would be forced into an apical position.[28] An analogous explanation could be advanced to explain the failure of any trigonal-bipyramid complex of **2** formed to undergo exchange since pseudorotation would require two alkyl groups to occupy apical positions in a trigonal-bipyramid complex.

Thus while it should be possible to resolve an optically active organotin compound with four carbon–tin bonds, it seems unlikely that such a compound would be very useful in investigating the stereochemistry of substitution at tin.

Experimental Section

The preparation of **1** and **2** will be reported shortly in connection with synthetic studies.[9]

Deuterated solvents were obtained from Merck Sharp and Dohme of Canada, Ltd. Other reagent grade solvents and chemicals were used as received.

Spectra were determined on a Varian Associates HA-100 spectrometer and where it was necessary to check for long-range coupling between the $Sn^{117/119}$-Hγ on a Varian Associates HA-56–60A spectrometer. The 100-MHz spectrometer was equipped with a variable temperature probe standardized against an iron-constantan thermocouple. Line positions were measured directly from calibrated chart paper or by using standard side band techniques.

Samples were degassed and sealed under vacuum prior to study, except in those cases where subsequent ligand addition was desired.

Acknowledgment. We thank the Petroleum Research Fund, administered by the American Chemical Society, and the National Science Foundation for financial support and Mr. D. Gifford for running the HA-100 spectra.

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Stereochemistry of Nucleic Acids and Their Constituents. VIII.[1a] Metal Binding Studies. Crystal Structure of a Guanine–Copper Chloride Complex, a Trigonal-Bipyramidally Coordinated Copper

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Abstract: The X-ray crystal structure of the complex $(C_5H_6N_5O)CuCl_3 \cdot H_2O$ has been determined using diffractometric single-crystal methods. The crystals are monoclinic, $a = 16.952$, $b = 10.183$, $c = 13.185$ Å, $\beta = 99.968°$, and the space group is C2/c. The structure consists of a binuclear complex with chlorine-bridged copper atoms bound to the N(9) atoms of center-related guanine moieties. Both the N(3) and N(7) sites on the guanine ring are protonated, and these sites participate in hydrogen bonding with neighboring molecules. The combined effect of metal and proton binding severely perturbs the π-electron system of the guanine ring, causing a significant shrinking of the imidazole portion of the ring relative to neutral guanine. The pentacoordinated copper complex displays trigonal-bipyramidal geometry as opposed to the more common square-pyramidal environment. Three chlorine atoms occupy the trigonal plane, while the N(9) atom of guanine and another chlorine take up the axial positions. The axial Cu–Cl bond length is found to be about 0.11 Å shorter than the in-plane Cu–Cl bond length, a feature which may be characteristic of trigonal-bipyramidal coordination of copper.

The importance of metal ions in protein chemistry has long been recognized, and exhaustive studies have been reported in this area. More recently, the related and equally important involvement of metal ions in nucleic acid processes has received considerable attention.[2,3] Model studies with DNA and its constituents have shown that metals bind to various sites of the double helix, bringing about either stabilization (*e.g.*, Mg^{2+}, Na^+, Ni^{2+}) or destabilization (*e.g.*, Cu^{2+}, Cd^{2+}, Pb^{2+}) of the ordered structure. While spectral and potentiometric studies have shed some light on these interactions,[2,3] very few X-ray crystal structures are available to show the precise binding sites of metals to the nucleic acid components.[4,5] We are engaged in an X-ray crystallographic study of pertinent complexes, not only to explain metal binding, but also to provide analog structures which may facilitate work in progress on the structure of transfer RNA. Here we report the crystal structure of a guanine–copper chloride complex showing preferential binding of copper to the N(9) of the imidazole ring, a site normally blocked by the sugar–base glycosidic bond in DNA and RNA.

Yellow-brown crystals of $(C_5H_6N_5O)CuCl_3 \cdot H_2O$ were prepared by treating guanine with an approximate 4:1 molar excess of $CuCl_2 \cdot 2H_2O$ in hot, aqueous HCl. Preliminary oscillation, Weissenberg, and precession photographs showed the space group to be either Cc or C2/c. The successful structure analysis and refinement in the centrosymmetric space group C2/c are taken as confirmation of that choice. Crystal data are: $a = 16.952 \pm 0.001$, $b = 10.183 \pm 0.001$, $c = 13.185 \pm 0.001$ Å; $\beta = 99.968 \pm 0.004°$; $D_m = 2.024$ g cm^{-3},

(1) (a) Parts VII and VI are in press in "Synthetic Procedures in Nucleic Acid Chemistry," Vol. 2, W. W. Zorbach and R. S. Tipson, Ed., and *Acta Crystallogr.*, respectively; (b) to whom inquiries and reprint requests should be sent at this address: Department of Biochemistry, University of Wisconsin, Madison, Wisconsin 53706.

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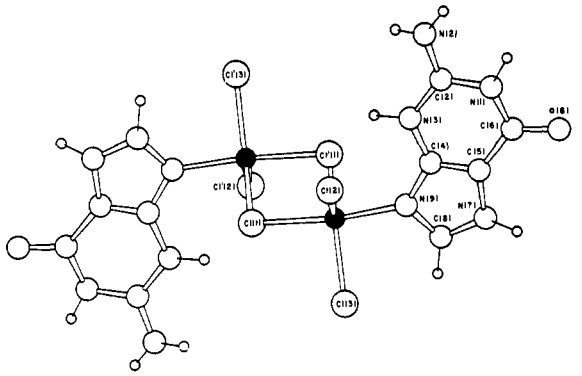

Figure 1.

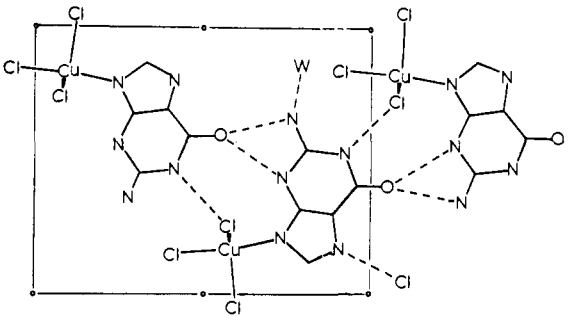

Figure 2.

D_x = 2.016 g cm^{-3} based on eight formula units per unit cell.

A total of 1602 independent reflections were recorded from a crystal mounted about the c axis, using a Picker four-circle automatic diffractometer, Cu Kα radiation (λ 1.5418 Å), and a 2θ scan mode. Of these reflections, 1403 were significantly above background. The structure was solved using the heavy atom method. A three-dimensional Patterson synthesis showed several strong, nonHarker peaks in the Harker section at y = 0, one of which corresponded reasonably well to a copper–chlorine vector. This would require that copper and chlorine atoms have roughly the same y coordinate, and that three related peaks occur in the Harker section corresponding to copper–copper, copper–chlorine, and chlorine–chlorine interactions, respectively. The latter three peaks were easily found, and the corresponding copper and chlorine positions were used to phase an initial Fourier synthesis, resulting in a residual factor ($R = \Sigma||F_o| - |F_c||/\Sigma|F_o|$) of 0.54. The position, but not the orientation, of the purine ring was found from this synthesis, together with the two other independent chlorine atoms and the water oxygen. Isotropic full-matrix least-squares refinement of this model, and a subsequent difference Fourier map, confirmed the orientation of the purine ring and revealed the hydrogen atoms, except those of the water molecule. Further anisotropic refinement led to the present R factor of 0.052. The full crystallographic details will be published elsewhere.

The molecular structure of the complex is shown in Figure 1, while bond lengths and bond angles involving copper are given in Table I. The binuclear complex is seen to consist of chlorine-bridged copper atoms, each having a trigonal-bipyramidal environment. Copper is bonded to N(9) of guanine and to one of the bridge chlorines in the axial direction. The trigonal plane consists of three copper–chlorine bonds. The Cu, Cl′(1), Cl(2), and Cl(3) atoms are coplanar within experimental error. A recent survey[6] of solid copper(II) complexes indicates that, while pentacoordination is fairly common, the trigonal-bipyramidal geometry is seen infrequently. The more common arrangement is the distorted square pyramidal, with copper displaced 0.1–0.2 Å in the direction of the fifth ligand.

Under the strongly acidic conditions used, both N(3) and N(7) are protonated, and participate in hydrogen bonding, as shown in Figure 2. In addition to coordinate bonding to copper, each guanine base is hydrogen bonded to four neighboring molecules and to a water molecule. The structure is rather strongly hydrogen bonded, including two N–H···Cl bonds. Compared to similar guanine derivatives, the carbonyl group here is unique in that it participates simultaneously in hydrogen bonding to N(2) and N(3) of an adjacent base.

Table I. Bond Lengths and Bond Angles in the Copper Coordination Sphere

	Bond lengths, Å
Cu–N(9)	1.976
Cu–Cl(1)	2.288[a]
Cu–Cl′(1)	2.447
Cu–Cl(2)	2.365
Cu–Cl(3)	2.329
	Bond angles, deg
Cl(1)–Cu–Cl(2)	95
Cl(2)–Cu–N(9)	91
N(9)–Cu–Cl′(1)	87
Cl′(1)–Cu–Cl(1)	82
Cl(3)–Cu–Cl(1)	94
Cl(3)–Cu–Cl(2)	112
Cl(3)–Cu–N(9)	92
Cl(3)–Cu–Cl′(1)	134
Cl(1)–Cu–N(9)	169
Cl′(1)–Cu–Cl(2)	114

[a] It may be noted that the axial Cu–Cl(1) bond distance is about 0.11 Å shorter than the average value of the equatorial Cu–Cl bond, a feature that may be characteristic of a trigonal-bipyramidal coordination around a copper: J. A. Carrabine and M. Sundaralingam, in preparation.

A comparison of the bond lengths and bond angles of the present structure with those of guanine·HCl[7] is given in Table II, showing the effects of both metal binding and protonation (at N(3)) on the electronic structure of the ring system. The most significant difference occurs in the vicinity of N(3). The adjacent bonds are significantly lengthened in the metal complex, relative to guanine·HCl, presumably due to protonation in the former case. In addition, the bond angles N(1)–C(2)–N(3), C(2)–N(3)–C(4), and N(3)–C(4)–C(5) are noticeably different. The bond lengths in the imidazole ring, to which copper is directly bound, are generally shorter than those of guanine. In effect, copper serves as an electron sink for the imidazole ring, which was initially π-electron excessive.[8] A significant shortening of the C(2)–N(2) bond is also seen in the com-

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Table II. Bond Lengths and Bond Angles for the Guanine Ring

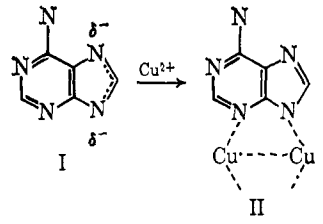
	This work	Guanine·HCl[a]
	Bond lengths, Å	
N(1)–C(2)	1.361	1.374
C(2)–N(3)	1.346	1.318
N(3)–C(4)	1.382	1.345
C(4)–C(5)	1.367	1.377
C(5)–C(6)	1.398	1.414
C(6)–N(1)	1.396	1.390
C(5)–N(7)	1.378	1.378
N(7)–C(8)	1.312	1.322
C(8)–N(9)	1.345	1.335
N(9)–C(4)	1.361	1.375
C(2)–N(2)	1.296	1.339
C(6)–O(6)	1.242	1.237
	Bond angles, deg	
N(1)–C(2)–N(3)	119.0	123.4
C(2)–N(3)–C(4)	118.1	112.8
N(3)–C(4)–C(5)	122.1	127.6
C(4)–C(5)–C(6)	122.0	119.9
C(5)–C(6)–N(1)	112.3	110.8
C(6)–N(1)–C(2)	126.4	126.4
C(4)–C(5)–N(7)	104.9	107.4
C(5)–N(7)–C(8)	107.8	108.2
N(7)–C(8)–N(9)	112.3	109.6
C(8)–N(9)–C(4)	104.1	108.6
N(9)–C(4)–C(5)	110.9	106.2
N(1)–C(6)–O(6)	119.0	120.3
C(5)–C(6)–O(6)	127.7	128.9
C(6)–C(5)–N(7)	133.1	132.7
N(1)–C(2)–N(2)	121.5	116.0
N(3)–C(2)–N(2)	119.5	120.6
N(3)–C(4)–N(9)	127.0	126.3

[a] Reference 7.

plex, indicating that the amino group is even more highly conjugated with the heterocyclic ring than it is in guanine·HCl.

These effects demonstrate that combined metal and proton binding disturbs the entire electronic system of the ring. This observation must be considered when studying binding sites with methods which measure localized perturbations.

Consideration of this and other structures allows some generalizations regarding preferred binding sites and coordination for copper with the nucleic acid bases. In the case of the purines, a strong preference for N(9) binding is observed. Since, in the present case, guanine was initially dissolved in HCl, it is expected that both N(7) and N(9) were protonated prior to the addition of copper.[7] Then the preference of copper for N(9) must be strong enough for copper to successfully compete with the proton for that site. The N(3) site appears to be the least basic relative to protonation in guanine.[8] Crystals of copper–adenine[9] were prepared in strongly basic solution and presumably the initial anionic species would be as shown in I. The addition of copper resulted in the structure shown in II,[4] again



I II

showing a strong preference for N(9) binding. The only known structure of copper with a pyrimidine base is that of copper–cytosine. Here cytosine exists as the neutral species and copper binds to the N(3) of the ring.[5]

Significantly, all of the known metal–base structures are those possessing an amino substituent on the base. Previous workers have invoked this substituent as a donor site in metal–nucleic acid complex formation,[2,10] notably, the structure suggested by Szent-Györgyi for metal–ATP complexes.[11] As has been pointed out,[8,12] such a proposal involves the incorrect but persistently held view that heterocyclic amines are analogous to aromatic amines, or to amino acids, in regard to the basic properties of the amino group. Clearly, the structures cited here substantiate the noninvolvement of the amino group in metal complexes, even in the case of cytosine, where the primary coordination site, N(3), is adjacent to the amino substituent. The lack of involvement of the amino group is consistent with the strong delocalization of the lone-pair electrons into the heterocyclic ring.

The preferred binding of copper to N(9) of the purine ring does not preclude the involvement of N(7) in cases where N (9) is blocked, *e.g.*, in DNA or RNA. In fact, Eichhorn[13] and Tu[14] offer reasonable spectral evidence for N(7) participation in copper–guanosine complexes. As seen in the present structure, however, considerable electronic perturbations can occur at ring sites other than those involved in metal binding. Such perturbations can complicate interpretation of spectral data, and could lead to erroneous conclusions.

Acknowledgment. This work was supported by National Institutes of Health Grants No. GM14828 and GM42412.

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