H_a), 2.62 (1 H, dd, J_{bx} = 9.5 Hz and J_{ab} = 13 Hz, H_b), 4.51 (1 H, dd, J_{ax} = 11.5 Hz and J_{bx} = 9.5 Hz, H_x); ^{13}C NMR (DCl + D_2O; ref 1,4-dioxane = δ 67.40 ppm) δ 7.71 and 8.14 (2 q, 2 Me), 31.03 and 31.20 (2 t, 2 CH_2), 35.16 (t, CH_2CH), 50.29 (d, CH), 92.40 (s, CEt_2), 174.19 (s, C=O).

3-Amino-5,5-di-*n*-propyltetrahydro-2-furanone, 24c (hydrochloride): mp >260 °C; IR (KBr) 3600-2500 (NH_3^+), 1770 cm^{-1} (C=O); ^1H NMR (DCl + D_2O; ref 1,4-dioxane = δ 3.64 ppm) δ 0.82 (2 × 3 H, t, overlap, 2 Me), 1.0-2.0 (4 × 2 H, m, 4 CH_2), 2.18 (1 H, dd, J_{ax} = 11.5 Hz and 13 Hz, H_a), 2.68 (1 H, dd, J_{bx} = 9 Hz and J_{ab} = 13 Hz, H_b), 4.56 (1 H, dd, J_{ax} = 11.5 Hz and J_{bx} = 9 Hz, H_x); ^{13}C NMR (DCl + D_2O; ref 1,4-dioxane = δ 67.40 ppm) δ 14.39 (q, 2 Me, overlap), 16.98 and 17.38 (2 t, $(CH_3CH_2CH_2)_2$), 36.18 (t, CH_2CH), 39.64 and 40.96 (2 t, $(CH_3CH_2CH_2)_2$), 50.28 (d, CH), 91.79 (s, CPr_2), 174.16 (s, C=O).

Retention Values. Retention values for TLC using Kieselgel 60 F_{254} plates (5 × 10 cm; thickness 0.25 mm) with 1-butanol-acetic acid-water (4:1:1) as eluent: Compound **22a**, 0.43; compound **22b**, 0.60; compound **22c**, 0.65 (ninhydrin positive spots of compounds **22** appeared light purple); compound **23a**, 0.28; compound **23b**, 0.50 (ninhydrin positive spots of compounds **23** appeared dark yellow to light brown); compound **24a**, 0.39; compound **24b**, 0.57; compound **24c**, 0.59 (ninhydrin positive spots of compounds **24** appeared yellow).

Registry No. **11a**, 4091-39-8; **11b**, 13280-00-7; **11c**, 2832-55-5; **11d**, 2907-70-2; **12a**, 78827-37-9; **12b**, 118231-23-5; **12c**, 118231-24-6; **12d**, 128753-38-8; **14a**, 118231-19-9; **14b**, 118231-20-2; **14c**, 118231-21-3; **14e**, 128753-39-9; **14f**, 128753-40-2; **21a**, 123445-50-1; **21b**, 123445-51-2; **21c**, 123445-52-3; *cis*-**18f**, 128753-41-3; *trans*-**18f**, 128753-42-4; **19a**, 114809-78-8; **22a**, 123445-53-4; **22b**, 123445-54-5; **22c**, 123445-55-6; **23a**, 104302-37-6; **23b**, 123445-56-7; **24a**·HCl, 15722-67-5; **24b**·HCl, 128753-43-5; **24c**·HCl, 128779-80-6; **25a**, 128753-44-6; **25b**, 128753-45-7; **26a**, 128753-46-8; **26b**, 128753-47-9; **27a**, 128753-48-0; **27b**, 128753-49-1; **28a**, 128753-50-4; **28b**, 128779-81-7; **29a**, 128753-51-5; **29b**, 128779-82-8.

Syn-Anti Conformational Analysis of Regular and Modified Nucleosides by 1D ^1H NOE Difference Spectroscopy: A Simple Graphical Method Based on Conformationally Rigid Molecules

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The 1D ^1H NOE difference spectra of 50 base- and/or sugar-modified nucleosides were measured in $(CD_3)_2SO$ with irradiation of various protons. The resulting NOE data were used for a conformational analysis with respect to their syn-anti conformer equilibrium. Irradiation of H-8 [purine numbering (purine and pyrimidine numbering has been used for all nucleosides throughout the paper)] of the conformationally fixed compounds **25**β and **41**β resulted in NOE values at H-1′, H_β-2′, and H_β-3′, respectively, which were used to establish a calibration graph for a semiquantitative estimation of syn and anti conformer populations of β-D nucleosides. Moreover, the preferred conformations of a number of α-D nucleosides were qualitatively deduced from their 1D ^1H NOE difference spectra. Measurement of the NOE spectra of sterically hindered nucleosides implied that both the chemical properties as well as the van der Waals radius of a nucleobase substituent are of decisive importance for the conformation around the N-glycosylic bond.

Introduction

Nucleosides exist in solution in distinct conformational ranges with a Gaussian distribution of conformer populations within these ranges. Concerning the overall shape of a nucleoside, the most important conformational parameters are the torsion angle around the glycosylic bond (χ) as well as the sugar puckering, which are interdependent.[1] The energy barrier between the different conformational states is usually low (≈25 kJ/mol),[2,3] implying dynamic equilibria between them which might be more or less biased toward one side. Normally, the different conformational modes can be reliably described by two-state models (syn-anti; N/S-type sugar puckering).[1]

Rare nucleotides characterized by unusual aglycon moieties like 2-thiouridine, pseudouridine, wyosine (**42**β), and others are particularly common in tRNA's. Some of these manifest either the syn or the anti conformation around the glycosylic bond in the solid state.[4] Moreover, the syn-anti equilibrium is a key event in going from a right-handed B-DNA to a left-handed Z-DNA involving a conformational change in guanylate residues from anti to syn.[5,6]

As substrate or inhibitor activities of nucleosides and nucleotides might be correlated with their preferred structure in solution, the evaluation of thermodynamic and conformational parameters is of key importance in eluci-

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dating the mechanism of a biological process. If in an enzymatic reaction the initial encounter between an enzyme and its binding partner is fast compared to the rate of conformational interconversion of the latter,[7] then the enzyme can distinguish between the different conformations. If the interconversion between the conformations is so fast that both conformers are rapidly exposed to the enzyme, then the most reactive conformer is sought out even if it is only present in minute concentrations (Curtin–Hammett principle).[8]

1D ^{1}H Nuclear Overhauser enhancement spectroscopy (NOE) has been found to allow a direct approach to qualitative or semiquantitative information about the configuration as well as the preferred conformation[9] of nucleosides and nucleotides in solution. NOE and CD measurements of some regular nucleosides in different solvents or solvent mixtures indicated that no gross conformational differences exist between D_2O and $(CD_3)_2SO$ solutions.[10,11] As $(CD_3)_2SO$ is the most universal solvent for nucleosides where aggregate formation can be excluded,[10,11] we measured the NOE difference spectra of the 50 sugar- and/or base-modified as well as regular nucleosides shown in the formula schemes in $(CD_3)_2SO$ solution and attempted to correlate the data with structural parameters. This may be important for an assessment of the conformation of oligo- and polynucleotides[12,13] and may help to explain their biological activity.

Results and Discussion

Recently we have reported on the results of homonuclear ^{1}H NOE difference spectra with respect to the unequivocal assignment of anomeric configuration of N-nucleosides.[14a,b] α- and β-anomers can easily be distinguished by saturating H-1′ and measuring the NOE factors at H-4′ and H-3′.[15] Occurrence of an NOE at H-4′ proves β-configuration at the anomeric center while α-anomers show an NOE at H-3′ upon irradiation of H-1′. This has been successfully applied to D-ribo-, 2′-deoxy-D-ribo-, D-arabino-, 2′,3′-dideoxy-D-ribo-,[14a,b] 2′,3′-didehydro-2′,3′-dideoxy-D-ribo-, as well as 2′-deoxy-D-xylo- and 2′,3′-dideoxy-3′-fluoro-D-ribonucleosides.[16]

Besides such stereochemical assignments,[17] 1D ^{1}H NOE difference spectroscopy displays a direct approach to the conformational analysis of nucleosides with respect to the torsion angle around the glycosylic bond.

The orientation of the base relative to the sugar moiety can adopt two main ranges (syn and anti) defined by torsion angle χ (purine nucleosides: χ, O-4′–C-1′–N-9–C-4; pyrimidine nucleosides: χ, O-4′–C-1′–N-1–C-2).[18] This nucleobase orientation has been analyzed in several ways: (i) spin relaxation times;[19–22] (ii) NOE effects;[10,11,23–26] (iii) perturbation of sugar ^{1}H and ^{13}C chemical shifts due to anisotropy effects of the nucleobase;[27,28] (iv) a Karplus-like dependence of the ^3J(C-8,H-1′) coupling constant from the torsion angle of the glycosylic bond.[29] While the first three methods furnish information about the conformer populations, the last one results in distinct torsion angles but without information regarding a dynamic syn–anti equilibrium. Nevertheless, characteristic discrepancies concerning the conformer populations emerge also from the comparison of the results of the first three techniques depending on the various initial assumptions and implications.

Table I. Computed Proton–Proton Distances (Å) and Torsion Angles (deg) for 25β and 41β

compd	$r_{i,j}$ of H_i–H_j (Å)	torsion angle (deg)
25β	H-8–H-1′, 2.29	O-4′–C-1′–N-9–C-4, 47.2
	H-8–H-2′, 3.31	O-4′–C-1′–N-9–C-8, 147.9
	H-1′–H-4′, 4.01	C-1′–C-2′–C-3′–C-4′, 6.8
	H-1′–H-2′, 2.82	O-4′–C-1′–C-2′–C-3′, −25.6
		C-3′–C-4′–C-5′–N-3, 59.8
		C-8–N-9–C-1′–H-1′, −28.9
		H-1′–C-1′–C-2′–H-2′, 103.6
		H-2′–C-2′–C-3′–H-3′, 8.1
		H-3′–C-3′–C-4′–H-4′, −106.8
		H-4′–C-4′–C-5′–H-5′, 60.2
		H-4′–C-4′–C-5′–H-5″, −55.5
41β	H-8–H_β-2′, 2.75	O-4′–C-1′–N-9–C-4, −141.0
	H-8–H-3′, 4.33	O-4′–C-1′–N-9–C-8, 38.6
	H-8–H-1′, 3.66	C-8–N-9–C-1′–H-1′, 155.9
	H-8–H-5′, 2.20	C-1′–C-2′–C-3′–C-4′, −37.3
	H-1′–CH_3, 2.20	C-3′–C-4′–C-5′–O-5′, 166.6
	H-1′–H-4′, 3.65	H-1′–C-1′–C-2′–H_α-2′, 37.3
	H-1′–H_α-2′, 2.39	H-1′–C-1′–C-2′–H_β-2′, 160.0
		H_β-2′–C-2′–C-3′–H-3′, −40.6
		H_α-2′–C-2′–C-3′–H-3′, 80.8
		H-3′–C-3′–C-4′–H-4′, −84.5

A Calibration Graph Based on the NOE Data of the Conformationally Rigid Nucleosides 25β and 41β/42β. Computer modeling based on force-field calculations of e.g. adenosine (1β) or its 7-deazaisostere (=tubercidin, 5β) show that H-8 is the closest proton to H-1′ if the conformation is syn while in the anti conformation the closest protons to H-8 are H_β-2′ and H-3′.[23] Only a "perfect" syn orientation of a nucleobase ($\chi \approx 40$–$50°$) relative to the sugar moiety goes along with a minimum distance between H-8 and H-1′. In contrast, a "perfect" anti orientation ($-140° \leq \chi \leq -150°$) does not agree with the minimum distances of H-8–H_β-2′ and H-8–H-3′. If the distance H-8–H_β-2′ is minimized, a nucleoside adopts the rare high-anti conformation (-sc) in which the bonds C-1′–C-2′ and N-9–C-8 are almost eclipsed.

One can presume if saturation of H-8 or β-D configured purine nucleosides or isosteres thereof (H-6 of pyrimidine

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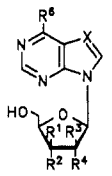
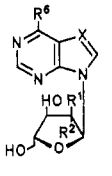
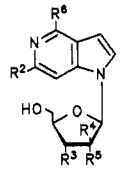


	X	R^1	R^2	R^3	R^4	R^6
1β	N	H	OH	H	OH	NH_2
2β	N	H	OH	OH	H	NH_2
3β	N	H	OH	H	H	NH_2
4β	N	H	H	H	H	NH_2
5β	CH	H	OH	H	OH	NH_2
6β	CH	H	OH	H	H	NH_2
7β	CH	OH	H	H	H	NH_2
8β	CH	H	OH	H	OH	Cl
9β	CH	H	H	H	H	Cl
10β	N	H	OH	H	OH	OH

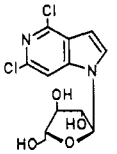


	X	R^1	R^2	R^6
11α	N	OH	H	NH_2
12α	N	H	OH	NH_2
13α	CH	OH	H	NH_2
14α	CH	H	H	NH_2
15α	CH	OH	H	Cl

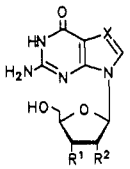


16β: $R^2 = R^6 = Cl$; $R^3 = R^4 = OH$; $R^5 = H$

17β: $R^2 = H$; $R^6 = NH_2$; $R^3 = R^4 = R^5 = H$



18α



19β: $R^1 = R^2 = OH$; X = N

20β: $R^1 = OH$; $R^2 = H$; X = N

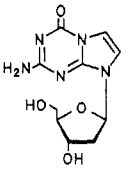
21β: $R^1 = R^2 = H$; X = N

22β: $R^1 = R^2 = OH$; X = CH

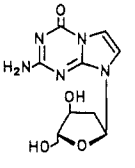
nucleosides) produces a strong NOE at H-1′ and small ones at H_β-2′ and H-3′, then syn orientation of the nucleobase should be preferred. In a reverse experiment saturation of H-1′ should yield a significant NOE at H-8/H-6. This should be almost unaffected by the sugar puckering. If, on the other hand, saturation of H-8/H-6 results in a strong NOE at H_β-2′ and a smaller one at H-1′, the anti orientation should dominate.

To obtain a semiquantitative estimation of the syn and anti populations of nucleosides (formula schemes) using NOE difference spectroscopy, we used the conformationally fixed compounds **25β** (syn) and **41β** (anti)[30] as calibration points. First, force-field calculations were made on both nucleosides using the Alchemy II molecular modeling program (Tripos Ass., Inc., 1988). After energy minimization of the model structures, torsion angles as well as interproton distances ($r_{i,j}$) were measured (Table I). As the data of Table I show, compound **25β** represents an ideal syn-fixed nucleoside. Moreover, the distance H-8–H-1′ is minimal and found to be 2.29 Å. Therefore, a maximal NOE is observed at H-1′ upon irradiation of H-8 (η(H-1′) = 11.3%). Simultaneously, no NOE can be observed at H-2′ (Table I).

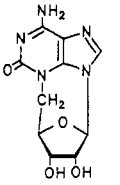
On the other hand, computer modeling shows that compound **41β** (2′-deoxywyosine) exhibits almost perfect anti conformation with a glycosylic torsion angle $\chi = -141°$



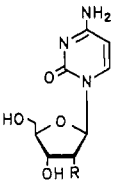
23β



24α

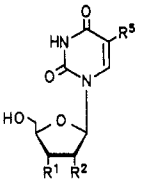


25β



26β: R = OH

27β: R = H

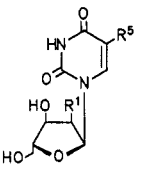


28β: $R^5 = H$; $R^1 = R^2 = OH$

29β: $R^5 = CH_3$; $R^1 = OH$; $R^2 = H$

30β: $R^5 = CH{=}CHBr$; $R^1 = OH$; $R^2 = H$

31β: $R^5 = CH_3$; $R^1 = N_3$; $R^2 = H$



32α: $R^5 = H$; $R^1 = OH$

33α: $R^5 = CH_3$; $R^1 = H$

and r(H-8,H_β-2′) = 2.75 Å. This conformation is not consistent with a minimal distance H-8–H_β-2′ which can easily be assessed by altering the torsion angle χ stepwise toward a high-anti conformation. Applying this method the minimum distance is found to be 2.00 Å. Notwithstanding this fact, 2′-deoxywyosine (**41β**) exhibits the largest NOE values [$\eta(H_\beta\text{-}2') + \eta$(H-3′)] upon irradiation of H-8 (9.5%, Table IV); simultaneously, the η value at H-1′ is found to be zero. Analogous results were obtained for the corresponding β-D-ribonucleoside (wyosine, **42β**,[31] Table II). With the NOE data of **25β** and **41β**/**42β** an empirical calibration graph can be set up. In the following this graph is used for the determination of the syn–anti conformation of regular and modified nucleosides. Scope and limitations will be discussed.

Analysis of the NOE Data of β-D-Ribonucleosides. The NOE data (Table II) of a number of β-D-ribonucleosides shown in the formula schemes have been measured. As can be seen from Figure 1, most β-D-ribonucleosides exhibit preferentially anti conformation around the N-glycosylic bond or show an almost equal distribution of syn and anti conformers. The two-state equilibrium (syn–anti), represented by the model compounds **25β** and **41β**, can be deduced from the fact that for most compounds studied, the syn conformer population calculated from graph A (Figure 1) and the anti conformer population calculated from B (Figure 1) add to 100% (±10%).

It can be seen from Figure 1 that adenosine (**1β**) prefers slightly the syn range (60% syn) while other regular purine nucleosides like guanosine (**19β**) and inosine (**10β**) exhibit anti orientation of the nucleobase (**19β**, 70% anti; **10β**, 65% anti). Introduction of an *O*-2′,3′-isopropylidene moiety (**48β**–**50β**) shifts the syn–anti equilibrium toward the syn range—a finding which is consistent with results earlier described. Applying ^{1}H NOE spectroscopy it has been found that adenosine exhibits a 60–70% population of syn rotamers[32] while *O*-2′,3′-isopropylidenadenosine

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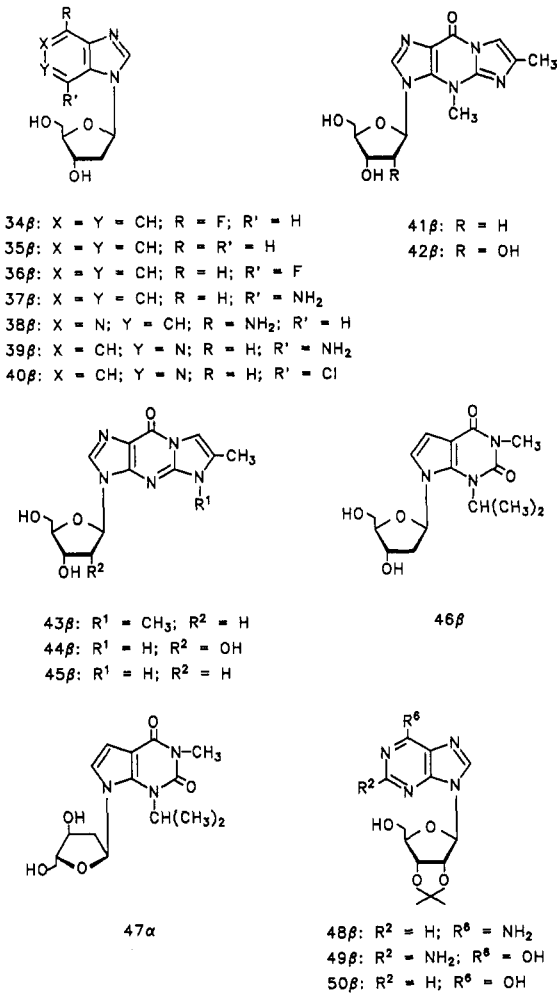
(31) Golankiewicz, B.; Folkman, W. *Nucl. Acid Res.* **1983**, *11*, 5243.



(48β) shows a 70–80% population of syn conformers.[24] Using the graph of Figure 1, 60% syn in the case of adenosine and 65% syn of *O*-2′,3′-isopropylideneadenosine can be estimated. Switching to the 7-deazapurine ribonucleosides **5β** (7-deazaadenosine) a shift of populations toward the anti range by 15–20% compared to the parent nucleoside can be estimated.

Inspection of the NOE data of uridine (**28β**) and cytidine (**26β**) show a highly preferred anti orientation of the nucleobase which is consistent with X-ray data. However, the anti conformer populations calculated from graph B (Figure 1) are slightly overestimated. This may be explained by slightly different interproton distances of H-8–H-1′ vs H-6–H-1′. Furthermore, the anti conformation of **26β** and **28β** may be slightly shifted toward high-anti which would result in an enhanced sum [η(H_β-2′) + η-(H_β-3′)] compared to the corresponding NOE values of **41β**/**42β** (9.5%). Nevertheless, the NOE data of **26β** and **28β** clearly demonstrate a preferred conformation in the anti range. From the fit of the NOE data of various purine β-D-ribonucleosides—with certain limitations in the case of pyrimidine β-D-nucleosides—the applicability of the calibration graph (Figure 1) is demonstrated. The conformation at the glycosylic bond of new β-D-ribonucleosides can now be estimated from this empirical graph.

Analysis of NOE Data of 2′-Deoxy-β-D-ribonucleosides. The graph of Figure 1 is also useful for a semiquantitative estimation of syn and anti conformer populations for 2′-deoxy-β-D-ribonucleosides (Table IV).

(32) Plochacka, D.; Rabczenko, A.; Davis, D. B. *Biochim. Biophys. Acta* **1977**, *476*, 1.

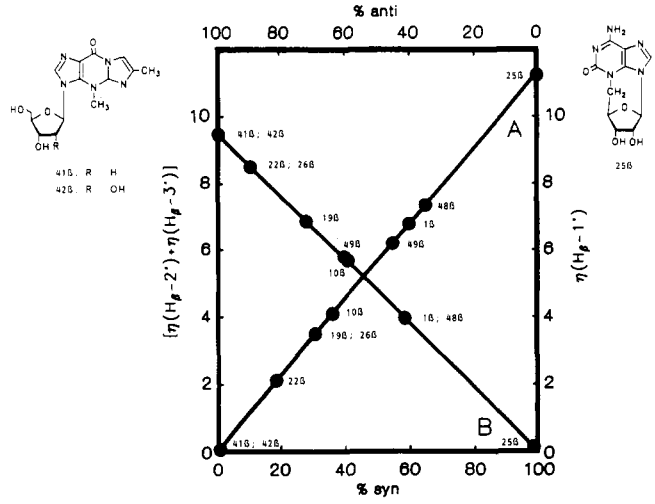


Figure 1. Calibration graph for the estimation of syn and anti conformer populations of β-D-nucleosides applying ^{1}H NOE difference spectroscopy.

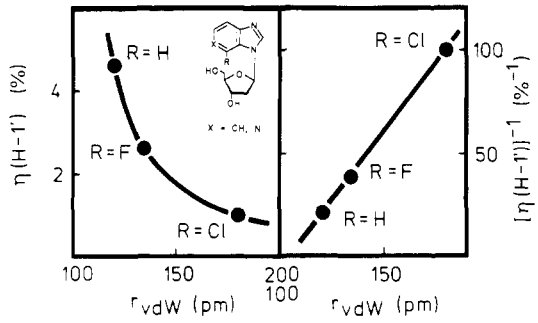


Figure 2. NOE Values (η(H-1′), irr. of H-8) of compounds **34β**, **35β**, and **40β** as a function of the van der Waals radius of *R*.

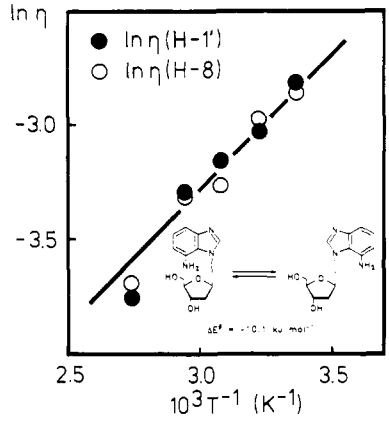


Figure 3. Arrhenius plot of η(H-1′) and η(H-8), respectively, versus T^{-1} for compound **37β**.

However, as the H-2′ signals do often overlap with the solvent signal, correct integration of the NOE difference spectrum is difficult. Therefore, the most reliable method for an assessment of conformer populations is the use of η(H-1′) upon irradiation of H-8/H-6.

Comparison of the η(H-1′) values of compounds **35β**, **36β**, and **40β** show a decrease with increasing van der Waals radius of the chromophore substituents (H, F, Cl) being in proximity to the β-D-ribofuranosyl residue (Figure 2). A plot of the reciprocal NOE values versus the van der Waals radii show a linear dependence demonstrating the steric influence of the substituent on the syn conformer population. Electronic effects can be excluded as chlorine and fluorine show similar field effect parameters. Compounds **35β**, **34β**, and **38β** bearing substituents (H, F, NH_2)

Table II. Results of Proton–Proton 1D NOE Experiments on D-Ribonucleosides

	proton irradiated	NOE (%)
1β	H-1′	H-2′ (1.9), H-4′ (2.1), H-8 (6.8), 2′-OH (3.4), 3′-OH (1.3)
	H-4′	H-1′ (3.9), H-3′ (1.6), H_a-5′ (3.1), H_b-5′ (4.5), 2′-OH (2.4), 3′-OH (4.6)
	H-8	H-1′ (6.7), H-2′ (3.2), H-3′ (0.8)
11α	H-1′	H-2′ (10.9), H-3′ (1.5), H-8 (2.7), 5′-OH (0.5)
	H-3′[a]	H-1′ (3.6), H-2′ (9.2), H_a-5′ (1.7), H_b-5′ (3.3), H-8 (1.4), 3′-OH (20.6), 5′-OH (3.9)
	H-8	H-1′ (1.7), H-4′ (1.8), 2′-OH + 3′-OH (3.8)
5β	H-1′	H-2′ (1.6), H-4′ (1.8), H-8 (4.2), 2′-OH (2.7), 3′-OH (1)
	H-4′	H-1′ (2.7), H-3′ (1.2), H_2-5′ (4.3), 2′-OH (1.1), 3′-OH (2.1)
	H-8	H-1′ (4.8), H-2′ (4.8), H-3′ (1.0), H-7 (5.8)
13α	H-1′	H-2′ (11.3), H-3′ (3.5), H-8 (3.5)
	H-4′[b]	H_a-5′ (5.1), H_b-5′ (5.8), H-8 (5.2), 3′-OH (5.9), 5′-OH (2.6)
	H-8	H-1′ (3.1), H-4′ (4.0), H-7 (11.3), 2′-OH (2.9), 3′-OH (2.4)
8β	H-1′	H-2′ (2.1), H-4′ (2.1), H-8 (2.6)
	H-4′	H-1′ (4.0), H-3′ (1.5), H_2-5′ (3.8)
	H-8	H-1′ (3.4), H-2′ (6.9), H-3′ (1), H-7 (10.6)
15α	H-1′[c]	H-2′ (10.3), H-3′ (1.5), H-8 (2.7)
	H-8	H-1′ (1.2), H-4′ (2.7), H-7 (10.0)
28β	H-1′	H-2′ (2.2), H-4′ (1.7), H-6 (2.1)
	H-4′	H-1′ (2.8), H_2-5′ (2.9), 2′-OH (1.5), 3′-OH + 5′-OH (2.8)
	H-6	H-1′ (2.9), H-2′ (7.0), H-3′ (2.5), H-5 (12.4)
32α	H-1′	H-2′ (10.0), H-3′ (3.7), H-6 (1.4)
	H-6	H-1′ (1.3), H-4′ (5.3), H-5 (17.7)
25β	H-8	H-1′ (11.3), H-2′ (0)
	H-1′	H-8 (10.1), H-4′ (3.0)
19β	H-8	H-1′ (3.6), H-2′ (5.7), H-3′ (1.1)
	H-1′	H-8 (3.0), H-2′ (1.8), H-4′ (1.8)
	H-2′	H-8 (7.6), 2′-OH (4.8), 3′-OH (2.1), H-3′ (6.8)
	H-3′	H-8 (1.5), H-2′ (5.7), H-4′ (1.2)
26β	H-6	H-1′ (3.6), H-5 (9.2), 5′-OH (1.6), H-2′ + H-3′ (8.5)
49β	H-8	H-1′ (6.2), H-2′ (5.8), H-3′ (0.5), H_2-5′ (0.9)
	H-1′	H-8 (5.7), H-2′ (3.4), H-4′ (2.4)
48β	H-8	H-1′ (7.4), H-2′ (4.0)
	H-1′	H-8 (8.2), H-2′ (2.8), H-4′ (2.3)
22β	H-8	H-7 (8.5), H-1′ (2.1), H-2′ (7.3), H-3′ (1.3)
	H-1′	H-8 (1.8), H-2′ (2.1), H-4′ (2.2)
	H-2′	H-8 (10.4), H-1′ (3.0), H-3′ (6.1)
	H-3′	H-8 (2.2), H-1′ (0.8), H-2′ (4.7), H-4′ (1.5), H_2-5′ (2.5)
10β	H-8	H-1′ (4.1), H-2′ (4.2), H-3′ (1.5)
	H-1′	H-8 (4.0), H-2′ (2.0), H-4′ (1.6)
	H-2′	H-8 (6.5), H-1′ (2.9), H-3′ (7.1)
	H-3′	H-8 (1.6), H-2′ (6.4), H_2-5′ (1.8)
50β	H-8	H-1′ (5.8), H-2′ (5.1), H-3′ (0.5)
	H-1′	H-8 (5.7), H-2′ (3.1), H-4′ (2.2)
	H-2′	H-8 (6.5), H-1′ (3.4), H-3′ (6.2), H_2-5′ (1.7)
	H-3	H-8 (1), H-2′ (6.6), H-4′ (3.3), H_2-5′ (4.0)
42β	H-8	H-1′ (0.5), 5′-OH (0.8), H-2′ (7.4), H-3′ (2.1)
	H-2′	H-8 (9.1), H-3′ (4.8)
44β	H-8	H-1′ (2.1), H-2′ (2.6), H-3′ (1.2)
	H-1′	H-8 (1.8)

[a] H-4′, 15%. [b] H-3′, 8%. [c] H-7, 20%.

of increasing van der Waals radii but far away from the glyconic moiety exhibit almost identical η(H-1′) data upon saturation of H-8 (Table IV).

For 2′-deoxywyosine (**41β**) an almost perfect anti conformation of the nucleobase was stated. Interestingly, if the methyl group at N-4 (IUPAC numbering) is shifted to N-5 as in compound **43β**[30] the nucleobase is now able to rotate around the glycosylic bond which can be seen from an NOE value of 5.2% at H-1′ (Table IV) upon saturation of H-8. The syn/anti populations assessed from the graph of Figure 1 are similar (50:50) as found for a corresponding 2′-deoxywyosine congener bearing no methyl group at one of the nitrogen atoms (**45β**).[30]

Table III. Results of Proton–Proton 1D NOE Experiments on D-Arabinonucleosides

	proton irradiated	NOE (%)
2β	H-1′	H-2′ (9.9), H-4′ (2.0), H-8 (2.0)
	H-4′	H-1′ (2.1), H-3′ (3.0), 3′-OH (3.6), 5′-OH (2.6)
	H-8	H-1′ (1.7), H-2′ + H-3′ (3.1), 2′-OH (1.3)
12α	H-1′	H-2′ (4.1), H-3′ (3.0), H-8 (6.4)
	H-3′	H-1′ (3.4), H-2′ (2.4), 2′-OH (4.5), 3′-OH (16.8), 5′-OH (2.8)
	H-4′	H-2′ (3.7), H_2-5′ (3.0), H-8 (2.0), 3′-OH (4.4), 5′-OH (2.2)
	H-8	H-1′ (5.7), H-2′ (4.2), H-4′ (1.9), 3′-OH (0.8)
16β	H-1′	H-2′ (12.1), H-4′ (2.5), H-3 (17.8), H-8 (6.4)
	H-8[a]	H-1′ (4.2), H-3′ (4.9), H-7 (10.3), 5′-OH (2.3)
	H-3[b]	H-1′ (10.4), H-2′ (1)
18α	H-1′	H-2′ (2.3), H-3′ (3.5), H-3 (14.1), 2′-OH (3.5)
	H-8[c]	H-1′ (7.2), H-2′ (8.3), H-4′ (3.1), H-7 (13.4)

[a] H-3, 12%. [b] H-8, 10%. [c] H-3, 25%.

Switching to the 2′-deoxynucleosides **37β** and **39β** a high anti conformer population was expected due to the steric effect of the amino group. However, it was found that in both nucleosides irradiation of H-8 (purine numbering) produces a strong NOE at H-1′ and vice versa (Table IV), which points to a considerable population of syn conformers. This can be explained by a hydrogen bridge between the exocyclic amino group and either 5′-OH or O-4′. Increase of the temperature from 298 to 365 K significantly reduces the NOE value of H-1′ upon saturation of H-8 and vice versa. The reason for this is obviously the breakup of the bonding interactions resulting in an almost free rotation around the N-glycosylic bond. Assuming temperature independence of all dipolar relaxation terms, $\Delta E^{\ddagger}$ values can be estimated from corresponding Arrhenius plots (ln η(H-8 or H-1′) vs T^{-1} (Figure 3)). For both nucleosides similar values (**37β**, −10 kJ/mol; **39β**, −11 kJ/mol[44]) were assessed. In order to exclude any solvent effects we measured the NOE value at H-1′ (irr. of H-8) of compound **38β** as a regioisomer of **39β** at three different temperatures between 295 and 330 K and found identical results (⟨η(H-1′)⟩ = 4.4%). Also compound **40β** exhibits identical η(H-1′) values (1%) within a temperature range of 300–365 K.

Enhancement of the bulkiness of a substituent at N-3 like in the 7-deazapurine 2′-deoxy nucleoside **46β** leads obviously to a fixed high-syn conformation as irradiation of H-8 does not result in an NOE at one of the sugar protons (Table IV).

In conclusion, both the chemical properties as well as the van der Waals radius of a substituent is of decisive importance for the conformation around their N-glycosylic bond.

Analysis of NOE Data of α-D Configured Nucleosides. Despite the fact that the calibration graph shown in Figure 1 is developed on the basis of NOE data of β-D-nucleosides, it is also useful for the determination of the syn–anti conformation of α-D anomers. Qualitative information about the distribution of syn and anti conformers of α-D-ribonucleosides (**11α**, **13α**, **15α**, **32α**) can be drawn from the NOE data of H-1′ (syn) and H-4′ (anti) upon irradiation of H-8/H-6: if the intensity enhancement of the H-1′ signal is large and that of H-4′ small then the syn conformers are preferred. If, on the other hand, the NOE value of H-4′ is relatively large and that of H-1′ is small then anti conformation is preferred. It can be seen from molecular models that the distance between H-8/H-6 and H-1′ in α-D-ribonucleosides is almost the same as in β-D-ribonucleosides. Therefore, it can be assumed that the

Table IV. Results of Proton–Proton 1D NOE Experiments on 2′-Deoxy- and 2′,3′-Dideoxy-D-ribofuranosides

	proton irradiated	NOE (%)
6β	H-1′	$H_α$-2′ (5.6), H-4′ (2.0), H-8 (2.5)
	$H_α$-2′	H-1′ (15.7), $H_β$-2′ (21.9), H-3′ (3.0), H-4′ (1.1)
	H-4′	H-1′ (2.0), H-3′ (2.5), H_2-5′ (2.2)
	H-8	H-1′ (4.1), $H_β$-2′ (3.8), H-3′ (0.8), H-7 (6.7)
14α	H-1′	$H_β$-2′ (5.6), H-3′ (1), H-8 (4.0)
	$H_α$-2′	H-1′ (1.0), $H_β$-2′ (21.0), H-3′ (1.0), H-4′ (1.0), H-8 (8.6)
	$H_β$-2′	H-1′ (17.9), $H_α$-2′ (30.9), H-3′ (9.4), H-8 (−1.8)
	H-4′	H-3′ (1.5), H-8 (3.2)
	H-8	H-1′ (3.9), $H_α$-2′ (3.6), H-4′ (2.5), H-7 (10.3)
23β	H-1′	$H_α$-2′ (5.1), H-4′ (1.5), H-8 (1.5)
	H-3′	$H_α$-2′ (1.0), $H_β$-2′ (4.1), H-4′ (2.4), H-8 (2.0), 3′-OH (3.4), 5′-OH (1.5)
	H-4′	H-1′ (1.9), H-3′ (2.4), H_2-5′ (3.5), 3′-OH (3.4), 5′-OH (1.5)
	H-8	H-1′ (1.8), $H_β$-2′ (4.3), H-3′ (1.3), H_2-5′ (1.0), 5′-OH (1.0)
	3′-OH	H-1′ (1.2), $H_α$-2′ (2.2), H-3′ (9.2), H-4′ (5.0), H_2-5′ (1.0)
24α	H-1′	$H_β$-2′ (5.0), H-8 (1.0)
	H-3′	$H_β$-2′ (3.6), 3′-OH (5.5)
	H-4′	H-8 (2.4), 3′-OH (2.0)
	H-8	H-1′ (1.3), $H_α$-2′ (2.8), H-4′ (2.3), H-7 (2.7)
29β	H-1′	$H_α$-2′ (6.3), H-4′ (2.3), H-6 (2.1)
	H-3′	$H_β$-2′ (6.3), H-4′ (3.7), H_2-5′ (2.7), H-6 (2.2), 3′-OH (5.3), 5′-OH (3.0)
	H-4′	H-1′ (3.2), H-3′ (2.6), H_2-5′ (2.6), 3′-OH (2.2), 5′-OH (1.5)
	H-6	H-1′ (2.5), H_2-2′ (4.6), H-3′ (1.5), H_2-5′ (1.0), 5-CH_3 (7.4), 5′-OH (1.0)
33α	H-1′	$H_β$-2′ (7.0), H-3′ (1), H-6 (2.3)
	$H_α$-2′	H-1′ (1.8), $H_β$-2′ (36.4), H-3′ (2.9), H-4′ (1.2), H-6 (14.4), 3′-OH (5.5)
	H-3′	H-1′ (1.2), $H_α$-2′ (1.1), $H_β$-2′ (5.8), H-6 (1.1), 3′-OH (13.4), 5′-OH (3.1)
	H-4′	H-6 (6.2), 3′-OH (5.3), 5′-OH (2.1)
	H-6	H-1′ (2.0), $H_α$-2′ (3.4), H-4′ (4.3), 5-CH_3 (7.2), 3′-OH (1.7)
30β	H-1′	H_2-2′ (5.9), H-4′ (2.3), H-6 (1.5)
	H-4′	H-1′ (2.8), H_2-2′ (0.8), H-3′ (2.3), 3′-OH (3.6), 5′-OH (1.6)
	H-6	H-1′ (2.4), H_2-2′ (3.8), H-3′ (2.1), H-7 (17.0), H-8 (4.1), 5′-OH (1.7)
	H-7	H-6 (10.5)
	H-8	H-6 (1.8)
4β	H-1′	H_2-2′ (6.6), H-4′ (1.8), H-8 (4.8)
	H_2-3′	H-1′ (1.8), H_2-2′ (6.5), H-4′ (12.1), H-8 (5.2), 5′-OH (1.4)
	H-4′	H-1′ (1.9), H_2-2′ (1.6), H_2-3′ (5.8), H_a-5′ (2.2), H_b-5′ (2.7)
	H-8	H-1′ (4.3), H_2-2′ (1.4), $H_β$-3′ (2.1)
17β[a]	H-1′	$H_α$-2′ (6.4), H-4′ (2.6), H-3 (10.3), H-8 (2.6)
	H-4′	H-1′ (2.6), H_2-3′ (5.7), H_2-5′ (5.6)
	H-8	H-1′ (1.9), $H_β$-2′ (3.0), $H_β$-3′ (2.4), H_2-5′ (1.0), H-7 (6.3)
21β	H-1′	H_2-2′ (7.8), H-4′ (2.0), H-8 (2.6)
	H_2-3′	H-1′ (1.7), H-4′ (12.4), H_2-5′ (3.6), H-8 (5.6), 5′-OH (1.0)
	H-4′	H-1′ (1.7), $H_α$-2′ (1.9), H_2-3′ (5.5), H_2-5′ (4.8)
	H-8	H-1′ (2.7), $H_β$-2′ (3.2), $H_β$-3′ (2.8), 5′-OH (0.8)
37β	H-8	H-1′ (6.1), $H_β$-2′ (5.3), H-3′ (0.8)
	H-1′	$H_α$-2′ (10.0), H-4′ (3.2), H-8 (6.1), NH_2 (4.2)
46β	H-8	H-1′ $H_β$-2′, and H-3′ (0%, each)
	H-1′	H-8 (0.5), CH (12.6), H-4′ (2.0), $H_α$-2′ (4.7)
41β	H-8	H-1′ (0), $H_β$-2′ (6.8), H-3′ (2.8)
	H-1′	CH_3 (13.7)
45β	H-8	H-1′ (6.2), $H_β$-2′ (3.1), H-3′ (2.3)
	H-1′	H-8 (3.5), H-4′ (1.4)
43β	H-8	H-1′ (5.2), $H_β$-2′ (4.1), H-3′ (1.4)
47α	H-8	H-1′ (0), H-4′ (2.3), $H_α$-2′ (6.5), H-7 (8.7)
	H-1′	H-8 (0), CH (14.0), H-3′ (1.1), $H_β$-2′ (6.2)
27β	H-6	H-5 (9.3), H-1′ (2.2), H-3′ (1.9), H_2-2′ (2.9)
	H-1′	H-6 (2.1), H-4′ (1.7), $H_α$-2′ (6.9)
	H-3′	H-6 (1.9), H-4′ (3.1), H_2-5′ (2.6) H_2-2′ (6.2)
3β	H-8	H-1′ (6.0), $H_β$-2′ (2.2), H-3′ (0.5)
	H-1′	H-8 (6.3), H-4′ (1.3), $H_α$-2′ (6.1)
	H-3′	H-8 (0.5), H-4′ (2.1), H_2-5′ (1.6), $H_β$-2′ (4.0)
	$H_β$-2′	H-8 (2.8), H-3′ (7.0), $H_α$-2′ (20.0)
20β	H-8	H-1′ (3.1), H-3′ (1.1), $H_β$-2′ (3.7)
	H-1′	H-8 (3.1), H-4′ (1.6), $H_α$-2′ (5.6)
	H-3′	H-8 (1.7), H-4′ (3.4), $H_β$-2′ (4.2), H_2-5′ (1.5)
	H-4′	H-1′ (1.8), H-3′ (2.3)
31β	H-6	H-1′ (2.7), H-3′ (3.0), $H_β$-2′ (4.6), CH_3 (6.4)
	H-1′	H-6 (2.3), H-4′ (2.0), $H_α$-2′ (8.0)
9β	H-8	H-7 (10.7), H-1′ (1.4), $H_β$-2′ (2.2), $H_β$-3′ (2.3)
	H-1′	H-8 (1.1), H-4′ (1.5)
40β	H-8	H-1′ (1), H-3′ (1.2), $H_β$-2′ (3.7)
	H-1′	H-8 (1), H-4′ (1.7), $H_α$-2′ (5)
	H-3′	H-8 (2.4), $H_β$-2′ (6.1)
39β	H-8	H-1′ (4.5), $H_β$-2′ (4.2)
	H-1′	H-8 (5.2), H-4′ (2.9), $H_α$-2′ (6.3)
34β	H-8	H-1′ (4.4), $H_β$-2′ (3.0), H-3′ (0.7)
35β	H-8	H-1′ (4.6)
	H-1′	H-8 (5.5), H-3 (5.2), H-4′ (2.0), $H_β$-2′ (7.6)
	H-4′	H-1′ (2.4), H-3′ (2.1), H_2-5′ (5.7)
36β	H-8	H-1′ (2.6), $H_β$-2′ (3.5), H-3′ (0.9)
38β	H-8	H-1′ (4.2), $H_β$-2′ (3.5), H-3′ (0.7)
7β	$H_β$-2′	$H_α$-2′ (22), H-3′ (2.0), 3′-OH (1.9), H-1′ (1), H-6 (4.3)
	$H_α$-2′	$H_β$-2′ (23), H-4′ (1.6), H-3′ (7.8) H-1′ (12.3)
	H-3′	$H_α$-2′ (4.0), H-4′ (8.6), 3′-OH (2.5)
	H-1′	$H_α$-2′ (5.7), H-4′ (2.3), H-6 (4.8)
	H-6	$H_β$-2′ (1.9), H-1′ (4.8), H-5 (7.6)

[a] Measured at 50 °C.

maximal NOE value at H-1′ (irradiation of H-8)—determined for the syn-fixed β-D-ribonucleoside **25β**—can also be used as a calibration for the estimation of syn/anti conformer populations in the case of α-D-ribonucleosides. In general, these rules should also be valid for α-D-arabinonucleosides (Table III) as well as α-D-2′-deoxyribonucleosides (Table IV). Within this series, however, the intensity enhancement of the $H_α$-2′ signal upon saturation of H-8/H-6 can also be used as an indicator of the anti conformation of the nucleobase.

Inspection of the NOE data of α-D configured compounds (Tables II–IV) shows that the α-D-ribonucleosides **11α**, **13α**, **15α**, and **32α** exhibit preferentially anti conformation at the glycosylic bond as the η(H-1′) values amount only to 1.2–3.1%. α-D-Arabinoadenosine (**12α**) exhibits a significantly larger η(H-1′) value (5.7%) which points to an almost equal distribution of syn and anti conformers. Simultaneous irradiation of H-8 and H-3 in the case of the base-modified α-D-arabino nucleoside **18α** (Table III) prevents a reliable estimation of syn/anti conformer populations. In Table IV the NOE data of four α-D-2′-deoxyribonucleosides are included (**14α**, **24α**, **33α**, and **47α**). The first three of them exhibit η(H-1′) values of 1.3–3.9% upon irradiation of H-8/H-6, which points to a preferred anti orientation of the nucleobase.

A special phenomenon was observed for compound **47α** bearing a bulky isopropyl group at N-3 of the purine isosteric aglycon which hinders rotation around the N-glycosylic bond. As the NOE at the $H_α$-2′ signal upon saturation of H-8 amounts to 6.5% (Table IV) which is the largest value in the series of α-D-nucleosides the conformation at the glycosylic bond seems to be high-anti or at least near to this. This finding shows that in the case of the sterically hindered 2′-deoxyribonucleosides **46β** and **47α** a change of the anomeric configuration goes along with a change of the conformation around the glycosylic bond.

In conclusion, NOE measurements on the conformationally rigid nucleosides **25β** and **41β** allows the setting

up of a calibration graph for a semiquantitative estimation of syn and anti conformer populations of regular and modified nucleosides. Deviations from the yardstick NOE values obtained on the compounds **25β** and **41β** are also of diagnostic value as they imply an unusual conformation around the glycosylic bond (e.g. high-syn, **46β**; high-anti, **47α**), which usually does not play an important role for the two-state equilibrium (syn–anti) of nucleosides and nucleotides.

Experimental Section

All NMR measurements were performed at 298 K with $(CD_3)_2SO$ (99.5%) as solvent using its deuterium for internal lock.

For the NOE measurements the solutions (ca. 0.1 M) were degassed by bubbling N_2 through it followed by ultrasound sonication. As it is known that, in contrast to all other nucleic acid constituents, guanosine forms gels from aqueous solution,[33] NOE measurements (irr. of H-8) were run on this nucleoside in $(CD_3)_2SO$ at concentrations of 0.05, 0.1, and 0.2 M. In all cases identical η(H-1′) values ($\langle\eta$(H-1′)$\rangle$ = 3.6%) were found. All compounds were measured under identical spectral and processing conditions by applying either the NOEDIFF or the NOEMULT[34] pulse sequence of the Bruker software package (release version 1988 or 1989) applying its recommendations for steady-state NOE measurements. As irradiation time of 1.5 s with an irradiation power of 40–45 dB below 0.2 W yielded a saturation of ≤95%.

The analysis of spectral data was performed in two different ways: (i) sequential exponential multiplication (line broadening: 0.25) and fourier transformation of two FIDs (one entry for a desired irradiation point plus one off-resonance control value for O-2) and then subtraction of the two spectra; (ii) subtraction of two FIDs followed by exponential multiplication and fourier transformation of the differential FID. All NOE values (η, in %) were obtained by repeated integration of the peaks of the difference spectra.

Force-field calculations were performed using the Alchemy II software package, release 1988 (Tripos Ass., Inc., St. Louis, MO). Minimization of the potential energy of the constructed molecule was performed with a force-field equation that involves the five energy terms: bond-stretching, angle bending, torsion deformation, van der Waals interactions, and out-of-plane bending.

Compounds **1β**, **2β**, **11α**, **28β**, **29β**, **33α**, **3β**, **10β**, **19β**, **20β**, **26β**, **27β**, **31β**, **48β**, **49β**, and **50β** were purchased from either Pharma Waldhof (Darmstadt, FRG) or Sigma Chemicals Co. (St. Louis, MO). Compounds **4β** and **21β** were provided by Boehringer Mannheim (Mannheim, FRG). Compounds **12α** and **32α** were generous gifts of Dr. F. Hansske (Boehringer Mannheim, FRG), compound **30β** was a gift of Prof. Dr. E. de Clercq (University of Leuven, Belgium). Compounds **41β–45β** were provided by Prof. Dr. B. Golankiewicz.[30,31,46] All other compounds were synthesized in our laboratory: **5β**, **8β**, **13α**, **15α**;[35] **6β**;[36] **7β**;[16] **9β**;[37] **14α**;[14] **16β**, **18α**;[38] **17β**;[39] **22β**;[40] **23β**, **24α**;[41] **34β**;[38] **35β**;[43] **36β**;[38] **37β**;[43] **38β**, **39β**, **40β**;[44] **46β**, **47α**.[45]

6-Amino-9-(5-chloro-β-D-ribofuranosyl)-9*H*-purin-2-one. 6-Amino-9-(β-D-ribofuranosyl)-9*H*-purin-2-one (isoguanosine, 285 mg, 1 mmol) was dissolved in hexamethylphosphoric triamide (15 mL) by heating. The solution was brought to room temperature, and thionyl chloride (0.4 mL, 5.5 mmol) was added during 1 h. The reaction mixture was stirred 1 h at ambient temperature, diluted with water (50 mL), and chromatographed on Dowex 50 W (H^+ form, column: 1 × 15 cm). After washing with water (200 mL), 5% aqueous ammonia (100 mL) eluted one main zone which was pooled and evaporated to a volume of 15 mL whereupon the title compound (240 mg, 80%) crystallized as colorless needles: mp 240 °C dec; UV (0.01 N HCl) λ_{max} 281 nm (ε 13 900), (0.01 M phosphate buffer, pH 7) λ_{max} 245 (ε 9300), 288 nm (ε 11 600), (0.01 N NaOH) λ_{max} 282 nm (ε 11 200); ^1H NMR ($(CD_3)_2SO$–D_2O, 1:1) δ 3.85 (2 H, m, H_2-5′), 4.02 (1 H, q, H-4′), 4.11 (1 H, t, H-3′), 4.57 (1 H, t, H-2′), 5.68 (1 H, d, J = 5.8 Hz, H-1′), 7.96 (1 H, s, H-8). Anal. Calcd for $C_{10}H_{12}N_5O_4Cl$ (301.7): C, 39.65; H, 4.11; N, 23.01. Found: C, 39.65; H, 4.11; N, 23.01.

6-Amino-N^3,5′-cyclo-9-(β-D-ribofuranosyl)-2-oxopurine (N^3,5′-Anhydroisoguanosine, 25β). 6-Amino-9-(5-chloro-β-D-ribofuranosyl)-9*H*-purin-2-one (150 mg, 0.5 mmol) and K_2CO_3 (500 mg), dissolved in water, were refluxed for 30 min. The title compound crystallized in colorless plates upon cooling and storage overnight at 0 °C (90 mg, 68%): mp 270 °C dec; UV (0.01 N HCl) λ_{max} 238 (ε 5500), 286 nm (ε 13 100); (0.01 M phosphate buffer, pH 7 and 0.01 N NaOH) λ_{max} 279 nm (ε 11 500); ^1H NMR ($(CD_3)_2SO$–D_2O, 1:1) δ 3.70 (2 H, m, H_2-5′), 3.87 (1 H, d, H-4′), 4.05 (1 H, t, H-3′), 4.52 (1 H, m, H-2′), 6.11 (1 H, s, H-1′), 7.76 (1 H, s, H-8). Anal. Calcd for $C_{10}H_{11}N_5O_4$ (265.2): C, 45.29; H, 4.18; N, 26.41. Found: C, 45.19; H, 4.26; N, 26.39.

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Registry No. **1β**, 58-61-7; **2β**, 5536-17-4; **3β**, 958-09-8; **4β**, 4097-22-7; **5β**, 69-33-0; **6β**, 60129-59-1; **7β**, 107729-48-6; **8β**, 16754-80-6; **9β**, 115899-34-8; **10β**, 58-63-9; **11α**, 5682-25-7; **12α**, 3228-71-5; **13α**, 72933-38-1; **14α**, 103194-72-5; **15α**, 120401-32-3; **16β**, 124469-57-4; **17β**, 120552-21-8; **18α**, 124469-58-5; **19β**, 118-00-3; **20β**, 961-07-9; **21β**, 85326-06-3; **22β**, 62160-23-0; **23β**, 110457-87-9; **24α**, 110457-88-0; **25β**, 129285-58-1; **26β**, 65-46-3; **27β**, 951-77-9; **28β**, 58-96-8; **29β**, 50-89-5; **30β**, 82768-44-3; **31β**, 30516-87-1; **32α**, 3258-07-9; **33α**, 4449-43-8; **34β**, 129266-17-7; **35β**, 4845-21-0; **36β**, 129266-18-8; **37β**, 127553-28-0; **38β**, 78582-17-9; **39β**, 129266-19-9; **40β**, 129266-20-2; **41β**, 129266-21-3; **42β**, 52662-10-9; **43β**, 101803-01-4; **44β**, 59327-60-5; **45β**, 101803-00-3; **46β**, 128751-25-7; **47α**, 128751-27-9; **48β**, 362-75-4; **49β**, 362-76-5; **50β**, 2140-11-6; isoguanosine, 1818-71-9; 6-amino-9-(5-chloro-β-D-ribofuranosyl)-9*H*-purin-2-one, 129266-22-4.

Supplementary Material Available: 1D ^1H NOE difference spectra (7 pages). Ordering information is given on any current masthead page.

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