Synthesis and Crystal Structure Determinations of the Bis-(5,5-diethylbarbiturato)-bisimidazole Complexes of Cobalt(II) and Zinc(II)

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Summary In the molecular structures of the bis-(5,5-diethylbarbiturato)-bisimidazole complexes of cobalt(II) and zinc(II) there is tetrahedral co-ordination of the metal atom by nitrogen atoms, and a conformation stabilized by C–H · · · O intramolecular interactions between almost coplanar pairs of imidazole and barbiturate rings.

WE report the first determinations of crystal structures of transition-metal complexes in which the anion of a drug-active barbiturate (5,5-diethylbarbituric acid or barbital) is a ligand. Many such complexes have been prepared,[1] because of their potential use in clinical detection and estimation of barbiturate drugs. They are of general formula $M^{II}(barb)_2L_2$ where M is Co, Cu, Zn, or Cd; barb is the anion of barbital, phenobarbital, amobarbital, cyclobarbital, or one of a number of 5,5-dialkyl-2-thiobarbituric acids; L is an organic base such as ammonia, pyridine, or one of the picolines or lutidines. The structures of these molecules are unknown, although in some cases, it has been suggested, on the basis of i.r. spectral data, that the barbiturate ligand is bound to metal through oxygen or sulphur atoms. Complexes in which L is imidazole have not been previously described. We chose this ligand because the resulting complexes might be more illustrative of possible barbiturate binding to metalloenzymes.

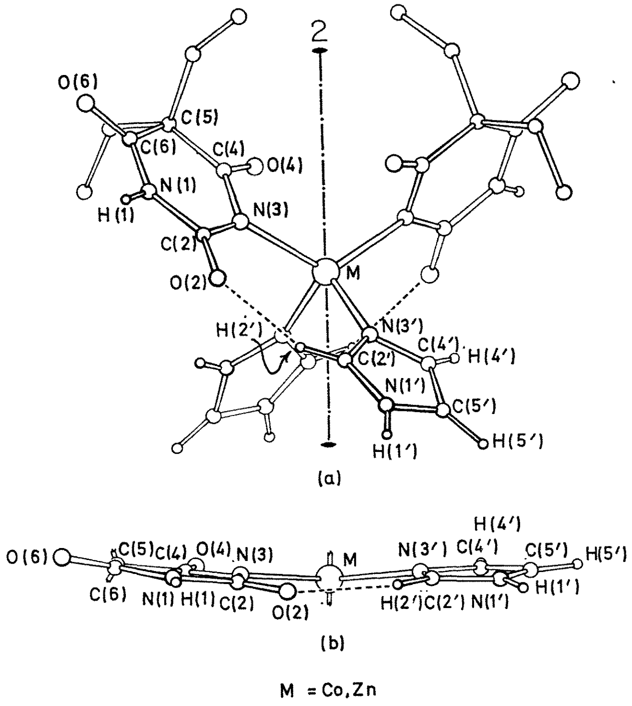

FIGURE 1. *Molecular structure* (a) *Molecule complete except for ethyl hydrogen atoms,* (b) *almost coplanar barbiturate and imidazole rings.*

The bis-(5,5-diethylbarbiturato)-bisimidazole complexes of cobalt(II) and zinc(II) were prepared at room temperature by dissolving imidazole, sodium barbital, and metal chloride in water in the mole ratio 2 : 2 : 1. The crystals (purple or transparent for the cobalt or zinc complexes, respectively) are monoclinic prisms, which are approximately ellipsoidal and have many small facets. The crystal structures are isomorphous, space group $C2/c$; $a = 13{\cdot}362(2)$, $b = 10{\cdot}133(2)$, $c = 20{\cdot}544(4)$ Å, $\beta = 100°\,20(2)'$ for the cobalt complex and $a = 13{\cdot}333(2)$, $b = 10{\cdot}204(2)$, $c = 20{\cdot}512(4)$ Å, $\beta = 100°24(1)'$ for the zinc complex; $D_m = 1{\cdot}37$ g cm^{-3} for both, $Z = 4$. X-Ray intensity data (2329 and 2333 non-symmetry related reflections for the cobalt and zinc complexes, respectively) were measured using nickel-filtered Cu-K_α radiation, and a computer-controlled four-circle diffractometer. The phase problem was solved by inspection of the Patterson function. All hydrogen atoms were found in a difference Fourier synthesis. Atomic parameters, including anisotropic thermal parameters for non-hydrogen atoms were refined by full-matrix least-squares methods to give final R factors of 0·074 and 0·039 for the cobalt and zinc complexes, respectively.

The molecules (Figure 1a) have two-fold crystallographic symmetry. The metal atom is tetrahedrally co-ordinated by the deprotonated nitrogen atoms from two barbital anions and by nitrogen atoms from two imidazole molecules. Each barbiturate ring is almost coplanar with an adjacent imidazole ligand (Figure 1b). This configuration would not be readily predicted by comparison with other crystal structures of metal–imidazole complexes, since these show no correlations in the orientation of the imidazole ring about the metal-nitrogen bond such as might arise from interactions with the *d*-electron system of the metal atom.[2] Manipulation of a molecular model gave no indication of steric hindrance to concerted rotations from coplanarity of the barbiturate and imidazole rings. Such a non-coplanar configuration might be expected, since from the observed openings of bond angles at the metal atom and adjacent nitrogen atoms (Figure 2) it is implied that coplanarity of the two rings induces molecular strain. We conclude that this configuration is stabilized by C-H · · · O interactions involving carbon atoms C(2) of imidazole and carbonyl oxygen atoms O(2) of barbital at a C · · · O distance of 3·02 Å. There has been disagreement as to whether such interactions should be called hydrogen bonds.[3] However, there is increasing evidence that they have some structure-determining influence. In the xanthines, atoms H(8) have a similar molecular environment to that of H(2) in imidazole. In crystal structures of xanthines, short H(8) · · · O intermolecular distances are commonly found, *e.g.* in the monohydrates of caffeine and theophylline,[3] the 1 : 1 complexes of 5-chlorosalicyclic acid with caffeine and theophylline,[4] and the 2 : 1 complex of barbital and caffeine.[5] The latter is of interest in that it has the shortest of these C(8) · · · O and H · · · O distances (3·16 and 2·32 Å). As in the presently reported barbital–imidazole interaction, the short C • • • O distance in the barbital–caffeine complex involves the barbital oxygen atom O(2).

The corresponding bond lengths and angles in the cobalt and zinc complexes are very similar, *e.g.*, the M–N(barb) and M–N(im) bond lengths are 2·020(3) and 2·022(3) Å in the cobalt complex and 2·009(2) and 2·023(2) Å in the zinc complex. In Figure 2, only the more accurate values determined for the zinc complex are shown. These are uncorrected for the effects of thermal motion. Bond lengths and angles in the barbital ligand are intermediate between those found in the crystal structures of the parent acid[6] and in sodium barbital,[7] where the sodium ion is co-ordinated through oxygen atoms O(4) and O(6) of the barbital anion.

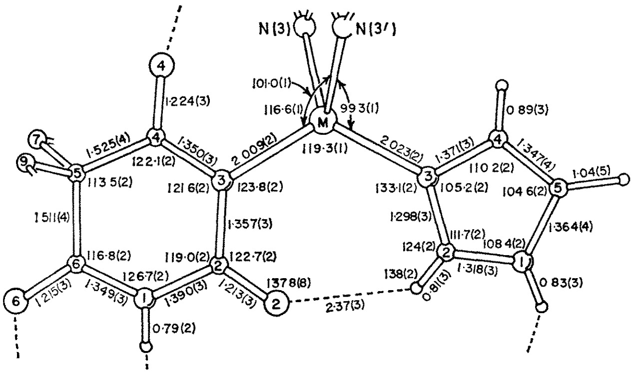

FIGURE 2. *Bond lengths and angles for the fragment of the zinc complex shown in Figure* 1b. *E.s.d.'s in parentheses.*

In the imidazole ligand, three of the bond lengths are in close agreement with the values found in the crystal structure of imidazole itself.[8] However, in the ligand there are shortenings (0·03 Å) of both C-N bonds at atom C(2), which are significant in terms of their e.s.d.'s (0·006 Å). We cannot explain these differences. If they are real, they may be related to the C(2) • • • O interaction which is formed in the crystal structure of the metal complex but not in imidazole.

The most important intermolecular interactions in the crystal structures of these metal complexes are hydrogen bonds of the usual type from the NH groups of the barbital and imidazole moieties to the barbital oxygen atoms O(6) and O(4), respectively. These link the molecules to form a three-dimensional hydrogen-bonded framework.

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