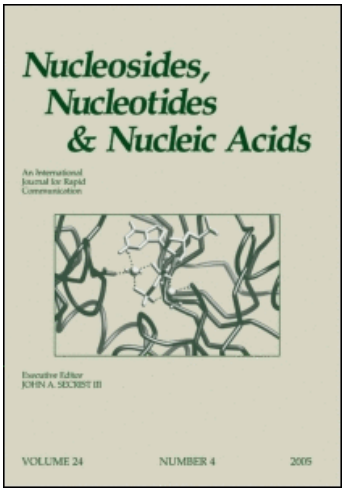

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Novel Types of N⁶,2'-Cyclonucleosides

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NOVEL TYPES OF N^6,2'-CYCLONUCLEOSIDES

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Abstract : Upon oxidation followed by treatment with hydroxylamine, the 3',5'-diblocked uridine **1** gave the expected oxime **2** together with the N^6,2'.cyclonucleoside **3** formed by nucleophilic attack of hydroxylamine at both C-6 and C-2' positions. Reduction of **2** took place predominantly from the α face and the major D-*arabino* compound obtained gave the cyclonucleoside **7** *via* Michael type addition. The structures of the novel cyclonucleosides, particularly their configuration at C-6 were established by X-ray diffraction.

Deoxy *N*-hydroxyamino sugars and nucleosides are very close analogs of their oxygenated counterparts and present the interesting property of oxidizing spontaneously in solution to give the corresponding nitroxide free radical in a stationnary concentration sufficient to provide good EPR spectra and too small to significantly degrade the resolution of their NMR spectra.[1] We have previously described 3'-deoxy-3'-*N*-hydroxyamino analogs of nucleosides[2] and report here the synthesis and properties of some derivatives of 2'-deoxy-2'-*N*-hydroxyamino uridine. Owing principally to the so-called α-effect,[3] hydroxylamines are very efficient nucleophiles towards activated C-C double bonds and this property renders feasible a scarcely encountered mode of formation of cyclonucleosides : Michael type reactions.[4] This led to a novel type of cyclonucleosides N^6,2'-cyclo-5,6-dihydrouridine derivatives. Part of this work has been the subject of a preliminary communication.[5]

TABLE 1. ^{1}H NMR Chemical Shifts of Uridine Derivatives (200 MHz)

Compd	H-1'	H-2'	H-3'	H-4'	H-5'	H-5	H-6
2a[a]	6.16		5.22	3.84	4.02 4.08	5.69	7.10
2b[a]	6.18		5.24	3.90	4.11	5.73	7.12
3[a]	5.58		4.73	3.83	4.10	2.85 3.08	4.69
4[b]	5.55		4.42	3.77	3.66 3.86	2.75 2.95	4.65
5[a]	5.77		5.60	4.22	4.22	3.0	4.95
6a[b]	6.55		4.93	3.72- 3.95	3.72- 3.95	5.67	7.57
6b[b]	6.42		4.81	3.72- 3.95	3.72- 3.95	5.66	7.52
7[c]	5.85	3.83	3.72	3.39	3.42 3.61	2.80 2.91	4.58
9[a]	6.20	4.41	5.35	4.07	4.19 4.33	2.93 3.10	5.02
10[b] D-*arabino*	6.38	4.90	5.06	3.96	3.87 3.96	5.59	8.03
10[b] D-*ribo*	6.49	4.90	4.60	4.39	3.82 3.98	5.70	8.02

[a] *In* $CDCl_3$. [b] *In* CD_3OD. [c] *In* $(CD_3)_2SO$.

The 3',5'-diblocked uridine **1**[6] was found the most suitable substrate for modifying the 2' position. It was oxidized by chromic anhydride following Garegg's procedure[7] to the expected ketonucleoside which was not isolated but directly oximated to a 1:3 mixture of the geometrical isomers (**2a** and **2b**) of **2** (45.5%). The cyclonucleoside **3** (10%) was also obtained. As evident from the NMR data of **2** (TABLES 1-3), a reliable assignment of the *E-Z*

TABLE 2. ^{1}H NMR Coupling Constants of Uridine Derivatives[a]

Compd	$J_{1',2'}$	$J_{1',3'}$	$J_{2',3'}$	$J_{3',4'}$	$J_{4',5'}$	$J_{5',5''}$	$J_{5,6}$	$J_{5,5}$
2a		1.8		8.0	3.5 5.0	12.0	8.0	
2b		1.8		8.0	4.0 5.0		8.4	
3				8.0	2.7		10.0 5.2	16.5
4				8.7	4.0 1.0	12.0	9.5 5.5	16.2
5				8.0			8.0	
6a		1.5		6.0			8.0	
6b		1.5		7.0			8.0	
7	6.0		6.0	8.5	5.5 5.5	10.5	6.7	17.7
9	6.2		6.0	7.5	5.0 3.2	12.5	8.0 7.0	17.5
10 D-*arabino*	7.0			6.2	? 2.5	14.5	8.0	
10 D-*ribo*	2.0		7.5	8.5	3.0 2.2	14.5	8.0	

[a] *Same solvents as in TABLE 1.*

configuration was not possible (very close values of δ_{H-1} and δ_{H-3} of the two isomers in particular). The 5,6-dihydrouracil moiety of compound **3** gave the expected NMR signals and the structure of **3** was further established by its acetylation to an unisolated di-*O*-acetyl [(NMR: δ 2.06, 2.08, 2s, 2x3H, 2 OAc; MS: 558 (10.3, $M^{\cdot+}$ - Ac), 542 (3.1, $M^{\cdot+}$ - AcO)] derivative. Glycosidation at position 2' and de-*O*-silylation of compound **3** using acidic methanol gave **4** (94%) which was acetylated to **5** (SCHEME 1). X-ray diffraction study of

TABLE 3. ^{13}C NMR Chemical Shifts of Uridine Derivatives (50.4 MHz)[a]

Compd	C-1'	C-2'	C-3'	C-4'	C-5'	C-5	C-6
2a	84.66	155.60	69.20	83.55	63.59	102.76	141.88
2b	82.45	156.88	70.59	82.45	62.23	102.85	142.75
3	89.27	97.96	67.82	82.04	60.48	35.66	67.82
4	87.28	102.37	68.79	84.46	61.76	37.26	72.44
6a	85.49	151.57	69.55	83.36	62.33	102.81	144.89
6b	86.08	152.19	66.96	83.79	62.49	103.21	144.12
7	87.62	71.77	73.92	83.94	61.39	31.26	81.66
9	86.73	72.35	72.35	76.61	62.69	31.67	79.29
10 D-*arabino*			71.40		62.00	101.60	
10 D-*ribo*			70.50		62.00	103.00	

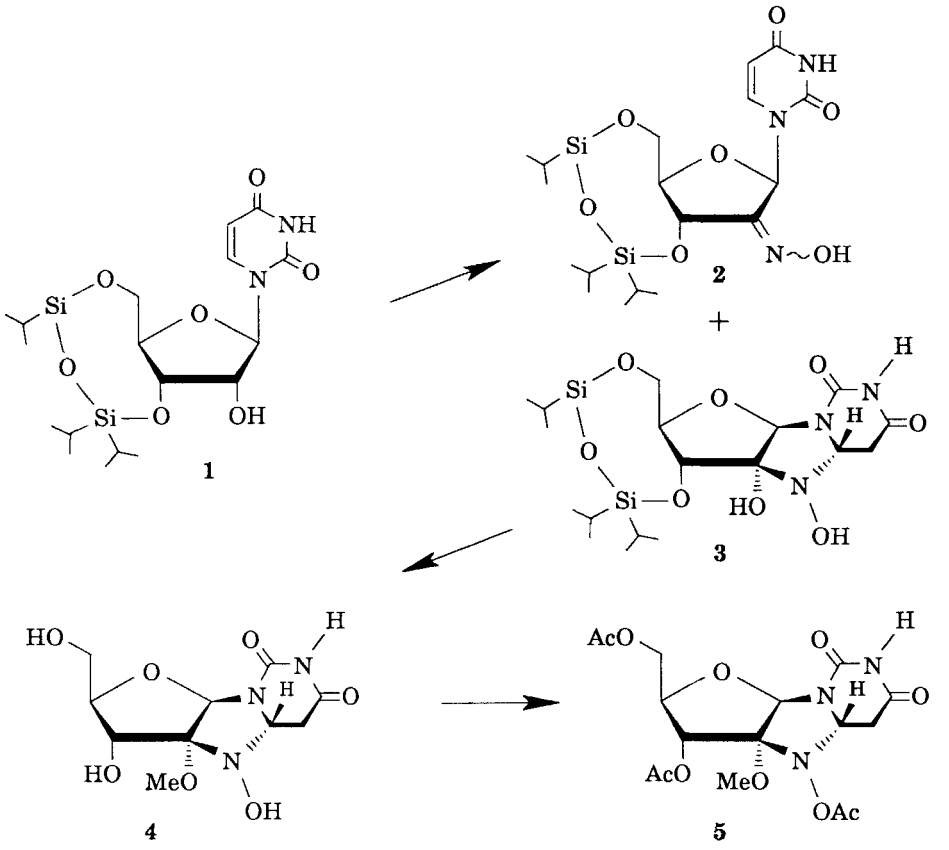
[a] *Same solvents as in TABLE 1 except for* **7** *(CD_3OD + DMSO-d_6).*

5 (FIG. 1) showed the configuration at the two new asymmetric carbon atoms to be *6S,2'R*.

De-*O*-silylation of **2** gave a 3:7 mixture of geometrical isomers **6** as a hygroscopic solid for which no acceptable elementary analysis could be obtained. Its structure was instead asserted by high resolution mass spectroscopy ($M^{\cdot+}$ *m/z* calcd : 257.0647, found : 257.0672).

Upon acidic desilylation followed by reduction (BH_3-pyridine), **2** gave a mixture, in variable proportions, of the cyclonucleoside **7** and an unresolvable unstable mixture of the epimers **8** (SCHEME 2).

Compound **7** was acetylated to **9** (64%) and **8** converted to the corresponding nitrones **10**. Typically, we did not isolate **7** after the reduction stage but treated the reaction mixture containing **7** and **8** with veratraldehyde to obtain unreacted **7** (75% from **2**) and the unresolvable epimeric mixture of the nitrones **10** (18.5% from **2**) in an 3:7 *arabino/ribo ratio*. The configuration



SCHEME 1

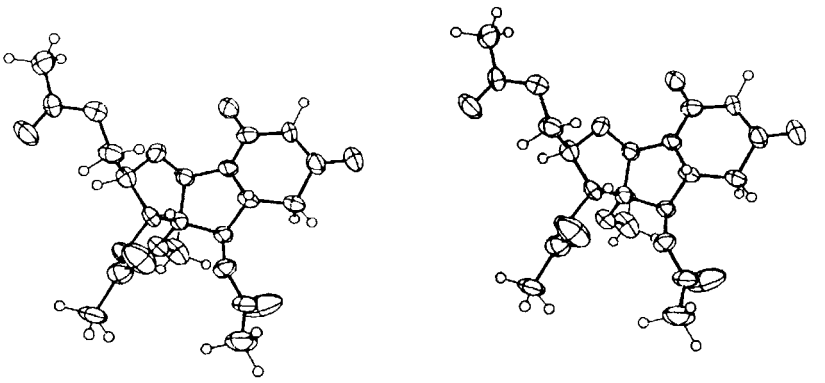
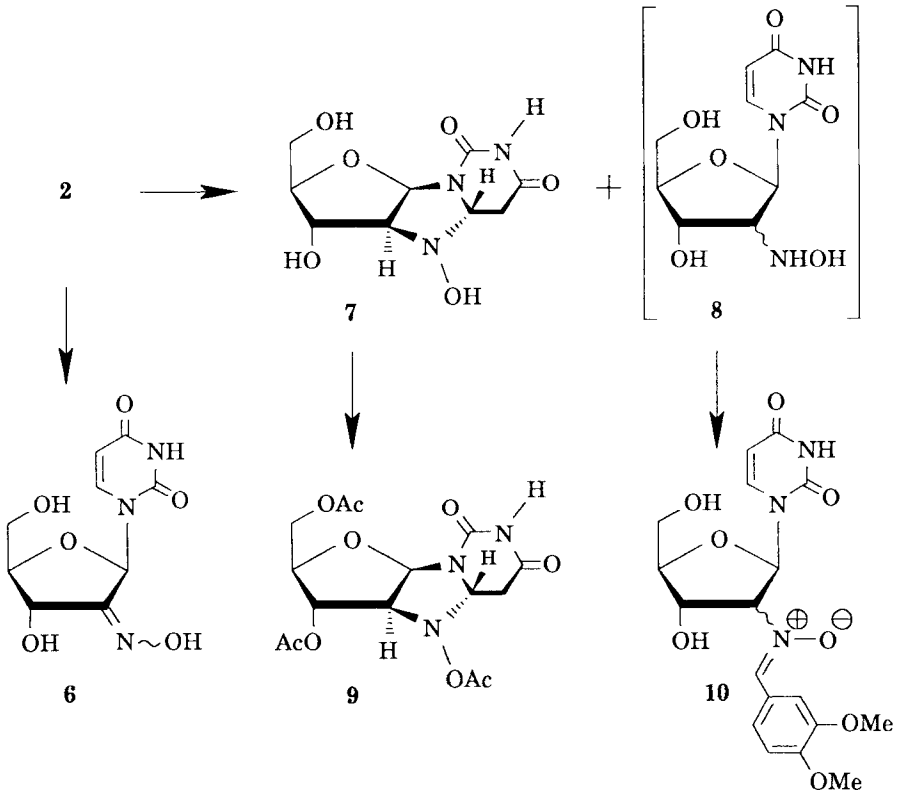


FIG 1. An ORTEP stereoview of cyclonucleoside **5**



SCHEME 2

of each of the epimers **10** was easily assigned from the $J_{1',2'}$ values (TABLE 2) in particular the low value (2.0 Hz) for the *ribo* isomer establishing the *trans* relationship of H-1' and H-2'. This showed that the reduction proceeded predominantly from the α side of the furanose ring and that most of the D-*arabino* hydroxylamine **8** underwent conjugate addition onto the uracil moiety leading to **7**. An X-ray diffraction study of **7** established its *(6S)*-β-D-*arabino* configuration (FIG. 2).

Besides the configurational assessment they allowed, the X-ray studies provided useful structural information on the novel family of cyclonucleosides represented by **5** and **7**. The furanose ring of **5** adopts a $^3T_4$ conformation[8] whereas **7** exhibits a quasi perfect ^3E [(C3')-endo] conformation with a minimum value of the asymmetry parameter[9] $\Delta C_s = 0.005$. Both

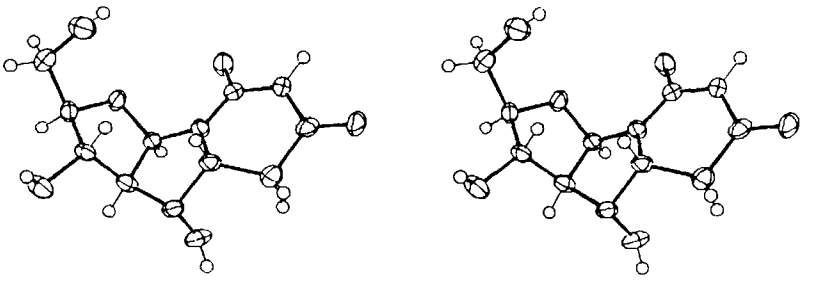


FIG. 2. An ORTEP stereoview of cyclonucleoside **7**

furanose rings show maximum puckering amplitude[10] associated with the C(3') atom. In compound **7** the C(4')-C(5') bond adopts the prefered *gauche-gauche* conformation (φ_{CO} = 62.2(5)°, φ_{OO} = -55.3(5)°) and the hydroxyl group participate to a bifurcated intermolecular hydrogen bond (TABLE 4). This was not observed in compound **5** where the hydroxyl group was blocked and the C(4')-C(5') bond shows the less favourable *trans-gauche* conformation [φ_{CO} = 168(1)°, φ_{OO} = -54(1)°].

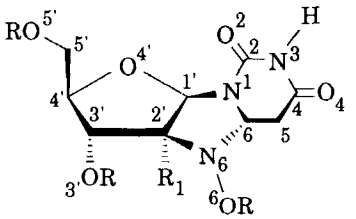
Even if the absolute configuration at the N(6) atom of the imidazolidine rings is *R* for both **5** and **7**, their relative configuration differs. In **5**, the OAc group is *endo* (pseudo equatorial) relative to the tetrahydrofuranoimidazolidine bicycle and steric interaction of O(6) with H(C(3')) leads N(6) to be *exo* in a $^{C(6)}T_{N(6)}$ conformation of the imidazolidine. In compound **7**, the hydroxyl substituent of N(6) is *exo* (pseudo-axial) and the imidazolidine ring adopt a $^{N(6)}T_{C(2')}$ conformation. It is clear that the orientation of the base relative to the sugar moiety, described by the glycosidic torsion angle χ_{CN} [O(4')-C(1')-N(1)-C(2)],[11] is fixed by the presence of the nitrogen bridge. In both cases, the glycosidic linkage is restricted to a *syn* arrangement with χ_{CN} values of -70(2)° and -62.1(5)° for compounds **5** and **7** respectively. The C(1')-N(1) glycosidic bond lengths (1.44 and 1.45 Å) are significantly shorter than the mean value of 1.52 Å observed[12] for compounds where χ_{CN} is 180°.

Both dihydrouracil moieties exhibit a half-chair conformation with a minimum value of the asymmety parameter (TABLE 5) associated with a pseudo C_2 symmetry passing through the C(2)-N(3) bond. In **5**, the half-

TABLE 4. Selected Interatomic Distances and Hydrogen Bonds (Å) with e.s.d.'s in parenthesis.

	5	7		5	7
O(4') - C(1')	1.40(1)	1.424(5)	N(1) - C(6)	1.44(1)	1.475(5)
O(4') - C(4')	1.43(1)	1.468(5)	C(2) - O(2)	1.25(1)	1.221(5)
C(1') - C(2')	1.55(1)	1.545(6)	C(2) - N(3)	1.37(2)	1.391(6)
C(1') - N(1)	1.44(2)	1.450(5)	N(3) - C(4)	1.37(2)	1.393(6)
C(2') - C(3')	1.53(2)	1.522(6)	C(4) - O(4)	1.20(2)	1.205(6)
C(2') - N(6)	1.46(1)	1.497(5)	C(4) - C(5)	1.52(1)	1.507(7)
C(3') - C(4')	1.52(2)	1.533(6)	C(5) - C(6)	1.50(1)	1.514(6)
C(3') - O(3')	1.44(1)	1.417(5)	C(6) - N(6)	1.47(2)	1.484(5)
C(4') - C(5')	1.48(2)	1.513(7)	N(6) - O(6)	1.47(1)	1.461(5)
N(1) - C(2)	1.33(1)	1.347(5)			

5			7		
$O(H_2O)$....O(4')	x, y, z-1	2.98(1)	O(3')....O(5')	x-1/2, 1/2-y, 1-z	2.703(5)
$O(H_2O)$....O(2)	x, y, z-1	2.93(1)	O(5')....N(6)	x+1, y, z	3.015(5)
$O(H_2O)$....O(5')	x, y, z-1	3.16(1)	O(6).....O(4')	x-1, y, z	3.021(4)
N(3).....O(5'')	x+1, y, z	2.90(1)	O(6).....O(2)	x-1, y, z	2.808(5)



5 R = Ac, R_1 = OMe

7 R = R_1 = H

chair conformation is quasi perfect (ΔC_2 = 0.011) whereas **7** shows a small deformation toward the twist-boat form (ΔC_2 = 0.044). In both compounds the molecular packing is fixed by hydrogen bonds involving all potential donors (TABLE 4).

Diglyme solutions of **3**, **4** and **7** gave, upon spontaneous oxidation in the air, well-resolved EPR spectra. The data corresponding to experiments run at 20 °C are collected in TABLE 6. Increasing the temperature to 40 and 80 °C did not significantly change the aspect of the spectra but at 110°, the radical generated from **7** decomposed. This indicated that the hyperfine couplings measured at 20 °C corresponded already to time-averaged values. All these compounds showed hyperfine couplings with nitrogen (12.9-14

TABLE 5. Selected Torsional Angles(°), Ring-Puckering Parameters and Minimum Values of Asymmetry Parameters[a]

	5	7
Furanose ring	Conformation $^3T_4$	Conformation ^3E
C(4')-O(4')-C(1')-C(2')	-9(1)	-1.2(4)
O(4')-C(1')-C(2')-C(3')	-14(1)	-22.3(4)
C(1')-C(2')-C(3')-C(4')	29(1)	35.3(4)
C(2')-C(3')-C(4')-O(4')	-35(1)	-36.7(4)
C(3')-C(4')-O(4')-C(1')	28(1)	24.1(4)
Q_2	0.337	0.374
φ_2	-60.6	-71.4
ΔC_2	C(1') = 0.019	-
ΔC_s	-	C(3') = 0.005
Dihydrouracil	*half-chair*	*half-chair*
C(6)-N(1)-C(2)-N(3)	6(2)	3.6(6)
N(1)-C(2)-N(3)-C(4)	13(2)	23.7(6)
C(2)-N(3)-C(4)-C(5)	0(2)	-11.4(6)
N(3)-C(4)-C(5)-C(6)	-30(2)	-25.2(5)
C(4)-C(5)-C(6)-N(1)	44(2)	46.3(5)
C(5)-C(6)-N(1)-C(2)	-34(2)	-37.9(5)
Q_T	0.382	0.443
φ_2	92.4	99.7
θ_2	117.5	109.2
ΔC_2	(C(2)-N(3)) 0.011	(C(2)-N(3)) 0.044
Imidazolidine ring	Conformation $^{C(6)}T_{N(6)}$	Conformation $^{N(6)}T_{C(2')}$
N(1)-C(1')-C(2')-N(6)	-16(1)	-25.7(4)
C(1')-C(2')-N(6)-C(6)	35(1)	37.1(4)
C(2')-N(6)-C(6)-N(1)	-40(1)	-33.0(4)
N(6)-C(6)-N(1)-C(1')	30(1)	17.8(4)
C(6)-N(1)-C(1')-C(2')	-9(1)	4.8(4)
Q_2	0.371	0.355
φ_2	83.2	63.2
ΔC_2	C(1') = 0.025	N(1) = 0.034
Miscellaneous		
φ_{CO} [C(3')-C(4')-C(5')-O(5')]	168(1)	62.2(5)
φ_{OO} [O(4')-C(4')-C(5')-O(5')]	54(1)	-55.3(5)
χ_{CN} [O(4')-C(1')-N(1)-C(2)]	-70(2)	-62.1(5)
C(3')-C(2')-N(6)-C(6)	-75(1)	-76.6(4)
C(2')-N(6)-C(6)-C(5)	-157(1)	-152.9(4)

[a] *For ring-puckering parameters (Q_2, Q_T, φ_2, θ_2),[10] the starting position and direction for ring puckering calculations are O(4') to C(4') for furanose, N(1) to C(6) for dihydrouracil and C(1') to N(1) for imidazolidine. Asymmetry parameters (ΔC_s, ΔC_2) are expressed according to Nardelli[9] and conformational nomenclature (E, T, χ_{CN}, φ_{OO}, φ_{CO}) based on Sundaralingam's proposals.[8,11]*

TABLE 6. EPR Data (diglyme, 20 °C) of Nitroxide Free Radicals from Cyclonucleosides **3**, **4** and **7**

Compd	g	a_N	a_H^β	Extra signal splittings
3	2.0054	13.6	16.4	3x0.5
4	2.0062	12.9	16.0	3x0.5
7	2.0060	14.0	19.3 18.0	0.6, 0.6, 0.5

G). For compounds **3** and **4**, one large coupling with a β hydrogen atom was noted. From the modified[13] Rassat's equation[14] [$a_H = (25 \pm 1) \cos^2\theta$] where θ stands for the dihedral angle between the C-H bond and the axis of the p_z orbital on the nitroxide nitrogen atom, this corresponded to an averaged θ value of *ca* 38°. As expected from its structure, **7** showed two such a_H^β couplings, both large, this ruling out an envelope conformation of the imidazolidine *N*-oxyl ring in which the nitrogen atom bearing the oxygen would be out of the plane of the four remaining atoms. The measured values of 19.3 and 18.0 G corresponded to θ ranges of 26.3-30.5° and 30-33.7° respectively, which indicated a conformation where either C-1' or N-1 (or both) would be out of the general plane of the imidazolidine ring. Some very small long-range hyperfine couplings were also noted but the resolution of the signals did not allow a reliable assignment either to the β nitrogen atom (N-1) or to some of the four γ hydrogen atoms.

Antibacterial activities of compounds **3**, **6**, **7** and **9** against *E. coli* and *B. subtilis* and activity of **7**, **9** and **10** against Polyoma A2 virus have been measured using described procedures.[2] No activity against *E. coli* was found for any of these compounds. A marginal activity against *B. subtilis* was noted for **7** and **9** (minimum inhibitory concentration 5 and 4 μM respectively). Concerning the antiviral testing, the only somewhat active compound was the nitrone **10** (partial inhibition of Polyoma A2 virus for a 235 μM concentration).

EXPERIMENTAL

General Methods. Melting points (uncorrected) were determined under microscope with a Mettler FP52 melting-point apparatus. Thin layer chromatographies (TLC) were performed on silica gel HF_{254} (Merck) with detection by UV light and phosphomolybdic-sulfuric acid.[15] Dry column chromatography[16] was conducted on silica gel $60F_{254}$ (0.063-0.200 mm). Silica gel 60 (0.040-0.200 mm) Merck was used for flash column chromatography.[17] IR spectra were recorded with a Perkin-Elmer Model 357 or a FT-IR Nicolet 20 SXB spectrometers. UV spectra were measured on a Kontron Uvicon 810 spectrophotometer. NMR spectra were recorded at 20 °C on a Bruker WP 200 SY spectrometer (^1H 200 MHz; ^{13}C 50.4 MHz; chemical shifts in ppm from TMS; δ units). Optical rotations were measured with a Schmidt-Haensch polarimeter and circular dichroism studied with a Jasco S-20 spectropolarimeter. Mass spectra (EIMS, 70 eV) were recorded on a VG-70-70E spectrometer. EPR spectra were recorded on a Varian E-9 spectrometer (X band, 100 KHz modulation) equipped with a variable temperature device. The g values were measured by using a DPPH sample and the magnetic field was calibrated with an NMR marker. All hyperfine coupling constants were checked by simulating the corresponding EPR spectra using a PC program developed in this Laboratory.[18]

Cristallography. Experimental data and structure refinement are summarized in TABLE 7. Single crystals were grown at room temperature from H_2O and EtOH for compound **5** and **7** respectively. Data collection were performed at room temperature on a Nonius CAD4 diffractometer with graphite monochromated Mo Kα radiation (λ = 0.71069 Å). Diffracted intensities were corrected for Lorentz-polarization but not for absorption. The structures were solved by direct methods (MULTAN-87)[19] and refined by full-matrix least squares with XTAL program.[20] All coordinates of H atoms were calculated for **5** and observed and refined for **7**. The polar origin of **5** have been constrained by fixing the *y* coordinate of O(4'). Crystallographic data have been previously[5] deposited with the Cambridge Crystallographic Data Center, University Chemical Laboratory, Lensfield Road, Cambridge CB21EW, England.

TABLE 7. Summary of Crystal Data, Intensity Measurement and Structure Refinement for Compounds **5** and **7**

	5	**7**
Formula	$C_{16}H_{21}N_3O_{10} \cdot H_2O$	$C_9H_{13}N_3O_6$
Mol. wt.	433.4	259.2
Crystal system	Monoclinic	Orthorhombic
Space Group	$P2_1$	$P2_12_12_1$
a (Å)	10.6418(12)	6.7051(9)
b (Å)	7.4341(7)	10.2824(13)
c (Å)	12.7910(14)	15.593(2)
β (°)	96.04(1)	-
V (Å^3)	1006.3(2)	1075.1(2)
Z	2	4
F(000)	456	544
Dc gr.cm^{-3}	1.43	1.60
μ(MoKα) mm^{-1}	0.114	0.127
$((\sin\theta)/\lambda)_{max}$ (Å^{-1})	0.55	0.55
Temperature (K)	298	298
No. measured reflc.	1614	1056
No. observed reflc.	1099	812
Criterion for observed	$\|Fo\| > 4\sigma(Fo)$	$\|Fo\| > 4\sigma(Fo)$
No. parameters	270	202
Weighting scheme	$1/\sigma^2(Fo)$	$1/\sigma^2(Fo)$
Max. and average Δ/σ	0.018, 0.004	0.089, 0.011 (for H)
Max. and min. Δρ (e.Å^{-3})	0.38, -0.46	0.24, -0.26
S	1.23	1.92
R, ωR (%)	6.8, 6.7	3.6, 2.8

(*E*+*Z*)-2'-Deoxy-5,6-dihydro-2'-*N*-hydroxyimino-3',5'-*O*-(1",1",3",3"-tetraisopropyldisiloxan-1",3"-diyl)-β-D-*erythro*-pentofuranosyluracil (2). A solution of **1** (5 g, 10 mmol) in CH_2Cl_2 (200 mL) was treated at 0 °C with an excess of Garegg's reagent (CrO_3, 9 g; pyridine, 15 mL; Ac_2O, 9 mL). After completion of the reaction (TLC), the reaction mixture was filtered on a column of silica gel WOELM impregnated with AcOEt and the solvent

evaporated. The crude ketone was dissolved in a mixture of MeOH (100 mL) and pyridine (8 mL) and hydroxylamine chlorhydrate (2.1 g, 30.4 mmol) was added. After 2 h, the solvents were distilled, the residue extracted with AcOEt (3x50 mL) and the organic phase washed (H_2O, 100 mL) concentrated and submitted to column chromatography (1:2 AcOEt/CH_2Cl_2) to give **2a** (0.71 g, 11.5%), **2b** (2.09 g, 34%) and **3** (0.63 g, 9.8%).

Properties of **2a** : mp 96.6-97.2 °C, R_F 0.35 (1:4 AcOEt/hexane); $[\alpha]_D^{25}$ -96.1° (*c* 1.0, $CHCl_3$); UV ($CHCl_3$) 259 nm (10600); IR (KBr) 3250 (OH), 3110 (NH), 1710 and 1690 cm^{-1} (C=O); MS (*m/z*, %) 112 (100, Ur + H), 69 (74), 120 (60), 146 (44), 135 (43), 105 (39), 175 (39), 289 (22), 163 (15), ...456 (11, $M^{\cdot+}$ -$CHMe_2$).

Anal. Calcd for $C_{21}H_{37}N_3O_7Si_2$ (499.72): C, 50.48; H, 7.46; N, 8.41. Found: C, 50.32; H, 7.52; N, 8.19.

Properties of **2b** : mp 101.1-101.8 °C; R_F 0.11 (1:4 AcOEt/CH_2Cl_2); $[\alpha]_D^{21}$ -67° (*c* 1.6, $CHCl_3$); UV ($CHCl_3$) 259 nm (10200); IR (KBr) 3300 (OH), 1720 and 1690 cm^{-1} (C=O); MS (*m/z*, %) 112 (100, Ur + H), 69 (90), 317 (66), 456 (48, $M^{\cdot+}$ - $CHMe_2$), 329 (46), 120 (33), 344 (31), 147 (26), 135 (23), 175 (22).

Anal. calcd for $C_{21}H_{37}N_3O_7Si_2$ (499.72): C, 50.48; H, 7.46; N, 8.41. Found: C, 50.33; H, 7.46; N, 8.32.

(6*S*)-6,2'-Anhydro-5,6-dihydro-6-hydroxy-2'-*N*-hydroxyamino-3',5'-*O*-(1",1",3",3"-tetraisopropyldisiloxan-1"-3"-diyl)uridine (3). Obtained as described for the preparation of **2**. Mp 108.5-109.6 °C; R_F 0.26 (1:10 MeOH/CH_2Cl_2); $[\alpha]_D^{23}$ +6° (*c* 1.0, $CHCl_3$); UV ($CHCl_3$) 240 nm (1300); IR (KBr) 3490 (OH), 3230 (NH), 1720 and 1690 cm^{-1} (C=O, C=N). MS (*m/z*, %) 70 (100), 119 (97), 235 (86), 135 (85), 55 (78), 105 (68), 147 (62), 120 (57), 123 (53), ...474 (4, $M^{\cdot+}$ - $CHMe_2$).

Anal. Calcd for $C_{21}H_{39}N_3O_8Si_2$ (517.73): C, 48.72; H, 7.59; N, 8.12. Found: C, 48.64; H, 7.68; N, 8.09.

(6*S*)-6,2'-Anhydro-5,6-dihydro-6-hydroxy-2'-*N*-hydroxyamino-2'-*O*-methyl-3',5'-*O*-(1",1",3",3"-tetraisopropyldisiloxan-1",3"-diyl)uridine (4). To a solution of **3** (0.91 g, 1.75 mmol) in MeOH (50 mL), HCl 3N in MeOH was added and the solution stirred at room temp for 15 h. The reaction mixture was brought to pH 6 (saturated aqueous $NaHCO_3$), concentrated and submitted to a column chromatography (1:6 MeOH/CH_2Cl_2) to give **4** (0.43 g, 94.4 %) as very hygroscopic crystals: mp 99.6-101 °C; R_F 0.35 (1:6

MeOH/CH_2Cl_2); $[\alpha]_D^{26}$ -48.3° (*c* 1.2, MeOH); UV (MeOH) 209 nm (5240); IR (KBr) 3380, 3240 (OH, NH), 1710, and 1690 cm^{-1} (C=O); MS (*m/z*, %) 112 (100, Ur + H), 69 (52), 107 (16), 128 (10), 145 (6), 150 (6), 146 (4), 151 (3), 239 (0.3, $M^{\cdot+}$ - MeOH - H_2O), 257 (0.2, $M^{\cdot+}$ - MeOH).

Anal. calcd for $C_{10}H_{15}N_3O_7$ (289.25): C, 41.53; H, 5.23; N, 14,53. Found: C, 41.49; H, 5.61; N, 14.04.

***(6S)*-3',5'-di-*O*-Acetyl-2'-*N*-acetoxyamino-6,2'-anhydro-5,6-dihydro-6-hydroxyuridine (5).** A solution of compound **4** (200 mg, 0.69 mmol) in a mixture of pyridine (5 mL) and acetic anhydride (2 mL) was stirred at room temp for 10 h, then treated as usual. The analytical sample of **5** (127 mg, 41%) was obtained by column chromatography (1:1 AcOEt/hexane) followed by recrystallization (EtOH/H_2O): mp 122.2-122.7 °C; $[\alpha]_D^{25}$ -11.1° (*c* 0.7, $CHCl_3$); UV ($CHCl_3$) 240 nm (400); IR (KBr) 3260 (NH), 1790, 1770, 1740 and 1710 cm^{-1} (C=O); MS (*m/z*, %) 373 (100, $M^{\cdot+}$ - AcOH), 331 (66), 112 (26), 113 (26), 299 (21), 198 (19), 356 (19), 341 (18), 230 (14).

Anal. calcd for $C_{16}H_{21}N_3O_{10}.H_2O$ (433.38); C, 44.34; H, 5.35; N, 9.70. Found; C, 43.99; H, 5.23; N, 9.58.

***(Z+E)*-2'-Deoxy-2'-*N*-hydroxyimino-β-D-*erythro*-pentofurano-syluracil (6).** To a solution of **2** (0.5 g, 1 mmol) in methanol (40 mL), 2N HCl in MeOH (2 mL) was added and the mixture stirred at room temp for 38 h. The pH was brought to 6 (saturated aqueous $NaHCO_3$) and the concentrated reaction mixture, submitted to a column chromatography (1:4 MeOH/CH_2Cl_2), gave a 3:7 mixture (193 mg, 75%) of the two geometrical isomers (**6a** and **6b**) of **6** as a hygroscopic solid : mp 130-130.3 °C; R_F 0.33 (**6a**) and 0.43 (**6b**) (1:4 MeOH/CH_2Cl_2); $[\alpha]_D^{22}$ -43° (*c* 0.8, MeOH); UV (MeOH) 206 (9000) and 259 nm (6950); IR (KBr) 3380, 3240 (OH, NH) 1710, 1690 and 1660 cm^{-1} (C=O, C=N); MS (*m/z*, %) 112 (100, Ur + H), 69 (66), 145 (21), 128 (7), 226 (7), 257 (3, $M^{\cdot+}$), 239 (2, $M^{\cdot+}$ - H2O), 258 (1, $M^{\cdot+}$ + H).

High resolution mass spectrum: calcd for $C_9H_{11}N_3O_6$ 257.0647. Found: 257.0672.

***(6S)*-2'-deoxy-5,6-dihydro-6,2'-*N*-hydroxyimino-β-D-arabino-furanosyluracil (7).** To a solution of **2** (1.02 g, 2.04 mmol) in MeOH (50 mL) 3N HCl in MeOH (2 mL) was added and the solution stirred at room temp for 24 h to give **6** which was not isolated but reduced to **8** with BH_3-pyridine (1 mL, 9.9 mmol) for 24 h at room temp. The reaction mixture was then

brought to pH 5 (saturated aqueous $NaHCO_3$), concentrated to dryness, the residue washed with CH_2Cl_2 (20 mL), tthen extracted with water (3x10 mL). The aqueous solution was concentrated to dryness, the residue dissolved in MeOH (30 mL) and reacted 15 h at room temp with veratraldehyde (0.5 g, 3.01 mmol). The reaction mixture concentrated gave, after column chromatography (1:10 MeOH/CH_2Cl_2) a 3:7 *arabino/ribo* mixture of **10** (154 mg, 18.5 %) and **7** (0.4 g, 75%): mp 196.5-198.2 °C; R_F 0.3 (1:4 MeOH/CH_2Cl_2); $[\alpha]_D^{25}$ +130° (*c* 1.0, MeOH); UV (MeOH) 204 nm (6400); IR (KBr) 3390, 3290, 3240 (OH, NH), 1720, and 1680 cm^{-1} (C=O); MS (*m/z*, %) 113 (100), 152 (73), 70 (65), 84 (60), 130 (51), 169 (51), 81 (46), 56 (37), 97 (20) ...259 (3, $M^{\cdot+}$).

Anal. calcd for $C_9H_{13}N_3O_6$ (259.22): C, 41.70; H, 5.06; N, 16.21. Found: C, 41.67; H, 5.08; N, 16.18.

***(6S)*-3',5'-di-*O*-Acetyl-6,2'-*N*-acetoxyimino-2'-deoxy-5,6-dihydro-β-D-arabinofuranoslyuracil (9).** A solution of **7** (0.16 g, 0.6 mmol) in a mixture of pyridine (10 mL) and acetic anhydride (5 mL) was stirred at room temp for 1 h, concentrated, then the solvents codistilled with toluene. Water (20 mL) was added to the residue and the mixture extracted with CH_2Cl_2 (3x10 mL). The organic phases were dried (Na_2SO_4), concentrated and submitted to a column chromatography (1:1 AcOEt/CH_2Cl_2) which yielded **9** (152 mg, 64%); mp 73.0-73.9 °C; R_F 0.25 (1:1 AcOEt/CH_2Cl_2); $[\alpha]_D^{29}$ -43° (*c* 0.6, $CHCl_3$); UV (EtOH) 256 nm (1040); IR (KBr) 3240 (NH), 1760, 1730 and 1690 cm^{-1} (C=O); MS (*m/z*, %) 81 (100), 113 (50, Ur + 2 H), 112 (43, Ur + H), 60 (38), 70 (34), 109 (28), 152 (21), 97 (20), 121 (13), ...325 (1, $M^{\cdot+}$ - AcOH).

Anal. calcd for $C_{15}H_{19}N_3O_9$ (385.33): C, 46.76; H, 4.97; N, 10.90. Found C, 46.71; H, 5.05; N, 10.81.

2'-Deoxy-2'-(3",4"-dimethoxybenzylidenimino)-β-D-*arabino*(and *ribo*)furanosyluracil *N'*-oxyde (10). Obtained as described for the preparation of **7**: mp > 220 °C; R_F 0.2 (1:10 MeOH/CH_2Cl_2); UV (EtOH) 205 (19800), 231 (12200), 264 (12500), and 320 nm (13000); IR (KBr) 3400, 3230 (OH, NH), 1690 (C=O) and 1590 cm^{-1} (C=N); MS (*m/z*, %) 112 (100, Ur + H), 69 (64), 165 (50), 77 (18), 261 (17), 231 (16), 151 (16), 259 (13), 247 (10), ...295 (4, $M^{\cdot+}$ - UrH).

Anal. calcd for $C_{18}H_{21}N_3O_8.H_2O$ (425.40): C, 50.82; H, 5.45; N, 9.88. Found: C, 50.59; H, 5.43; N, 9.47.

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