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RELATIVE SPIN-LATTICE RELAXATION TIMES OF H-8 AND H-1' IN PURINE RIBONUCLEOSIDES AND RIBONUCLEOTIDES AS A MEASURE OF SYN OR ANTI CONFORMATION

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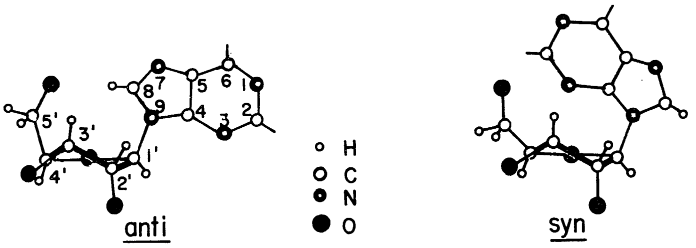
Proton relaxation measurements with the pulse Fourier transform method have revealed that the spin-lattice relaxation times(T_1) of H-8 and H-1' in purine ribonucleosides and ribonucleotides depend strongly on the syn-anti conformation. The ratio of T_1's for the two protons is shown to be a convenient measure of the syn-anti conformational equilibrium.

Elucidation of molecular structure and conformation from nuclear relaxation rate measurements has become promising with the recent development of pulse Fourier transform(FT) NMR technique. In a course of work on proton relaxation studies of nucleic acid components with the FT method, we have found that the ratio of the spin-lattice relaxation time(T_1) of H-8 and that of H-1' is strongly dependent on the syn-anti conformational equilibrium of purine ribonucleosides and ribonucleotides.



In Table I, we have summarized T_1 values for H-8 and H-1' and their ratios for various purine ribonucleosides and ribonucleotides and their derivatives. For example, for 2',3'-isopropylidene-3,5'-cycloguanosine for which the conformation is nearly strictly syn because of the covalent bond between N-3 and C-5', we have $(T_1)_8/(T_1)_{1'} = 1.47$, whereas for adenosine and 5'-adenosine monophosphate in D_2O for which near-anti conformations are accepted from shift measurements[1,2], the ratios are 0.76 and 0.70, respectively. Moreover, for some nucleosides such as adenosine, 2',3'-isopropylideneadenosine, and 2',3'-isopropylideneguanosine in DMSO-d_6 for which allowance of having both syn-like and anti-like conformations has been proposed[3,4], the ratio takes intermediate values which are close to unity.

In general, we should have the ratio more than unity in a syn conformation, while less than unity for anti, because of the following reason: For a syn conformation, T_1 of H-8 would be determined almost entirely by the dipolar interaction with H-1', while T_1 of H-1' would not only be determined by H-8 but also by H-2' and possibly by H-3'. As a result, $(T_1)_{1'}$ would become shorter than $(T_1)_8$, rendering $(T_1)_8/(T_1)_{1'} > 1$. On the other hand, in an anti conformation, where H-8

Table I. Spin-lattice relaxation times(T_1) of H-8 and H-1' and their ratio for various purine ribonucleosides and ribonucleotides.*

compounds	$(T_1)_8$ (sec)	$(T_1)_{1'}$ (sec)	$(T_1)_8/(T_1)_{1'}$
2',3'-isopropylidene-3,5'-cycloguanosine 0.1 M, 35°C in DMSO-d_6	1.25	0.85	1.47
2',3'-isopropylideneguanosine 0.5 M, 60°C in DMSO-d_6	1.39	1.58	0.88
2',3'-isopropylideneadenosine 1.0 M, 30°C in DMSO-d_6	0.54	0.53	1.02
adenosine 0.1 M, 35°C in DMSO-d_6	1.07	1.07	1.00
adenosine 0.1 M, 50°C in D_2O	3.23	4.23	0.76
5'-adenosine monophosphate-Na_2 0.1 M, 30°C in D_2O	1.66	2.36	0.70
poly-adenylic acid 0.045 M, 81°C in D_2O	0.71	1.14	0.63
anti conformation	(estimated from a Dreiding model)		0.53**
syn conformation			1.52**

* Measured with the pulse Fourier transform mode by applying 180°-τ-90° pulse sequences on a JEOL PS-100 equipped with a PFT-100 and a JEC-6.

** Contributions other than those from H-8, H-1', H-2', H-3', and H-4' are neglected. Inclusion of the contribution from H-5' will only increase the deviation of the ratio from unity.

would interact with all the ribose protons more or less strongly except for H-1', $(T_1)_8$ could easily become shorter than $(T_1)_{1'}$, making the ratio less than unity.

These situations can quantitatively be shown by calculating the ratio of the expected relaxation rates for H-8 and H-1' as determined by mutual dipolar interaction as well as the interaction with other ribose protons. This is reduced to calculating $\sum_{i \neq 8} r(8,i)^{-6} / \sum_{i \neq 1'} r(1',i)^{-6}$, where r(8,i) and r(1',i) represent distances to H-i from H-8 and H-1', respectively. The result of the calculation is given in Table I as the average for the 3'-_endo_ and 2'-_endo_ conformation of the ribose moiety. The results show indeed that the ratio $(T_1)_8/(T_1)_{1'}$ is sensitive to the conformation and may be used as a criterion for the _syn_ or _anti_ conformation. This criterion may particularly be useful in a system for which a method like Nuclear Overhauser Effect is difficult to apply. Poly-riboadenylic acid(poly-A) is one of such candidates. For poly-A in a single stranded region(pH 6.0, 81°C), we have found that the ratio becomes 0.63, which suggests strongly that the conformation of a nucleotide in the single-stranded poly-A is _anti_. This criterion may also be used in cases where purine ribonucleosides or ribonucleotides change their conformations when they associate with other molecules.

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