C-Glycosyl Nucleosides. 9.[1] An Approach to the Synthesis of Purine-Related C-Glycosides

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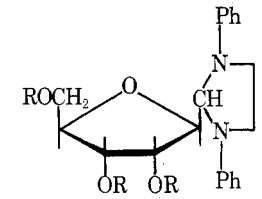
Several approaches to the synthesis of 4-(2,3,5-tri-*O*-benzyl-β-D-ribofuranosyl)-3(5)-carbomethoxypyrazole (**4b**) have been investigated. One route involves conversion of 2,5-anhydro-3,4,6-tri-*O*-benzyl-D-allose to the *C*-glycosyl acrylate **3** via a Wittig reaction followed by cycloaddition of diazomethane and dehydrogenation with chlorine. Alternatively **4b** could be directly prepared via cycloaddition of diazomethane to methyl 3-(2,3,5-tri-*O*-benzyl-β-D-ribofuranosyl)propiolate (**16a**). Condensation of 2,3,5-tri-*O*-benzyl-D-ribose with a Grignard reagent derived from propiolic acid gave, after esterification, an essentially stereoselective synthesis of methyl 5,6,8-tri-*O*-benzyl-2,3-dideoxy-D-*altro*-oct-2-ynonate (**7a**). Reaction of this material with diazomethane followed by acid-catalyzed cyclization gave the desired **4b**. While acid-catalyzed cyclization of **7a** was unsuccessful, reaction with methyltriphenoxyphosphonium iodide gave **16a** together with a number of isomeric products. Characterization of these substances was achieved by conversion to pyrazole derivatives and by use of ^{13}C NMR spectroscopy. The pyrazole ester **4b** was converted into a 3-aminopyrazole via a Curtius reaction on the acyl azide. Cyclization with phenoxycarbonyl isocyanate followed by debenzylation with boron trichloride gave the purine-related *C*-glycoside 2,4-dioxo-8-β-D-ribofuranosyl-1*H*,3*H*-pyrazolo[1,5-*a*]-1,3,5-triazine.

The natural occurrence of a number of *C*-glycosyl nucleosides,[3] some of which possess antibiotic or antitumor activities, has stimulated much recent effort toward the synthesis of this class of compound. In some cases a direct forging of the critical C–C glycosyl linkage has been successfully accomplished via condensation of an appropriate carbohydrate derivative with a suitably activated heterocyclic component.[4] A much more versatile route, however, involves the synthesis of functionally substituted anhydro sugar derivatives, already containing the elusive *C*-glycosyl bond, that can be further elaborated into a variety of heterocyclic substituents.[5] Our own activities have centered about this latter approach and have led to the development of efficient syntheses of a number of differently protected derivatives of 2,5-anhydro-D-allose.[6] The latter compounds have then been elaborated into a variety of maleimide,[1,7] pyrazole,[8] isoxazole,[9] and 1,2,4-oxadiazole[8b] *C*-glycosides. In addition, we have developed stereochemically controlled methods for the synthesis of other functionally substituted anhydro sugars.[10] These compounds, which have also been briefly reported on by others,[11] provide attractive intermediates for the synthesis of further *C*-glycosyl nucleosides.[12]

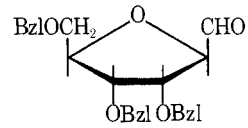
While the above methods have been rather successful for the synthesis of five- and six-membered heterocyclic ring *C*-glycosides, the development of routes leading to condensed heterocyclic *C*-glycosides related to purine nucleosides has been considerably more difficult. Quite facile routes to 2- and 8-ribofuranosyladenines and their sugar analogues are available,[13] but the preparation of the more interesting purine nucleoside analogues in which the *C*-glycosyl linkage is adjacent to the heterocyclic ring junction is challenging. Toward this end, elegant syntheses of formycin B[5a] and oxoformycin[5c] have been achieved.

One attractive approach to the above problem involves the annulation of a fused pyrimidine ring onto one of the 4-(β-D-ribofuranosyl)pyrazoles that we have previously described.[8] The readily available 4-(2,3,5-tri-*O*-benzoyl-β-D-ribofuranosyl)-3(5)-carbomethoxypyrazole (**4a**) appeared to be a suitable starting material if the carbomethoxyl group could be converted into an amino function via the Curtius reaction.[14] Unfortunately, as has been pointed out previously,[8] the carbomethoxyl group of **4a** is relatively nonreactive toward amidation and accordingly we have been unable to convert **4a** into the requisite hydrazide. Upon reaction with hydrazine under a variety of conditions a number of products were obtained, presumably due to side reactions with the benzoate functions. Accordingly, it was decided to prepare 4-(tri-*O*-benzyl-β-D-ribofuranosyl)-3(5)-carbomethoxypyrazole (**4b**), a compound in which the sugar protecting groups should be completely stable.

We have previously described the preparation of 2,5-anhydro-3,4,6-tri-*O*-benzyl-D-allose (**2**) via benzylation of



1a, R = H
b, R = $CH_2C_6H_5$(Bzl)
c, R = COC_6H_5



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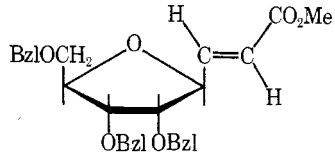

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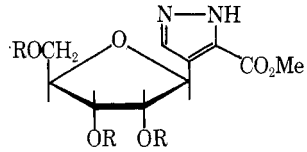


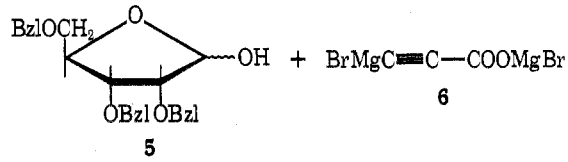
4a, R = COC_6H_5
b, R = $CH_2C_6H_5$
c, R = H

1,3-diphenyl-2-(β-D-ribofuranosyl)imidazolidine (**1a**) using benzyl chloride and sodium hydride in dimethyl sulfoxide followed by mild acidic hydrolysis.[6] This method, however, required purification of the fully protected intermediate **1b** by chromatography on silicic acid. We have now found that by conducting the benzylation with benzyl bromide in dimethylformamide at room temperature the chromatographic step is unnecessary and crystalline **1b** can be directly obtained in 84% yield. An improved procedure for the preparation of **1a** from its tri-*O*-benzoyl precursor **1c** without the necessity of chromatography is also to be found in the Experimental Section. The free aldehyde **2** was liberated from its imidazolidine derivative **1b** by treatment with *p*-toluenesulfonic acid monohydrate[6] and reacted with carbomethoxymethylenetriphenylphosphorane giving methyl *trans*-4,7-anhydro-5,6,8-tri-*O*-benzyl-2,3-dideoxy-D-*allo*-oct-2-enonate (**3**) in essentially quantitative yield. The ^1H NMR spectrum of **3** confirms that the trans olefin ($J_{2,3}$ = 15.5 Hz) was the predominant product. Subsequent treatment of **3** with an excess of diazomethane in ether at room temperature gave an in-

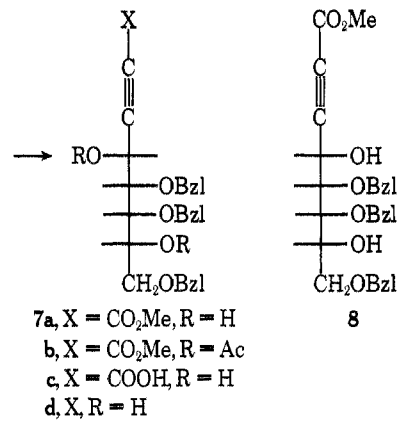
termediate 2-pyrazoline that was not purified, but rather directly treated with chlorine in carbon tetrachloride[8a] giving 4-(2,3,5-tri-*O*-benzyl-β-D-ribofuranosyl)-3(5)-carbomethoxypyrazole (**4b**) in 72% yield. The ^{1}H NMR spectrum of **4b** shows the pyrazole ring proton[15] as a singlet at 7.91 ppm, a figure very similar to that previously reported for **4a** (7.87 ppm)[8] and supporting the well-established principal mode of 1,3-dipolar cycloaddition.[16] There was no indication of any product resulting from inverse addition of diazomethane giving a 4-methoxycarbonyl-3-β-D-ribofuranosylpyrazole. Debenzylation of **4b** using boron trichloride in methylene chloride at −78 °C gave crystalline **4c** identical with that prepared from the tribenzoate[8] in 77% yield.

While the procedure described above for the preparation of **4b** via the glycosylacrylate **3** was quite efficient on a small scale, we have found the chlorine oxidation of the intermediate pyrazoline to be rather capricious, giving quite variable yields of **4b** when scaled up. Accordingly, we were also interested in examining an alternate synthesis via direct 1,3-dipolar cycloaddition of diazomethane to an acetylenic ester. In a previous paper[8] we reported an attempt to prepare such a 3-β-D-ribofuranosylpropiolate via condensation of 2,3,5-tri-*O*-benzoyl-D-ribofuranosyl bromide with the silver derivative of methyl propiolate. The 2-*O*-benzoyl group, however, participated in the displacement of the 1-bromide and a 1,2-α-ethynylbenzylidene derivative was formed rather than the desired glycosylethyne. The use of a 2-*O*-benzyl protecting group should avoid this problem, but recent extensive work by Buchanan et al.[17] has shown that the condensation of 2,3,5-tri-*O*-benzyl-D-ribofuranosyl halides with either Grignard or silver derivatives of acetylenes leads predominantly to the undesired α-D-ribofuranosylalkynes. On the other hand, subsequent to completion of our work, it has recently been reported that the related condensation of 2,3-*O*-isopropylidene-5-*O*-trityl-D-ribofuranosyl chloride with the silver derivative of ethyl propiolate leads primarily to the desired 3-β-D-ribofuranosylpropiolate.[18]

The probability that condensations of metal derivatives of propiolates with 2,3,5-tri-*O*-benzyl-D-ribofuranosyl halides will lead to α-*C*-glycosides[17] led us to first explore an alternate route in which the first step would be the reaction of 2,3,5-tri-*O*-benzyl-D-ribofuranose (**5**)[19] with the Grignard reagent derived from methyl propiolate. Preliminary experiments using the reagent prepared from equimolar amounts of methyl propiolate and ethylmagnesium bromide, however, suggest that side reactions are prevalent, probably due to self-condensation. Accordingly, we have preferred to react **5** with the reagent **6**[20] derived from propiolic acid and 2 equiv of ethylmagnesium bromide. The crude, acidic product **7c** from this reaction at room temperature was directly converted to its methyl esters by treatment with methanol and benzene in the presence of *p*-toluenesulfonic acid and then purified by chromatography on silicic acid. In this way an analytically pure, but noncrystalline, adduct was isolated in 73% yield. Unfortunately, the ^{1}H NMR spectrum of this substance is rather unrevealing since the benzyl resonances are superimposed upon those of several of the sugar protons. Only a single methyl ester singlet was apparent at 3.73 ppm, and while the compound appears homogeneous we could not rule out the presence of a trace of a second isomer. The ^{13}C NMR spectrum run on a rather large sample was very clean and gave no indication of the presence of a second isomer. Acetylation of the acetylenic ester **7a** with acetic anhydride and pyridine was relatively slow and accompanied by formation of some unidentified by-products. On the other hand, a comparable acetylation in the presence of a catalytic amount of 4-dimethylaminopyridine[21] was complete within 1 h at room temperature and gave a single spot product by TLC analysis. Following chromatographic isolation a TLC homogeneous diacetate was isolated as an oil in 82% yield and once again appeared to be a single isomer by ^{1}H and ^{13}C NMR analysis. Only the presence of a very small signal at 1.99 ppm in the ^{1}H NMR spectrum suggested the possible existence of another acetylated species. The closely related condensation of **5** with ethynylmagnesium bromide has been shown by degradative studies to lead predominantly (70%) to the D-*altro*-ethynylpentitol **7d**[17a] and this has been rationalized by consideration



5 **6**



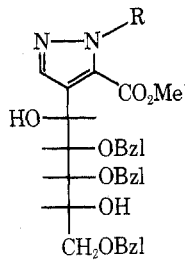
7a, X = CO_2Me, R = H
b, X = CO_2Me, R = Ac
c, X = COOH, R = H
d, X, R = H

8

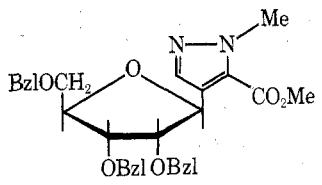
of the rules of asymmetric induction derived by Cram[22a] and Karabatsos.[22b] A direct extrapolation of these considerations leads us to believe that the present compound is essentially pure methyl 5,6,8-tri-*O*-benzyl-2,3-dideoxy-D-*altro*-oct-2-ynonate (**7a**), although the presence of a trace of the D-allo isomer **8** cannot be excluded.

In an effort to confirm the stereochemistry of **7a** we have attempted to decarboxylate the precursor acetylenic acid **7c** to the previously characterized **7d**.[17a] Upon heating **7c** in benzene under reflux, however, a number of neutral products were formed and no conclusions could be reached. Various attempts to acetylate the free hydroxyl groups in **7c** under either basic or acidic conditions led to extensive decomposition.

A copious literature exists concerning the cyclization of 1,4-diols to the corresponding tetrahydrofurans via treatment with anhydrous acids[23] or suitable sulfonyl chlorides in the presence of a base.[17,24] The acid-catalyzed cyclization is particularly facile when one of the hydroxyl groups is activated by being benzylic or allylic in nature.[4a] Unfortunately, treatment of **7a** with either *p*-toluenesulfonic acid in benzene under reflux or with 2.2 equiv of *p*-toluenesulfonyl chloride in pyridine at 60 °C[17] led to mixtures of products most of which no longer contained an acetylene function as judged from their infrared spectra. Accordingly, **7a** was first reacted with an excess of diazomethane in ether at 0 °C giving two pyrazoles in a ratio of roughly 10:1. These compounds were separated by preparative TLC and the major product was isolated in 76% yield. By a combination of the usual spectroscopic and analytical techniques this crystalline compound was shown to be the expected 4-(2,3,5-tri-*O*-benzyloxy-1,4-dihydroxy-D-*altro*-pent-1-yl)-3(5)-carbomethoxypyrazole (**9a**). The D-altro configuration of **9a** is based upon the assumed structure of **7a** and is supported by its ORD spectrum. It is well established that the ORD spectra of a variety of heterocyclic polyols derived from sugars are predominantly dependent upon the chirality of the carbinol adjacent to the heterocycle,[25] those with an *R* configuration showing a negative Cotton effect. The ORD spectrum of **9a** only showed a large trough at 267 nm, the low-wavelength region being



9a, R = H
b, R = Me



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poorly defined, probably due to the presence of the benzyl ethers. This nevertheless suggests a negative Cotton effect centered about 220 nm (λ_{max} for **4c** is 219 nm[8a]) and supports the D-altro configuration for **7a**. A second pyrazole was also isolated in 7% yield and shown by ^{1}H NMR spectroscopy to contain an *N*-methyl group which appeared as a singlet at 4.06 ppm. It is well known that N-methylation of pyrazoles can be achieved using a variety of alkylating agents including diazomethane.[16] In particular, the methylation of pyrazoles bearing electron-withdrawing substituents at the 3(5) position almost inevitably occurs on the nitrogen adjacent to that substituent.[16] Hence we consider this by-product to be the 1-methyl derivative **9b** arising by methylation of the initially formed **9a** by excess diazomethane. In support of this, we find that treatment of **7a** with an excess of diazomethane at room temperature for longer periods leads to the formation of the *N*-methylpyrazole **9b**. Further confirmation of the site of N-methylation will be presented later in this paper.

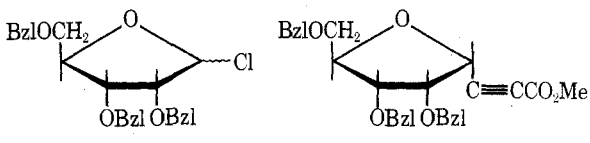
While acid-catalyzed cyclization of **7a** was not successful, treatment of **9a** with an excess of *p*-toluenesulfonic acid monohydrate in benzene under reflux for 17 h led to the smooth formation of a less polar product that no longer showed hydroxyl absorptions in its ir spectrum. By chromatography on silicic acid an 85% yield of the β-D-ribofuranosylpyrazole **4b** was isolated and shown to be identical (ir, ^{1}H and ^{13}C NMR spectra) with the compound prepared via the 3-β-D-ribofuranosylacrylate **3**. This identity confirms the β-D-ribofuranosyl structure for **4b**, the route of synthesis via **5** → **9** → **4b** being quite competitive or even superior to that via **2** and **3**.

The related cyclization of **9b** was also achieved using *p*-toluenesulfonic acid in benzene and gave crystalline 4-(2,3,5-tri-*O*-benzyl-5-carbomethoxymethyl-1-methylpyrazole (**10**) in 77% yield. The latter compound was found to be identical with the product slowly formed, and isolated in 42% yield, from the reaction of **4b** with an excess of diazomethane at room temperature for 3 days.

Recently, ^{13}C NMR spectroscopy has been shown to provide a convenient tool for determination of the position of N-alkylation in heterocycles.[26] Thus alkylation of a nitrogen leads to a substantial upfield shift of the adjacent carbons (α shift) and to a variable downfield shift of the β carbons. In the present case, the ^{13}C chemical shifts of the pyrazole ring carbons in **4b** are readily assigned by comparison with the spectra of other pyrazoles.[27] C_3 being immediately identified by being the only doublet in the nondecoupled spectrum. The *N*-methyl derivative (**10**) showed a 7.94-ppm upfield shift of C_5 and a 5.42-ppm downfield shift of C_3, both being related to the shifts reported for 1-methylpyrazole[27] and confirming the site of alkylation. It should also be noted that while the ^{13}C NMR spectrum of **9b** and **10** showed very sharp signals for the pyrazole ring carbons, the spectra of the nonmethylated compounds (e.g., **9a**) showed broadened signals, presumably as a consequence of tautomeric equilibria.

It is interesting to note that acid-catalyzed cyclization of **9a** and **9b** to the β-D-ribofuranosylpyrazoles **4b** and **10** appears to be a stereoselective process leading to inversion of configuration at $C_{1'}$. This same observation was previously reported during acid-catalyzed cyclization of 5-(D-*altro*-pentahydroxypentyl)uracil to β-pseudouridine.[4a] In the uracil series, cyclization of the related D-*allo*-pentitol led predominantly to α-pseudouridine, suggesting that the cyclization involved direct SN2 displacement of the protonated $C_{1'}$ hydroxyl rather than proceeding through a common, allylically stabilized carbonium ion. In the present work we have not had the D-allo isomer of **9a** available and hence can come to no firm conclusions regarding the mechanism of this cyclization.

In the pseudouridine series, acid-catalyzed cyclization was followed by a slower anomerization of the *C*-glycosyl linkage.[4a,28] We observed no comparable isomerization of **4b** to its α anomer (**13**) during cyclization of **9a**, but in order to clarify this point it was of interest to have a sample of pure 4-(2,3,5-tri-*O*-benzyl-α-D-ribofuranosyl)-3(5)-carbomethoxypyrazole (**13**) available. Previous work[17] has shown that condensation of 2,3,5-tri-*O*-benzyl-D-ribofuranosyl chloride (**11**, largely β)[29] with metal acetylides leads predominantly to the α-D-ribofuranosylalkynes. Accordingly, **11** was reacted with the propiolic acid Grignard derivative **6** in tetrahydrofuran at room temperature. Following the isolation of acidic materials by a partition process the crude reaction product was then converted into the methyl esters by treatment with methanol and benzene in the presence of *p*-toluenesulfonic acid. The overall yield of neutral products was not very good in this process and preparative TLC allowed the isolation of a hydroxyl-free acetylenic ester in only 27% yield. This reaction has not, however, been optimized. The product was homogeneous by TLC and NMR (^{1}H and ^{13}C) and by analogy with the work of Buchanan is considered to be methyl 4,7-anhydro-5,6,8-tri-*O*-benzyl-2,3-dideoxy-D-*altro*-oct-2-ynonate (**12**). Very recently,[17b] Buchanan et al. have briefly described the condensation of **11** with the silver derivative of methyl propiolate and obtained **12**, and its D-allo isomer **16a**, in a ratio of 2:1.



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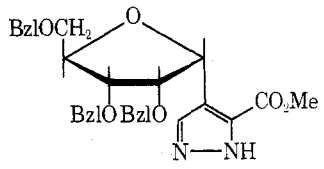
12



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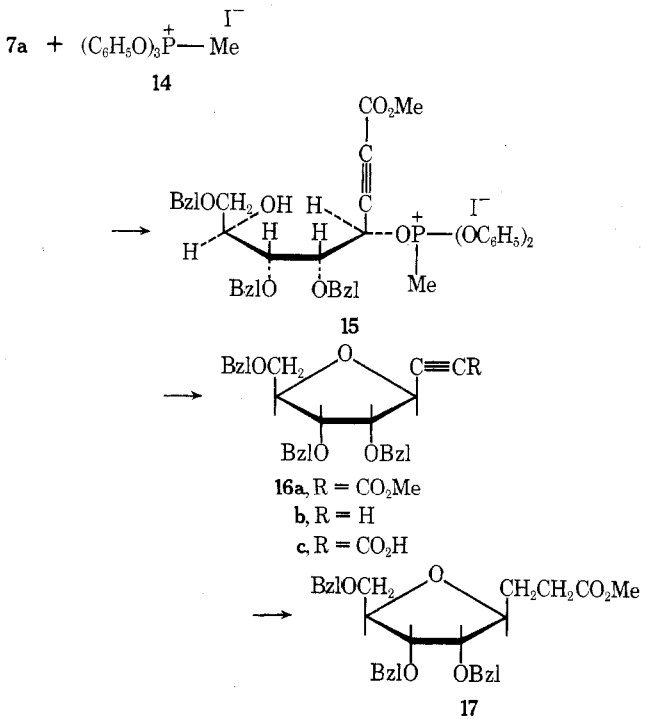
Treatment of **12** with diazomethane in ether at 0 °C led to the isolation, in 58% yield, of 4-(2,3,5-tri-*O*-benzyl-α-D-ribofuranosyl)-3(5)-carbomethoxypyrazole (**13**). The latter compound was clearly separable from its less polar β anomer **4b** by TLC and, since the method of synthesis would be expected to lead to structural ambiguity only at the "anomeric" carbon, its assigned α-D-ribofuranosyl structure seems assured. No equilibration of **4b** and **13** was observed upon treatment of either compound with *p*-toluenesulfonic acid in benzene under reflux for 16 h.

While attempted conversion of **7a** to furanose ring derivatives via treatment with either *p*-toluenesulfonic acid in benzene or *p*-toluenesulfonyl chloride in pyridine were unsuccessful, we considered that this transformation might be accomplished by conversion of one of the hydroxyl groups to a reactive, positively charged derivative. With this in mind **7a** was reacted with methyltriphenoxyphosphonium iodide (**14**)[30] in dimethylformamide at room temperature but led to only

a complex mixture of products. A comparable reaction between **7a** and **14** in methylene chloride was considerably

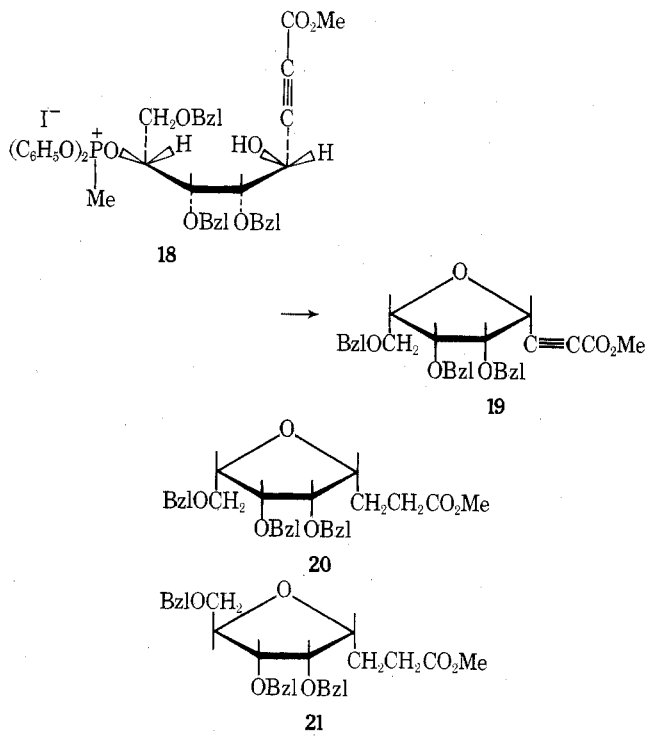


slower but led to the clean formation of two major and three minor carbohydrate products together with the expected diphenyl methylphosphonate and phenol. By chromatography on silicic acid the carbohydrate products were isolated in homogeneous form, and three of them were shown by ir and NMR (^{1}h and ^{13}C) analysis to correspond to the desired tetrahydrofuran derivatives. The two major products, isolated in yields of 33 and 19%, corresponded to the most polar and least polar of these products, respectively, while three minor products were of intermediate mobility.

The authentic α-D-ribofuranosylpropiolate **12**[31] corresponded to one of the minor products upon TLC and NMR examination and was obtained in only 2% yield. The less polar of the major products was shown to be the desired β-D-ribofuranosylpropiolate **16a** by several means. Thus, reduction of **16a** with diimide,[32] generated from potassium azodicarboxylate and acetic acid in pyridine,[33] was shown to give the same methyl 4,7-anhydro-5,6,8-tri-*O*-benzyl-2,3-dideoxy-D-*allo*-octonate (**17**) that was obtained by comparable reduction of the acrylate **3**. Also, the reaction of **16a** with diazomethane gave, in 83% yield, a pyrazole that was chromatographically and spectroscopically identical with **4b**. Finally, **16a** was hydrolyzed and the resulting propiolic acid was decarboxylated by heating in benzene as described by Buchanan et al.[17b] The resulting crystalline 3,6-anhydro-4,5,7-tri-*O*-benzyl-1,2-dideoxy-D-*allo*-hept-1-ynitol (**16b**) was found to be identical (ir, NMR, TLC, and melting point) with an authentic sample kindly provided by Dr. Buchanan.[17a] It therefore appears that the stereochemistry of the 3-ribofuranosylpropiolates with the α (**12**) and β (**16a**) configurations obtained in the above cyclization reaction is on safe grounds. It should be noted, however, that the optical rotation observed for **16a** was 25° less positive than that reported by Buchanan et al.[17b] The rotation we report has been consistent from several different preparations and we cannot readily explain this difference. It may be noted, however, that the values of $[\alpha]$D for these compounds vary widely in different solvents.

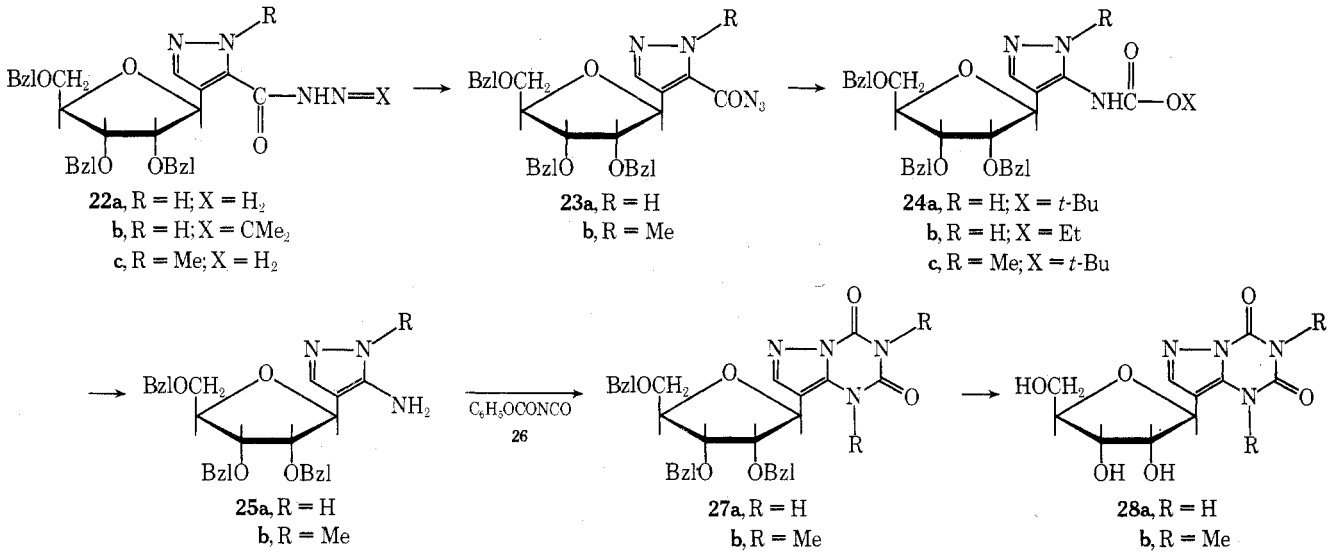
The two remaining minor products, each isolated in only 1% yield, were shown by ir spectroscopy to still contain a free hydroxyl group. While these compounds have not been rigorously characterized, one would appear to be an iodo sugar since its ^{13}C NMR spectrum showed a resonance at unusually high field (2.7 ppm).[34] The second product showed the presence of both an acetylene (ir 2240 cm^{-1}) and a vinyl proton as a doublet at 6.97 ppm. Purely on the basis of this evidence we tentatively suggest this compound to be methyl 5,6,8-tri-*O*-benzyl-2,3,4-trideoxy-D-*erythro*-oct-4-en-2-ynonate resulting from an elimination reaction.

The mechanism of the above cyclization must proceed through initial reaction between a free hydroxyl group of **7a** and the reagent **14** giving an oxyphosphonium intermediate such as **15**. Both the inductive effect of the acetylene and its relatively small steric bulk suggested to us that the C_4 hydroxyl of **7a** would be the principal site of reaction with **14** leading to the intermediate **15**. Direct SN2 displacement of diphenyl methylphosphonate by the C_7 hydroxyl group would then give the β-D-ribofuranosyl product **16a**. A similar activation of the C_4 hydroxyl group in any of the D-allo compound **8** that could be present as a minor contaminant of **7a** would lead to the α-D-ribofuranosyl product **12**. The possibility that cyclization proceeds via initial conversion of **15** to the 4-iodo compound with inversion of configuration seems unlikely since the major product from **7a** by this pathway would be **12**. Alternatively, reagent **14** could attack the C_7 hydroxyl of **7a** giving the intermediate **18**, and subsequent SN2 attack at C_7



by the C_4 hydroxyl of **18** would then lead to methyl 4,7-anhydro-5,6,8-tri-*O*-benzyl-2,3-dideoxy-L-*galacto*-oct-2-ynonate (**19**, 3-β-L-lyxofuranosyl propiolate). Neither of these pathways is clearly predominant since **16a** and **19** are both formed in substantial amounts in this reaction. Once again, diimide reduction of **19** and **12** cleanly gave the saturated esters **20** and **21**, respectively.

Unfortunately, the use of ^{1}H NMR spectroscopy has proved to be of minimal use for configurational assignments to the compounds described in the present work. The methylene protons of the benzyl ethers are generally nonequivalent and the resulting doublets are superimposed over a large portion of the pertinent sugar proton resonances. With the exception of well-defined signals due to methyl esters, and sometimes $C_{5'}$ and $C_{1'}$ protons, it is usually difficult to even ensure



chemical homogeneity from the ^1H NMR spectra alone. Hence the use of ^{13}C NMR spectra has been of critical importance in determination of chemical purity since resonances due to most of the nonbenzylic carbons are well separated and the presence of extraneous signals is readily detected. It is not always possible, however, to make specific assignments to all carbon resonances since the poorly defined ^1H NMR signals preclude comprehensive single frequency decoupling. The ^{13}C chemical shifts for pertinent compounds are shown in Table I, figures in parentheses being tentative assignments not supported by decoupling data. Regardless of specific assignments, the precise chemical shifts provide a useful fingerprint for comparative purposes.

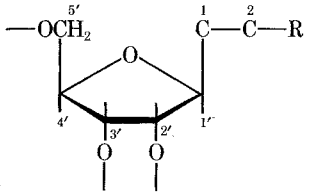
It is well known that the chemical shift of a carbon substituent on a five-membered ring is sensitive to steric crowding, especially by oxygen-containing neighbors, a cis orientation leading to upfield shifts relative to the trans counterpart.[35] We, and others, have made extensive use of this empirical rule in assignments of $C_{1'}$ and $C_{4'}$, configurations in pairs of nucleosides and *C*-glycosides where both isomers are available.[10,35b] In the case of the *C*-glycosyl propiolates **12, 16a,** and **19,** ^{13}C NMR was not of analytical value in assigning configurations at C_4 ("anomeric") and C_7. Thus the chemical shifts of C_3 in these three compounds were essentially identical (84.73 ± 0.05 ppm), probably as a result of the very small steric bulk and rigid geometry of such an acetylenic carbon. Unfortunately, the C_8 chemical shifts were also too close to be of diagnostic value. The fully reduced products **17, 20,** and **21** arising from diimide reduction of **16a, 19,** and **12,** respectively, were more amenable to ^{13}C analysis of "anomeric" configuration. As expected, the chemical shift of C_3 in the cis oriented *altro*-octonate **21** appeared 3.67 ppm upfield of the same carbon in the *allo*-octonate **17** which bears a trans vicinal substituent. Similarly, C_3 in **20** appeared at 26.23 ppm, which is 2.67 ppm upfield of C_3 in **17** and strongly supports the cis configuration in this compound and in its precursor **19.** Once again the chemical shifts of C_8 in **17, 20,** and **21** were too similar to allow confirmation of the configuration at C_7 in **20,** but previous arguments (see above) leave no doubt that its precursor (**19**) belonged to the L-lyxo series. This, together with the NMR assignment of "anomeric" configuration above, provides substantive evidence that the β-L-lyxo configuration of **19** predicted on mechanistic grounds is indeed true.

Since **4b** was available by several different routes described in this paper, we proceeded with attempts to convert this compound to purine-related *C*-glycosides via the route **22** → **28.** Thus **4b** was converted in 86% yield into the syrupy hydrazide **22a** by reaction with anhydrous hydrazine in methanol under reflux. Various attempts to convert **4a** into the corresponding hydrazide were unsuccessful owing to the lability of the benzoyl functions. For characterization, **22a** was readily transformed into the crystalline isopropylidene derivative **22b** by treatment with acetone. The hydrazide **22a** was converted into the acyl azide **23a** upon treatment with dilute hydrochloric acid and sodium nitrite in a mixture of aqueous acetic acid and ether at −10 °C. Without purification, **23a** was subjected to a Curtius rearrangement[14] by heating under reflux with *tert*-butyl alcohol, giving, after purification by chromatography on silicic acid, a 71% yield of 4-(2,3,5-tri-*O*-benzyl-β-D-ribofuranosyl-3(5)-*tert*-butoxycarboxamido)-pyrazole (**24a**). A similar treatment of **23a** with ethanol gave the corresponding urethane **24b** in 76% yield. In essentially identical ways the *N*-methylpyrazole **10** was converted into the *tert*-butoxycarboxamido derivative **24c** via the intermediate hydrazide **22c** and azide **23b.**

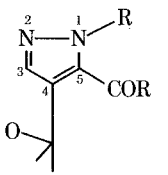
Treatment of **24a** with aqueous trifluoroacetic acid at room temperature for 7 h led to clean cleavage of the *tert*-butyl ester and decarboxylation of the resulting carbamic acid giving 3(5)-amino-4-(2,3,5-tri-*O*-benzyl-β-D-ribofuranosyl)pyrazole (**25a**) in 94% yield. Similar treatment of **24c** gave the corresponding crystalline *N*-methyl derivative **25b** in 65% yield. The aminopyrazole **25a** could also be obtained by alkaline hydrolysis of the urethane **24b,** but in this case the conditions were quite vigorous and the yield of **25a** was only 39%. While **25a** gave satisfactory ^1H and ^{13}C NMR spectra, it appeared to be unstable and quite rapidly gave several spots on TLC analysis. It was therefore used directly in the following steps. The N-methylated analogue **25b** was, on the other hand, a stable, crystalline substance.

Numerous examples of the cyclization of amino heterocycles to fused ring products by reaction with alkoxy- or aryloxycarbonyl isothiocyanates are to be found in the literature.[36] In particular, the reaction of 3-aminopyrazole with ethoxycarbonyl isothiocyanate to give 2-oxo-4-thiono-1*H*,3*H*-pyrazolo[1,5-*a*]-1,3,5-triazine[37] provides a close analogy for the type of cyclization that we desired. Accordingly, **25a** was reacted in dioxane with phenoxycarbonyl isocyanate (**26**),[38] a reagent that has found considerable use in this laboratory for other heterocyclic syntheses.[39] Without isolation of the acyclic ureido intermediate, crystalline 2,4-dioxo-8-(2,3,5-tri-*O*-benzyl-β-D-ribofuranosyl)-1*H*,3*H*-pyrazolo[1,5-*a*]-1,3,5-triazine (**27a**) was isolated in 50% yield. Debenzylation of **27a** was readily accomplished by treatment with boron trichloride in methylene chloride at −78 °C giving the crystalline, unprotected nucleoside **28a** in 73% yield. The latter compound was chromatographically homogeneous and had an electrophoretic mobility in pH 9.2 borate buffer very similar to that of β-pseudouridine.[4a] It is, of course, a *C*-gly-

Table I. 22.62-MHz ^{13}C NMR Chemical Shifts (ppm from Me_4Si)[a]



a



b

Compd	Solvent[b]	Pentose[c]					Side chain[c]		Ester		Other[d]
		C_1'	C_2'	C_3'	C_4'	C_5'	C_1	C_2	CO	OMe	
3	C	(80.04)	(81.40)	(77.53)	(81.86)	70.22	121.62	145.90	166.87	51.62	
4b	C	76.88	81.89	76.88	79.97	69.21			162.58	51.85	125.06 (C_4), 132.08 (C_3), 137.16 (C_5)
4c	D	76.66	(76.66)	(70.48)	(83.45)	61.48			162.06	51.40	121.67 (C_5), 124.64 (C_4), 131.99 (C_3)
7a	C	62.35	(80.23)	(79.36)	(70.84)	70.84	86.86	77.14	153.74	52.83	
7b	C	62.78	(77.11)	(79.19)	68.37	71.81	83.00	77.89	153.25	52.83	169.93, 169.47 (COMe), 21.10, 20.64 ($COCH_3$)
9a	C	66.94	(80.17)	(80.92)	70.32	71.29			163.00	52.08	127.01 (C_4), 131.99 (C_3), 136.70 (C_5)
9b	C	66.87	(80.23)	(80.65)	70.35	71.16			160.43	51.85	40.41 (NMe), 129.39 (C_5 or C_4), 138.20 (C_3)[e]
10	C	76.27	82.61	77.44	80.65	69.76			160.58	52.02	40.28 (NMe), 126.71 (C_4), 129.21 (C_5), 137.50 (C_3)
12	B	70.58	79.26	78.48	81.86	69.80	84.69	79.68	153.87	52.05	
13	C	(75.97)	(79.55)	(77.44)	(80.62)	70.35			162.74	51.82	122.40 (C_4), 132.87 (C_3)[e]
16a	C	70.74	(82.11)	(78.19)	(81.86)	69.93	84.72	(77.93)	153.67	52.79	
16b	C	70.90	(82.12)	(78.19)	(81.76)	70.22	81.66	74.97			
17	C	79.84	80.95	77.66	81.57	70.64	28.90	30.23	173.99	51.66	
19	C	68.63	(79.84)	(77.47)	(80.43)	69.44	84.78	(78.41)	153.93	52.60	
20	C	(77.96)	(79.13)	(78.15)	(79.55)	70.25	26.23	30.62	174.38	51.49	
21	C	(78.09)	(79.84)	(79.29)	(79.84)	70.32	25.23	30.53	174.19	51.53	
22a	C	(76.69)	(81.47)	(76.43)	(80.56)	69.38			162.55		122.0 (C_4), 132.5 (C_3)[e]
24a	C	(77.89)	(82.05)	(76.79)	(81.76)	69.08			153.15		28.25 (CMe_3), 102.89 (Me_3C)
25a	C	(77.86)	(81.76)	(76.40)	(81.11)	70.22					130.00 (pyrazole)

		Heterocycle					
		C_2	C_4	C_7	C_8	C_9	
27a	C	(143.53)	(148.02)	144.50	103.74	136.96	
28a	D	(144.18)	(148.27)	144.18	103.18	137.84	
28b	D	(144.54)	(148.73)	144.73	104.06	138.03	29.13, 31.83 (NMe)

[a] Assignments that are ambiguous and could not be confirmed by single frequency decoupling are written in parentheses. [b] Solvents are C, $CDCl_3$; D, Me_2SO-d_6; B, benzene-d_6. [c] In an effort at consistency, the various non-N-heterocyclic sugar derivatives, including the acyclic compounds **7** and **9**, are numbered as in a. The pyrazole derivatives are all numbered as in b in order to be consistent with the nontautomeric *N*-methyl derivatives (**9b**, **10**). [d] In addition, all tribenzyl derivatives showed three signals (OCH_2Ar) at 71.59–74.51 ppm, nine overlapping aryl carbons at 127–129 ppm, and three aryl C_i carbons at 136–138 ppm in the spectra in $CDCl_3$. [e] One pyrazole carbon is masked by aryl resonances.

coside analogue of xanthosine in which N^9 is transposed to a bridgehead position and represents one of the few reported syntheses of purine-related *C*-glycosides.[5a,5c,13] The heterocyclic base related to **28a** has recently been prepared[37] and considerable interest has centered upon the synthesis of *N*-glycosides derived from purine nucleoside analogues bearing a bridgehead nitrogen.[40] Debenzylation of **27a** by treatment with sodium in liquid ammonia required the use of a charcoal adsorption and elution step in order to free the produce from inorganic materials. The resulting product was found to consist of a mixture of the desired **28a** and an isomeric material with a similar, but different, chromatographic mobility. These substances could be cleanly separated by borate electrophoresis and the second product was found to have a mobility similar to that of α-pseudouridine. Presumably under the strongly basic conditions of the sodium in ammonia reduction, **28a** underwent partial isomerization to the corresponding α nucleoside via a mechanism similar to that previously proposed for pseudouridine.[28] There was, however, no indication of the formation of pyranosides. Fortunately, no similar isomerization was observed under the mild conditions for debenzylation with boron trichloride.

The similarity of the ^{13}C chemical shifts of urea and oxygen substituted azomethine carbons makes an unequivocal assignment of tautomeric structure for **27a** and **28a** difficult. The ^{13}C NMR spectra of both compounds show signals for C_2, C_4, C_7, and C_9 all between 137 and 148 ppm, making it difficult to reach any conclusions. Hence **28a** was treated with methyl iodide and potassium carbonate to give the crystalline N^1,N^3-dimethyl compound **27b** in >90% yield. Debenzylation of **27b** with boron trichloride proceeded readily giving crystalline 2,4-dioxo-1,3-dimethyl-8-β-D-ribofuranosylpyrazolo[1,5-*a*]-1,3,5-triazine (**28b**) in 61% yield. The ^1H NMR spectra of **27b** and **28b** left the site of alkylation ambiguous, but the ^{13}C NMR spectrum of **28b** clearly indicated that methylation had, as expected, occurred on nitrogen rather than oxygen. Thus the new methyl signals appeared at 29.13 and 31.83 ppm, positions compatible with those shown by N^1,N^3-dimethyluracil (27.5 and 36.8 ppm)[41] but distinctly different from those of aryl methyl ethers (55–60 ppm).[34,41]

The uv spectra of **28a** and **28b** were quite similar with both showing maxima at 253–254 nm. The N^1,N^3-dimethyl compound **28b**, however, showed a second maxima at 240 nm while **28a** only had a shoulder at 231 nm. Since these lower wavelength peaks are rather close to the beginning of intense end absorption it is difficult to reach firm conclusions regarding tautomeric structure without careful study on the pH dependence of the uv spectra. Finally, it is interesting to note that the ir spectra of **27a** and **28a** show intense carbonyl absorptions at roughly 1770 and 1710 cm^{-1}. The former are at rather high frequency when compared with other ketonucleosides[42a] such as xanthosine (1715 and 1690 cm^{-1})[42b] and are much closer to those exhibited by 2,4-dioxo-1,3,5-triazines such as substituted 5-azauracils (~1750 cm^{-1} in dioxane).[42c] The N^1,N^3-dimethyl derivatives **27b** and **28b** showed similar long-wavelength carbonyl absorptions which futher support the dioxo structures for the parent nucleosides.

In the present paper we have outlined a number of different routes for the preparation of selected pentofuranosylpropiolates. These compounds can, in turn, be converted into functionally substituted *C*-glycosylpyrazoles which are useful precursors of bicyclic *C*-glycosides related to purine nucleosides. In forthcoming papers in this series we hope to describe the preparation of other compounds of the latter class.

Experimental Section

General Methods. The general methods used are similar to those described previously.[7] Only limited ^1H NMR data are presented owing to the frequent complexity of the spectra of tri-*O*-benzylribose derivatives. In Table I, ^{13}C NMR data are accumulated and assignments are made based upon off-resonance and, whenever possible, single frequency proton decoupling studies. We are most grateful to Dr. M. L. Maddox for his help with ^{13}C NMR spectroscopy.

1,3-Diphenyl-2-(2,3,5-tri-*O*-benzyl-β-D-ribofuranosyl)imidazolidine (1b). A solution of **1c** (27.0 g, 40.4 mmol) in chloroform (275 ml) was added to methanolic sodium hydroxide (275 ml of 0.075 M) and stirred at room temperature for 2.5 h. After neutralization with Dowex 50 (H^+) resin the mixture was filtered and evaporated leaving a gum that was triturated with ether to remove methyl benzoate. The solid was crystallized from aqueous methanol giving 10.3 g (72%) of **1a**.[6] A solution of **1a** (14.25 g, 40 mmol) in anhydrous DMF (30 ml) was added dropwise at 0 °C under nitrogen to a suspension of 100% sodium hydride (4.8 g, 0.2 mol)[43] in DMF (35 ml). The mixture was stirred at room temperature for 2 h and then cooled to 0–5 °C while a solution of benzyl bromide (22.6 ml, 190 mmol) in DMF (15 ml) was added over 30 min. After 2 h at room temperature methanol (20 ml) was added and the solution was poured onto a mixture of ice water and ether. The aqueous phase was further extracted with ether and the combined organic layers were washed with water (three times), dried ($MgSO_4$), and evaporated. The residue was triturated with petroleum ether (bp 30–60 °C) and the solid residue was crystallized from ether–hexane giving 20.97 g (84%) of **1b** with mp 93–94 °C and in all ways identical with an authentic sample.[6]

Methyl *trans*-4,7-Anhydro-5,6,8-tri-*O*-benzyl-2,3-dideoxy-D-*allo*-oct-2-enonate (3). The aldehyde **2** was regenerated from **1b** (9.0 g, 14.4 mmol) with *p*-toluenesulfonic acid as previously described[6] and directly reacted with carbomethoxymethylenetriphenylphosphorane (9.6 g, 28.8 mmol) in methylene chloride (180 ml) at room temperature for 2 h. The solution was washed three times with water, diluted with ether, and filtered. The evaporated filtrate was chromatographed on a column of silicic acid using ether–hexane (1:1) giving 6.45 g (92%) of **3** as a colorless oil: $[\alpha]^{25}D$ −13.7° (*c* 1.0, $CHCl_3$); ν_{max} (film) 1725 cm^{-1} (CO); ^1H NMR ($CDCl_3$) inter alia 6.16 (dd, 1, $J_{2,3}$ = 15.5, $J_{2,4}$ = 2 Hz, C_2H), 6.92 ppm (dd, 1 $J_{3,4}$ = 5 Hz, C_3 H); ^{13}C NMR (see Table I) showed the presence of a little (5–10%) of the cis isomer by minor peaks at 148.9 (C_3), 120.0 (C_2), 80.5, 79.0, 77.9, 71.3, 69.3, and 51.5 ppm (OCH_3).

Anal. Calcd for $C_{30}H_{32}O_6$ (488.59): C, 73.75; H, 6.60. Found: C, 73.52; H, 6.89.

4-(2,3,5-Tri-*O*-benzyl-β-D-ribofuranosyl)-3(5)-carbomethoxypyrazole (4b). A. A solution of **3** (1.2 g, 2.5 mmol) and diazomethane (from 1.0 g, 10 mmol, of *N*-nitroso-*N*-methylurea) in ether was stored at room temperature for 2.5 h and then evaporated to dryness. A solution of chlorine (0.3 g, 4.1 mmol) in carbon tetrachloride (50 ml) was added dropwise to a solution of the residue in carbon tetrachloride (10 ml). After 1.5 h at room temperature the solvent was evaporated and the residue was chromatographed on a column of silicic acid using ether–hexane (2:1) giving 0.95 g (72%) of **4b** as a TLC-homogeneous syrup: $[\alpha]^{25}D$ 95.1° (*c* 0.8, $CHCl_3$), 69.5° (*c* 0.4, MeOH); ORD (MeOH) $[\Phi]_{260}^{pk}$ 12 100°, $[\Phi]_{240}^{tr}$ 7500°, $[\Phi]_{232}^{pk}$ 9100°; λ_{max} (MeOH) 236 nm (sh, ε 5400); ^1H NMR ($CDCl_3$) 3.78 (s, 3, OMe), 5.62 (d, 1, $J_{1',2'}$ = 2 Hz, $C_{1'}$ H), 7.91 ppm (s, 1, $C_{5(3)}$ H).

Anal. Calcd for $C_{31}H_{32}N_2O_6$ (528.61): C, 70.44; H, 6.10; N, 5.30. Found: C, 70.46; H, 6.15; N, 5.33.

B. A solution of **9a** (1.7 g, 3.1 mmol) and *p*-toluenesulfonic acid (0.3 g, 1.6 mmol) in benzene (50 ml) was stirred and heated under reflux for 17 h. The solution was diluted with ether, washed with aqueous sodium bicarbonate (three times) and water, dried ($MgSO_4$), and evaporated. The residue was chromatographed as in A giving 1.4 g (86%) of **4b** that was identical with that above by TLC and ir analysis. By ^1H and ^{13}C NMR the product was shown to be at least 90–95% pure with only a few very small signals suggesting the presence of a trace of a second isomer.

C. A solution of **16a** (130 mg, 0.27 mmol) and diazomethane (from 250 mg, 2.4 mmol, of *N*-nitroso-*N*-methylurea) in ether (15 ml) was kept at 0 °C for 1.5 h. Purification by preparative TLC using ether–hexane (3:1) gave 120 mg (83%) of **4b** identical with that above.

4-β-D-Ribofuranosyl-3(5)-carbomethoxypyrazole (4c). A solution of **4b** (240 mg, 0.45 mmol) in methylene chloride (2 ml) was added to a solution of boron trichloride (~1 ml) in methylene chloride (5.5 ml) cooled to −78 °C. After 40 min at −78 °C a mixture of methanol and methylene chloride (1:1, 6 ml) was added and the mixture was warmed to room temperature and evaporated to dryness. The residue was coevaporated five times with methanol and then crystallized from methanol–ether giving 90 mg (77%) of **4c** with mp 183–184.5 °C. This material was identical with an authentic sample of **4c** (mp 186–188 °C, mmp 182–187 °C).[8a]

Methyl 5,6,8-Tri-*O*-benzyl-2,3-dideoxy-D-*altro*-oct-2-ynonate (7a). Ethylmagnesium bromide (141 ml of a 1.32 *M* solution in tet-

rahydrofuran, 186 mmol) was added dropwise to a stirred solution of propiolic acid (6.7 g, 95.7 mmol) in tetrahydrofuran (100 ml) at 0 °C and the mixture was warmed to room temperature for 1 h. A solution of **5** (7.7 g, 18.3 mmol) in tetrahydrofuran (50 ml) was added dropwise to the resulting **6** and stirred at room temperature for 20 h. Following addition of excess saturated aqueous ammonium chloride and 6 N hydrochloric acid (35 ml) the mixture was extracted (three times) with ether and the extracts were washed with water (three times) and evaporated to a syrup. A solution of the latter in saturated aqueous sodium bicarbonate was washed three times with ether, acidified with 6 N hydrochloric acid, and extracted with ether. The extracts were washed with water, dried ($MgSO_4$), and evaporated, leaving 9.7 g of crude acid that was dissolved in benzene–methanol (1:1, 100 ml) containing *p*-toluenesulfonic acid (1.0 g) and heated under reflux for 5.5 h. The cooled solution was diluted with ether and washed with water, aqueous sodium bicarbonate (three times), and water, dried ($MgSO_4$), and evaporated, leaving 8.9 g of crude **7a**. Chromatography on a column of silicic acid using ether–hexane (2:1) gave 6.78 g (73%) of TLC-homogeneous **7a** that appeared to be a single isomer by ^1H and ^{13}C NMR analysis: $[\alpha]^{25}D$ −33° (*c* 1.0, MeOH); ^1H NMR ($CDCl_3$) 3.73 ppm (s, 3, OMe); ir (film) 2240 (C≡C), 1720 cm^{-1} (CO).

Anal. Calcd for $C_{30}H_{32}O_7$ (504.59): C, 71.41; H, 6.39. Found: C, 71.01; H, 6.35.

Methyl 4,7-Di-*O*-acetyl-5,6,8-tri-*O*-benzyl-2,3-dideoxy-D-*altro*-oct-2-ynonate (7b). A solution of **7a** (2.0 g, 4 mmol), acetic anhydride (10 ml), and 4-dimethylaminopyridine (20 mg) in pyridine (30 ml) was stirred at room temperature for 1 h and then poured into ice water. After 30 min the mixture was extracted with ether and the extracts were washed with 2 N hydrochloric acid (three times), aqueous sodium bicarbonate, and water. The dried solution was evaporated and the residue was chromatographed on a column of silicic acid using ether–hexane (3:2) to give 1.9 g (82%) of **7b** as a TLC-homogeneous syrup: $[\alpha]^{25}D$ −33.6° (*c* 0.4, MeOH); ^1H NMR ($CDCl_3$) 1.93 and 2.04 (s, 3, OAc), 3.67 ppm (s, 3, OMe).

Anal. Calcd for $C_{34}H_{36}O_9$ (588.63): C, 69.37; H, 6.16. Found: C, 69.53; H, 6.29.

4-(2,3,5-Tribenzyloxy-1,4-dihydroxy-D-*altro*-pent-1-yl)-3(5)-carbomethoxypyrazole (9a). A solution of **7a** (0.52 g, 1.03 mmol) and diazomethane (from 0.8 g, 8 mmol, of *N*-nitroso-*N*-methylurea) in ether (50 ml) was stored at 0 °C for 2 h. After removal of excess diazomethane with a stream of nitrogen the solvent was evaporated and the residue was purified by preparative TLC using ether–methanol (19:1) giving 0.43 g (76%) of **9a** with mp 47–50 °C from benzene–hexane: $[\alpha]^{25}D$ −44.8° (*c* 1.0 MeOH); ORD (MeOH) $[\Phi]_{267}^{tr}$ −16 400°; λ_{max} (MeOH) 247 nm (sh, ϵ 4600); ^1H NMR ($CDCl_3$) 7.72 (s, 1, $C_{5(3)}$ H), 3.73 ppm (s, 3, OMe).

Anal. Calcd for $C_{31}H_{34}N_2O_7$ (546.62): C, 68.12; H, 6.27; N, 5.12. Found: C, 67.94; H, 6.44; N, 4.74.

Two by-products were also isolated by preparative TLC. The one less polar than **9a** (40 mg, 7%) was shown by ^1H NMR to be the *N*-methyl derivative (**9b**), ^1H NMR ($CDCl_3$) 7.68 (s, 1, $C_{5(3)}$ H), 3.69 (s, 3, OMe), 4.06 ppm (s, 3, NMe), while a more polar substance (15 mg) was not identified.

4-(2,3,5-Tri-*O*-benzyl-β-D-ribofuranosyl)-5-carbomethoxy-1-methylpyrazole (10). A solution of **9b** (280 mg, 0.5 mmol) and *p*-toluenesulfonic acid (60 mg, 0.25 mmol) in benzene (25 ml) was heated under reflux for 17 h, diluted with ether, and washed with aqueous sodium bicarbonate and water. The dried solution was evaporated and the residue was triturated with hexane giving 210 mg (77%) of **10**. An analytical sample from hexane had mp 98–99 °C: $[\alpha]^{25}D$ 56.9° (*c* 1.0, MeOH); λ_{max} (MeOH) 231 nm (ϵ 9400); ^1H NMR ($CDCl_3$) 3.85 (s, 3, OMe), 4.11 (s, 3, NMe), 5.51 (d, 1, $J_{1',2'}$ = 4 Hz, $C_{1'}$ H), 7.60 ppm (s, 1, C_3H).

Anal. Calcd for $C_{32}H_{34}N_2O_6$ (542.63): C, 70.83; H, 6.32; N, 5.16. Found: C, 70.80; H, 6.36; N, 5.07.

Methyl 4,7-Anhydro-5,6,8-tri-*O*-benzyl-2,3-dideoxy-D-*altro*-oct-2-ynonate (12). A solution of **11** (prepared from 1.9 g, 3.3 mmol, of 2,3,5-tri-*O*-benzyl-1-*O*-*p*-nitrobenzoyl-D-ribose as previously described[29] and giving 81% of the theoretical *p*-nitrobenzoic acid) in dry tetrahydrofuran (15 ml) was added to a stirred suspension of **6** (prepared from 1.8 g, 25.7 mmol, of propiolic acid and 51.5 mmol of ethylmagnesium bromide as described for preparation of **7a**) in tetrahydrofuran (100 ml). After 16 h at room temperature excess saturated aqueous ammonium chloride and concentrated hydrochloric acid (20 ml) were added and the solution was extracted twice with ether. The extracts were washed with water and evaporated. A solution of the residue in aqueous sodium bicarbonate was washed with ether until the extracts were colorless, acidified with hydrochloric acid, and extracted with ether. The extracts were washed with water, dried ($MgSO_4$), and evaporated, leaving 1.3 g of crude acetylenic acid. A solution of this material in benzene (10 ml) and methanol (10 ml) containing *p*-toluenesulfonic acid (120 mg, 0.63 mmol) was heated under reflux for 5 h and then diluted with ether. The solution was washed twice with aqueous sodium bicarbonate and then with ice-cold water, dried ($MgSO_4$), and evaporated, leaving 780 mg of a light-colored oil. Preparative TLC using ether–hexane (3:1) gave 250 mg (15%) of **7a** and 430 mg (27%) of the less polar **12** as a homogeneous syrup. In various preparations the yield of **12** varied between 13 and 27%: $[\alpha]^{25}D$ 87.2° (*c* 0.1, $CHCl_3$) (reported[17b] $[\alpha]D$ 84.3°); ν_{max} (film) 2240 (C≡C), 1720 cm^{-1} (CO).

4-(2,3,5-Tri-*O*-benzyl-α-D-ribofuranosyl)-3(5)-carbomethoxypyrazole (13). A solution of **12** (130 mg, 0.27 mmol) in ether was treated with diazomethane as described for the preparation of **4b** (method C) giving 85 mg (58%) of homogeneous **13**: $[\alpha]^{25}D$ −25.0° (*c* 0.5, $CHCl_3$); $[\alpha]^{25}D$ −34.9° (*c* 0.5, MeOH); ORD (MeOH) $[\Phi]_{264}^{tr}$ −12 200°, $[\Phi]_{240}$ 0°; λ_{max} (MeOH) 230 nm (sh, ϵ 7000); ^1H NMR ($CDCl_3$) 3.76 (s, 3, OMe), 5.56 (d, 1, $J_{1',2'}$ = 2.5 Hz, $C_{1'}$ H), 7.86 ppm (s, 1, $C_{3(5)}$ H).

Anal. Calcd for $C_{31}H_{32}N_2O_6$ (528.61): C, 70.44; H, 6.10; N, 5.30. Found: C, 70.11; H, 6.20; N, 5.20.

Reaction of 7a with Methyltriphenoxyphosphonium Iodide (14). A solution of **7a** (2.0 g, 4 mmol) and **14** (5.5 g, 12 mmol) in dry methylene chloride (240 ml) was stored at room temperature for 91 h. Methanol (50 ml) was then added and after 30 min the solution was evaporated. A solution of the residue in ether was washed with ice-cold 5% potassium hydroxide (3 × 50 ml) and water, dried ($MgSO_4$), and evaporated. The residue was separated into five pure components by a combination of chromatography on a column of silicic acid and preparative TLC using ether–hexane (1:1). In order of increasing polarity these were identified as follows.

(a) The least polar band contained 375 mg (19%) of the β-D-ribofuranosylpropiolate (**16a**) as a homogeneous syrup: $[\alpha]^{25}D$ −23.4° (*c* 0.8, MeOH), −8.7° (*c* 0.9, $CHCl_3$) (reported[17b] $[\alpha]D$ 16°, $CHCl_3$); ν_{max} (film) 2240 (C≡C), 1720 cm^{-1} (CO); ^1H NMR ($CDCl_3$) 3.73 (s, 3, OMe), 4.74 ppm (d, 1, $J_{4,5}$ = 4.5 Hz, C_4 H).

Anal. Calcd for $C_{30}H_{30}O_6$ (486.59): C, 74.06; H, 6.21. Found: C, 73.53; H, 6.02.

(b) The second band contained 30 mg (1%) of a compound that was considered on spectral grounds to be an iodo sugar: ν_{max} (film) 3300 (OH), 2240 (C≡C), 1730 cm^{-1} (CO); ^1H NMR ($CDCl_3$) 3.69 ppm (s, 3, OMe); ^{13}C NMR ($CDCl_3$) 2.7 (C_4), 52.7 (OMe), 69.4 (C_8), 77.4 (C_6), 80.7 (C_5), 81.4 (C_7), 84.5 (C_2), 153.8 ppm (C_1) (tentative carbohydrate assignments).

(c) The third band contained 15 mg (1%) of what is tentatively considered to be methyl 5,6,8-tri-*O*-benzyl-2,3,4-trideoxy-D-*erythro*-oct-4-en-2-ynonate: ν_{max} (film) 3400 (OH), 2240 (C≡C), 1720 (CO), 1630 cm^{-1} (C=C); ^1H NMR ($CDCl_3$) 3.71 (s, 3, OMe), 6.97 ppm (d, 1, $J_{4,6}$ = 1.5 Hz, C_4 H).

(d) The next band contained 40 mg (2%) of the α-D-ribofuranosyl propiolate (**12**) that was identical with the sample prepared as above by ^1H and ^{13}C NMR and TLC analysis.

(e) The most polar band contained 630 mg (33%) of the β-L-lyxofuranosyl propiolate (**19**) as a homogeneous syrup: $[\alpha]^{25}D$ 69.7° (*c* 0.3, $CHCl_3$), 43.9° (*c* 0.3, MeOH); ν_{max} (film) 2240 (C≡C), 1725 cm^{-1} (CO); ^1H NMR ($CDCl_3$) 3.72 ppm (s, 3, OMe).

Anal. Calcd for $C_{30}H_{30}O_6$ (486.59): C, 74.06; H, 6.21. Found: C, 74.37; H, 6.04.

In another reaction similar to that above, the yields of the purified major products **16a** and **19** were 30 and 33%, respectively.

2,3,5-Tri-*O*-benzyl-β-D-ribofuranosylethyne (16b). A solution of **16a** (100 mg, 0.2 mmol) and aqueous potassium hydroxide (0.25 ml of 2 N) in dioxane (1.5 ml) was stirred at room temperature for 1 h and then evaporated to dryness. An aqueous solution of the residue was washed with ether, acidified to pH 4 with 2 N hydrochloric acid, and then extracted with chloroform (3 × 20 ml). The dried ($MgSO_4$) extracts were evaporated leaving 80 mg of the acid **16c** [ν_{max} 2240 (C≡C), 1715 cm^{-1} (CO_2H)] that was dissolved in benzene (10 ml) and heated under reflux for 27 h. The solution was diluted with ether, washed with aqueous sodium bicarbonate and water, dried ($MgSO_4$), and evaporated. The residue was purified by preparative TLC using ether–hexane (1:1) giving 45 mg (52%) of NMR and TLC homogeneous **16b** that was crystallized from hexane giving 30 mg of product with mp 63.5–64.5 °C (reported[17] mp 63–64 °C); $[\alpha]^{25}D$ 11.9° (*c* 0.4, $CHCl_3$); ν_{max} (film) 3280 cm^{-1} (C≡CH); ^1H NMR ($CDCl_3$) 2.47 (d, 1, $J_{1,3}$ = 2 Hz, C≡CH), 3.52 ppm (d, 2, $J_{6,7}$ = 4 Hz, C_7 H). This material was identical in all respects with a sample kindly provided by Professor J. G. Buchanan.

Methyl 4,7-Anhydro-5,6,8-tri-*O*-benzyl-2,3-dideoxy-D-*allo*-octonate (17). A. A mixture of **3** (244 mg, 0.5 mmol), potassium azodicarboxylate (485 mg, 2.5 mmol), glacial acetic acid (0.28 ml, 5 mmol),

and pyridine (5 ml) was stirred under nitrogen at room temperature for 17 h. It was then diluted with methanol, filtered, and evaporated in vacuo, leaving a residue that was partitioned between ethyl acetate and water. The organic phase was washed with aqueous sodium bicarbonate (3 × 20 ml), 2 N hydrochloric acid (5 × 20 ml), and ice-cold water (2 × 20 ml), dried ($MgSO_4$), and evaporated, leaving 220 mg (90%) of pure **17** as a syrup: $[\alpha]^{25}D$ −18.3° (*c* 0.6, $CHCl_3$); ν_{max} (film) 1735 cm^{-1} (CO_2Me); ^1H NMR ($CDCl_3$) 2.39 (t, 2, C_2H_2), 3.60 ppm (s, 3, OMe).

Anal. Calcd for $C_{30}H_{34}O_6$ (490.60): C, 73.44; H, 6.98. Found: C, 73.11; H, 702.

B. The propiolate **16a** (120 mg, 0.25 mmol) was reduced with diimide as in A giving 130 mg of a red syrup the major component of which was identical with **17** by TLC. Purification by preparative TLC using ether–hexane (3:2) gave 50 mg (41%) of pure **17** that was identical with that from A by ^1H and ^{13}C NMR.

Methyl 4,7-Anhydro-5,6,8-tri-*O*-benzyl-2,3-dideoxy-L-*galacto*-octonate (20). Reduction of the propiolate **19** (120 mg, 0.25 mmol) with diimide was carried out as described for preparation of **17.** Purification of the red syrup by preparative TLC gave 70 mg (57%) of pure **20** as a colorless syrup: $[\alpha]^{25}D$ 9.0° (*c* 0.5, $CHCl_3$); ν_{max} (film) 1730 cm^{-1} (CO_2Me); ^1H NMR ($CDCl_3$) 2.42 (t, 2, C_2H_2), 3.60 ppm (s, 3, OMe).

Anal. Calcd for $C_{30}H_{34}O_6$ (490.60): C, 73.44; H, 6.98. Found: C, 72.99; H, 6.59.

Methyl 4,7-Anhydro-5,6,8-tri-*O*-benzyl-2,3-dideoxy-D-*altro*-octonate (21). The reduction of **12** (120 mg) with diimide was carried out as described for preparation of **17.** The resulting crude product was purified by preparative TLC using ether–hexane (1:1) to give 42 mg (35%) of **21** as a clear syrup: $[\alpha]^{25}D$ 37.6° (*c* 0.3, $CHCl_3$); ν_{max} (film) 1735 cm^{-1}; ^1H NMR ($CDCl_3$) 3.58 ppm (s, 3, OMe).

Anal. Calcd for $C_{30}H_{34}O_6$ (490.60): C, 73.44; H, 6.98. Found: C, 73.84; H, 6.64.

4-(2,3,5-Tri-*O*-benzyl-β-D-ribofuranosyl)pyrazole-3(5)-carboxylic Acid Hydrazide (22a). A solution of **4b** (8.0 g, 15.1 mmol) in anhydrous hydrazine (25 ml) and methanol (50 ml) was heated under reflux for 3 h and then evaporated to dryness. A solution of the residue in ether was washed with water (three times), dried, and evaporated. Purification of the residue by chromatography on a column of silicic acid using ether–methanol (19:1) gave 6.89 g (86%) of **22a** as a homogeneous (TLC and NMR) syrup: ^1H NMR ($CDCl_3$) 3.57 (dd, 1, J_{gem} = 11, $J_{4',5'a}$ = 3 Hz, $C_{5'a}$ H), 3.78 (dd, 1, $J_{4',5'b}$ = 2 Hz, $C_{5'b}$ H), 5.57 (d, 1, $J_{1',2'}$ = 3 Hz, $C_{1'}$ H), 7.70 (s, 1, $C_{5(3)}$ H).

The hydrazide **22a** reacted rapidly with acetone to give crystalline **22b** with mp 157–159 °C: $[\alpha]^{25}D$ 72.3° (*c* 0.2, MeOH); ORD (MeOH) $[\Phi]_{250}^{pk}$ 10 000°, $[\Phi]_{230}^{tr}$ 5900°; ^1H NMR 1.79 and 2.01 (s, 3, CMe_2), 5.58 (d, 1, $J_{1',2'}$ = 2 Hz, $C_{1'}$ H), 7.78 ppm (s, 1, $C_{5(3)}$ H).

Anal. Calcd for $C_{33}H_{36}N_4O_5$ (568.68): C, 69.70; H, 6.38; N, 9.85. Found: C, 69.39; H, 6.24; N, 9.80.

4-(2,3,5-Tri-*O*-benzyl-β-D-ribofuranosyl)-1-methylpyrazole-5-carboxylic Acid Hydrazide (22c). A solution of **10** (1.8 g, 3.3 mmol) and anhydrous hydrazine (5 ml) in methanol (20 ml) was heated under reflux for 7 h and then evaporated to dryness. The residue was partitioned between water and ether and the aqueous phase was extracted twice with ether. The combined ether phases were dried ($MgSO_4$) and evaporated, leaving a residue that was triturated with hexane. The solid residue was crystallized from ether–hexane giving 1.6 g (89%) of **22c** with mp 85–87.5 °C: $[\alpha]^{25}D$ −28.4° (*c* 1.0, MeOH); ^1H NMR ($CDCl_3$) 4.07 (s, 3, NMe), 5.03 ppm (d, 1, $J_{1',2'}$ = 7.5 Hz, $C_{1'}$ H).

Anal. Calcd for $C_{31}H_{34}N_4O_5$ (542.61): C, 68.81; H, 6.31; N, 10.32. Found: C, 69.12; H, 6.27; N, 9.84.

4-(2,3,5-Tri-*O*-benzyl-β-D-ribofuranosyl)-3(5)-*tert*-butoxycarboxamidopyrazole (24a). A solution of sodium nitrite (0.72 g, 10.4 mmol) in water (8 ml) was added dropwise to a stirred mixture of **22a** (1.2 g, 2.27 mmol), 2.5 N hydrochloric acid (20 ml), acetic acid (10 ml), and ether (30 ml) at −10 °C. After a further 5 min at −10 °C the ether layer was separated and the aqueous phase was extracted twice with ether. The combined ether phases were washed repeatedly with cold aqueous sodium bicarbonate and with water, dried, and evaporated below 10 °C giving crude **23a** as a pale yellow glass that was essentially pure by TLC using ether–methanol (19:1). A solution of this material in *tert*-butyl alcohol (20 ml) was heated under reflux for 7 h and then evaporated to dryness. The residue was purified by preparative TLC using ether–methanol (98:2) giving 940 mg (71%) of pure **24a** as a dry foam: $[\alpha]^{25}D$ −4.0° (*c* 1.0, MeOH); λ_{max} (MeOH) 228 nm (sh, ε 6400), 258 (850), 264 (700); ^1H NMR ($CDCl_3$) 1.42 (s, 9, *t*-Bu), 3.37 (dd, 1, J_{gem} = 10, $J_{4',5'a}$ = 1.5 Hz, $C_{5'a}$ H), 3.71 (dd, 1, $J_{4',5'b}$ = 3 Hz, $C_{5'b}$ H), 5.04 ppm (d, 1, $J_{1',2'}$ = 6.5 Hz, $C_{1'}$ H).

Anal. Calcd for $C_{34}H_{39}N_3O_6$ (585.70): C, 69.72; H, 6.71; N, 7.17. Found: C, 69.66; H, 6.68; N, 7.12.

4-(2,3,5-Tri-*O*-benzyl-β-D-ribofuranosyl)-3(5)-ethoxycarboxamidopyrazole (24b). The hydrazide **22a** (200 mg, 0.38 mmol) was converted as above into the acyl azide **23a.** This was dissolved in ethanol and heated under reflux for 2 h. Evaporation of the solvent left 170 mg (80%) of essentially pure **24b** that was characterized only by its ^1H NMR spectrum ($CDCl_3$): 1.15 (t, 3, CH_2CH_3), 3.39 (dd, 1, J_{gem} = 11, $J_{4',5'a}$ = 1.5 Hz, $C_{5'a}$ H), 5.05 ppm (d, 1, $J_{1',2'}$ = 6.5 Hz, $C_{1'}$ H).

4-(2,3,5-Tri-*O*-benzyl-β-D-ribofuranosyl)-1-methyl-5-*tert*-butoxycarboxamidopyrazole (24c). The hydrazide **22c** (250 mg, 0.46 mmol) was converted to the acyl azide (**23b**) and thence to the *tert*-butylurethane (**24c**) as described above for **22a** → **24a.** The crude product was purified by preparative TLC using ether–methanol (99:1) giving 200 mg (72%) of **24c** as a homogeneous syrup: $[\alpha]^{25}D$ 3.9° (*c* 0.8, MeOH); λ_{max} (MeOH) 227 nm (sh, ε 6100), 257 (850), 263 (700); ^1H NMR ($CDCl_3$) 1.43 (s, 9, *t*-Bu), 3.49 (dd, 1, J_{gem} = 10, $J_{4',5'a}$ = 3 Hz, $C_{5'}H_a$), 3.66 (dd, 1, $J_{4',5'b}$ = 4 Hz, $C_{5'b}$ H), 3.67 (s, 3, NMe), 3.93 (dd, 1, $J_{1',2'} = J_{2',3'}$ = 5 Hz, $C_{2'}$ H), 4.00 (dd, 1, $J_{3',4'}$ = 8 Hz, $C_{3'}$ H), 4.22 (m, 1, $C_{4'}$ H), 4.4–4.75 (m, 6, OCH_2Ph), 4.99 (d, 1, $C_{1'}$ H), 7.7 (s, 16, Ar and C_3 H).

Anal. Calcd for $C_{35}H_{41}N_3O_6$ (599.74): C, 70.10; H, 6.89; N, 7.01. Found: C, 70.37, H, 6.72; N, 7.04.

A slightly more polar by-product (50 mg) was not identified.

3(5)-Amino-4-(2,3,5-tri-*O*-benzyl-β-D-ribofuranosyl)pyrazole (25a). A. A solution of **24a** (650 mg, 1.08 mmol) in trifluoroacetic acid (9 ml) and water (3 ml) was stirred at room temperature for 7 h. It was then diluted with water, neutralized with solid sodium bicarbonate, and extracted three times with ether. The extracts were dried ($MgSO_4$) and evaporated, leaving 490 mg (94%) of crude **25a** that was predominantly a single spot by TLC (ether–methanol, 19:1) and gave a clean ^{13}C NMR spectrum. It was, however, unstable and gradually decomposed during several days' storage at room temperature. Attempts to isolate a crystalline salt were not successful and accordingly **25a** was generated and used directly in subsequent experiments.

B. A solution of **24b** (160 mg, 0.29 mmol) in ethanol (5 ml) and 5.3 M sodium hydroxide (1 ml) was heated under reflux for 19 h and then evaporated to dryness. The residue was then treated with 6 N hydrochloric acid and extracted three times with ether. The aqueous phase was made basic and extracted four times with chloroform. The extracts were washed with water, dried ($MgSO_4$), and evaporated, leaving 55 mg (39%) of **25a** similar to that in A above.

5-Amino-4-(2,3,5-tri-*O*-benzyl-β-D-ribofuranosyl)-1-methylpyrazole (25b). A solution of **24c** (120 mg, 0.2 mmol) in trifluoroacetic acid (2 ml) and water (1 ml) was stirred at room temperature for 20 h and then worked up as for **25a.** After removal of a trace of unreacted **24c** by preparative TLC (ether–methanol, 98:2) crystallization from hexane gave 65 mg (65%) of **25b** with mp 82–83 °C: $[\alpha]^{25}D$ −31.4° (*c* 1.0, MeOH); λ_{max} (MeOH) 233 nm (ε 6000); ^1H NMR ($CDCl_3$) 3.49 ppm (dd, 1, J_{gem} = 10, $J_{4',5'a}$ = 3 Hz, $C_{5'a}$ H), 3.71 (dd, 1, $J_{4',5'b}$ = 3 Hz, $C_{5'b}$ H), 3.48 (s, 3, NMe), 3.78 (s, 2, NH_2), 3.91 (dd, 1, $J_{1',2'} = J_{2',3'}$ = 6 Hz, $C_{2'}$ H), 3.99 (dd, 1, $J_{3',4'}$ = 7 Hz, $C_{3'}$ H), 4.20 (m, 1, $C_{4'}$ H), 4.35–4.75 (m, 6, OCH_2Ph), 4.94 (d, 1, $C_{1'}$ H), 7.13 (s, 1, C_3 H), 7.2–7.4 (m, 15, Ar).

Anal. Calcd for $C_{30}H_{33}N_3O_4$ (499.61): C, 72.12; H, 6.66; N, 8.41. Found: C, 72.15; H, 6.68; N, 8.37.

2,4-Dioxo-8-(2,3,5-tri-*O*-benzyl-β-D-ribofuranosyl)-1*H*,-3*H*-pyrazolo[1,5-*a*]-1,3,5-triazine (27a). A solution of phenoxycarbonyl isocyanate (**26,** 200 mg, 1.2 mmol) in dry dioxane (3 ml) was added over 20 min to a stirred solution of crude **25a** (390 mg, 0.8 mmol) at room temperature. After a further 22 h the solution was heated under reflux for 4.5 h and then evaporated in vacuo. The residue was triturated with ether giving a solid that was further washed with ether and crystallized from chloroform–ether giving 220 mg (50%) of **27a** with mp 195–201°: $[\alpha]^{25}D$ −64.3° (*c* 0.24, MeOH); λ_{max} (MeOH) 235 nm (sh, ε 5400), 252 (5300), 257 (5300); ν_{max} (KBr) 1775, 1705, 1650 cm^{-1}; ^1H NMR ($CDCl_3$) 3.47 (br d, 1, J_{gem} = 11, $J_{4',5'a} \sim$ 2 Hz, $C_{5'a}$ H), 5.00 (d, 1, $J_{1',2'}$ = 4 Hz, $C_{1'}$ H), 7.46 (s, 1, C_7 H).

Anal. Calcd for $C_{31}H_{30}N_4O_6$ (554.61): C, 67.14; H, 5.45; N, 10.10. Found: C, 66.81; H, 5.34; N, 10.20.

2,4-Dioxo-8-(2,3,5-tri-*O*-benzyl-β-D-ribofuranosyl)-1,3-dimethylpyrazolo[1,5-*a*]-1,3,5-triazine (27b). A solution of **27a** (200 mg, 0.36 mmol) and methyl iodide (1.0 ml) in acetone (7 ml) was stirred for 16 h at room temperature in the presence of anhydrous potassium carbonate (200 mg, 0.36 mmol). The mixture was then filtered and the filtrate was evaporated leaving a residue that was triturated with water. The resulting solid was crystallized from chloroform–hexane, giving 165 mg (79%) of **27b** with mp 111–112 °C: $[\alpha]^{25}D$ −27.7° (*c* 0.4, MeOH); λ_{max} (MeOH) 239 nm (ε 5600), 252 (5800), 258 (6000); ν_{max} (KBr) 1755, 1685, 1620 cm^{-1}; ^1H NMR ($CDCl_3$) 3.46 and 3.60 ppm (s, 3, NMe), 5.09 (d, 1, $J_{1',2'}$ = 7.5 Hz, $C_{1'}$ H), 7.61 (s, 1, C_7 H).

Anal. Calcd for $C_{33}H_{34}N_4O_6$ (582.66): C, 68.03; H, 5.88; N, 9.62. Found: C, 68.28; H, 5.73; N, 9.67.

2,4-Dioxo-8-β-D-ribofuranosyl-1*H*,3*H*-pyrazolo[1,5-*a*]-1,3,5-triazine (28a). A. A solution of **27a** (200 mg, 0.36 mmol) in methylene chloride (2 ml) was added to a solution of boron trichloride (~1 ml) in methylene chloride (8 ml) at −78 °C and the mixture was stored at −78 °C for 1.5 h. A mixture of methanol (4 ml) and methylene chloride (4 ml) was then added dropwise and the mixture was allowed to warm to room temperature and evaporated in vacuo. The residue was coevaporated six times with methanol (10 ml) and crystallized from acetone–hexane, giving 75 mg (73%) of **28a** with mp 184–186 °C dec: $[\alpha]^{25}D$ −50.4° (*c* 0.36, MeOH); λ_{max} (MeOH) 231 nm (sh, ε 4900), 253 (4300); λ_{max} (KBr) 1765, 1715, 1640 cm^{-1}; ^1H NMR (Me_2SO-d_6) 4.69 (d, 1, $J_{1',2'}$ = 5.5 Hz, $C_{1'}$ H), 7.80 ppm (s, 1, C_7 H).

Anal. Calcd for $C_{10}H_{12}N_4O_6$ (284.24): C, 42.26; H, 4.26. Found, 42.23; H, 4.50.

This material showed a single spot on paper chromatography using 2-propanol–concentrated NH_4OH–water (7:1:2) and 1-butanol–acetic acid–water (5:2:3). Paper electrophoresis using pH 9.2 borate buffer showed a single spot with the same mobility as pseudouridine C.

B. Sodium (75 mg, 3 mmol) was added portionwise to a solution of **27a** (100 mg, 0.18 mmol) in dioxane (3 ml) and liquid ammonia (2.5 ml) until a blue color persisted. Ammonium chloride (100 mg) was added and the ammonia was evaporated. An aqueous solution of the residue was neutralized with dilute hydrochloric acid and extracted with chloroform giving 15 mg of unreacted **27a.** The aqueous phase was passed through a column of activated charcoal[44] (1.5 g) and washed thoroughly with water. Elution with ethanol–water–concentrated NH_4OH (50:45:5) followed by evaporation of the eluates gave 20 mg (39%) of material that was shown by paper chromatography and borate electrophoresis as in A to be a mixture of **28a** and presumably its α anomer.

2,4-Dioxo-8-β-D-ribofuranosyl-1,3-dimethylpyrazolo[1,5-*a*]-1,3,5-triazine (28b). Debenzylation of **27b** (170 mg, 0.29 mmol) with boron trichloride was done as described for **27b** above. Crystallization from methanol–ether gave 55 mg (61%) of **28b** with mp 184–184.5 °C: $[\alpha]^{25}D$ −31.0° (*c* 0.5, MeOH); λ_{max} (MeOH) 215 nm (ε 15 400), 240 (5600), 254 (5800); ν_{max} (KBr) 1750, 1670, 1600 cm^{-1}; ^1H NMR (Me_2SO-d_6) 3.25, 3.55 (s, 3, NMe), 4.80 (d, 1, $J_{1',2'}$ = 6 Hz, $C_{1'}$ H), 7.95 (s, 1, C_7 H).

Anal. Calcd for $C_{12}H_{16}N_4O_6$ (312.29): C, 46.15; H, 5.17; N, 17.94. Found: C, 45.70; H, 5.12; N, 17.81.

Registry No.—**1b,** 38821-04-4; **1c,** 39038-02-3; **2,** 37699-02-8; **3,** 59463-89-7; **4b,** 59463-90-0; **4c,** 50866-58-5; **7a,** 59463-91-1; **7b,** 59463-92-2; **9a,** 59463-93-3; **9b,** 59463-94-4; **10,** 59463-95-5; **11,** 16205-54-2; **12,** 57361-98-5; **13,** 59463-96-6; **14** isomer A, 17579-99-6; **14** isomer B, 4167-91-3; **16a,** 57361-95-2; **16b,** 3679-96-8; **16c,** 59463-97-7; **17,** 59463-98-8; **19,** 59463-99-9; **20,** 59464-00-5; **21,** 59464-01-6; **22a,** 59464-02-7; **22b,** 59464-03-8; **22c,** 59464-04-9; **24a,** 59464-05-0; **24b,** 59464-06-1; **24c,** 59492-70-5; **25a,** 59464-07-2; **25b,** 59464-08-3; **26,** 5843-43-6; **27a,** 59464-09-4; **27b,** 59464-10-7; **28a,** 59464-11-8; **28b,** 59492-71-6; benzyl bromide, 100-39-0; ethyl bromide, 74-96-4; propiolic acid, 471-25-0; acetic anhydride, 108-24-7; 5,6,8-tri-*O*-benzyl-2,3,4-trideoxy-D-*erythro*-oct-4-en-2-ynonate, 59464-12-9; acetone, 67-64-1; methyl iodide, 74-88-4.

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