

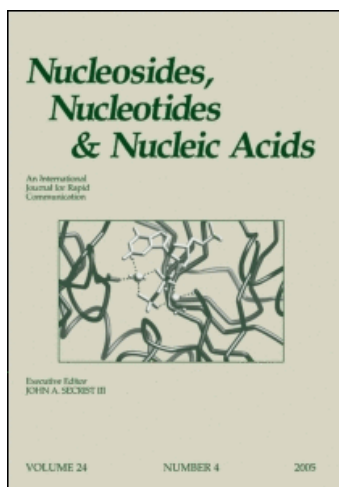
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Structural Studies of 5-Ethyl-2'-Deoxyuridine by Selective Pulse ¹H DPGSE NOE Spectroscopy and PM3 Calculations

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**STRUCTURAL STUDIES OF 5-ETHYL-2'-DEOXYURIDINE BY
SELECTIVE PULSE ¹H DPGSE 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 $v_j = a_j v_{\max} \cos(P + 0.8 \pi (j - 2))$ was used to calculate the pseudorotational parameters of the deoxyribose ring². 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 v_{\max} =35.

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

PARAMETER	COMPOUND					
	Solution conformation				Crystal conformation	
	dT ⁴		EDU		dT ⁵	EDU ⁶
	N	S	N	S		
Exocyclic torsions:						
χ (O4'-C1'-N1-C2)	263.1° (<i>anti</i>)		111.2° (<i>anti</i>)		220° (<i>anti</i>)	70.9° (<i>high anti</i>)
% <i>anti</i>	77.8		73.5			
γ (O5'-C5'-C4'-C3')	59.7	60.8	59.7	60.8	172.9° (<i>g-</i>)	-46.8° (<i>g+</i>)
% <i>g+</i> / <i>g-</i> / <i>t</i>	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
$\nu_{\max}^{(b)}$	42	42	59	35	37.2	11.2
X ^(c)	0.37	0.63	0.36	0.64		
Sugar pucker	³ T ₄	² T ₃	³ T ₄	² T ₃	³ T ₂ S	³ T ₄ N
	C3'-endo/C2'-endo		C3'-endo/C2'-endo		C3'-exo	C3'-endo

(a) $\tan P = [(v_4 + v_1) - (v_3 + v_0)] / [2v_2(\sin 36^\circ + \sin 72^\circ)]$ (b) $\nu_{\max} = v_2 / \cos P$ (c) Molar fraction.

The results reveal that another conformer with a North-type puckered conformation for the deoxyribose ring is also present in solution. ($P=25$, $\nu_{\max}=59$). The characterization of the minor conformer must be regarded as an essential complement to the results of X-ray crystallographic analysis. One dimensional DPGSE 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