Easy Synthesis and Different Conformational Behavior of Purine and Pyrimidine β-D-*glycero*-Pent-2′-enopyranosyl Nucleosides[1]

Bogdan Doboszewski,[†] Norbert Blaton,[‡] and Piet Herdewijn*,[†]

Rega Institute for Medical Research and Department of Pharmacy, Katholieke Universiteit Leuven, B-3000 Leuven, Belgium

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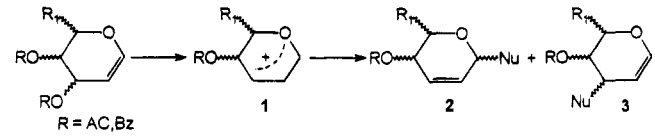
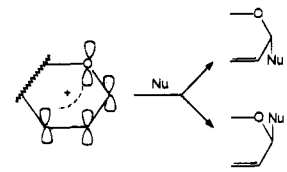
Condensation of 3,4-bis-*O*-(*p*-nitrobenzoyl)-D-xylal with purines and pyrimidines (A, C, 6-chloropurine, G, T, U) without externally added acid catalyst leads to the 2′,3′-unsaturated pentopyranosyl nucleosides in preparatively acceptable yields of both β and α anomers and near complete suppression of formation of the 3′-substituted 1′,2′-unsaturated regioisomers. Anomeric configurations of these analogues of nucleosides have been established for the 4′-*O*-deprotected derivatives by way of ^{13}C NMR. In all nine anomeric pairs the signals of the carbon atoms C-5′ in α anomers are shifted upfield when compared with the corresponding signals of the β anomers. Coupling constants $J_{4'5'ax}$ indicate pseudoaxial positions of purines in **33**–**40**, **45**, and **46**. This is rationalized in terms of a $\pi-\sigma^*_{C\text{-}1'-N\text{-}9}$ resonance and represents a case where aglycons occupy pseudoaxial positions via a mechanism different than the anomeric effect. The same coupling constants of the α-pyrimidines **30**, **32**, **42**, and **44** indicate $^4H_0 \leftrightarrow {}^0H_4$ equilibrium with a marginal preference toward the $^0H_4$ form, whereas the β-pyrimidines **29**, **31**, **41**, and **43** show a preference toward $^0H_4$ probably due to steric interactions.

Reaction of 1,2-unsaturated carbohydrates or glycals[2] with nucleophilic agents mediated by acids yielding 2,3-unsaturated glycosides (accompanied by 1,2-unsaturated regioisomers) (Scheme 1) is known as Ferrier rearrangement.[3–5] The reaction is believed to proceed via a delocalized cation, **1**, formed by departure of the acyloxy moiety from a starting glycal followed by attack of nucleophile from a side which provides maximum continuous overlap of orbitals in a way from transition state to product, i.e., leading to α-glycosides (Scheme 2). This overlap lowers the activation energy versus an alternative transition state leading to β-glycosides. (This idea has been put forward by Corey and Sneen in order to explain preferential formation of axial products during α halogenation of ketones[6] and later used to rationalize stereochemical aspects of reactivity of 4,6-*O*-benzylidene-1,2,3-trideoxy-3-*C*-methylene-D-*erythro*-hex-1-enopyranose activated by iodonium ions during a synthesis of saccharose[7] and also for 3,4,6-tri-*O*-acetyl-2-deoxy-2-nitroso glycals as starting compounds for syntheses of glycosides and 2-amino-2-deoxyglycosides having a 1,2-cis arrangement.[8]) Also, β-glycosides can be anomerized to α-glycosides in acidic medium, favoring therefore formation of the latter, additionally stabilized by the anomeric effect. In general, α-glycosides of *O*-, *N*-, and

Scheme 1



Scheme 2



S-nucleophiles are predominant products of the Ferrier rearrangements. This is not so for *C*-nucleophiles since the resulting *C*-glycosides lack anomeric stabilization in general.[9,10] Also, transition metal catalysts frequently employed for their formation alter the mechanism of a reaction.[11–14] Ferrier rearrangement can also proceed autocatalytically. Several nucleophilic agents react with acetylated glycals in the absence of externally added catalysts to give 2,3-unsaturated glycosides.[2] For example, phenol reacts with tri-*O*-acetyl glucal in boiling chlorobenzene to furnish 80% yield of the anomeric unsaturated glucosides (α:β = 85:15),[15] but methanol or ethanol requires elevated temperature (180 °C).[16] In these cases an effective catalyst can be acetic acid generated during thermal decomposition of a substrate, or a reaction involves initial migration of a double bond to give species **4** (Scheme 3) which reacts further to

[†] Rega Institute for Medical Research.
[‡] Department of Pharmacy.
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(1) Preliminary communication: Doboszewski, B.; Blaton, N.; Herdewijn, P. *Tetrahedron Lett.* **1995**, *36*, 1321–1324. The author has deposited atomic coordinates for **31**, **37**, and **45** with the Cambridge Crystallographic Data Centre. The coordinates can be obtained, on request, from the Director, Cambridge Crystallographic Data Centre, 12 Union RD., Cambridge, CB2 1EZ U.K.
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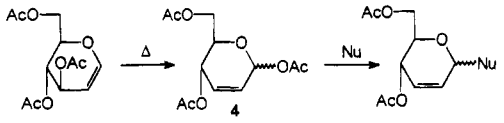
Scheme 3

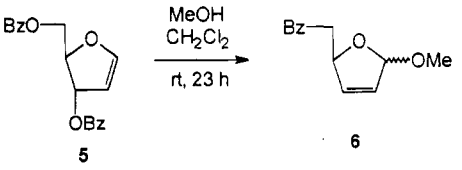


furnish 2,3-unsaturated products.[17] Compounds of the type **4** can be indeed prepared by either thermal or acid-catalyzed isomerization of acetylated glycals[18,19] (Scheme 3). It should be noted that protic acids can promote 1,2-addition to a double bond of a starting acetylated glycal. In order to suppress this reaction, Ferrier and co-workers have introduced $BF_3{\cdot}Et_2O$ as a catalyst.[17] Other catalysts used include J_2, $SnBr_4$, $EtAlCl_2$, HCl, H_2SO_4,[20] $SnCl_4$,[21] $SbCl_5$,[22] CCl_3CO_2H,[23] CF_3CO_2H,[24] $LiCl_4$-trityl-perchloride,[25] and $ZnCl_2$.[26]

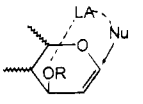
Regiochemical aspects of Ferrier rearrangement (C-1 vs C-3 reaction, Scheme 1) have been rationalized in terms of the hard acids-soft bases principle: carbon atom C-3 in cation **1** is soft, whereas C-1 is hard.[27] Hard bases like alcohols react preferentially at C-1 to form **2** and soft bases, e.g., 6-chloropurine of *N*-benzoyladenine, at C-3 to form **3**. Using nucleobases as nucleophilic agents, formation of both C-1- and C-3-substituted products has been frequently observed (see below). In these cases it can be speculated that either a system has not reached an equilibrium [formation of **3** as the most stable regioisomer (2′,3′-Unsaturated hexopyranosyl nucleosides of a type **2** have been published to rearrange to **3** in acidic media.[19] The same is true for pentopyranosyl nucleosides.[28])] or a nucleobase displays a boarderline character. Ferrier rearrangement has been used to prepare 2′,3′-unsaturated hexopyranosyl nucleosides as α,β mixtures accompanied by 3′-substituted product(s).[19,22-26,29-31]

Data on reactions of pentopyranosyl glycals with heterocyclic bases mediated by acid catalyst is much more limited and inconsistent. Either only α anomer[32] (using thymine and di-*O*-acetyl-D-xylal) or only 3′-substituted 1′,2′-unsaturated product[33] (using *N*-benzoyladenine and the same xylal) has been reported. In most cases, however, anomeric mixtures of 2′,3′-unsaturated pentopyranosyl nucleosides are formed accompanied by 3′-substituted 1′,2′-unsaturated product(s).[34-36] 1,2-Additions without migration of a double bond have been recorded.[37-39] Elimination of either benzoic acid or hydrogen chloride molecules from functionalized 2-deoxypentopyranoses have been reported to generate glycals in situ, which further reacted to yield olefinic pentopyranosyl nucleosides.[40,41] α(β)-2′,3′-Unsaturated pentopyranosyl nucleosides can be converted to β(α) counterparts (in the presence of trifluoroacetic acid) accompanied by the 3′-substituted products like **3**,[28] which do not rearrange back as the most stable compounds.

Scheme 4



It seems that there is no general method to make β/α-configured 2′,3′-unsaturated pentopyranosyl nucleosides with acceptable preparative yields and β/α ratio. A reason for this is the added acid catalyst which promotes formation of the desirable β/α-2′,3′-olefinic products **2** and also undesirable products **3**. Furthermore, it transforms **2** into **3** and anomerizes kinetically formed β anomers into α anomers. Omitting a catalyst therefore could be a way to suppress formation of **3** although formation of the α anomer can still be favored (for *O*-glycosides at least[15]). Several facts need to be pointed out here. (a) Furanosyl glycal **5** reacts with methanol at room temperature without acid catalyst to furnish a glycoside, **6**, believed to be β[42] (Scheme 4). (b) It has been suggested that some β selectivity could be obtained during early stage of reaction of glycals with nucleophiles as shown in **7**, where Lewis acid catalyst coordinates both a leaving group and an incoming nucleophile.[43] (c) The concept of



S_N2' reactivity (without a catalyst) has been realized using reactive glycals **8** and **9**,[44] which react with sodium methoxide to furnish products **10** and **11**, respectively (Scheme 5). In both cases the methoxide moiety enters on the anomeric position in a syn manner with respect

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Scheme 5

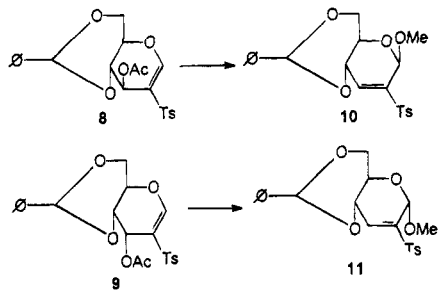
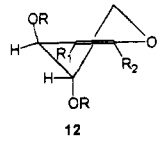


Chart 1[a]

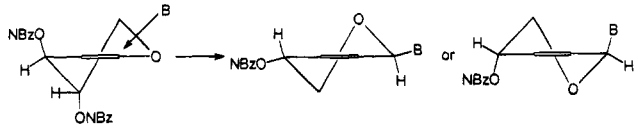


R = Ac	$R_1 = R_2 = H$[45-47]	
R = Bz	$R_1 = R_2 = H$[48]	
R = Ac	$R_1 = H$	$R_2 = NO_2$[49]
R = Ac	$R_1 = H$	$R_2 = OAc$[50]
R = Ac	$R_1 = CH_2OAc$	$R_2 = OAc$[51,*]

12

[a] Asterisk denotes that the compound was originally published as an L-isomer.

Scheme 6



13

to a leaving group at the carbon atom C-3. (d) ^1H NMR data of xylals uniformly point out that the compounds adapt the preponderant $^5H_4$ conformation **12** (up to 85% of the equilibrium mixture[45]) with pseudoaxial and axial functionalities at the carbon atoms C-3 and C-4, respectively (Chart 1). Ferrier and Sankey rationalized this in terms of "allylic effect",[51] a tendency of allylic acetoxy or benzoyloxy groups to adopt a pseudoaxial orientation in unsaturated carbohydrates. Many other examples are known where electronegative substituents on the allylic position occupy preferentially an axial orientation via a mechamism different than the anomeric effect, being either a $\sigma^*-\pi$ stabilization or a vinylogous anomeric effect.[9,10,52-54]

Facts a–d suggest that if a good leaving group is put on position C-3 of D-xylal, e.g., *p*-nitrobenzoyl as in compound **13**, then a nucleobase could approach the anomeric position from the same side to provide some β selectivity, without mediation of an acid catalyst (Scheme 6). If such stereochemical outcome would be a consequence of a stereoelectronic effect or a result of conformational properties of a transition state is not clear. This issue has been extensively discussed.[55,56] *p*-Nitrobenzoic acid liberated during a reaction turned out to be too weak to promote **2** → **3** rearrangement (Scheme 1) (see below). One could therefore anticipate formation of β/α anomeric mixtures only. This reasoning stimulated us to investigate the reaction of nucleobases with bis-*O*-(*p*-nitrobenzoyl)-D-xylal without added catalysts. We needed the β-D-*glycero*-pent-2′-enopyranosyl nucleosides as starting materials to introduce the 3′-hydroxymethyl appendix and eventually invert a configuration at the 4′-position to obtain nucleoside analogues for antisense/antiviral studies.[57] Also, since the nucleobases in the 2′,3′-unsaturated pentopyranosyl nucleosides occupy both an anomeric position and an allylic position, a study of the NMR spectra of the target compounds might give us insight in the predominant factor influencing the conformation of these compounds.

The starting compound **13**, a highly crystalline 3,4-bis-*O*-(*p*-nitrobenzoyl)-D-xylal, has been prepared from D-xylal[58,59] (*p*-nitrobenzoyl chloride, pyridine, DMAP). The compound adopts preferentially the conformation $^5H_4$ as evidenced by a coupling pattern of the protons H4, $H5_{eq}$, and $H5_{ax}$ (in C_6D_6: $J_{4,5ax} = 3.1$ Hz, $J_{4,5eq} = 1.5$ Hz). The following nucleobases have been used throughout this study: N^6-benzoyladenine,[60,61] 6-chloropurine, N^4-acetyl- and N^4-benzoylcytosine,[62] N^2-isobutyryl-O^6-[2-(*p*-nitrophenyl)ethyl]guanine,[63] thymine, N^3-benzoylthymine,[64] uracil, and N^3-benzoyluracil[64]. When these bases, their trimethylsilyl derivatives, or their sodium salts were incubated with **13** in dimethylformamide at elevated temperature without addition of any acid catalyst, anomeric mixtures of 2′,3′-unsaturated pentopyranosyl nucleosides **14A** were formed (Scheme 7).

Preparative yields varied between 22% and 76% and anomeric ratios between β/α = ca. 2/1 and 1/2. Relevant data are listed in Table 1. Only in the case of *N*-benzoylcytosine were we able to isolate a 3′-substituted product, **18** (**14C**, B = C^{Bz}), of unspecified configuration formed in ca. 3% yield. Our result with *N*-benzoyladenine and thymine (only formation of the 2′,3′-unsaturated products α,β-**22** and -**28**, respectively) stays in sharp contrast with the published data where exclusive formation of 3′-substituted 1′,2′-unsaturated product(s)[33,41] or the α anomer[32] has been reported. Uracil yielded two N^1,N^3-bis-substituted products, **27A,B**, besides the β,α products **25** and **26**. In an attempt to suppress this bis-glycosylation, we used N^3-benzoyluracil. Unexpectedly complex reaction mixtures were obtained, even though formation of **27A,B** had been suppressed. Also, condensation using trimethylsilylated N^3-benzoylthymine was more complex than TMS(T), and both pathways have not

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Scheme 7

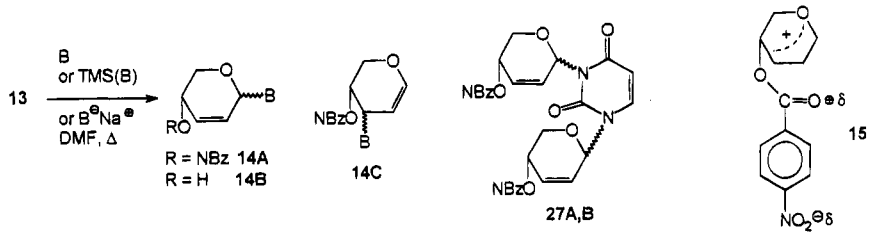
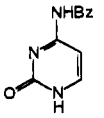
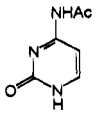
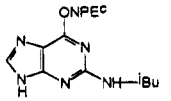
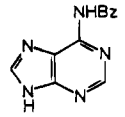
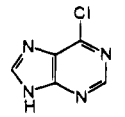
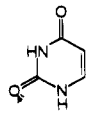
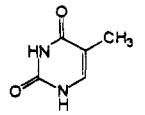


Table 1. Results of the Condensation Reaction of Different Bases with 3,4-di-*O*-(*p*-nitrobenzoyl)-D-xylal

Entry	Base	Reactive form, reaction time, temperature	Product number	Total yield of 14A, %	β:α
1	 , C^{Bz}	TMS derivative 15 min, bp	16(β); 17(α)	73%	1:1[a]
2	 , C^{AC}	TMS derivative, 5 h, 110°	19(α,β)	52%	1:1[b]
3	 , $G^{NPE^c}_{iBu}$	(i) TMS derivative 40 min, bp	20(β); 21(α)	76%	47:26[d]
4		(ii) used as such 45 min, bp		60%	1:1
5	 , A^{Bz}	(i) used as such 10 min, bp	22(α,β)	60%	25:20[d]
6		(ii) TMS-derivative 10 min, bp		28-44%[e]	ca 2:1
7		(i) used as such 10 min, bp	23(β); 24(α)	57%	1:1[a]
8		(ii) Na salt 15 min, bp		39%	1:2
9		Na salt 1 h, bp	25(β); 26(α)	23%	3:5[a]
10		TMS derivative 7 h, 110°	28(α,β)	48%	1:1[d]

[a] Separable as 4′-*O*-nitrobenzoates. [b] Unseparable. [c] NPE, (*p*-nitrophenyl)ethyl. [d] Separation much easier after 4′-deesterification (catalytic NaOMe in dioxane–HOMe). [e] Inconsistent yields and β/α ratios.

been further examined. It is noteworthy that only N^1 (pyrimidines) and N^9 (purines) regioisomers have been formed in these condensations. Moderate yields are not detrimental because of easy availability of the starting glycal **13** and simplicity of the condensation procedure.

These results can be rationalized as follows. Due to a favorable conformation of the glycal **13** and its sufficient reactivity, both purines and pyrimidines react with it as shown in Scheme 6 during initial stages of reaction providing β anomers. *p*-Nitrobenzoic acid liberated during the condensation and also during thermal decomposition of **13** starts to protonate the 3-(*p*-nitrobenzoyl) group to form a cation, **15**, which is not stabilized by anchimeric assistance of the carbonyl group of the 4-*p*-nitrobenzoate due to the electron-withdrawing effect of the *p*-nitro group. (The substrate **13** alone decomposes substantially in boiling DMF. At least six more polar products can be seen on TLC. Unchanged **13** can be isolated in ca. 20% of original amount after 45 min of heating). Therefore incoming nucleophiles attack only the anomeric carbon atom from both possible sides providing α,β mixtures **14A**, which are products of a kinetic control as stated in ref 26. No conversion of the α(β) to β(α) nor to 3′-substituted products takes place under the reaction conditions as evidenced by the following experiment. Incubation of either α-**17** or β-**16** with 2 mol equiv of

Table 2. Selected NMR Parameters of the 4′-*O*-Deprotected Pentopyranosyl Nucleosides[a]

	α anomers				β anomers			
base	compd no.	δ C-5′	$J_{4'5'}$	$J_{4'5''}$	compd no.	δ C-5′	$J_{4'5'}$	$J_{4'5''}$
C^{Bz}	**30**	67.05	4.1	4.9	**29**	68.00	4.4	6.1
C	**32**	67.04	3.9	4.5	**31**	68.07	4.6	6.6
U	**42**	67.36	3.9	4.4	**41**	68.18[68]	4.7	6.6[68]
T	**44**	67.72	3.7	4.0	**43**	68.30[68]	4.8	6.9[68]
G^{NPE}_{iBu}	**34**	65.02	4.4	n.d.	**33**	67.17	3.3	3.7
A^{Bz}	**36**	65.02	5.2	7.8	**35**	67.16	3.6	2.9
A	**38**	64.80	5.1	8.0	**37**	66.83	3.7	3.4
6-OMe-purine	**40**	64.75	5.4	7.8	**39**	66.94	3.5	3.3
G_{iBu}	**46**	64.17	5.5	7.8	**45**	67.50	3.7	3.3

[a] δ in ppm, $J_{4'5'}$, $J_{4'5''}$ in Hz for DMSO-d_6 solutions, recorded on a Varian Gemini 200 spectrometer.

p-nitrobenzoic acid in boiling DMF during a period of 6 times the effective condensation time did not produce any traces of the opposite anomer nor 3′-product **18**. This has been checked only for *N*-benzoylcytidines because all three products were available, and these results contrast with a similar experiment using trifluoroacetic acids as catalyst.[28] Suppression of formation of the 3′-substituted 1′,2′-unsaturated products **14C** therefore can be attributed to the lack of anchimeric stabilization of the cation **15** and the fact that liberated *p*-nitrobenzoic acid is too weak to force either α(β) to β(α) or **14A** ↔ **14C** equilibration.

As seen in Table 1, anomeric ratios of the compounds **14A** change from case to case. For trimethylsilylated guanine and adenine (entries 3 and 6), we were able to get some β selectivity probably due to the elevated nucleophilicity of these two bases. In most cases (entries 1, 2, 4, 7, and 10), equal proportions of anomers have been formed. When sodium salts were used (entries 8 and 9), the predominant anomer was α probably due to decomposition of the substrate **13** by the basic salts. In these circumstances more *p*-nitrobenzoic acid is produced which forces a reaction to proceed along the ionic intermediate **15**. This cation evidently displays elevated facial electrophilicity from a *re* side to provide α anomers which are stabilized by the $\pi-\sigma^*$ conjugation (see below).

Separation of the 4′-*O*-*p*-nitrobenzoylated β/α anomers **14A** was possible for B = C^{Bz} (**16** and **17**), 6-chloropurine (**23** and **24**), and uracil (**25** and **26**). Small amounts of anomerically pure guanosines **20** and **21** have been obtained for analytical purpose. It was much easier to separate β/α anomers **33/34** and **35/36** after 4′-*O*-deesterification (catalytic NaOMe in dioxane–HOMe) by either gravitational or flash chromatography. The only troublesome mixture is **43/44** where HPLC was necessary to obtain a complete separation. 6-Chloropurine nucleosides **23** and **24** have been treated with excess of sodium methoxide in methanol to furnish 6-methoxy derivatives **39** and **40** (further converted to adenosines **37** and **38**, respectively, by ammonolysis). All β-4′-*O*-deprotected nucleosides are chromatographically more polar than their corresponding α anomers.

Anomeric configurations have been established using chemical shifts of the carbon atoms C-5′ in the 4′-*O*-deprotected compounds **14B**. In all α/β pairs the signals of the C-5′ atoms in the α anomers are moved upfield compared to those in the β anomers, evidently as a result of increased steric congestion in the vicinity of the C-5′ nuclei (Table 2). This effect is not very pronounced (0.5–2 ppm) but is uniformly displayed by all nine anomeric pairs **14B** described here. Interestingly, the anomeric carbon atoms in **14B** do not demonstrate such changes of shielding. Coupling constants $J_{H1',H2'}$ are not informative due to a narrow range of their variation. These structural assignments were confirmed by X-ray analysis of **31**, **37**, and **45** (Figure 1) and by comparison with the data for the known (2′,3′-dideoxy-β-D-*glycero*-pent-2′-enopyranosyl)thymine **43**[65,66] and -uracil **41**[66]

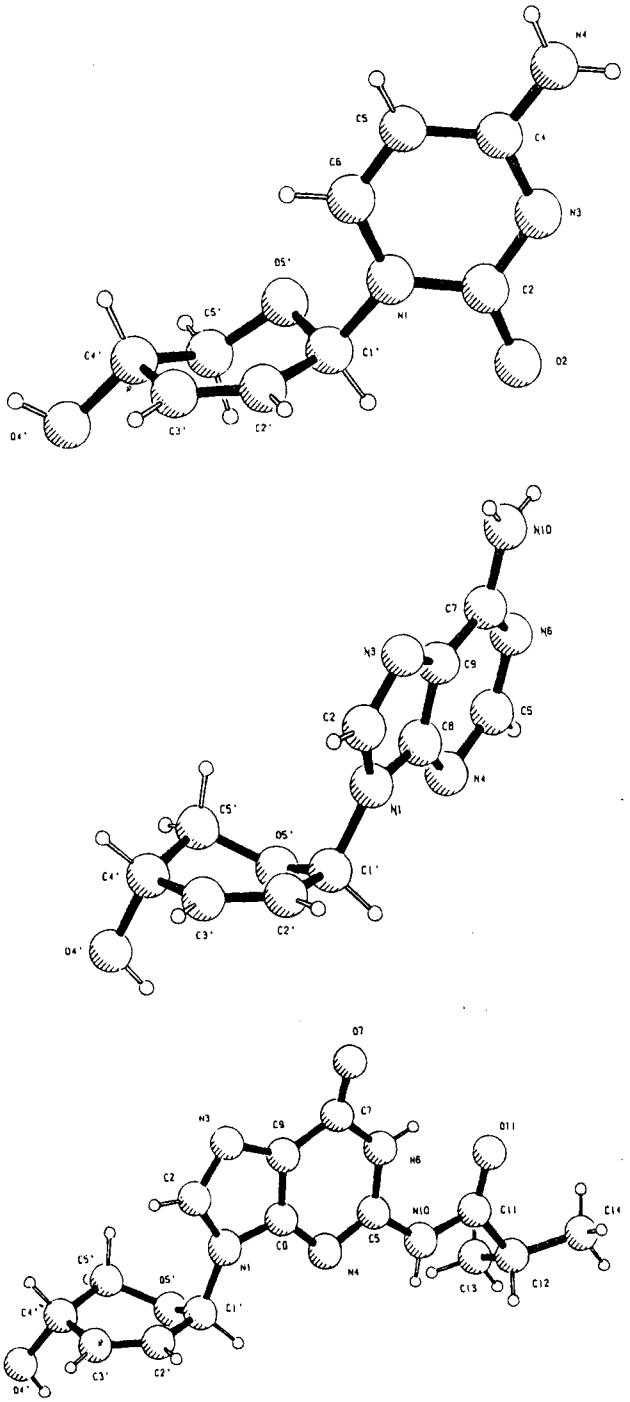


Figure 1. X-ray structures of **31**, **37**, and **45**.

(65) Pérez-Pérez, M. J.; Rozenski, J.; Herdewijn, P. *Bioorg. Med. Chem. Lett.* **1994**, *4*, 1199–1202.
(66) Doboszewski, B.; Blaton, N.; Rozenski, J.; De Bruyn, A.; Herdewijn, P. *Tetrahedron* **1995**, *51*, 5381–5396.

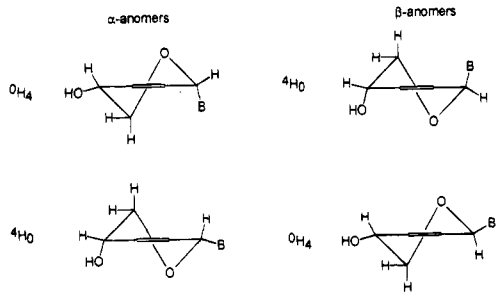
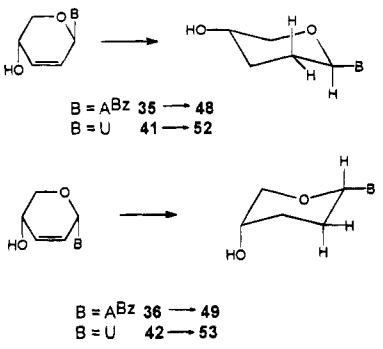


Figure 2. Conformational forms of the 2′,3′-unsaturated pentopyranosyl nucleosides.

Scheme 8

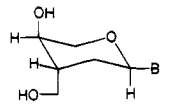


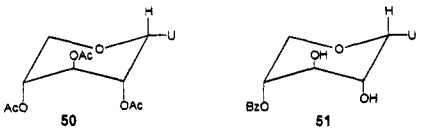
prepared by a stepwise procedure from (2′,3′,4′-tri-*O*-acetyl-β-D-xylopyranosyl)thymine and -uracil. It should be noted that Hudson's rules of isorotation can not be used to correlate the optical rotation values with anomeric configuration for nucleosides,[67,68] whereas generality of application of circular dichroism for the same purpose has been questioned for 2′,3′-unsaturated hexopyranosyl nucleosides.[29]

O,*N*-Bis-deprotected nucleosides **31**, **32**, **37**, and **38** have been prepared from their respective *N*-protected derivatives by either NaOMe/HOMe or NH_3/HOMe treatment. O^6-Deprotection of guanosines **33** and **34** has been done by DBU/Py treatment[63] to furnish **45** and **46**.

Inspection of the coupling constants $J_{4'5'}$ and $J_{4'5''}$ in 4′-*O*-deprotected nucleosides (Table 2) reveals the following pattern. Purines in **33**–**40**, and **45**, and **46** are oriented pseudoaxially via the predominant conformation $^0H_4$ for the α anomers and $^4H_0$ for the β anomers (Table 2, Figure 2) notwithstanding unfavorable steric repulsions. Clearly an overriding effect must operate, which is not an anomeric effect, though. This turned out clear after catalytic reduction of the 2′,3′-double bond in **35** and **36** to furnish **48** and **49**, respectively (Scheme 8). Coupling constants $J_{1'2'eq} = 2.1$ Hz and $J_{1'2'ax} = 11.0$ Hz in **48** and $J_{1'2'eq} = 2.1$ Hz and $J_{1'2'ax} = 10.2$ Hz in **49** indicate conformations $^4C_1$ and $^1C_4$, respectively, with equatorially oriented *N*-benzoyladenine. Steric bulk of this moiety is therefore the driving force which controls conformations of the saturated compounds **48** and **49**. If conformations of these two compounds were controlled by the anomeric effect of *N*-benzoyladenine, then this moiety would be oriented axially, which is obviously not the case. The anomeric effect of purines and pyrimidines is low. Thus, presence of the 2′,3′-double bond is essential to ensure pseudoaxial orientations of purines in compounds **33**–**40**, **45** and **46**. Since the anomeric position in 2′,3′-unsaturated nucleosides is also the allylic position, one can speculate that a resonance between a π electron cloud and an antibonding orbital of the C-1′–N-9 bond is responsible for the stabilizing effect which overrides steric repulsion. This resonance is possible only when purines are oriented (pseudo)axially. Such $\pi-\sigma^*$ interactions have been introduced to rationalize preferential axial orientations of electronegative substituents on allylic position in cyclic systems as already mentioned.[9,10,52-54] When examining structures **37** and **45** (Figure 1), the influence of the anomeric effect and of an O-5′–C-5′–C-4′–O-4′ gauche effect can still be present and contribute to the driving force for the conformational preference. Compounds **33**–**40**, **45**, and **46** represent an interesting case where substituents bound to the anomeric carbon atom adopt pseudoaxial orientation via a mechanism different than the anomeric effect.

The resonance $\pi-\sigma^*$ has also some influence on the conformational equilibria of the 2′,3′-unsaturated pentopyranosyl pyrimidines (Table 2, Figure 2). α Anomers **30**, **32**, **42**, and **44** show an equilibrium, $^4H_0 \leftrightarrow {}^0H_4$, with marginal preference toward the $^0H_4$ conformation with pseudoaxially oriented base moieties and pseudoequatorial 4′-OH groups. Energetic gain due to this resonance is nearly completely counterbalanced by steric repulsion between the aglycons and the axial proton H-5′. Steric bulk of pyrimidines is a factor strongly influencing conformations of pentopyranosyl nucleosides. For example, nucleosides **47** adapt a conformation, $^4C_1$, both in a solution and in a crystalline state with equatorially oriented thymine and uracil and diaxially disposed functionalities at the carbon atoms C-3′,4′.[66] (2′,3′,4′-Tri-*O*-acetyl-α-D-xylopyranosyl)uracil (**50**) and (4′-*O*-benzoyl-α-D-xylopyranosyl)uracil (**51**) adopt exclusively a conformation, $^1C_4$, with equatorial uracil and three functional groups at the atoms C-2′,3′,4′ oriented axially.[66]





Steric bulk of the aglycons and possibly also reversed anomeric effect due to a partial positive charge on the nitrogen atom N^1 seem to be the driving forces for these conformational features. (Interestingly, theoretical calculations performed for 2-aminotetrahydropyran and 2-tetrahydropyranylammonium ion indicate equatorial orientations of both $-NH_2$ and $-NH_3^+$ due to steric and electrostatic effects, respectively.[69]) Presence of the 2′,3′-double bond and consequently $\pi-\sigma^*$ conjugation in **30**, **32**, **42**, and **44** are therefore essential to explain roughly equal population of conformers $^4H_0$ and $^0H_4$. When this C–C double bond is reduced as in D-*glycero*-pentopyranosyluracils **52** and **53**, the uracil moiety occupies exclusively equatorial position as evidenced by the mag-

(67) Lemieux, R. U.; Lown, J. W. *Can. J. Chem.* **1963**, *41*, 889–897.
(68) Emerson, T. R.; Ulbricht, T. L. V. *Chem. Ind.* **1964**, 2129.
(69) Salzner, U.; von Ragué Schleyer, P. *J. Org. Chem.* **1994**, *59*, 2138–2155.

nitude of the coupling constants $J_{H1',2'eq}$ and $J_{H1',2'ax}$, just like adenine in **48** and **49**.

Coupling constants $J_{4'5'ax}$ in **29**, **31**, **41**, and **43** suggest a preferential conformation, $^0H_4$, with pseudoequatorial aglycons and 4′-OH groups. The percentage of this conformation could not be determined exactly due to a lack of experimental data on the magnitude of the diaxial coupling constant in a frozen conformation, $^0H_4$. An alternative conformation, $^4H_0$, with pseudoaxial aglycons and 4′-OH goups provides a $\pi-\sigma^*$ stabilization but also introduces unfavorable steric interactions; the latter are evidently stronger. The steric effect of pyrimidine base disfavors pseudoaxial orientation which should be preferred when the influence of stereoelectronic effects (O-5′−C-5′−C-4′−O-4′ gauche effect, anomeric effect, allylic effect of 4′-OH group, $\pi-\sigma^*_{C\text{-}1'-N\text{-}1}$ interaction) dominates. Interplay of these factors ensures a predominant $^0H_4$ form. It is clear that a $\pi-\sigma^*$ conjugation also operates for pyrimidines, but it is not as efficient as for purines.

Application of the olefinic nucleosides **29**, **35**, **41**, **43**, and **45** for the synthesis of branched derivatives like **47** for antiviral/antisense studies will be published separately.

Conclusions

"No acid-added" Ferrier rearrangement of glycal **13** and purines/pyrimidines (A, C, 6-chloropurine, G, T, U) provides preparatively acceptable yield of α,β-2′,3′-unsaturated pentopyranosyl nucleosides. Formation of the thermodynamically most stable 3′-substituted 1′,2′-unsaturated nucleosides has been practically avoided. Anomeric configurations in 4′-*O*-deprotected 2′,3′-unsaturated nucleosides **29**−**46** can be determined using only ^{13}C NMR. In all anomeric pairs studied here, chemical shifts of the carbon atoms C-5′ in the α anomers are smaller than in the corresponding β anomers. Purines adopt pseudoaxial orientiation in **33**−**40**, **45**, and **46** probably due to the $\pi-\sigma^*_{C\text{-}1'-N\text{-}9}$ stabilization. This stabilization is counterbalanced by steric repulsions in α pyrimidines **30**, **32**, **42**, and **44** which show a $^4H_0 \leftrightarrow {}^0H_4$ equilibrium with marginal preference toward the $^0H_4$ form. In β pyrimidines **29**, **31**, **41**, and **43**, steric interactions dominate a conformational equilibrium with marked preference toward the $^0H_4$ form.

Experimental Section

General. Glassware was dried at 130 °C and cooled under dry nitrogen. Reactions involving water-sensitive reagents were performed under dry nitrogen. After evaporations, vacuum was broken with dry nitrogen using a balloon. NMR spectra and mass exact measurements were performed as described in ref 66. NMR spectra are reported in δ units. X-ray diffractions intensities were measured on a Stoe STADI4 diffractometer using graphite-monochromated Mo Kα radiation. The atomic coordinates and other data for **31**, **37**, and **45** were deposited in the Cambridge Crystallographic Data Centre (see ref 1).

3,4-Bis-*O*-(*p*-nitrobenzoyl)-D-xylal (13). 3,4-Di-*O*-acetyl-D-xylal[58,59] (55 g, 0.275 mmol) in 900 mL of dry methanol was deacetylated with catalytic NaOMe overnight and treated with several pieces of solid CO_2. After evaporation and drying, pyridine (900 mL) was added followed by *p*-nitrobenzoyl chloride (122 g, 1.2 mol equiv) at 0 °C. After overnight reaction, a few milliliters of water was added to destroy excess acyl chloride, and extraction was performed ($CH_2Cl_2-H_2O$). The organic layer was successively washed with water, dilute HCl, aqueous saturated $NaHCO_3$, and finally water. After drying ($MgSO_4$) and evaporation, the residue was coevaporated with *p*-xylene to remove any remaining pyridine. The product crystallized from EtOAc after addition of hexane to turbidity: yield 86.5 g, 76%, for two steps; mp 123−124 °C (crystallized EtOAc−hexane); ^1H NMR (benzene-d_6) 7.88−7.74 (8H), 6.23 (1H, d, J_{12} = 6.2 Hz), 5.47−5.41 (1H), 5.29−5.22 (1H), 5.16 (1H, ddd, J_{21} = 6.4 Hz, J_{23} = 5.0 Hz, J_{24} = 1.6 Hz), 4.20 (1H, ddd, J_{5ax3} = 1.8 Hz, J_{5ax4} = 3.1 Hz, J_{5ax5eq} = 12.5 Hz, H5ax), 3.87 (1H, dd, J_{5eq4} = 1.5 Hz, J_{5eq5ax} = 12.3 Hz, H5 equiv); ^{13}C NMR (DMSO-d_6) 163.48, 150.64, 134.99, 134.72, 131.07, 131.11, 124.03 (C aromatic), 149.24, 96.78, 67.98, 64.36, 63.60; MS (CI, isobutane) calcd for $C_{19}H_{14}N_2O_9$ + H 415.0777, found 415.0672.

[4′-*O*-(*p*-Nitrobenzoyl)-2′,3′-dideoxy-β-D-*glycero*-pent-2′-enopyranosyl]-N^4-benzoylcytosine (16), α Anomer 17, and 3′-Substituted Product 18. A mixture of N^4-benzoylcytosine[62] (6.3 g, 29.3 mmol) in 70 mL of hexamethyldisilazane (HMDS) and a catalytic amount of $(NH_4)_2SO_4$ were boiled overnight. The solution was cooled to room temperature. DMF (200 mL) was added, and all volatiles were evaporated. To the resulting solid residue was added DMF (200 mL), and the flask was warmed up in a silicon oil bath (~190 °C). When the heterogenous solution reached boiling point, glycal **13** (12 g, 29 mmol) was added in one portion. After 15 min heating was discontinued. TLC (EtOAc−toluene, 4:1) showed a spot having R_f 0.55 of the 3′-substituted product **18**, R_f 0.42 of the β anomer **16**, and R_f 0.23 of the α anomer **17**. When the solution reached room temperature, some unidentified material crystallized (1.1 g) and was removed by filtration. DMF was evaporated. To the semisolid residue was added chloroform (~300 mL) resulting in a spontaneous crystallization of the β isomer **16**, which was filtered out. The crystals were washed with chloroform and dried. An amount of pure **26** (4.92 g) was obtained at this stage. The chloroform solution was washed with aqueous saturated $NaHCO_3$ and water, dried, and evaporated to furnish the dark-brown syrup. Flash chromatography (gradient EtOAc−toluene, 3:1, EtOAc−toluene, 4:1, neat EtOAc) furnished 0.463 g (3.4%) of **18**, 0.30 g of **16** (total 5.22 g), and 4.62 g of **17**. Total yield of β/α products was 73%. No interconversion of β(α) into α(β) nor **18** was detected by TLC when **16** or **17** was incubated with 2 mol equiv of *p*-nitrobenzoic acid in DMF at bp during 90 min.

16: mp dec ca. 250 °C (crystallized dioxane−MeOH); ^1H NMR (DMSO-d_6) 11.40 (1H, s), 8.42−7.50 (11H), 6.60 ($^1/_2$H, dd, J = 1.4, 4.3 Hz), 6.58−6.49 (1.5H), 6.27 (1H, dd, $J_{1'2'}$ = 2.9 Hz, $J_{2'3'}$ = 10.3 Hz), 5.51 (1H, q, $J_{4'5'} = J_{4'5''} = J_{4'3'}$ = 3.7 Hz), 4.15 (1H, dd, $J_{5'4'}$ = 3.3 Hz, $J_{5'5''}$ = 13.6 Hz), 4.04 (1H, dd, $J_{5''4'}$ = 2.9 Hz, $J_{5''5'}$ = 13.6 Hz); ^{13}C NMR (DMSO-d_6) 164.10, 163.81 (C carbonyl), 154.77, 150.63, 147.25, 135.10, 133.36, 133.09, 131.10, 129.19, 128.98, 128.74, 124.23, 96.29, 77.47, 66.61, 63.04 (C-5′); UV (MeOH) λ_{max} 262.4 nm (ε = 44 202); MS (thioglycerol) calcd for $C_{23}H_{18}N_4O_7$ + H 463.1254, found 463.1238.

17: mp 171−172 °C (crystallized dioxane−MeOH); ^1H NMR (DMSO-d_6) 11.38 (1H, s, NH), 8.44−8.25, 8.10−7.97, 7.72−7.39 (11H), 6.59−6.44 (2H), 6.25 (1H, dd, $J_{2'3'}$ = 11.3 Hz), 5.42 (1H, bs, half-width = 10.9 Hz), 4.20 (2H, AB, $J_{5'4'}$ = 2.7 Hz, $J_{5''4'}$ = 1.9 Hz, $J_{5'5''}$ = 13.2 Hz); ^{13}C NMR (DMSO-d_6) 167.65, 164.20, 163.84, 154.62, 150.60, 146.19, 135.17, 133.30, 133.07, 131.63, 131.17, 128.70, 128.20, 124.15, 97.48, 78.83, 65.89 (C-5′), 65.05; UV (MeOH) λ_{max} 260.7 nm (ε = 42 319); MS (thioglycerol) calcd for $C_{23}H_{18}N_4O_7$ + H 463.1254, found 463.1249.

18: mp 105−120 °C (crystallizeddioxane−MeOH); ^1H NMR (DMSO-d_6) 11.27 (1H, s), 8.44−7.99 and 7.69−7.14 (11H), 7.05 (1H, dd, $J_{1'2'}$ = 6.2 Hz, $J_{1'3'}$ = 1.5 Hz), 5.43 (1H, bs, half-width = 9.5 Hz), 5.22 (1H, t, $J_{3'4'} = J_{3'2'}$ = 4.7 Hz), 4.94 (1H, ddd, $J_{2'1'}$ = 6.0 Hz, $J_{2'3'}$ = 4.6 Hz, $J_{2'4'}$ = 1.1 Hz), 4.26 (1H, ddd, $J_{5'4'}$ = 4.5 Hz, $J_{5'5''}$ = 11.9 Hz, $J_{5'3'}$ = 0.8 Hz), 4.06 (1H, dd, $J_{5''4'}$ = 1.7 Hz, $J_{5''5'}$ = 12.4 Hz); ^{13}C NMR (DMSO-d_6) 167.53, 163.40, 163.21, 155.31, 147.65, 150.74, 149.70, 134.72, 133.39, 132.99, 131.10, 129.16, 128.70, 96.86, 96.00, 69.11, 63.08 (C-5′), 51.86; UV (MeOH) λ_{max} 261.2 nm (ε = 36 801), 301.6 (ε = 14 100); MS (thioglycerol) calcd for $C_{23}H_{18}N_4O_7$ + H 463.1254, found 463.1241.

When *N*-acetylcytosine was used instead of *N*-benzoylcytosine, unseparable mixture of α,β anomers **19** was isolated

in 52% yield (β:α = 1:1) after 5 h of reaction time at 110 °C. **19**: ^{1}H NMR data not presented due to complexity of the 200 MHz spectrum; ^{13}C NMR (DMSO-d_6) 171.33, 164.17, 164.06, 163.02, 154.94, 154.69, 150.57, 147.23, 146.16, 135.13, 131.64, 131.13, 131.04, 129.10, 128.99, 128.07, 124.01, 96.64, 95.47, 78.77, 77.42, 65.86, 65.01, 64.74, 63.01, 24.61.

[4′-*O*-(*p*-Nitrobenzoyl)-2′,3′-dideoxy-β-D-*glycero*-pento-2′-enopyranosyl]-N^2-isobutyryl-O^6-[2-(*p*-nitrophenyl)ethyl]guanine (20) and α Anomer 21. Coupling of trimethylsilylated N^2-isobutyryl-O^6-[2-(*p*-nitrophenyl)ethyl]guanine[63] (12 g, 32.4 mmol) and **13** (12.8 g, 31 mmol) in 250 mL of DMF at bp, during 40 min, was performed as above. After evaporation of the solvent and coevaporation with *p*-xylene, extraction was performed ($CHCl_3$–aqueous saturated $NaHCO_3$). Unreacted guanine was crystallized in a chloroform phase and filtered out (3.7 g). Organic phase was dried ($MgSO_4$) and evaporated. TLC (CH_2Cl_2–MeOH, 20:0.7) showed two principal products, R_f 0.78 (α anomer **21**) and 0.70 (β anomer **20**), in approximate proportions 1:2, accompanied by two minor products, R_f 0.56 and 0.31.

Chromatography (CH_2Cl_2–MeOH, 20:0.3) furnished 10.49 g of a mixture of **20** and **21** (76% counting on a guanine which had effectively reacted or 52% on a total guanine taken for condensation), 0.60 g of the product R_f 0.56, and 0.62 g of the product R_f 0.31. Separation of the anomers **20** and **21** was difficult, and only small amounts of pure compounds were obtained for analytical purpose. The two more polar minor product were not further studied, since they decomposed during 6-*O*-deprotection (DBU/Py). Coupling of the glycal **13** (1.5 g, 3.6 mmol) with N^2-isobutyryl-O^6-[2-(*p*-nitrophenyl)ethyl]-guanine (1.34 g, 3.6 mmol) in boiling DMF during 45 min yielded 60% of **20/21** mixture in approximate ratio 1:1.

20: amorphous; ^{1}H NMR (DMSO-d_6) 10.45 (1H, s), 8.41–9.16 and 7.70–7.65 (9H), 6.61–6.40 (3H), 5.49 (1H, d, $J_{4'5'}$ = 4.1 Hz), 4.82 (2H, t, $J_{CH_2\text{-}CH_2}$ = 6.6 Hz), 4.22 (1H, dd, $J_{5'4'}$ = 3.4 Hz, $J_{5'5''}$ = 14.0 Hz), 4.07 (1H, d, $J_{5''5'}$ = 13.4 Hz), 3.40–3.29 (CH_2PhNO_2, superimposed on the residual H_2O signal), 2.93 (1H, quint, $J_{CH\text{-}CH_3}$ = 7.0 Hz), 1.12 (6H, d, $J_{CH_3\text{-}CH}$ = 6.7 Hz); ^{13}C NMR (DMSO-d_6) 175.43, 164.13, 160.13, 153.08, 152.60, 146.80, 146.55, 141.93, 135.19, 131.07, 130.63, 128.62, 127.55, 124.21, 123.67, 117.60, 74.39, 66.74, 64.66, 63.01 (C-5′), 34.61, 34.49, 19.59; UV (MeOH) λ_{max} 264.8 nm (ϵ = 37 403); MS (thioglycerol) calcd for $C_{29}H_{27}N_7O_9$ + H 618.1948, found 618.1926.

21: amorphous; ^{1}H NMR (DMSO-d_6) 10.49 (1H, s), 8.40–8.17 and 7.70–7.66 (9H), 6.55–6.38 (3H), 5.57–5.46 (1H, m), 4.82 (2H, t, $J_{CH_2\text{-}CH_2}$ = 6.9 Hz), 4.22 (1H, dd, $J_{5'4'}$ = 4.2 Hz, $J_{5'5''}$ = 12.7 Hz), 4.06 (1H, dd, $J_{5''4'}$ = 4.8 Hz, $J_{5''5'}$ = 12.4 Hz), 3.35 (t, J = 6.1 Hz, overlapped on the residual H_2O peak), 2.91 (1H, sept, $J_{CH\text{-}CH_3}$ = 6.9 Hz), 1.10 (6H, d, $J_{CH_3\text{-}CH}$ = 6.6 Hz); ^{13}C NMR (DMSO-d_6) 175.38, 164.17, 160.12, 153.08, 152.71, 150.62, 146.78, 146.54, 141.20, 135.14, 131.18, 130.65, 129.31, 129.01, 124.12, 123.67, 117.28, 75.87, 66.79, 65.23, 64.03 (C-5′), 34.62, 34.48, 19.56; UV (MeOH) λ_{max} 264.9 nm (ϵ = 35 918); MS (thioglycerol) calcd for $C_{29}H_{27}N_7O_9$ + H 618.1948, found 618.1950.

[4′-*O*-(*p*-Nitrobenzoyl)-2′,3′-dideoxy-α,β-D-*glycero*-pent-2′-enopyranosyl]-N^6-benzoyladenine 22. A. Using *N*-Benzoyladenine. To a boiling solution of N^6-benzoyladenine[60,61] (1.0 g, 4.2 mmol) in dry DMF (30 mL) was added glycal **13** (1.73 g, 4.2 mmol). After 10 min heating was discontinued. The solvent was evaporated. Extractive workup (CH_2Cl_2–aqueous saturated $NaHCO_3$) and evaporation of CH_2Cl_2 furnished a brown syrup. TLC (CH_2Cl_2–MeOH, 20:0.4) showed a spot corresponding to a mixture of **22** (R_f 0.34) and minor more and less polar impurities. Chromatography furnished 1.27 g (60%) of unseparated **22** (in proportion α/β = 2/2.5; see 4′-*O*′-deprotection step): MS (EI) calcd for $C_{24}H_{18}N_6O_6$ 486.1288, found 486.1299.

B. Using Trimethylsilylated *N*-Benzoyladenine. Glycal **13** (13.0 g, 31.4 mmol) was reacted with A^{Bz} (7.7 g, 32.2 mmol) (trimethylsilylated and worked up as in the case of C^{Bz}) in DMF (150 mL) at bp during exactly 10 min. TLC showed a UV-absorbing, noncharring spot, R_f 0.46 (solvent system as above), a product **22** spot (R_f 0.34), and three more polar charring compounds (not identified). Extractive workup and chromatography furnished 6.79 g (44%) of **22** (in ratio β/α = 27/17 after 4′-*O*-deprotection, see below).

In separate experiments, the yield of **22** was 28–51%. Prolongation of reaction time resulted in more complex reaction mixtures. *N*-Benzoyladenine prepared as in ref 61 was inferior probably due to the presence of benzoic acid.

[4′-*O*-(*p*-Nitrobenzoyl)-2′,3′-dideoxy-β-D-*glycero*-pent-2′-enopyranosyl]-6-chloropurine (23) and α Anomer 24. A. Using Sodium Salt of 6-Chloropurine. 6-Chloropurine (1.6 g, 10.35 mmol) in dry DMF (45 mL) and sodium hydride (60% in mineral oil, 0.45 g, 11.4 mmol) were stirred at room temperature. After 2 h, the flask was immersed in an oil bath (t = ~150 °C), and glycal **13** (5.14 g, 12.4 mmol) was added. The mixture turned dark immediately. After 35 min heating was discontinued. TLC (CH_2Cl_2–MeOH, 20:0.2) showed two spots corresponding to **23/24** (R_f 0.31). After evaporation of the solvent and extractive workup (CH_2Cl_2–aqueous saturated $NaHCO_3$), 5.2 g of the brown glassy material was obtained. Flash chromatography furnished 1.065 g of the less polar α anomer **24**, 0.438 g of **23**, and 0.260 g of mixed fractions in roughly equal proportion. Total yield of **23/24**: 1.76 g, 42%, counting on 6-chloropurine.

B. Using 6-Chloropurine. 6-Chloropurine (0.37 g, 2.4 mmol) in DMF (20 mL) was brought to bp, whereupon glycal **13**, 1.0 g (2.4 mmol), was added. After 12 min heating was discontinued. Workup as above and chromatography furnished a total of 0.55 g, 57%, of **23/24** formed in equal proportion.

23: amorphous; ^{1}H NMR (DMSO-d_6) 8.84, 8.76 (2s), 8.39–8.19 (4H), 6.71 (1H, dd, $J_{1'3'}$ = 1.8 Hz, $J_{1'2'}$ = 3.1 Hz), 6.61 (1H, ddd, $J_{3'1'}$ = 1.7 Hz, $J_{3'4'}$ = 4.9 Hz, $J_{3'2'}$ = 10.2 Hz), 6.48 (1H, dd, $J_{2'1'}$ = 3.1 Hz, $J_{2'3'}$ = 9.9 Hz), 5.48 (1H, dt, $J_{4'5'}$ = $J_{4'5''}$ = 2.4 Hz), ^{13}C NMR (DMSO-d_6) 163.97, 152.12, 151.84, 150.47, 149.54, 146.43, 134.96, 131.35, 130.91, 128.04, 127.86, 124.05, 74.90, 64.35, 62.86 (C-5′); UV (MeOH) λ_{max} 264.6 nm; MS (thioglycerol) calcd for $C_{17}H_{12}ClN_5O_5$ + H 402.0605, found 402.0609.

24: amorphous; ^{1}H NMR (DMSO-d_6) 8.85, 8.80 (1H, 2s), 8.39–8.23 (4H), 6.63 (1H, q, $J_{1'2'}$ = $J_{1'3'}$ = $J_{1'4'}$ = 2.0 Hz), 6.54 (1H, ddd, $J_{3'1'}$ = 1.6 Hz, $J_{3'4'}$ = 3.6 Hz, $J_{3'2'}$ = 10.3 Hz), 6.42 (1H, ddd, $J_{2'4'}$ = 1.2 Hz, $J_{2'1'}$ = 2.2 Hz, $J_{2'3'}$ = 10.1 Hz), 5.52 (1H, bs, half-width = 10 Hz), 4.26 (1H, dd, $J_{5'4'}$ = 3.9 Hz, $J_{5'5''}$ = 12.3 Hz), 4.05 (1H, dd, $J_{5''4'}$ = 4.1 Hz, $J_{5''5'}$ = 12.2 Hz); ^{13}C NMR (DMSO-d_6) 164.01, 152.17, 151.79, 150.50, 149.57, 146.06, 134.99, 131.19, 129.03, 128.74, 131.00, 123.99, 76.59, 65.03, 64.05 (C-5′); UV (MeOH) λ_{max} 263.6 nm; MS (thioglycerol) calcd for $C_{17}H_{12}ClN_5O_5$ + H 402.0605, found 402.0582.

[4′-*O*-(*p*-Nitrobenzoyl)-2′,3′-dideoxy-β-D-*glycero*-pent-2′-enopyranosyl]uracil (25), α Anomer 26, and N^1,N^3-Bisglycosylated Products 27A,B. Uracil (1.12 g, 10 mmol) in dry DMF (40 mL) was treated with sodium hydride (60% suspension in mineral oil, 0.4 g, 10 mmol) at room temperature, and after 30 min the flask was immersed in a silicon oil bath (t = 170 °C). After 15 min glycal **13** (3.1 g, 15 mmol) was added. Reaction time was 1 h. TLC showed four spots: in CH_2Cl_2–MeOH (20:0.15) R_f 0.52 and 0.33 corresponding to two compounds (**27A,B**) and in CH_2Cl_2–MeOH (20:0.5) R_f 0.40 corresponding to a midpoint of two compounds (**25** and **26**). The solvent was evaporated. Extractive workup gave a brown syrup. Chromatography using a gradient of CH_2Cl_2–MeOH (20:0.1 → 20:0.5) gave 0.53 g of **26** (less polar) and 0.311 g of **25** (total yield 23%). Both products **27A,B** were repurified using CH_2Cl_2–MeOH (20:0.1) to give 0.36 g of **27A** (less polar) and 0.17 g of **27B**. When sodium salt of N^3-benzoyluracil[64] was used instead of uracil, more complex reaction mixture resulted despite suppression of formation of **27A,B**. This was not further examined.

25: mp 252–258 °C, dec (crystallized dioxane); ^{1}H NMR (DMSO-d_6) 11.43 (1H, s), 8.37 (2H, d, J = 8.5 Hz), 8.19 (2H, d, J = 8.5 Hz), 7.59 (1H, d, J_{65} = 8.0 Hz), 6.49 (1H, ddd, $J_{3'1'}$ = 1.5 Hz, $J_{3'4'}$ = 3.7 Hz, $J_{3'2'}$ = 10.3 Hz), 6.30 (1H, t, $J_{1'2'}$ = $J_{1'3'}$ = 2.4 Hz), 6.15 (1H, dd, $J_{2'1'}$ = 2.8 Hz, $J_{2'3'}$ = 10.1 Hz), 5.59 (1H, d, J_{56} = 7.9 Hz), 5.47 (1H, q, $J_{4'3'}$ = $J_{4'5'}$ = $J_{4'5''}$ = 3.6 Hz), 4.10 (1H, dd, $J_{5'4'}$ = 3.4 Hz, $J_{5'5''}$ = 12.9 Hz), 3.99 (1H, dd, $J_{5''4'}$ = 3.6 Hz, $J_{5''5'}$ = 12.8 Hz); ^{13}C NMR (DMSO-d_6) 163.93, 163.33, 150.77, 150.47, 142.18, 134.93, 130.91, 129.41, 128.63, 124.04,

101.40, 76.13, 64.62, 63.21 (C-5′); MS (3-nitrobenzyl alcohol, negative mode) calcd for $C_{16}H_{13}N_3O_7$ 359.0753, found 359.0748.

26: amorphous; ^{1}H NMR (DMSO-d_6) 11.44 (1H, s), 8.36 (2H, dd, J = 2.0, 8.9 Hz), 8.22 (2H, dd, J = 2.2, 9.0 Hz), 7.44 (1H, d, J_{65} = 8.0 Hz), 6.45 (1H, ddd, $J_{3'1'}$ = 1.3 Hz, $J_{3'4'}$ = 4.7 Hz, $J_{3'2'}$ = 10.1 Hz), 6.30 (1H, q, $J_{1'2'} = J_{1'3'} = J_{1'4'}$ = 1.7 Hz), 6.17 (1H, dd, $J_{2'1'}$ = 1.2 Hz, $J_{2'3'}$ = 10.1 Hz), 5.69 (1H, d, J_{56} = 8.1 Hz), 5.34 (1H), 4.18 (1H, dd, $J_{5'4'}$ = 2.6 Hz, $J_{5'5''}$ = 12.9 Hz), 4.09 (1H, dd, $J_{5''4'}$ = 1.9 Hz, $J_{5''5'}$ = 12.4 Hz); ^{13}C NMR (DMSO-d_6) 164.03, 163.21, 150.55, 150.48, 141.04, 135.03, 131.51, 130.94, 128.39, 124.03, 102.62, 77.37, 65.74 (C-5′), 64.85; MS (thioglycerol) calcd for $C_{16}H_{13}N_3O_7$ + H 360.0832, found 360.0831.

27A: amorphous; (^{1}H NMR data not present due to complexity of the 200 MHz spectrum) ^{1}H NMR data not presented due to complexity of the 200 MHz spectrum; ^{13}C NMR (DMSO-d_6) 164.19, 162.30, 150.75, 150.64, 140.72, 135.25, 131.52, 131.31, 131.08, 129.77, 124.22, 123.35, 102.16, 78.55, 74.15, 66.02, 65.85, 65.56, 64.97; MS (thioglycerol) calcd for $C_{28}H_{22}N_4O_{12}$ 606.1234, found 606.1214.

27B: amorphous; (^{1}H NMR data not present due to complexity of the 200 MHz spectrum) ^{13}C NMR (DMSO-d_6) 164.04, 163.91, 162.22, 150.82, 150.42, 141.58, 135.10, 134.91, 131.38, 130.88, 129.59, 128.36, 124.02, 123.14, 100.80, 77.14, 73.97, 65.89, 65.37, 64.56, 63.22; MS (thioglycerol) calcd for $C_{28}H_{22}N_4O_{12}$ 606.1234, found 606.1259.

[4′-*O*-(*p*-Nitrobenzoyl)-2′,3′-dideoxy-α,β-D-*glycero*-pent-2′-enopyranosyl]thymine 28. Thymine (1.0 g, 7.9 mmol) was trimethylsilyated and worked up as described for *N*-benzoylcytosine. DMF (40 mL) solution of this compound was warmed up in an oil bath at ca. 112 °C. Glycal **13** (3.94 g, 9.5 mmol) was added, and heating was continued during 7 h. TLC (CH_2Cl_2–MeOH, 20:0.3) showed a product (**28**, R_f 0.22) and a solvent front migrating compound. After evaporation of the solvent, extractive workup ($CHCl_3$–aqueous saturated $NaHCO_3$) and chromatography gave **28** (1.42 g, 48%) as a 1:1 mixture of both anomers by ^{1}H and ^{13}C NMR. When N^3-benzoylthymine[64] was used instead of thymine, more complex reaction mixture resulted, which was not further investigated.

28: (^{1}H NMR data not present due to complexity of the 200 MHz spectrum) ^{13}C NMR (DMSO-d_6) 164.17, 164.10, 164.04, 162.57, 150.95, 150.74, 150.60, 137.67, 136.42, 135.20, 135.09, 131.90, 131.08, 129.57, 128.95, 128.40, 124.17, 110.34, 109.34, 77.44, 76.14, 66.04, 65.05, 64.91, 63.49, 12.35, 12.18; MS (thioglycerol) calcd for $C_{17}H_{15}N_3O_7$ + H 374.1077, found 374.0996.

(2′,3′-Dideoxy-β-D-*glycero*-pent-2′-enopyranosyl)-*N*-benzoylcytosine (29) and α Anomer 30. Compound **16** (4.99 g, 10.8 mmol) was dissolved in dry dioxane (300 mL) with warming. The homogenous solution was brought to room temperature, and dry methanol (400 mL) was added followed by solution of sodium methoxide in methanol (6.5 mL) (prepared from 0.088 g of sodium and 50 mL of methanol). The amount of catalyst was 0.5 mmol. After 5 h the reaction was quenched with a few pieces of solid CO_2. TLC showed a small amount of unreacted substrate still present as well as the *O,N*-bis-deprotected compound **31**. After evaporation of the solvent and chromatography in CH_2Cl_2–MeOH (20:1), 2.34 g (69%) of **29** was obtained. Similarly, 4.24 g of **17** furnished 2.73 g (86%) of **30**. Even though the β-4′-nitrobenzoate **16** is less polar on TLC than the α anomer **17**, 4′-*O*-deprotected β anomer **29** is more polar than **30**.

29: mp >250 °C (crystallized MeOH–CH_2Cl_2); ^{1}H NMR (DMSO-d_6) 11.27 (1H, bs), 8.00–7.27 (7H), 6.34 (1H, q, $J_{1'2'} = J_{1'3'} = J_{1'4'}$ = 1.8 Hz), 6.27 (1H, dt, $J_{3'2'}$ = 10.0 Hz, $J_{3'4'}$ = 2.9 Hz, $J_{3'1'}$ = 2.2 Hz), 5.80 (1H, dt, $J_{2'1'}$ = 2.0 Hz, $J_{2'4'}$ = 1.8 Hz), 5.28 (1H, d, $J_{OH\text{-}4'}$ = 5.9 Hz), 4.12 (1H, bs, half-width = 13 Hz), 3.90 (1H, dd, $J_{5'4'}$ = 4.4 Hz, $J_{5'5''}$ = 11.4 Hz), 3.53 (1H, dd, $J_{5''4'}$ = 6.1 Hz, $J_{5''5'}$ = 11.5 Hz); ^{13}C NMR (DMSO-d_6) 167.61, 163.42, 154.53 (C-4), 146.52, 135.89, 133.21, 132.88, 128.55, 124.64, 96.54, 78.20, 67.84 (C-5′), 60.22; UV (MeOH) λ_{max} 261.6 nm (ε = 17 259), 304.4 (ε = 6700); MS (thioglycerol) calcd for $C_{16}H_{15}N_3O_4$ + H 314.1141, found 314.1153.

30: mp >250 °C (crystallized CH_2Cl_2–MeOH); ^{1}H NMR (DMSO-d_6) 11.33 (1H, bs), 8.14 (1H, d, J_{56} = 7.6 Hz), 8.09–8.00 and 7.70–7.48 (5H), 7.37 (1H, d, J_{56} = 6.6 Hz), 6.25–6.30 (2H), 5.87 (1H, dt, $J_{2'1'}$ = 2.1 Hz, $J_{2'4'}$ = 1.4 Hz, $J_{2'3'}$ = 11.0 Hz), 5.29 (1H, d, $J_{OH\text{-}4'}$ = 7.2 Hz), 4.06 (1H, bs, half-width = 14.9 Hz), 3.88 (1H, dd, $J_{5'5''}$ = 11.7 Hz, $J_{5'4'}$ = 4.1 Hz), 3.60 (1H, dd, $J_{5''5'}$ = 11.6 Hz, $J_{5''4'}$ = 4.9 Hz); ^{13}C NMR (DMSO-d_6) 167.56, 163.69, 154.79, 146.67, 135.33, 133.33, 133.04, 128.72, 125.63, 96.48, 78.25, 66.94 (C-5′), 60.62; UV (MeOH) λ_{max} 262.0 nm (ε = 15 143), 304.7 (ε = 5970); MS (thioglycerol) calcd for $C_{16}H_{15}N_3O_4$ + H 314.1141, found 314.1153.

(2′,3′-Dideoxy-β-D-*glycero*-pent-2′-enopyranosyl)cytosine (31) and α Anomer 32. Compounds **31** and **32** were prepared from **16** and **17**, respectively, by overnight treatment with methanolic ammonia, evaporation, and chromatography in CH_2Cl_2–MeOH (4:1).

31: mp dec >200 °C (crystallized MeOH); ^{1}H NMR (DMSO-d_6) 7.36 (1H, d, J_{56} = 7.3 Hz), 7.26 (2H, bs, half-width = 10.8 Hz), 6.25 (1H, q, $J_{1'2'} = J_{1'3'} = J_{1'4'}$ = 1.9 Hz), 6.18 (1H, dt, $J_{3'4'}$ = 2.5 Hz, $J_{3'1'}$ = 2.0 Hz, $J_{3'2'}$ = 10.3 Hz), 5.71 (1H, d, J_{56} = 7.3 Hz); 5.64 (t, $J_{2'1'} = J_{2'4'}$ = 1.8 Hz), 5.24 (1H, d, $J_{OH\text{-}4'}$ = 5.9 Hz), 4.10 (1H, bs, half-width = 10.0 Hz), 3.87 (1H, dd, $J_{5'4'}$ = 4.6 Hz, $J_{5'5''}$ = 11.4 Hz), 3.44 (1H, dd, $J_{5''4'}$ = 6.6 Hz, $J_{5''5'}$ = 11.4 Hz); ^{13}C NMR (DMSO-d_6) 165.85, 155.18, 142.16, 135.74, 125.62, 94.38, 77.51, 68.07 (C-5′), 60.48; UV (MeOH) λ_{max} 241.6 nm (ε = 7899), 269.6 (ε = 7879); MS (thioglycerol) calcd for $C_9H_{12}N_3O_3$ 210.0879, found 210.0878.

32: mp 193–194 °C (crystallized MeOH); ^{1}H NMR (DMSO-d_6) 7.67 (1H, d, J_{65} = 7.4 Hz), 7.21 (2H, bs, half-width = 18 Hz), 6.26–6.14 (2H), 5.71 (d, J_{56} = 7.3 Hz), 5.68 (upfield part of H2′ signal, t, $J_{2'1'} = J_{2'4'}$ = 1.3 Hz), 5.17 (1H, $J_{OH\text{-}4'}$ = 6.8 Hz), 3.94 (1H, bs, half-width = 15 Hz), 3.77 (1H, dd, $J_{5'5''}$ = 11.7 Hz, $J_{5'4'}$ = 3.9 Hz), 3.53 (1H, dd, $J_{5''5'}$ = 11.5 Hz, $J_{5''4'}$ = 4.5 Hz), ^{13}C NMR (DMSO-d_6) 165.87, 155.16, 142.31, 134.31, 126.75, 94.02, 77.26, 67.04 (C-5′), 60.45; UV (MeOH) λ_{max} 269.2 nm (ε = 7844), 241.0 (ε = 7800); MS (thioglycerol) calcd for $C_9H_{12}N_3O_3$ 210.0879, found 210.0872.

(2′,3′-Dideoxy-β-D-*glycero*-pent-2′-enopyranosyl)-N^2-isobutyryl-O^6-[2-(*p*-nitrophenyl)ethyl]guanine (33) and α Anomer 34. A mixture of **20/21** (10.49 g) was 4′-*O*-deprotected as for **29** or **30** using dioxane (200 mL), methanol (300 mL), and catalytic NaOMe. Since N^2-isobutyrate is less prone to be removed under Zemplen conditions than *N*-benzoate, the amount of sodium methoxide is not a critical factor. Chromatography (CH_2Cl_2–MeOH, 20:1) gave 2.58 g of the less polar α anomer **34** and 4.67 g of **33**. Total yield of **33** + **34**: 94%. Both **33** and **34** are amorphous.

33: ^{1}H NMR (DMSO-d_6) 10.45 (1H, s), 8.17 (1H, s), 8.17 (2H, d, J = 8.5 Hz), 7.66 (2H, d, J = 8.5 Hz), 6.38–6.32 (2H), 6.07 (1H, dd, $J_{2'1'}$ = 2.9 Hz, $J_{2'3'}$ = 10.0 Hz), 5.29 (1H, d, $J_{OH\text{-}4'}$ = 5.9 Hz), 4.81 (2H, t, $J_{CH_2\text{-}CH_2}$ = 6.9 Hz), 4.09 (1H), 3.90 (1H, dd, $J_{5'4'}$ = 3.3 Hz, $J_{5'5''}$ = 12.1 Hz), 3.65 (1H, dd, $J_{5''4'}$ = 3.7 Hz, $J_{5''5'}$ = 12.1 Hz), 3.30 (2H, t, $J_{CH_2\text{-}CH_2}$ = 6.6 Hz), 2.93 (1H, quint, $J_{CH\text{-}CH_3}$ = 6.7 Hz), 1.11 (6H, d, $J_{CH_3\text{-}CH}$ = 6.6 Hz); ^{13}C NMR (DMSO-d_6) 175.43, 163.05, 153.01, 152.57, 146.80, 146.53, 141.56, 134.05, 130.63, 124.18, 123.67, 117.47, 75.09, 67.11, 66.71 (C-5′), 59.98, 34.59, 34.47, 19.57; UV (MeOH) λ_{max} 270.9 nm (ε = 28 197); MS (thioglycerol) calcd for $C_{22}H_{24}N_6O_6$ + H 469.1835, found 469.1832.

34: ^{1}H NMR (DMSO-d_6) 10.47 (1H, s), 8.24 (1H, d, $J_{81'}$ = 1.1 Hz), 8.18 (2H, d, J = 7.8 Hz), 7.67 (2H, d, J = 8.1 Hz), 6.35–6.29 (2H), 6.04 (1H, d, half-width = 5 Hz, $J_{2'3'}$ = 9.7 Hz) (after H4′ irradiation dt, $J_{2'3'}$ = 10.1 Hz, $J_{1'2'} = J_{2'4'}$ = 2.6 Hz), 5.23 (1H, d, $J_{OH\text{-}4'}$ = 6.9 Hz), 4.82 (2H, t, $J_{CH_2\text{-}CH_2}$ = 6.4 Hz), 4.19 (1H, bs, half-width = 14 Hz), 4.83 (1H, dd, $J_{5'4'}$ = 4.4 Hz, $J_{5'5''}$ = 11.2 Hz), 3.48–3.32 (3H, superimposed on H_2O signal), 2.92 (1H, quint, $J_{CH\text{-}CH_3}$ = 6.3 Hz), 1.12 (6H, d, $J_{CH_3\text{-}CH}$ = 6.9 Hz); ^{13}C NMR (DMSO-d_6) 175.43, 160.09, 153.09, 152.58, 146.79, 146.53, 141.46, 136.32, 130.62, 123.66, 117.48, 75.02, 66.73, 64.95 (C-5′), 61.06, 34.64, 34.47, 19.56; UV (MeOH) λ_{max} 271.0 nm (ε = 24 072); MS (thioglycerol) calcd for $C_{22}H_{24}N_6O_6$ + H 469.1835, found 469.1855.

(2′,3′-Dideoxy-β-D-*glycero*-pent-2′-enopyranosyl)-N^6-benzoyladenine (35) and α Anomer 36. A. 4′-*O*-Deprotection of **22** (1.27 g) (prepared by coupling A^{Bz} with **13**) was carried out exactly as described for the cytidine analogue **19**. Flash chromatography (CH_2Cl_2–MeOH, 20:2.2) furnished 0.20 g of the less polar α anomer **36** and 0.25 g of the β anomer **35** (α:β = 44:56). Total yield of **35** and **36** was 74%. Small amounts

of the unreacted substrate and *O,N*-bis-deprotected products **37/38** were invariably present in deprotection reactions of **22**.

B. Total yield of β/α anomers (and, to a smaller extend, their proportion) formed in a coupling between TMS(A^{Bz}) and **13** varied from experiment to experiment as already mentioned. Selective 4′-*O*-deprotection of **22** (6.79 g) (formed in 44% yield) gave **36** (1.66 g) and **35** (2.26 g) after gravitational column chromatography using CH_2Cl_2–MEOH (20:0.3 → 20:0.4) (α:β = 42:58); **22** (4.39 g) formed in a separate experiment in 28% yield and gave **36** (0.93 g) and **35** (1.75 g) (α:β = 35:65).

35: amorphous; ^{1}H NMR (DMSO-d_6) 11.27 (bs), 8.81, 8.47 (2s), 8.13–8.28 and 7.73–7.51 (5H), 6.55 (1H, bs, half-width = 6 Hz), 6.40 (1H, ddd, $J_{3'1'}$ = 2.0 Hz, $J_{3'4'}$ = 4.2 Hz, $J_{3'2'}$ = 10.3 Hz), 6.14 (1H, ddd, $J_{2'4'}$ = 1.1 Hz, $J_{2'1'}$ = 2.9 Hz, $J_{2'3'}$ = 10.2 Hz), 5.34 (1H, d, $J_{OH\text{-}4'}$ = 4.6 Hz), 4.10 (1H, bs, half-width = 12 Hz), 3.91 (1H, dd, $J_{5'4'}$ = 3.6 Hz, $J_{5'5''}$ = 12.2 Hz), 3.71 (1H, dd, $J_{5''4'}$ = 2.9 Hz, $J_{5''5'}$ = 12.0 Hz); ^{13}C NMR (DMSO-d_6) 165.90, 152.36, 152.08, 150.62, 143.43, 134.05, 133.61, 132.72, 128.73, 125.86, 124.20, 75.27, 67.14 (C-5′), 60.01; MS (EJ) calcd for $C_{17}H_{15}N_5O_3$ 337.1175, found 337.1183.

36: amorphous; ^{1}H NMR (DMSO-d_6) 11.29 (1H, bs), 8.81, 8.53 (1H each, s), 8.14–8.03 and 7.73–7.52 (5H), 6.53 (1H, q, $J_{1'2'} = J_{1'3'} = J_{1'4'}$ = 2.2 Hz), 6.38 (1H, dt, $J_{3'1'} = J_{3'4'}$ = 1.8 Hz, $J_{3'2'}$ = 10.3 Hz), 6.10 (1H, ddd, $J_{2'4'}$ = 1.6 Hz, $J_{2'1'}$ = 2.6 Hz, $J_{2'3'}$ = 10.3 Hz), 5.32 (1H, d, $J_{OH\text{-}4'}$ = 7.3 Hz), 4.23 (1H), 3.87 (1H, dd, $J_{5'4'}$ = 5.2 Hz, $J_{5'5''}$ = 11.1 Hz), 3.45 (1H, dd, $J_{5''4'}$ = 7.8 Hz, $J_{5''5'}$ = 11.3 Hz); ^{13}C NMR (DMSO-d_6) 165.91, 152.44, 152.12, 150.73, 143.20, 136.67, 133.61, 132.74, 128.76, 125.89, 123.56, 75.20, 65.02 (C-5′), 61.14; MS (EJ) calcd for $C_{17}H_{15}N_5O_3$ 337.1175, found 337.1159.

(2′,3′-Dideoxy-β-D-*glycero*-pent-2′-enopyranosyl)adenine (37) and α Anomer 38. A. *O,N*-Bis-deprotection of **22** in NH_3/MeOH or NaOM/MeOH gave **37** and **38**; in CH_2Cl_2–MEOH (10:1) R_f of the α anomer **38** is 0.30 and R_f of the β anomer **37** is 0.24. Flash chromatography in CH_2Cl_2–MeOH (20:3) can be used to separate **37** and **38**.

B. In a separate experiment, it has been established that the compound α-**36** (less polar than β-**35**) is transformed into **38** (less polar than **37**).

C. 6-Methoxypurine derivative β-**39** (0.113 g) on ammonolysis in saturated NH_3/MeOH (80 mL) at 100 °C during 20 h furnished 0.060 g (56%) of **37**. Similarly, the α anomer **40** funished **38**, in 16% yield. The reaction was performed at 150 °C during 10 h. These conditions were evidently too harsh as evidenced by the low yield of the product and formation of other unidentified compounds.

37: mp 172–174 °C (crystallized MeOH); ^{1}H NMR (DMSO-d_6) 8.16, 8.08 (s), 7.31 (s, 2H), 6.36–6.30 (2H), 6.27 (dd, $J_{3'1'}$ = 1.8 Hz, $J_{3'4'}$ = 4.3 Hz), 6.03 (1H, ddd, $J_{2'1'}$ = 3.0 Hz, $J_{2'4'}$ = 1.1 Hz, $J_{2'3'}$ = 9.9 Hz), 4.09–3.98 (1H), 3.84 (1H, dd, $J_{5'4'}$ = 3.7 Hz, $J_{5'5''}$ = 12.1 Hz), 3.62 (1H, dd, $J_{5''4'}$ = 3.4 Hz, $J_{5''5'}$ = 12.1 Hz); ^{13}C NMR (DMSO-d_6) 156.29, 153.09, 149.52, 139.66, 133.75, 124.61, 119.16, 74.84, 67.01 (C-5′), 60.06; UV (MeOH) λ_{max} 261.2 nm (ε = 11 140); MS (EJ) calcd for $C_{10}H_{11}N_5O_2$ 233.0913, found 233.0905.

38: no sharp mp 98–110 °C (crystallized MeOH); ^{1}H NMR (DMSO-d_6) 8.17 (2H, s), 7.34 (2H, s), 6.34–6.29 (2H), 6.26 (t, $J_{3'4'}$ = 2.0 Hz, $J_{3'1'}$ = 1.9 Hz), 5.99 (1H, ddd, $J_{2'4'}$ = 1.6 Hz, $J_{2'1'}$ = 3.0 Hz, $J_{2'3'}$ = 9.9 Hz), 5.32 (1H, bs), 4.18 (1H, bs, half-width = 16 Hz), 3.81 (1H, dd, $J_{5'4'}$ = 5.1 Hz, $J_{5'5''}$ = 11.4 Hz), 3.41 (1H, dd, $J_{5''4'}$ = 8.0 Hz, $J_{5''5'}$ = 11.6 Hz); ^{13}C NMR (DMSO-d_6) 156.29, 153.08, 149.56, 139.54, 136.06, 124.03, 119.17, 74.82, 64.94 (C-5′), 61.10; UV (MeOH) λ_{max} 160.5 nm (ε = 14 460); MS (EJ) calcd for $C_{10}H_{11}N_5O_2$ 233.0913, found 233.0898.

(2′,3′-Dideoxy-β-D-*glycero*-pent-2′-enopyranosyl)-6-methoxypurine (39) and α Anomer 40. The β anomer **23** (0.35 g) was dissolved in dry dioxane (8 mL). Methanol (30 mL) was added followed by a piece of sodium. After the substrate reacted, the reaction mixture was neutralized with solid CO_2. After evaporation of solvents and chromatographic isolation (in CH_2Cl_2–MeOH, 20:0.7), 0.17 g (78%) of **39** was obtained.

Using the same procedure, the α anomer **24** (0.84 g) furnished 0.34 g (65%) of **40**. Compound α-**40** is chromatographically less polar than the β anomer **39**.

39: amorphous; ^{1}H NMR (DMSO-d_6) 8.54, 8.33 (2s), 6.45 (1H, s), 6.33 (1H, ddd, $J_{3'1'}$ = 1.9 Hz, $J_{3'4'}$ = 4.3 Hz, $J_{3'2'}$ = 10.3 Hz), 6.06 (1H, ddd, $J_{2'4'}$ = 1.0 Hz, $J_{2'1'}$ = 2.9 Hz, $J_{2'3'}$ = 10.1 Hz), 5.28 (1H, bs), 4.10–3.99 (1H), 4.08 (3H, s), 3.84 (1H, dd, $J_{5'4'}$ = 3.5 Hz, $J_{5'5''}$ = 12.0 Hz), 3.64 (1H, dd, $J_{5''4'}$ = 3.3 Hz, $J_{5''5'}$ = 12.1 Hz); ^{13}C NMR (DMSO-d_6) 160.63, 152.15, 151.98, 142.66, 134.01, 124.19, 121.17, 75.37, 67.11 (C-5′), 60.00, 54.23; UV (MeOH) λ_{max} 248.0 nm (ε = 10 511); MS (thioglycerol) calcd for $C_{11}H_{12}N_4O_3$ + H 249.0988, found 249.0984.

40: amorphous; ^{1}H NMR (DMSO-d_6) 8.59, 8.42 (2s), 6.45 (1H, q, $J_{1'2'} = J_{1'3'} = J_{1'4'}$ = 2.2 Hz), 6.34 (1H, dt, $J_{3'4'} = J_{3'1'}$ = 1.9 Hz, $J_{3'2'}$ = 10.2 Hz), 6.06 (1H, ddd, $J_{2'1'}$ = 1.8 Hz, $J_{2'4'}$ = 2.7 Hz, $J_{2'3'}$ = 10.3 Hz), 4.28–4.14 (1H, m), 4.12 (3H, s), 3.83 (1H, dd, $J_{5'4'}$ = 5.4 Hz, $J_{5'5''}$ = 11.4 Hz), 3.39 (1H, dd, $J_{5''4'}$ = 7.8 Hz, $J_{5''5'}$ = 11.4 Hz); ^{13}C NMR (DMSO-d_6) 160.68, 152.18, 152.03, 142.49, 136.52, 123.56, 121.17, 75.28, 64.91 (C-5′), 61.10, 54.27; UV (MeOH) λ_{max} 248.5 nm (ε = 12 057); MS (thioglycerol) calcd for $C_{11}H_{12}N_4O_3$ + H 249.0988, found 249.0988.

(2′,3′-Dideoxy-β-D-*glycero*-pent-2′-enopyranosyl)-uracil (41) and α Anomer 42. 4′-*O*-Deprotected compounds **41** and **42** were prepared by NaOMe/HOMe deesterification of **25** and **26**, respectively, and chromatographic isolation (CH_2Cl_2–MeOH, 10:1). The α anomer **42** is slightly less polar on TLC than **41**. Spectroscopic properties of **41** prepared as above are identical with those of the compound obtained in a stepwise procedure starting from (2′,3′,4′-tri-*O*-acetyl-β-D-xylopyranosyl)uracil.[65]

42: mp 150–155 °C (crystallized MeOH); ^{1}H NMR (DMSO-d_6) 11.35 (1H, bs), 7.60 (1H, d, J_{65} = 8.0 Hz), 6.25 (1H, ddd, $J_{3'1'}$ = 1.9 Hz, $J_{3'4'}$ = 3.8 Hz, $J_{3'2'}$ = 10.3 Hz), 6.11 (1H, q, $J_{1'2'} = J_{1'3'} = J_{1'4'}$ = 1.9 Hz), 5.75 (1H, ddd, $J_{2'1'}$ = 2.1 Hz, $J_{2'4'}$ = 1.1 Hz, $J_{2'3'}$ = 10.1 Hz), 5.63 (1H, d, J_{56} = 8.0 Hz), 5.20 (1H, d, $J_{OH\text{-}4'}$ = 6.1 Hz), 3.94 (1H, bs, half-width = 12 Hz), 3.80 (1H, dd, $J_{5'4'}$ = 3.9 Hz, $J_{5'5''}$ = 11.8 Hz), 3.54 (1H, dd, $J_{5''4'}$ = 4.4 Hz, $J_{5''5'}$ = 11.7 Hz); ^{13}C NMR (DMSO-d_6) 163.36, 150.71, 141.77, 135.10, 125.70, 101.56, 76.81, 67.22 (C-5′), 60.27; UV (MeOH) λ_{max} 259.6 nm (ε = 8197); MS (glycerol) calcd for $C_9H_{10}N_2O_4$ + H 211.0719, found 211.0716.

(2′,3′-Dideoxy-β-D-*glycero*-pent-2′-enopyranosyl)thymine (43) and α Anomer 44. Deprotection of **28** as described for **41** and **42** followed by flash chromatography (CH_2Cl_2–MeOH, 20:1.3) gave a small amount of the less polar α anomer **44**. Complete separation was possible using HPLC.

Spectroscopic properties of the β anomer **43** are identical with those of the compound obtained in a stepwise procedure starting from (2′,3′,4′-tri-*O*-acetyl-β-D-xylopyranosyl)uracil.[65]

44: mp 178–180 °C (crystallized MeOH–CH_2Cl_2) [lit.[32] mp 171 °C (MeOH)]; ^{1}H NMR (DMSO-d_6) 11.37 (1H, s), 7.46 (1H, q, $J_{6\text{-}CH_3}$ = 1.1 Hz), 6.26 (1H, ddd, $J_{3'1'}$ = 1.9 Hz, $J_{3'4'}$ = 3.8 Hz, $J_{3'2'}$ = 10.3 Hz), 6.12 (1H, q, $J_{1'2'} = J_{1'3'} = J_{1'4'}$ = 2.0 Hz), 5.76 (1H, ddd, $J_{2'1'}$ = 1.8 Hz, $J_{2'4'}$ = 0.8 Hz, $J_{2'2'}$ = 10.2 Hz), 5.20 (1H, d, $J_{OH\text{-}4'}$ = 6.8 Hz), 3.92 (1H, bs, half-width = 13 Hz), 3.81 (1H, dd, $J_{5'4'}$ = 3.7 Hz, $J_{5'5''}$ = 11.7 Hz), 3.60 (1H, dd, $J_{5''4'}$ = 4.0 Hz, $J_{5''5'}$ = 11.7 Hz), 1.77 (3H, d, $J_{CH_3\text{-}6}$ = 1.1 Hz); ^{13}C NMR (DMSO-d_6) 163.98, 150.71, 137.19, 134.67, 126.29, 109.22, 76.79, 67.72 (C-5′), 60.29, 12.11; UV (MeOH) λ_{max} 264.4 nm (ε = 8431); MS (thioglycerol) calcd for $C_{10}H_{12}N_2O_4$ + H 225.0875, found 225.0863.

(2′,3′-Dideoxy-β-D-*glycero*-pent-2′-enopyranosyl)-*N*-isobutyrylguanosine (45) and α Anomer 46. 6-*O*-[(*p*-Nitrophenyl)ethyl] derivative **33** (2.81 g, 6.0 mmol) in dry pyridine (140 mL) and diazabicycloundecene (1.70 mL, 11.3 mmol) was left overnight. After evaporation and coevaporation with *p*-xylene, column chromatography (CH_2Cl_2–MeOH, 10:1.8) furnished the amorphous O^6-deprotected compound **45** (1.56 g, 81%). Using the same procedure, **34** (2.09 g) furnished **46** (1.21 g, 85%).

45: no mp up to 280 °C dec (crystallized MeOH); ^{1}H NMR (DMSO-d_6) 12.01, 11.77 (2H, 2bs), 7.88 (1H, s), 6.31 (1H, ddd, $J_{3'1'}$ = 1.5 Hz, $J_{3'4'}$ = 4.0 Hz, $J_{3'2'}$ = 10.3 Hz), 6.16 (1H, bs), 6.04 (1H, dd, $J_{2'1'}$ = 2.6 Hz, $J_{2'3'}$ = 10.3 Hz), 5.24 (1H, d, $J_{OH\text{-}4'}$ = 5.1 Hz), 4.02 (1H, bs), 3.78 (1H, dd, $J_{5'4'}$ = 3.7 Hz, $J_{5'5''}$ = 12.1 Hz), 3.58 (1H, dd, $J_{5''4'}$ = 3.3 Hz, $J_{5''5'}$ = 12.1 Hz), 2.76 (1H, quint, $J_{CH\text{-}CH_3}$ = 6.9 Hz), 1.10 (6H, d, $J_{CH_3\text{-}CH}$ = 6.7 Hz); ^{13}C NMR (DMSO-d_6) 181.14, 155.76, 149.39, 149.14, 139.02, 134.81, 124.74, 121.35, 75.66, 67.50 (C-5′), 60.57, 35.62, 19.77

(CH_3); UV (MeOH) λ_{max} 260.4 nm (ϵ = 18 890), 278.0 (ϵ = 13 620); MS (thioglycerol) calcd for $C_{14}H_{17}N_5O_4$ + H 320.1359, found 320.1361.

46: no mp up to 300 °C, dec (crystallized MeOH−CH_2Cl_2); ^{1}H NMR (DMSO-d_6) 12.02, 11.79 (2bs), 7.97 (1H, s), 6.29 (1H, dt, $J_{3'1'} = J_{3'4'}$ = 1.8 Hz, $J_{3'2'}$ = 10.3 Hz), 6.13 (1H, q, $J_{1'2'} = J_{1'3'} = J_{1'4'}$ = 2.0 Hz), 6.01 (1H, ddd, $J_{2'4'}$ = 1.7 Hz, $J_{2'1'}$ = 2.7 Hz, $J_{2'3'}$ = 10.3 Hz), 5.19 (1H, d, $J_{OH\text{-}4'}$ = 6.9 Hz), 4.13 (1H, bs), 3.76 (1H, dd, $J_{5'4'}$ = 5.5 Hz, $J_{5'5''}$ = 11.4 Hz), 3.31 (1H, dd, $J_{5''4'}$ = 7.8 Hz, $J_{5''5'}$ = 11.1 Hz), 2.76 (1H, quint, $J_{CH\text{-}CH_3}$ = 6.8 Hz), 1.10 (6H, d, $J_{CH_3\text{-}CH}$ = 6.9 Hz); ^{13}C NMR (DMSO-d_6) 181.14, 155.80, 149.51, 149.21, 139.00, 137.30, 124.13, 121.36, 75.54, 65.17 (C-5′), 61.72, 35.62, 19.76; UV (MeOH) λ_{max} 260.4 nm (ϵ = 16 244), 280.0 (ϵ = 12 000); MS (thioglycerol) calcd for $C_{22}H_{24}N_6O_6$ + H 469.1835, found 469.1855.

(2′,3′-Dideoxy-β-D-*glycero*-pentopyranosyl)-*N*-benzoyladenine (48) and α Anomer 49. Catalytic reductions of the 2′,3′-double bond in a Parr apparatus at 15 psi overnight using EtOH solutions of **35** and **36** and 10% Pd/C followed by chromatographic purification (CH_2Cl_2, 18:1) furnished **48** (62%) and **49** (36%). It is difficult to follow these reductions on TLC because R_f values of the starting olefins and the corresponding reduction products are the same.

48: amorphous; ^{1}H NMR (DMSO-d_6) 11.24 (bs), 8.78, 8.70 (2s), 8.08−8.04 and 7.70−7.52 (5H), 5.81 (1H, dd, $J_{1'2'eq}$ = 2.1 Hz, $J_{1'2'ax}$ = 11.0 Hz), 5.06 (1H, d, $J_{OH\text{-}4'}$ = 4.8 Hz), 3.96 (1H, ddd, $J_{5'eq3'}$ = 1.8 Hz, $J_{5'eq4'}$ = 4.6 Hz, $J_{5'eq5'ax}$ = 10.5 Hz), 3.79−3.61 (1H, m), 3.37 (1H, t, $J_{5''ax5'eq} = J_{5'ax4'}$ = 10.3 Hz), 2.62−2.36 (overlapped on DMSO-d_6 signal), 2.25−2.04, 1.76−1.52 (three groups of signals, H3′), ^{13}C NMR (DMSO-d_6) 165.93, 152.18, 151.96, 150.62, 142.85, 133.63, 132.70, 128.73, 125.69 (adenine), 81.08, 72.21 (C-5′), 64.06, 31.81, 28.67; MS (thiglycerol) calcd for $C_{17}H_{17}N_5O_3$ + H 340.1410, found 340.1415.

49: amorphous; ^{1}H NMR (DMSO-d_6) 11.23 (1H, s), 8.78, 8.72 (2s), 8.09−8.05 and 7.71−7.52 (5H), 5.85 (1H, dd, $J_{1'2'eq}$ = 2.1 Hz, $J_{1'2'ax}$ = 10.2 Hz), 4.91 (1H, d, $J_{OH\text{-}4'}$ = 4.7 Hz), 3.85 (2H, s, 2 × 5′), 3.71 (1H, bs, half-width = 5.8 Hz), 2.88−2.60 and 2.30−1.80 (unresolved, 4H); ^{13}C NMR (DMSO-d_6) 165.93, 152.10, 151.95, 150.59, 142.77, 133.64, 132.70, 128.73, 125.59 (adenine), 80.80, 72.13 (C-5′), 62.21, 29.45, 24.99; MS (thiglycerol) calcd for $C_{17}H_{17}N_5O_3$ + H 340.1410, found 340.1413.

(2′,3′-Dideoxy-β-D-*glycero*-pentopyranosyl)uracil (52) and α Anomer 53. Compounds **52** and **53** were prepared from **41** and **42**, respectively, as described for *N*-benzoyladenine counterparts and purified by column chromatography using CH_2Cl_2−MeOH (10:1) system.

52: mp 200−202 °C (crystallized CH_2Cl_2−MeOH); ^{1}H NMR (DMSO-d_6) 11.30 (bs), 7.66 (d, 1H, J_{65} = 8.1 Hz), 5.60 (d, 1H, J_{56} = 8.1 Hz), 5.45 (dd, 1H, $J_{1'2'eq}$ = 4.0 Hz, $J_{1'2'ax}$ = 9.2 Hz), 3.88 (ddd, 1H, $J_{5'eq5'ax}$ = 11.0 Hz, $J_{5'eq4'}$ = 4.0 Hz, J = 1.5 Hz), 3.60−3.47 (m, 1H), 3.19 (t, 1H, $J_{5'ax4'}$ = 10.4 Hz, $J_{5'ax5'eq}$ = 10.4 Hz), 2.02 (dt, 1H, $J_{3'eq3'ax}$ = 11.6 Hz, $J_{3'eq4'} = J_{3'eq2'ax}$ = 3.1 Hz), 1.85−1.71 (unresolved, 2H), 1.51 (dq, 1H, $J_{3'ax2'eq}$ = 5.1 Hz, $J_{3'ax3'eq} = J_{3'ax4'} = J_{3'ax2'ax}$ = 11.4 Hz); ^{13}C NMR (DMSO-d_6) 163.24, 150.41, 141.03, 101.97, 81.19, 72.40 (C-5′), 63.92, 31.70, 28.30; MS (thioglycerol) calcd for $C_9H_{12}N_2O_4$ + H 213.0875, found 213.0864.

53: mp 173−178 °C (crystallized CH_2Cl_2-MeOH); ^{1}H NMR (DMSO-d_6) 11.34 (bs, 1H), 7.75 (d, 1H, J_{65} = 8.1 Hz), 5.66 (d, 1H, J_{56} = 8.1 Hz), 5.51 (dd, 1H, $J_{1'2'eq}$ = 1.9 Hz, $J_{1'2'ax}$ = 10.5 Hz), 4.85 (bs, 1H), 3.84 (d, 1H, $J_{5'eq5'ax}$ = 12.1 Hz), 3.71 (dd, 1H, $J_{5'ax4'}$ = 10.0 Hz, $J_{5'ax5'eq}$ = 12.2 Hz), 3.59 (bs, 1H), 2.40−2.25 (unresolved, 2 H), 2.16−1.93 (m, 1H), 1.52 (dq, 1H, $J_{2'eq2'ax}$ = 12.1 Hz, J = 2.6 Hz); ^{13}C NMR (DMSO-d_6) 163.27, 150.32, 141.14, 101.94, 81.10, 72.64 (C-5′), 61.95, 29.23, 24.39; MS (thioglycerol) calcd for $C_9H_{12}N_2O_4$ + H 213.0875, found 213.0864.

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Supporting Information Available: Copies of ^{13}C NMR spectra of **17**, **20**−**25**, **27**−**44**, **46**, **48**−**50**, **52**, **53**, **56**, and **57** and details of crystallographic data collections and refinement parameters (36 pages). This material is contained in libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.

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