are valid in spite of the limitations inherent in the Breit–Pauli approximation. At any rate, no alternative way to do the calculation is presently feasible in our estimate. For example, it would be meaningless to calculate the atomic relativistic energy using a relativistic Hartree–Fock procedure since the formalism for doing a similar molecular calculation has not yet been developed and the two calculations must be performed in exactly the same manner. A more detailed analysis of these results and general validity of the various approximations and alternate methods of obtaining relativistic corrections is in preparation.

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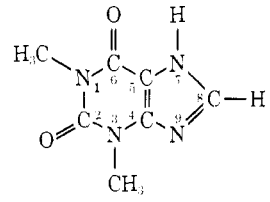
Intramolecular Hydrogen Bonding in Metal–Purine Systems. Synthesis and Structure of a Cobalt(III)–Theophylline Complex

Sir:

The role of metal ions in nucleic acid chemistry is both widespread and under considerable investigation. Several areas of metal nucleic acid chemistry under study include: (1) alteration of coding specificity in protein synthesis;[1] (2) stabilization of the manifold structure of nucleic acids;[2] (3) preparation of "heavy molecule" derivatives of yeast phenylalanine transfer RNA as aids in phasing the structure by X-ray methods;[3] (4) the use of heavy-metal-containing moieties in attempts to sequence nucleic acid biopolymers by electron microscope techniques.[4] Our interest stems primarily from this last consideration. We have been attempting to find and study inert metal complexes which will specifically react with one of the four purine or pyrimidine residues in the biopolymer—selectivity of reaction being a prerequisite for the sequencing method.

Our approach to the induction of selectivity is to utilize the different hydrogen bonding potentials of the nucleotides in the formation of hydrogen bonds to ligands of the reacting complex. The assignment of the metal binding site in biopolymers is best preceded by studies on model systems. Generally, the bases, the nucleosides, and the nucleotides have disadvantages as models. The bases may bind *via* N-9, a site blocked in the nucleic acid, and the nucleosides are generally weak ligands. On the other hand, the nucleotides often bind using the phosphate group, and this minimizes the possibility of selectivity toward nucleotides of different bases. However, we believe that the substituted purine, theophylline (1,3-dimethyl-2,6-oxopurine (I)), serves as



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a good model for the guanine class of nucleosides, *i.e.*, those nucleosides with a carbonyl group at position 6 of the pyrimidine ring, and possibly for the nucleotides (nucleic acid). The coordination in the complex reported here is through N-7, a site which is accessible and presumedly favorable in the biopolymer. Specific interligand hydrogen bonds (*e.g.*, with the ligand ethylenediamine) are present in the complex. These specific interactions may be sufficient to induce selective reaction of such complexes with the guanine residues in the nucleic acid biopolymer.

The complex was prepared in a similar fashion to the previously reported adenine complex[5] and formally contains in the coordination sphere of the cobalt(III) the monoanion of theophylline ($C_7N_4O_2H_7^-$), a chloride anion, and two ethylenediamine groups ($[Co(en)_2Cl(C_7N_4O_2H_7)]^+Cl^-$). The complex crystallizes in the triclinic system, space group $P\bar{1}$, with Friedel-reduced cell constants: $a = 10.034$ (3), $b = 10.711$ (4), and $c = 9.499$ (4) Å; $\alpha = 109.49$ (3), $\beta = 93.17$ (3), and $\gamma = 75.87$ (2)°; $V = 932.8$ (5) Å^3; and $Z = 2$. Besides the complex cation and chloride anion, there are two independent water molecules in the asymmetric unit. Intensity data were collected with Mo Kα radiation ($\lambda = 0.71069$ Å) on a Syntex $P\bar{1}$ computer-controlled diffractometer. A highly orientated graphite crystal monochromatized the incident beam of the spectrometer. A total of 4315 independent intensities (4202 above zero) were collected on a crystal which was a cut cube 0.25 mm on an edge. The θ–2θ scan method was employed (maximum 2θ of 55°) in the data collection. Atomic positions for the cobalt and its primary coordination sphere were obtained from a Patterson map. A Fourier synthesis then revealed the rest of the atoms in the structure including the two water molecules. It was noted early in the analysis that one of the ethylenediamine groups was disordered; this group has been treated isotropically in the least-squares refinement, and the 16 one-half hydrogen atoms have been positioned by geometrical considerations. The ordered hydrogen atoms were located on a ΔF map. Full-matrix least-squares refinement, with all nonhydrogen atoms anisotropic and hydrogens isotropic, with the exceptions noted above, has led to a final R value of 0.043 (4202 intensities above zero) and a final weighted R value of 0.052.

The cobalt is octahedrally coordinated with the six coordination sites occupied by the four nitrogens of the two ethylenediamine groups, a chlorine atom, and N-7 of the theophylline moiety. The chlorine ligand and N-7 have assumed trans positions in the coordination sphere (Figure 1). In the previously determined

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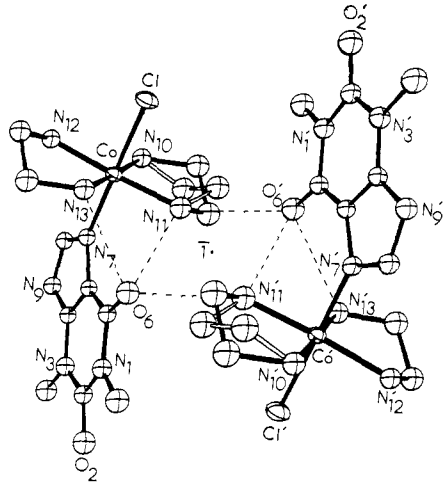

Figure 1. A perspective view of the molecular conformation of the complex *trans*-$[Co(en)_2Cl(C_7H_7N_4O_2)]^+$. The two complex ions shown are symmetry related by the center of inversion at ($^1/_2$, 0, $^1/_2$).

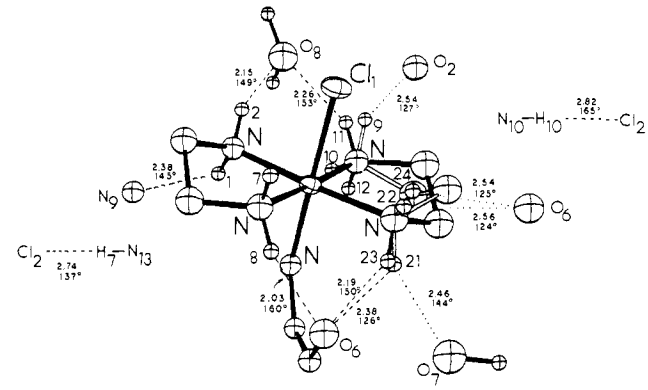

Figure 2. A perspective view showing some of the intramolecular and intermolecular hydrogen bonds stabilizing the molecular conformation of the complex. Hydrogen bonds are indicated by dashed lines; interatomic contacts are indicated by dotted lines.

adenine complex,[5] the coordination to cobalt was through N-9, and N-3 was found to be hydrogen bonded to the ethylenediamine groups (displayed in a cis conformation about the cobalt). Several important features appear immediately on comparison of the two complexes: (1) the N-3–N-11, N-3–N-13 intramolecular hydrogen bond system in the adenine complex has been supplanted by the O-6–N-11, O-6–N-13 intramolecular hydrogen bond system in the theophylline complex; (2) the angles C-5–N-7–Co, 132.0°, and C-8–N-7–Co, 124.9°, are highly dissymmetric. The analogous angles in the adenine complex are C-4–N-9–Co, 127.7°, and C-8–N-9–Co, 128.4°. This dissymmetry in the theophylline complex is unusual for metal–purine[6] or metal–imidazole[7] complexes. The asymmetry is obviously a result of molecular adjustment in order to accommodate the enlargement of the intramolecular hydrogen ring system from a five-membered ring in the adenine complex to a six-membered ring in the theophylline complex. The important feature is that the noted angles have been significantly altered in order to form the intramolecular hydrogen bond system. The particulars of the intermolecular and intramolecular hydrogen bonding are illustrated in Figure 2.

The hydrogen bonding of the carbonyl group, C-6–O-6, of the theophylline to the ligated ethylenediamines is specific for the guanine class of bases. Reaction of the complex with an adenine residue *via* N-7 would cause severe steric repulsion between the ethylenediamine ligands and the amino group at C-6. This suggests then that selectivity for guanine over adenine residues may be achieved by using octahedral complexes with *hydrogen donor ligands* attached.

Furthermore, reaction of the complex with a biopolymer may be achieved without severe disruption of intermolecular purine–pyrimidine hydrogen bonding. The Watson–Crick hydrogen bonding scheme[8] for G:C pairs has been recently confirmed at atomic resolution for the dinucleoside phosphate guanylyl-3′,5′-cytidine.[9]

The carbonyl oxygen O-6 of guanine is involved in an intermolecular hydrogen bond with the amino group N-4 of the cytidine base. Coordination of the complex at N-7 could result in two possibilities: (1) rupture of the $O\text{-}6_G\text{–}N\text{-}4_C$ hydrogen bond and formation of an $O\text{-}6_G$–N(ethylenediamine) hydrogen bond; (2) O-6 acting as a bifurcated acceptor between $N\text{-}4_C$ and N-(ethylenediamine). In either case the other two hydrogen bonds of the G:C pair could remain intact.

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The [2.2.2]Propellane System[1,2]

Sir:

We report now the first synthesis, isolation and characterization of a [2.2.2]propellane. Our successful synthesis of this elusive system is outlined in Chart I. The route to the diazo ketone **1** shown there is described in more detail in our earlier communication on the synthesis of [4.2.2]- and [3.2.2]propellanes.[3] Photolysis of **1** at −70° in methylene chloride gave the ketene **2**.[4] The reaction was monitored by infrared spectroscopy, following the disappearance of the carbonyl band of **1** at 6.12 μ. The ketene was not isolated but was cleaved directly to ketone **3** by ozonolysis at −70° in 2:1 by

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(1) A preliminary report of this work was presented at the 165th National Meeting of the American Chemical Society, Dallas, Tex., April 1973.
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(4) For other examples of photochemical Wolff reactions see ref 3, footnote 8 therein, and A. Hassner, A. W. Coulter, and W. S. Seese, *Tetrahedron Lett.*, 759 (1962).