Conformation of the^{7}Gadolinium Complexes of Adenosine 3′,5′ Cyclic Monophosphoric Acid and Inosine 3′,5′ Cyclic Monophosphoric Acid

By G. VICTOR FAZAKERLEY,* JILL C. RUSSELL, and MELANIE A. WOLFE

(Department of Inorganic Chemistry, University of Cape Town, Rondebosch 7700, South Africa)

Summary The title compounds do not exist in a rigid conformation but in a rapid *syn–anti*-equilibrium.

Two recent studies[1,2] on cAMP (adenosine 3′,5′ cyclic monophosphoric acid) with lanthanide shift reagents have arrived at contrary conclusions on the sugar to base conformation of the complex. In one case a predominantly *syn* conformation (though also observing some conflicting evidence from relaxation measurements) was deduced,[1] while in the other an *anti* conformation.[2] Both forms have been found in the crystalline state of the nucleotide.[3]

The Gd–ethylenediaminetetra-acetic acid complex (1 : 1) binds to both oxygen donors of the phosphate at pH 5·5[1,2]† and induces broadening of the resonances without observable shifts. The concentration dependence of T_2 is related to the metal ion–observed nucleus internuclear distance r, by equation (1) where f is the mole ratio of total Gd$^{\text{III}}$ to total

$$(fT_{2\text{P}})^{-1} = Kr^{-6} \qquad (1)$$

nucleotide and K a constant during the experiment.[4]

Nucleotides are known to exist in either *syn* or *anti* conformations or very rapid equilibrium between these two. No-one has yet succeeded in slowing down this equilibrium. The bottoms of the potential energy wells correspond to torsional angles (ϕ) of *ca.* +110° (*anti*) and −50° (*syn*) [1,5]. Very little time is spent in any intermediate conformation so that equation (1) becomes equation (2). A similar

$$1/fT_{2\text{P}}(\text{H-2}) = K[\tau_a/r^6(\text{H-2}\mathit{anti}) + (1-\tau_a/r^6(\text{H-2}\mathit{syn}) \qquad (2)$$

relationship holds for H-8. τ_a is the fraction of time spent in the *anti* conformation. The values of r were obtained from the crystal data[3] but to allow for movement in the potential energy well r^6 was averaged over +110° (±10°) and −50° (±10°).

TABLE

	cAMP[a]		cIMP[a]	
	H-2	H-8	H-2	H-8
$(fT_{2\text{P}})^{-1}$/Hz[b]	1427	1506	167	609

[a] Nucleotides 0·04 M in ^{2}H$_2$O at pH 5·5. [b] f was in the range 10^{-4}—10^{-2}.

cAMP. The observed data are given in the Table. Solving equation (2) gives τ_a = 0·60 (±0·05). The error arises almost wholly from the uncertainty in ϕ and thus in r^6, as T_2 (H-2)/T_2 (H-8) is very sensitive to τ_a for defined ϕ values ranging from *ca.* 60 (τ_a 1·0) to *ca.* 0·015 (τ_a 0·0). Clearly the lanthanide complex does not exist in any single conformation.

cIMP. Similar experiments were carried out but the solution was also 0·04M in praseodymium–ethylenediaminetetra-acetic acid complex which shifted H-8 downfield from H-2 as the resonances were otherwise coincident. The data in the Table give τ_a 0·90 (±0·05), in good agreement with coupling constant studies.[6]

For both cAMP and cIMP the results were the same within experimental error at 0·015 M nucleotide indicating that base stacking is not a major source of error.

We thank the University of Cape Town and the Council for Scientific and Industrial Research for financial support.

(*Received, 5th February* 1975; *Com.* 130.)

---

† This position is supported by our preliminary data on the broadening of the ribose protons.

[1] C. D. Barry, D. R. Martin, R. J. P. Williams, and A. V. Xavier, *J. Mol. Biol.*, 1974, 84, 491.

[2] D. K. Lavallee and A. H. Zeltmann, *J. Amer. Chem. Soc.*, 1974, **96**, 5552.

[3] K. Watenpaugh, J. Dow, L. H. Jensen, and S. Furberg, *Science*, 1968, **159**, 206.

[4] R. G. Shulman, H. Sternlicht, and B. J. Wyluda, *J. Chem. Phys.*, 1965, **43**, 3116.

[5] N. Yathindra and M. Sundaralingam, *Biochem. Biophys. Res. Comm.*, 1974, **56**, 119.

[6] M. P. Schweizer and R. K. Robins, in 'Conformation of Biological Molecules and Polymers.' Proceedings of the Vth Jerusalem Symposia, p. 329, 1973.