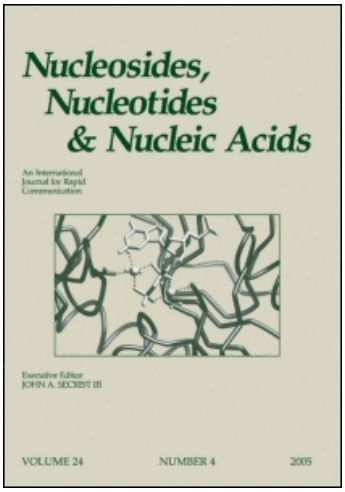

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STRUCTURAL STUDIES OF 5-ETHYL-2'-DEOXYURIDINE BY SELECTIVE PULSE ^{1}H DPFGSE NOE SPECTROSCOPY AND PM3 CALCULATIONS.

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Abstract: The solution conformation of 5-ethyl-2'-deoxyuridine (EDU) has been calculated from the vicinyl proton-proton NMR coupling constants and nuclear Overhauser (NOE) distances using excitation sculpting of selective pulses (Double Pulsed Field Gradient Spin Echo NOE) at 500 MHz and molecular modelling (PM3) studies.

A structural study is reported on 5-ethyl-2'-deoxyuridine (EDU), a thymidine (dT) analogue with antiviral activity. The conformations in phosphate buffer saline solution (PBS) at pH 7.4 were inferred from the vicinyl proton-proton NMR coupling constants and nuclear Overhauser (NOE) distances using excitation sculpting of selective pulses (Double Pulsed Field Gradient Spin Echo NOE)[1] at 500 MHz and molecular modelling (PM3) studies. A pseudorotational equation of the form $\nu_j=a_j\nu_{max}\cos(P + 0.8\ \pi\ (j - 2)$ was used to calculate the pseudorotational parameters of the deoxyribose ring[2]. Analysis of the J-coupling constants measured from simulated spectra revealed that: (i) the C4'-C5' bond is primarily in the g+ conformation, to an extent of 55% for g+, 29% for t and 16% for g- at 310 K and (ii) the deoxyribose ring has a preference for a South-type (C2'-*endo*/C3'-*exo*) puckered conformation (approximately 64% at 310 K). The pseudorotational parameters of the South conformer are as follows: P=177 and ν_{max}=35.

TABLE 1. Solution and crystal structure conformations of EDU and dT.

	COMPOUND					
	Solution conformation				Crystal conformation	
PARAMETER	dT[4]		EDU		dT[5]	EDU[6]
	N	S	N	S		
Exocyclic torsions:						
χ (O4'-C1'-N1-C2)	263.1° (*anti*)		111.2° (*anti*)		220° (*anti*)	70.9° (*high anti*)
% *anti*	77.8		73.5			
γ (O5'-C5'-C4'-C3')	59.7	60.8	59.7	60.8	172.9° (*g-*)	-46.8° (*g+*)
% g+ /g- / t	52.2; 18.1; 29.7		55.0; 16.3; 28.7			
Endocyclic torsions:						
ν_0 C4'-O4'-C1'-C2	-0.73	-8.01	-7.19	-12.54	-7.0°	-1.8°
ν_1 O4'-C1'-C2'-C3'	-27.34	30.72	-28.60	29.35	27.8°	-5.9°
ν_2 C1'-C2'-C3'-C4'	39.71	-41.69	53.47	-34.95	-36.9°	9.9°
ν_3 C2'-C3'-C4'-O4'	-40.17	36.73	-57.92	27.20	33.1°	-10.8°
ν_4 C3'-C4'-O4'-C1'	25.28	-17.75	40.24	-9.06	-16.6°	8.8°
P[(a)]	19	185	25	177	187.5	27.2
ν_{max}[(b)]	42	42	59	35	37.2	11.2
X[(c)]	0.37	0.63	0.36	0.64		
Sugar pucker	$^3T_4$	$^2T_3$	$^3T_4$	$^2T_3$	$_3T^2$ S	$^3T_4$ N
	C3'-*endo*/C2'-*endo*		C3'-*endo*/C2'-*endo*		C3'-*exo*	C3'-*endo*

(a) tan P = $[(\nu_4 + \nu_1)-(\nu_3 + \nu_0)] / [2\nu_2(\text{sen } 36° + \text{sen } 72°)]$ (b) $\nu_{max} = \nu_2 / \cos P$ (c) Molar fraction.

The results reveal that another conformer with a North-type puckered conformation for the deoxyribose ring is also present in solution. (P=25, ν_{max}=59). The characterization of the minor conformer must be regarded as an essential complement to the results of X-ray crystallographic analysis. One dimensional DPFGSE NOE measurements indicated a predominant *anti* conformation (73.5%)[3].

It is concluded that the preferred conformation of 5-ethyl 2'-deoxyuridine in solution is in close agreement with the X-ray crystal structure.

REFERENCES

1. Stott, K.; Stonehouse, J.; Keeler, J.; Hwang, T.; Shaka, A. (1995) *J. Am. Chem. Soc.* **117**, 4199-4200.
2. Haasnoot, C. A. G.; de Leeuw, F. A. A. M.; Altona, C. (1980) *Tetrahedron* **36**, 2783-2792.
3. Rosemeyer, H.; Tóth, G.; Golankiewicz, B.; Kazimierczuk, Z.; Bourgeois, W.; Kretschmer, U.; Muth, H.; Seela, F. (1990) *J. Org. Chem.* **55**, 5784-5790.
4. Koole, L. H.; Plavec, J.; Liu, H.; Vincent, B. R.; Dyson, M. R.; Coe, P. L.; Walker, R. T.; Hardy, G. W.; Rahim, S. G.; Chattopadhyaya, J. (1992) *J. Am. Chem. Soc.* **114**, 9936-9943.
5. Young, D. W.; Tollin, P.; Wilson, H. R. (1969) *Acta Cryst.* **B25**, 1423-1432.
6. Czugler, M.; Kálmán, A. (1994) *Zeits. für Krist.* **209**, 907