Dalton Communications

A Model Complex for the Carboxylate–Histidine–Zinc System in Zinc Enzymes. Crystal Structure of $[Zn(Him)_2(MeCO_2)_2]$ (Him = imidazole)

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The novel monomeric zinc(II) complex $[Zn(Him)_2(MeCO_2)_2]$ (Him = imidazole) has been prepared and structurally characterized; it is the first structural model for the carboxylate–histidine–zinc interactions frequently observed in zinc enzymes.

The simple compound, imidazole, can serve as a biomimetic ligand for the histidine residues which frequently participate in the co-ordination spheres of metalloenzyme active sites, especially in those of zinc-containing enzymes.[1] It is somewhat surprising that structural information about model zinc complexes containing neutral imidazole ligands is rather limited, and so far only two examples have been reported.[2,3] In contrast, zinc complexes containing imidazolate bridges have recently been described.[4–6] Recent systematic investigations have shown that carboxylate–histidine–zinc triad systems are frequently observed, and play important roles in the catalytic processes of more than 30 zinc enzymes.[7] The hydrogen bonding between the co-ordinated imidazole of a histidine residue and the carboxylate group of a nearby aspartate or glutamate can modulate the basicity of the ligating nitrogen atom of the histidine residue towards the zinc atom. Two types of hydrogen bonding with respect to the carboxylate modes have been observed (Fig. 1).

In order to provide a low molecular-weight model complex for the triad interactions we have prepared the first zinc acetate complex containing imidazole (Him), $[Zn(Him)_2(MeCO_2)_2]$ **1**, which was simply synthesized by reacting $Zn(MeCO_2)_2 \cdot 2H_2O$ (0.220 g, 1.0 mmol) with imidazole (0.136 g, 2.0 mmol) in aqueous ethanol solution (1:2 v/v, 15 cm^3). The resulting mixture was adjusted to pH ≈6 with acetic acid and then stirred at 50 °C for 20 min. The colourless crystalline product (0.27 g, 84.4%)† was collected after slow evaporation at room temperature for several days.

X-Ray crystallography‡ has established the crystal structure of complex **1**, which consists of monomeric $[Zn(Him)_2(MeCO_2)_2]$ molecules (Fig. 2) The Zn^{II} atom is co-ordinated

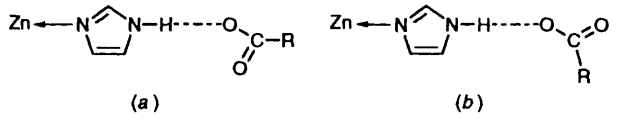

Fig. 1 Carboxylate–histidine–zinc triad system with the carboxylate acting in *syn* (*a*) and *anti* (*b*) modes

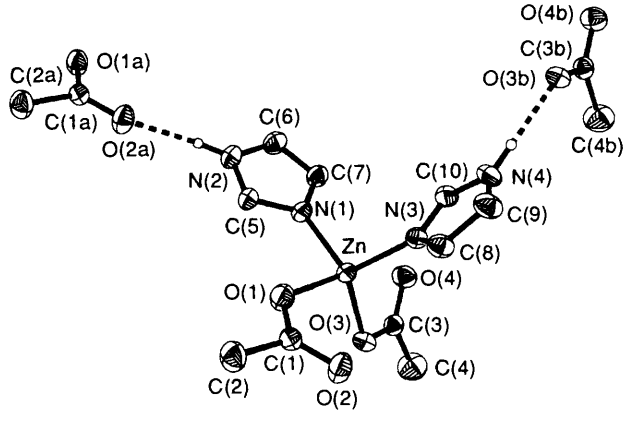

Fig. 2 Molecular structure of $[Zn(Him)_2(MeCO_2)_2]$ **1** with the atom-numbering scheme used and hydrogen bonding indicated. Selected bond lengths (Å) and angles (°): Zn–O(1) 1.965(3), Zn–O(3) 1.991(2), Zn–N(1) 2.003(3), Zn–N(3) 1.996(2); O(1)–Zn–O(3) 105.1(1), O(1)–Zn–N(1) 96.0(1), O(3)–Zn–N(1) 118.2(1), O(1)–Zn–N(3) 113.6(1), O(3)–Zn–N(3) 113.1(1), N(1)–Zn–N(3) 109.8(1), Zn–O(1)–C(1) 120.9(2), Zn–O(3)–C(3) 107.2(2), O(1)–C(1)–O(2) 124.0(3), O(3)–C(3)–O(4) 120.9(3). Symmetry codes: (a) x, 1 + y, z; (b) −1 + x, y, z

by a pair of monodentate imidazole ligands and further by a pair of *syn* monodentate acetate groups, forming a distorted tetrahedral N_2O_2 geometry. The Zn–N and Zn–O bond lengths are in the ranges 1.996(2)–2.003(3) and 1.965(3)–1.991(2) Å respectively; the most distorted bond angle is O(1)–Zn–N(1) at 96.0(1)°.

The most important finding in complex **1** is the carboxylate–imidazole–zinc system, which strikingly resembles the triad systems in zinc enzymes. Both of the unco-ordinated nitrogen atoms of the imidazole ligands form donor hydrogen bonds with carboxylate groups from adjacent molecules. The hydrogen bond distances for N(2) · · · O(2a) and N(4) · · · O(3b)

† Satisfactory C, H and N elemental analyses were obtained.

‡ Crystal data for **1**. $C_{10}H_{14}N_4O_4Zn$, M_r = 319.6, triclinic, space group $P\bar{1}$ (no. 2), a = 7.732(2), b = 8.068(2), c = 11.338(3) Å, α = 92.32(3), β = 99.77(2), γ = 96.31(3)°, U = 691.5 $Å^3$, Z = 2, D_c = 1.535 g cm^{-3}, $F(000)$ = 328, μ = 17.9 cm^{-1}. Data collection ($5 \leqslant 2\theta \leqslant 53°$) was performed at 294 K on an Enraf–Nonius CAD4 diffractometer (Mo-Kα, λ = 0.710 73 Å). The structure was solved using direct methods (SHELXS)[8] and refined by full-matrix least squares (SHELXL 93)[9] to final $R(R')$ values of 0.040 (0.052) for 172 parameters and 2132 observed data [$I \geqslant 2\sigma(I)$]. Atomic coordinates, thermal parameters and bond lengths and angles have been deposited at the Cambridge Crystallographic Data Centre. See Instructions for Authors, *J. Chem. Soc., Dalton Trans.*, 1994, Issue 1, pp. xxiii–xxviii.

are 2.724(5) and 2.783(5) Å, respectively, which are comparable to the average value (2.8 Å) found for those in zinc enzymes.[7] It is noteworthy that the two carboxylate moieties behave differently in their hydrogen bonding: the acetate defined by O(1), O(2), C(1) and C(2) utilizes the pendant oxygen atom O(2) in hydrogen bonding, and the carboxylate group acts in the *syn* mode; the other acetate uses the co-ordinated oxygen atom O(3), and hence acts in the *anti* mode. Thus the crystal structure of complex **1** comprises the two types of carboxylate–imidazole–zinc triad (Fig. 1) found in zinc enzymes.[7]

The other structural details of the triad system **1** also compare favourably with those of the zinc enzymes. The oxygen atoms involved in hydrogen bonding are almost co-planar with the corresponding imidazole moieties (deviations *ca.* 0.3 Å). Likewise, the zinc atom is virtually co-planar with both imidazole moieties within deviations of *ca.* 0.2 Å. Hence the structure mimics the head-on and in-plane interactions of the imidazole moiety with zinc and carboxylate groups in the biological triad systems.

In summary, complex **1** can serve as the first, simple structural model for the carboxylate–imidazole–zinc triad system, featuring both *syn* and *anti* modes for the carboxylate groups in hydrogen bonding. Further exploration of related model complexes is in progress.

Acknowledgements

This work was supported by the National Natural Science Foundation of China (Grant No. 29303024). We also thank Mr. Xiao-Ying Huang and Mr. Yong-Jin Xu for their help in the data collection.

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Received 24*th May* 1994; *Communication* 4/03095H