar), 4.61 (s, 2, $C_{5'}O$-CH_2Ar), 5.15 (d, 1, $C_{1'}H$), 5.86 (s, 1, C_4H), 7.25 ppm (m, 15, Ar).

Anal. Calcd for $C_{30}H_{32}N_2O_4$ (484.57): C, 74.35; H, 6.66; N, 5.78. Found: C, 74.37; H, 6.60; N, 5.89.

(*E*)-5,8-Anhydro-6,7,9-tri-*O*-benzyl-1,3,4-trideoxy-D-*allo*-non-3-eneulose (12). A solution of **8b** [regenerated, as above, from

4.05 g (6.5 mmol) of the diphenylimidazolidine derivative][4] and acetonylidenetriphenylphosphorane (4.2 g, 13 mmol) were allowed to react in methylene chloride (500 ml) at room temperature for 16 hr. The solution was washed with water, evaporated to dryness, and chromatographed on a column of silicic acid using ether–hexane (2:1), giving 2.6 g (85%) of a single geometrical isomer (**12**) as a syrup: λ_{max} (MeOH) 225 nm (sh, ϵ 9400); $[\alpha]^{23}D$ −14.6° (*c* 0.2, $CHCl_3$); NMR ($CDCl_3$) 2.10 (s, 3, $COCH_3$), 3.51 (d, 1, $J_{8,9}$ = 4 Hz, C_9H_2), 3.70 (dd, 1, $J_{5,6}$ = 6.5, $J_{6,7}$ = 5 Hz, C_6H), 3.91 (dd, 1, $J_{7,8}$ = 4 Hz, C_7H), 4.24 (dt, 1, C_8H), 4.45–4.6 (m, 6, CH_2Ar), 4.6 (under CH_2Ar, 1, C_5H), 6.27 (dd, 1, $J_{3,4}$ = 16, $J_{3,5}$ = 1 Hz, C_3H), 6.62 (dd, 1, $J_{4,5}$ = 5 Hz, C_4H), 7.3 ppm (m, 15, Ar).

Anal. Calcd for $C_{30}H_{32}O_5$ (472.56); C, 76.24; H, 6.83. Found: C, 75.87; H, 6.86.

***N*-Acetyl-3-(2,3,5-tri-*O*-benzyl-β-D-ribofuranosyl)-5-methylpyrazoline (13).** A solution of **12** (2.6 g, 5.5 mmol) and 90% hydrazine hydrate (2.5 g, ~50 mmol) in glacial acetic acid (200 ml) was heated at 100° for 1.5 hr. After evaporation of the cooled solution the residue was dissolved in chloroform, washed with aqueous sodium bicarbonate and water, dried, and evaporated. The residue was chromatographed on a column of silicic acid (200 g) using chloroform–ethyl acetate (10:3). Crystallization of the major product from ethyl acetate–hexane gave 2.15 g (74%) of a roughly equal mixture of diastereomers of **13** with mp 114–116°: λ_{max} (MeOH) 238 nm (ϵ 11,700); $[\alpha]^{23}D$ 129.9° (*c* 1.0, $CHCl_3$); ir (KBr) 1645 cm^{-1} (NAc), no NH or amide II: NMR ($CDCl_3$) 1.86 (s, 3, $COCH_3$), 2.13 and 2.19 (s, total 3, CH_3), 2.70 ppm (m, 2, C_4H_2), other sugar protons appearing as doubled signals in the expected regions.

Anal. Calcd for $C_{32}H_{36}N_2O_5$ (528.62): C, 72.70; H, 6.86; N, 5.30. Found: C, 72.38; H, 6.79; N, 5.30.

4-Bromo-5-methyl-3-(2,3,5-tri-*O*-benzoyl-β-D-ribofuranosyl)pyrazole (14). Bromine (0.25 ml) was added to a solution of **11a** (100 mg, 0.19 mmol) in chloroform (20 ml) and the mixture was heated under reflux for 1.5 hr. The mixture was diluted with chloroform, washed with aqueous bicarbonate and water, dried ($MgSO_4$), and evaporated, leaving a solid residue. The latter was purified by preparative TLC using benzene–ether (3:2), giving 100 mg (87%) of **14** as a homogeneous foam: λ_{max} (MeOH) 230 nm (ϵ 42,300), 275 (3100), 282 (2500); $[\alpha]^{23}D$ −27.1° (*c* 0.2, $CHCl_3$); NMR ($CDCl_3$) 2.21 (s, 3, CH_3), 4.70 (apparent s, 3, $C_{4'}H$, $C_{5'}H_2$), 5.42 (d, 1, $J_{1',2'}$ = 4.5 Hz, $C_{1'}H$), 5.98 (m, 2, $C_{2'}H$, $C_{3'}H$), 7.35 (m, 9, Ar). 7.95 ppm (m, 6, Ar).

Anal. Calcd for $C_{30}H_{25}N_2O_7Br$ (605.44): C, 59.51; H, 4.16; N, 4.63. Found: C, 59.45; H, 4.27; N, 4.79.

Ethyl N^2-(2-Nitro-1-phenylethyl)glyoxylate Hydrazone (17a). A solution of β-nitrostyrene (7.7 g, 52 mmol) and (*E*)-ethyl glyoxylate hydrazone (**16**, 6.0 g, 52 mmol)[32] in tetrahydrofuran (200 ml) was heated under reflux for 48 hr. Following evaporation of the solvent the residue was chromatographed on a column of silicic acid using ether–hexane (2:1) and the major product was crystallized from chloroform–hexane, giving 5.0 g (36%) of **17a** with mp 93–94°: λ_{max} (MeOH) 280 nm (ϵ 16,600); NMR ($CDCl_3$) 1.28 (t, 3, CH_3), 4.21 (q, 2, OCH_2), 4.67 (dd, 1, J_{gem} = 13, J_{vic} = 5 Hz, NO_2CH), 5.01 (dd, 1, J_{vic} = 7.5 Hz, NO_2CH), 5.23 (m, 1, ArCH), 6.84 (s, 1, N=CH), 7.04 (d, 1, NH), 7.30 ppm (s, 5, Ar).

Anal. Calcd for $C_{12}H_{15}N_3O_4$ (265.26): C, 54.33; H, 5.70; N, 15.84. Found: C, 53.94; H, 5.67; N, 15.58.

Ethyl N^2-(2-Nitro-1-phenylethyl)-2-chloroglyoxylate Hydrazone (17b). A solution of chlorine in carbon tetrachloride (13.2 ml of 1.36 *M*, 18.5 mmol) was added dropwise over 30 min to a stirred solution of **17a** (1.0 g, 3.8 mmol) in methylene chloride (30 ml) at −70°. The solvent was then evaporated in vacuo (below 0°) and the residue was crystallized from chloroform–hexane, giving 790 mg (70%) of **17b** with mp 77–78°: λ_{max} (MeOH) 276 nm (λ 17,300); ir (KBr) 1710 (CO), 1550 cm^{-1} (NO_2); mass spectrum (70 eV) *m/e* 299, 301 (M^+), 252, 254, (M − HNO_2), 239, 241 (M − CH_2NO_2), 104 ($ArCH{=}CH_2$); NMR ($CDCl_3$) 1.32 (t, 3, CH_3), 4.28 (q, 2, OCH_2), 4.67 (dd, 1, J_{gem} = 12.5, J_{vic} = 5 Hz, $CHNO_2$), 5.08 (dd, 1, J_{vic} = 8 Hz, $CHNO_2$), 5.33 (ddd, 1, $J_{H,NH}$ = 4 Hz, ArCH), 6.91 (d, 1, NH), 7.32 ppm (s, 5, Ar).

Anal. Calcd for $C_{12}H_{14}N_3O_4Cl$ (299.75): C, 48.09; H, 4.71; N, 14.02. Found: C, 47.95; H, 4.58; N, 13.87.

Ethyl N^2-(2-Nitro-1'-phenylvinyl)-2-chloroglyoxylate Hydrazone (18). A reaction similar to that for preparation of **17b** was conducted on 320 mg (1.2 mmol) of **17a** but using a large excess of chlorine and allowing the mixture to gradually warm to room temperature during the addition. Under these conditions a new yellow spot with an R_f just greater than that of **17b** was gradually formed. Following evaporation of the solvent the residue was purified by preparative TLC using two developments with ether–hexane (1:1). Elution of the slower of the resulting two bands gave 100 mg (30%) of **17b** identical with that above while the faster band gave 80 mg (22%) of **18** with mp 124–125° from chloroform–hexane: λ_{max} (MeOH) 220 nm (ϵ 8600), 273 (10,600), 370 (18,400); ir (KBr) 1725 (CO), 1615 (Ar), 1565 (NO_2), 1500 cm^{-1} (Ar); mass spectrum (70 eV) *m/e* 297, 299 (M^+), 251, 253, (M − EtOH), 216 (*m/e* 251 − Cl), 103, 77 (C_6H_5); NMR ($CDCl_3$) 1.26 (t, 3, CH_3), 4.28 (q, 2, OCH_2), 6.80 (s, 1, $C{=}CHNO_2$), 7.50 ppm (s, 5, Ar).

Anal. Calcd for $C_{12}H_{123}O_4Cl$ (297.75): C, 48.41; H, 4.06; N, 14.11. Found: C, 48.26; H, 4.18; N, 13.71.

3-Ethoxycarbonyl-5-phenylpyrazole (19). A solution of **17b** (100 mg) in triethylamine (1 ml) and tetrahydrofuran (10 ml) was heated under reflux overnight. The solvent was evaporated and the residue was partitioned between chloroform and water. The dried organic phase was purified by preparative TLC using ether–hexane (2:1). Elution of the major band and crystallization from ether–hexane gave 10 mg (14%) of **19** with mp 139–141° (reported[27] mp 140°): mass spectrum (70 eV) *m/e* 216 (M^+), 170 (M − EtOH), 142 (*m/e* 170 − CO); NMR ($CDCl_3$) 1.25 (t, 3, CH_3), 4.23 (q, 2, OCH_2), 7.00 (s, 1, C_4H), 7.35 (m, 3, Ar), 7.70 ppm (m, 2, Ar).

3,6-Anhydro-4,5,7-tri-*O*-benzyl-1-deoxy-1-nitro-D-*glycero*-D-*altro*-heptitol (20). A solution of **8b** [regenerated from 4.0 g (6.40 mmol) of the diphenylimidazolidine derivative[4]] in a mixture of methanol (200 ml) and nitromethane (20 ml) was stirred at 0° while methanolic sodium methoxide (10 ml of 0.48 *M*) was added dropwise. After an additional 1 hr at 0° the mixture was neutralized with Dowex 50 (H^+) resin, filtered, and evaporated. The residue was partitioned between chloroform and water, the dried organic phase was evaporated and the residue was crystallized from ether–hexane, giving 2.35 g (74%) of **20** with mp 42–44°: λ_{max} (MeOH) 207 nm (ϵ 31,500), 247 (500), 252 (600), 258 (750), 264 (600), 267 (400); $[\alpha]^{23}D$ −12.4° (*c* 0.18, $CHCl_3$); ORD (MeOH) $[\Phi]_{320}$ (pk) 1100°, $[\Phi]_{284}$ 0°, $[\Phi]_{229}$ (tr) −3000°, $[\Phi]_{220}$ 0°; ν_{max} (KBr) 1555 cm^{-1} (NO_2); NMR ($CDCl_3$) 3.19 (br s, 1, C_2OH), 3.38 (dd, 1, J_{gem} = 10.5, $J_{6,7a}$ = 3 Hz, $C_{7a}H$), 3.58 (dd, 1, $J_{6,7b}$ = 3 Hz, $C_{7b}H$), 4.00 (s, 2, C_4H, C_5H), 4.17 (m, 1, C_6H), 4.3–4.6 (m, 10, C_1H_2, C_2H, C_3H, and CH_2Ar), 7.27 ppm (m, 15, Ar).

Anal. Calcd for $C_{28}H_{31}NO_7$ (493.54): C, 68.14; H, 6.33; N, 2.84. Found: C, 68.00; H, 6.54; N, 2.98.

(*E*)-3,6-Anhydro-4,5,7-tri-*O*-benzyl-1,2-dideoxy-1-nitro-D-*allo*-hept-1-eneitol (21). A solution of acetic anhydride (1 ml) and pyridine (2 ml) in benzene (5 ml) was added to a stirred solution of **20** (1.5 g, 3.0 mmol) in benzene at 0°. After storage overnight at 4° the solvent was evaporated and the residue was dissolved in chloroform and washed with aqueous sodium bicarbonate and water. The dried organic phase was evaporated and purified by preparative TLC using ether–hexane (2:1). Elution of the major band gave 1.20 g (84%) of **21** as a syrup: λ_{max} (MeOH) 245 nm (sh, ϵ 4100), 250 (sh, 4050), 257 (sh, 3800); $[\alpha]^{23}D$ −17.6° (*c* 0.3, $CHCl_3$); NMR ($CDCl_3$) 3.44 (dd, 1, J_{gem} = 11, $J_{6,7a}$ = 3.5 Hz, $C_{7a}H$), 3.56 (dd, 1, $J_{6,7b}$ = 3.5 Hz, $C_{7b}H$), 3.76 (dd, 1, $J_{3,4}$ = 6.5 Hz, C_4H), 3.95 (dd, 1, $J_{4,5}$ = 4.5 Hz, C_5H), 4.23 (dt, 1, $J_{5,6}$ = 3.5 Hz, C_6H), 4.35–4.7 (m, 7, C_3H and CH_2Ar), 7.1–7.35 ppm (m, 17, C_1H, C_2H, and Ar).

Anal. Calcd for $C_{28}H_{29}NO_6$ (475.52): C, 70.20; H, 6.15; N, 2.95. Found: C, 70.42; H, 6.31; N, 2.69.

2-(2,3,5-Tri-*O*-benzyl-β-D-ribofuranosyl)-2-(2-carboethoxymethylenehydrazino)-1-nitroethane (22a). A solution of **21** (3.0 g, 6.3 mmol) and **16** (4 g, 34 mmol)[32] in tetrahydrofuran (100 ml) was stored at room temperature for 48 hr. Following evaporation of the solvent the residue was purified by preparative TLC using CCl_4–ethyl acetate (4:1), giving 2.2 g (59%) of **22a** as a mixture of isomers suitable for direct use in the next step. A portion of this material was separated into its diastereomers by further preparative TLC using two developments with chloroform–ethyl acetate (10:1). The major, more polar isomer was then crystallized from ethyl acetate–hexane with mp 83–87°: λ_{max} (MeOH) 283 nm (ϵ 12,400); $[\alpha]^{23}D$ 36.7° (*c* 0.1, $CHCl_3$); NMR ($CDCl_3$) 1.28 (t, 3, CH_3), 3.37 (dd, 1, J_{gem} = 10.5, $J_{4',5'a}$ = 3 Hz, $C_{5'a}H$), 3.54 (dd, 1, $J_{4',5'b}$ = 3.5 Hz, $C_{5'b}H$), 3.93 (m, 1, $C_{2'}H$), 4.22 (q, 2, OCH_2CH_3), 4.1–4.8 (m, 12, CH_2CH, $C_{1'}H$, $C_{3'}H$, $C_{4'}H$, OCH_2Ar), 6.68 (s, 1, N=CH), 7.25 ppm (m, 15, Ar).

Anal. Calcd for $C_{32}H_{37}N_3O_8$ (590.63): C, 65.07; H, 6.14; N, 7.11. Found: C, 65.27; H, 6.28; N, 6.93.

Chlorination of the Hydrazone 22a. A. A 7.3% solution of chlorine in carbon tetrachloride (3 ml) was added dropwise to a stirred solution of **22a** (250 mg, 0.42 mmol) in tetrahydrofuran at −65°. After 15 min TLC using carbon tetrachloride–ethyl acetate (4:1) showed complete conversion of **22a** to a faster spot and excess chlorine was removed with a stream of nitrogen at −60°. The sol-

vent was then evaporated in vacuo below 0° and the resulting syrup was purified by preparative TLC using CCl_4–ethyl acetate (4:1). Elution of the major band gave 220 mg (84%) of the chlorohydrazone **22b** as a very pale yellow oil: λ_{max} (MeOH) 274 nm (ε 13,700); $[\alpha]^{23}D$ −0.7° (*c* 0.7, $CHCl_3$); NMR ($CDCl_3$) 1.31 (t, 3, CH_3), 3.37 (dd, 1, J_{gem} = 12, $J_{4',5'a}$ = 3 Hz, $C_{5'a}H$), 3.52 (dd, 1, $J_{4',5'b}$ = 3.5 Hz, $C_{5'b}H$), 3.8–4.7 (m, 13), 4.30 (q, 2, OCH_2), 7.3 ppm (m, 15, Ar); mass spectrum (70 eV) *m/e* 626, 628 (M^+).

Anal. Calcd for $C_{32}H_{36}N_3O_8Cl$ (626.12): C, 61.39; H, 5.80; N, 6.71. Found: C, 61.17; H, 5.69; N, 6.43.

Elution of the faster yellow band gave 10 mg (4%) of crystalline **23** (see below).

B. The hydrazone **22a** (100 mg) was treated with chlorine in carbon tetrachloride (2 ml of 7.3%) at −60° as above in A, giving essentially a single spot of **22b.** The solvent was directly evaporated at room temperature and the residue was purified by preparative TLC using CCl_4–ethyl acetate (4:1), giving two well-resolved bands. Elution of the slower band gave 60 mg (57%) of **22b** identical with that above. Elution of the faster band gave 50 mg (46%) of the nitroolefin **23** that crystallized spontaneously. Recrystallization from ethyl acetate–hexane at −15° gave **23** as fine white needles with mp 107–108°: λ_{max} (MeOH) 263 nm (ε 9400), 366 (21,600); $[\alpha]^{23}D$ 69.6° (*c* 0.5, $CHCl_3$); NMR ($CDCl_3$) 1.24 (t, 3, CH_3), 3.60 (dd, 1, J_{gem} = 11, $J_{4',5'a}$ = 2.5 HZ, $C_{5'a}H$), 3.88 (dd, 1, $J_{4',5'b}$ = 1.5 Hz, $C_{5'b}H$), 4.05–5.05 (m, 11, $C_{2'}H$, $C_{3'}H$, $C_{4'}H$, OCH_2), 5.47 (s, $J_{allylic} \simeq 1$ Hz, $C_{1'}H$), 7.3 (m, 15, Ar), 7.55 (d, 1, $J_{allylic} \simeq 1$ Hz, $NO_2CH{=}C$), 12.1 ppm (s, 1, NH).

Anal. Calcd for $C_{32}H_{34}N_3O_8Cl$ (624.10): C, 61.58; H, 5.49; N, 6.73. Found: C, 61.46; H, 5.65; N, 6.58.

Registry No.—**1,** 23316-67-8; **2a,** 55428-60-9; **2b,** 55428-61-0; **3,** 50720-88-2; **4,** 50720-94-0; **5a,** 55428-62-1; **5b,** 55428-63-2; (*S*)-**6,** 55428-64-3; (*R*)-**6,** 55515-13-4; **7,** 55428-65-4; **8a,** 39037-99-5; **8b,** 37699-02-8; **9,** 6161-37-1; **10a,** 55428-66-5; **10b,** 55428-67-6; (*E*)-**10b,** 55428-68-7; **11a,** 55428-69-8; **11b,** 55428-70-1; **11c,** 55428-71-2; **12,** 55428-72-3; (*S*)-**13,** 55428-73-4; (*R*)-**13,** 55428-74-5; **14,** 55428-75-6; **16,** 55428-76-7; **17a,** 55428-77-8; **17b,** 55428-78-9; **18,** 55428-79-0; **19,** 5932-30-9; **20,** 55428-80-3; **21,** 55428-81-4; (*S*)-**22a,** 55428-82-5; (*R*)-**22a,** 55515-14-5; (*S*)-**22b,** 55428-83-6; (*R*)-**22b,** 55428-84-7; **23,** 55428-85-8; hydroxylamine, 7803-49-8; bromine, 7726-95-6; β-nitrostyrene, 102-96-5; chlorine, 7782-50-5.

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