SHORT PAPER

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A model complex for carbonic anhydrases: crystal structure of *tris*-imidazole maleato zinc(II) dihydrate[†]

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A novel zinc complex containing three simple imidazole rings as a model compound for carbonic anhydrase and as a rare model for the carboxylate–imidazole–zinc triad interactions frequently observed in zinc enzymes has been made and its structure determined by X-ray diffraction in which the zinc atom has a distorted tetrahedral geometry.

The simple compound, imidazole, can serve as a biomimetic ligand for the histidine residues which frequently participate in the coordination spheres of metalloenzyme active sites, especially in those zinc-containing enzymes.[1,2] X-ray structure determination of carbonic anhydrase confirmed that the zinc center is coordinated by three imidazole residues of histidine 93, histidine 95 and histidine 113.[3] The zinc ion is in a distorted tetrahedral geometry with a fourth ligand, possibly OH or H_2O, coordinated to it to complete the coordination. In spite of the obvious interest such systems would have, few chelating ligands using imidazole rings have been made so far,[4] and no model complex which combine three simple imidazole rings have been characterized by single crystal X-ray diffraction. This is because of the lability of zinc complexes and the diverse coordination possibilities for zinc. It is not surprising that structural information about model zinc complexes containing neutral imidazole ligands is rather limited, and so far only three examples have been reported.[4–6] Breslow *et al.* have designed synthesized a model complex containing an organic ligand, *tris*(2-imidazolyl)carbinol, which can act as three imidazole moieties of histidines[7]. We have recently obtained a monomeric zinc(II) complex where three imidazole molecules coordinate to a zinc atom via nitrogen atom and the fourth coordination site is completed by an O atom from the maleato-ligand.

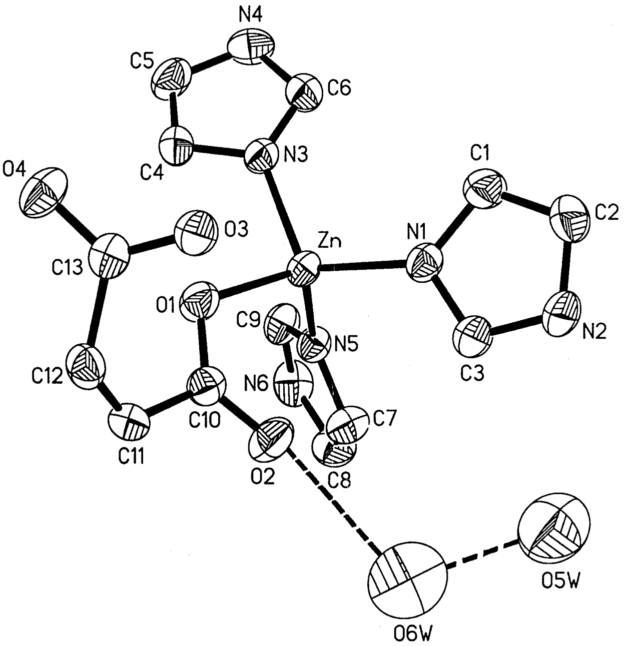

Fig. 1 Molecular structure of $[Zn(Him)_3(maleato)]\cdot 2H_2O$ 1 with the atom-numbering scheme used and hydrogen bonding indicated. Selected bond lengths (Å) and angles (°): Zn–O(1) 1.961(2), Zn–N(1) 1.990(3), Zn–N(2) 2.013(3), Zn–N(3) 2.016(3) O(2)---O(6w) 2.785(5), O(5w)---O(6w) 2.604(5); O(1)–Zn–N(1) 113.88(12), O(1)–ZN–N(2) 101.77(11), N(1)–Zn–N(2) 116.21(12), O(1)–Zn–N(3) 113.82(12), N(1)–Zn–N(3) 109.43(12), N(2)–Zn–N(3) 101.02(12), C(13)–O(1)–Zn 111.8(2), C(4)–N(1)–Zn 124.1(3), C(1)–N(1)–Zn 128.8(3), C(8)–N(2)–Zn 131.9(3), C(5)–N(2)–Zn 121.5(2), C(9)–N(3)–Zn 124.4(3), C(12)–N(3)–Zn 129.8(3).

In order to provide a low molecular-weight model complex for the zinc centre of carbonic anhydrase, we have prepared the first zinc maleate complex containing imidazole (Him), $[Zn(Him)_3(maleato)]\cdot 2H_2O$**1**, which was simply synthesized by reacting $ZnSO_4\cdot 7H_2O$ with sodium maleate and Him in a molar ratio of 1:1:3 in 30 mL of aqueous solution. The complex consists of monomeric $[Zn(Him)_3(maleato)]\ \cdot 2H_2O$ molecules (Fig. 1). The zinc(II) atom is coordinated by three monodentate imidazole ligands and further by a *syn* monodentate carboxylate group of maleate ion, forming a distorted tetrahedral N_3O geometry. The Zn–N bond lengths are in the range 1.988(2)–2.016(2) Å. The Zn–O bond length is 1.961(2) Å. The most distorted bond angle is N(1)–Zn–N(3) at 116.30(9)°.

The most important finding in complex **1** is the structural geometry which strikingly resembles those of the carbonic anhydrase which contains one zinc atom with three imidazole moieties from three histidines. The second important finding is the carboxylate-imidazole-zinc system,[4] which is comparable favourably to the triad system in zinc enzymes. All three uncoordinated nitrogen atoms of the imidazole ligands form donor hydrogen bonds with carboxylate groups from adjacent molecules. The hydrogen bond distances for N(2)...O(3^i), N(4)...O(3^{ii}) and N(6)...O(4^{iii}) are 2.766(5), 2.823(5) and 2.743(5) Å, respectively, which are comparable to the average value (2.8 Å) found for those in zinc enzymes[8] (i: 1–*x*, –*y*, 1–*z*; ii: 1–*x*, –*y*, 2–*z*; iii: –*x*, –*y*, 2–*z*).

Experimental

Crystal data for **1**: $C_{13}H_{18}N_6O_6Zn$, crystal size: 0.52 × 0.36 × 0.16 mm, triclinic, space group, P-1, $a = 8.6180(10)$, $b = 8.8590(10)$, $c = 11.856(2)$ Å, $\alpha = 88.370(10)$, $\beta = 75.500(10)$, $\gamma = 81.060(10)$°, $U = 865.6(2)$ Å^3, $Z = 2$, $D_c = 1.610$ g cm^{-3}, μ (Mo–Kα) = 14.63 cm^{-1}, 3044 reflections collected at 291 (2)K (Siemens P4 diffractometer) in the 1.77–25° θ range, 3044 unique used with $I > 2\sigma(I)$, 236 parameters refined on F^2 to final R indices: $R1$ $[I > 2\sigma(I)] = 0.031$, $wR2 = 0.090$. The structure was solved using direct methods (SHELX)[9] and refined by full-matrix least squares (SHELXL 93).[10] Atomic coordinates, thermal parameters and bond lengths and angles have been deposited at the Cambridge Crystallographic Data Centre.

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