

tor-bound ligand molecules the combined use of the two aforementioned 2D NMR experiments appears preferable on various practical grounds.

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Selective Recognition and Coordination by the $[\text{Rh}^{\text{III}}(\text{tris}(\text{aminoethyl})\text{amine})(\text{H}_2\text{O})_2]^{3+}$ Cation of the Adenine Nucleobase Only When It Is a Constituent of a 5'-Nucleotide

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We report the unusual observation of highly selective coordination of a nucleobase when it is a constituent in a 5'-nucleotide but not when it is in a nucleoside or in a 3'- or 2'-nucleotide. Such an example of molecular recognition is unprecedented. Several recent elegant syntheses of organic compounds have made possible the discovery of selective interactions with nucleobase derivatives in organic solvents.¹⁻⁷ In the present case, we demonstrate the use of an octahedral metal center in aqueous solution to arrange groups for the recognition of both base and phosphate groups. The tripodal tren (tris(aminoethyl)amine) ligand was selected because it can adopt only one geometry in octahedral complexes. The size and charge of the central metal can be varied; the resulting versatility should allow fine tuning of interactions of octahedral complexes with the molecular target not readily achieved with typical organic compounds containing a limited number of atom types.

An aqueous solution of $[\text{Rh}^{\text{III}}(\text{tren})(\text{H}_2\text{O})_2]^{3+}$ (0.056 M) and adenosine (Ado) in a 1:1 ratio was brought to 60 °C. After 48 h, essentially no evidence of reaction was observed by ¹H NMR (Figure 1). On the other hand, both guanosine (Guo) and inosine (Ino) react with $[\text{Rh}(\text{tren})(\text{H}_2\text{O})_2]^{3+}$ ($t_{1/2} < 2$ h) under the same conditions to form complexes with the H8 signal shifted strongly downfield. For example, the H8 signal of Guo shifts from 8.05 ppm to 8.49 ppm; for Ino, from 8.36 ppm to 8.75 ppm. Such ~0.5 ppm downfield shifts are characteristic of N7 coordination.

These differences in reactivity for the nucleosides can be understood by the nature of the tren-nucleobase interactions, which are unfavorable and repulsive between tren and the exocyclic 6-NH₂ group of Ado but favorable for H-bonding interactions between tren and the 6-oxo group of Guo and Ino.⁸

In contrast to Ado, 5'-AMP does react with $[\text{Rh}(\text{tren})(\text{H}_2\text{O})_2]^{3+}$ ($t_{1/2} \sim 2$ h at 60 °C) to form a complex (I-5'-AMP) with the following spectral characteristics: H8 signal at 9.10 ppm, H2 at 8.26 ppm, and H1' (doublet) at 6.26 ppm (Figure 1). Compared to free 5'-AMP (H8 at 8.52 ppm, H2 at 8.15 ppm, and H1' (doublet) at 6.09 ppm), the large downfield shift of the H8 signal

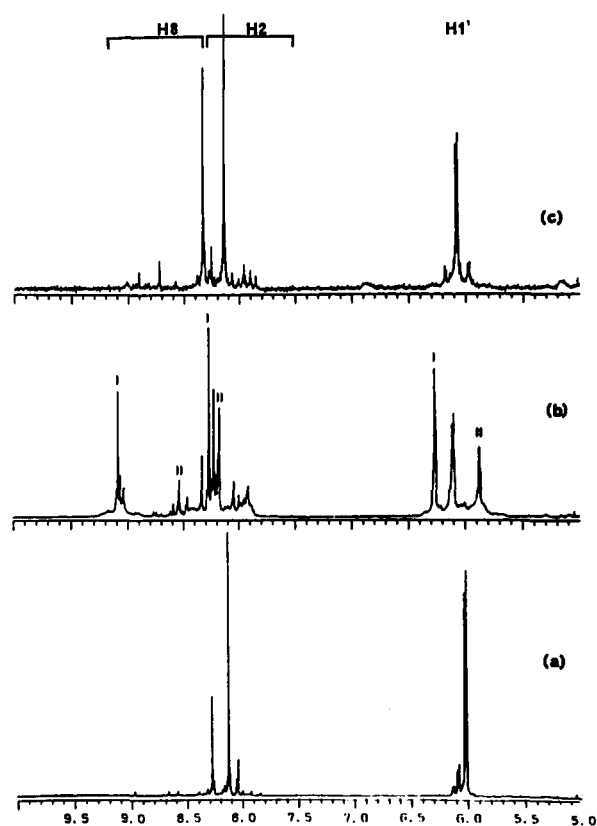


Figure 1. H8, H2, H1' region of the 360-MHz spectra of 1:1 mixtures of $[\text{Rh}(\text{tren})(\text{H}_2\text{O})_2]^{3+}$ with (a) Ado, $t = 48$ h, 60 °C; (b) 5'-AMP, $t = 2$ h, 60 °C (signals for I-5'-AMP and II-5'-AMP are labeled I and II, respectively); and (c) 3'-AMP, $t = 48$ h, 60 °C (Nicolet 360-MHz spectrometer, 99.98% D₂O, sodium 3-(trimethylsilyl)propionate-*d*₄ internal reference, pD = 6.9, 23 °C).

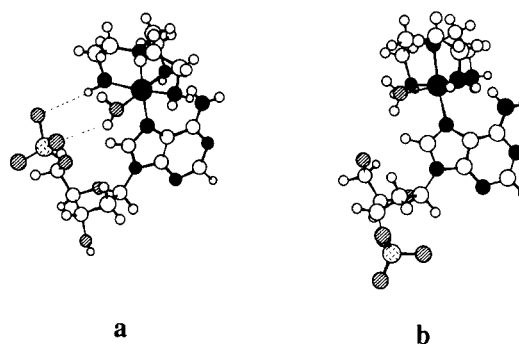


Figure 2. (a) Graphic depictions based on crystallographic data⁹⁻²¹ indicating potential favorable interligand H bonding of the phosphate group in $[\text{Rh}(\text{tren})(\text{H}_2\text{O})(5'-\text{AMP}-\text{N}7)]^+$. (b) The absence of such interactions in a hypothetical $[\text{Rh}(\text{tren})(\text{H}_2\text{O})(3'-\text{AMP}-\text{N}7)]^+$.

and smaller shifts of H2 and H1' are characteristic of N7 binding.⁹⁻¹³ Further evidence for N7 coordination was obtained from experiments using a paramagnetic probe. Addition of Cu²⁺ to a solution containing free 5'-AMP and I-5'-AMP resulted in line broadening of the H8 and H2 signals of the free ligand, while the H8 signal of I-5'-AMP was not affected.^{9,10} The ³¹P signal corresponding to complex I-5'-AMP appears at 1.1 ppm, only 1.4 ppm downfield from the free ligand. A similar behavior was observed with 5'-dAMP.

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These spectral features and behavior are entirely consistent with a monodentate, N7-coordinated 5'-AMP with the 5'-PO₄ group limited to an outer-sphere role.¹¹ Direct phosphate coordination, as observed for Rh(III)-inorganic phosphate or Rh(III)-methyl phosphate, causes downfield shifts of 8-10 ppm in ³¹P spectra.^{14,15} However, this outer-sphere interaction appears to be crucial, since it facilitates coordination of N7. Inspection of plastic or graphic models of [Rh(tren)(H₂O)(5'-AMP-N7)]⁺ (I-5'-AMP) reveals that the 5'-PO₄ is ideally positioned for H bonding with the tren and H₂O ligands (Figure 2).

Further evidence for the outer-sphere role of the 5'-PO₄ group in the formation of I-5'-AMP is found in the absence of N7 coordination in the Rh(tren) complexes formed with both 3'- and 2'-AMP. For complexes of these nucleotides, the ¹H signal did not shift significantly; the principal spectral change was a 7-10 ppm downfield shift of the ³¹P NMR signal, indicative of phosphate group coordination. The position of the phosphate groups of these nucleotides is not correct for an outer-sphere role in promoting N7 coordination as illustrated for the hypothetical N7-bound 3'-AMP in Figure 2.

As expected from the Guo results, 5'-GMP initially forms an analogous N7-bound complex, I-5'-GMP (*t*_{1/2} ~ 1 h). However, after 24 h, this species converted into a second complex II-5'-GMP (*t*_{1/2} ~ 5 h). The chemical shift of the H8 signal of this species at 8.41 ppm can be compared with values of 8.89 ppm for I-5'-GMP and 8.14 ppm for 5'-GMP, respectively. The H1' signal is a doublet at 5.93 ppm for I-5'-GMP and at 5.88 ppm for 5'-GMP, but a singlet at 6.02 ppm for II-5'-GMP. Furthermore, the H2' signal has shifted downfield to 5.2 ppm from 4.8 ppm in the free nucleotide. This pattern of shifts is characteristic of an N⁷,5'-PO₄ chelate.⁹⁻¹² Distortion of the sugar ring into an N pucker (*J*_{H1'-H2'} ~ 0) accounts for the singlet, and the placement of H2' in the guanine base deshielding region accounts for the downfield shift.¹² The same behavior was observed for 5'-IMP and 5'-dGMP. The ³¹P signals for these complexes have shifted downfield by 5-7 ppm, a shift also consistent with chelation. We conclude that I-5'-GMP and II-5'-GMP are [Rh(tren)(H₂O)-(5'-GMP-N7)]⁺ and [Rh(tren)(H₂O)(5'-GMP-N⁷,5'-PO₄)]⁺, respectively.

I-5'-AMP and I-5'-dAMP also convert to second species, II-5'-AMP and II-5'-dAMP (*t*_{1/2} ~ 24 h and 20 h, respectively), with some spectral characteristics of an N⁷,5'-PO₄ chelate (H8 at 8.55 ppm, *J*_{H1'-H2'} = 4.4 Hz, and H1' at 5.88 ppm for 5'-AMP; H8 at 8.43 ppm, *J*_{H1'-H2'} = 5.6 Hz, and H1' at 6.23 ppm for 5'-dAMP; 5-6 ppm downfield shift of the ³¹P signal). In the only reported 5'-dAMP N⁷,5'-PO₄ chelate, [Cp₂Mo(5'-dAMP-N⁷,5'-PO₄)], *J*_{H1'-H2'} is 4.6 Hz.¹³ The reason for this difference between 5'-AMP and 5'-GMP chelates, including the absence of a large downfield shift of the H2' signal for 5'-AMP, is not clear.

One problem encountered when Ado and 5'-AMP reactions are followed by ¹H NMR is the relatively fast rate of H8 exchange in D₂O. After 24 h at 60 °C, ~70% of the original H8 signal has been lost. To follow changes in the H8 peak, the reactions were also carried out in H₂O.¹⁶ The fast formation (*t*_{1/2} < 2 h) of I-5'-AMP, followed by slow conversion to a second complex, was confirmed.

The role that the phosphate group plays in directing the attack of a metal center on a nucleobase has been the subject of speculation.^{7,17} Our results demonstrate that a 5'-phosphate can direct nucleobase coordination. Qualitative molecular modelling with unperturbed B-DNA suggests that H-bond donor ligands equatorial to the axial attack direction could form H bonds to phosphate

oxygens. The role such interactions may play in the attack of Pt(II) anticancer drugs on DNA^{17,18} merits investigation. Unlike our Rh(III) results, the Pt(II) drugs readily form adducts with both Ado and 5'-AMP,¹¹ and therefore the outer-sphere role of the phosphate group is difficult to detect experimentally. The clear demonstration of the formation of an N⁷,5'-PO₄ chelate with a fourth metal center, Rh(III), in addition to recently discovered examples with Pt(II),^{10,11} Ru(II),¹² and Mo(IV),¹³ in the short time since the initial recognition of the characteristics of such species in 1986¹⁰ argues that such chelates may indeed be ubiquitous, although elusive, species in metal nucleotide chemistry.

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The Structure and Remarkable Stability of a Perypyridinium-Substituted Allyl Radical

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Allyl radical, the simplest example of a conjugated hydrocarbon possessing an unpaired electron, has been the subject of many theoretical and experimental studies. Recent multiconfiguration self-consistent field (MCSCF) calculations have shown that allyl radical has C_{2v} symmetry,¹ in agreement with the experimental data from electron diffraction² and electron spin resonance.³ Several examples of stable allyl radicals include 1,1,3,3-tetra-phenylallyl,⁴ the polycrystalline 1,3-bis(diphenylene)-2-(*p*-chlorophenyl)allyl⁵ and trifluoromethyl-substituted allyl radicals.⁶ To our knowledge no crystal structure has been reported for an allylic radical. Here we report the preparation, properties, and

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