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# AN ACTIVE SITE MODEL FOR CARBONIC ANHYDRASE. SYNTHESIS AND CRYSTAL STRUCTURE OF [$\eta^3$-HB(3-Phpz)$_3$]ZnBr

**KEWU YANG, YUANQI YIN* and DAOSIN JIN**

Lanzhou Institute of Chemical Physics, Academia Sinica, Lanzhou 730000, P.R. China

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**Abstract**—Reaction of potassium hydrotris(3-phenylpyrazol-1-yl)borate [KHB(3-Phpz)$_3$] with zinc bromide in methanol solution yielded hydrotris(3-phenylpyrazol-1-yl)boratozinc bromide [$\eta^3$-HB(3-Phpz)$_3$]ZnBr. Crystal structure determination showed that a zinc ion is coordinated with three nitrogen atoms and one bromine atom; the coordination environment about the zinc centre in [$\eta^3$-HB(3-Phpz)$_3$]ZnBr is trigonally distorted tetrahedral.

Carbonic anhydrase (CA) is a ubiquitous zinc containing metalloenzyme, its only known physiological function being to catalyse the interconversion of

$$CO_2 + H_2O \rightleftharpoons H^+ + HCO_3^- \qquad (1)$$

$CO_2$ and $HCO_3^-$ [1] [eq. (1)]. Complete X-ray crystallographic structures[2] have been determined for the human B and C isozymes and show the active site to be comprised of a $Zn^{2+}$ ion coordinated in a distorted tetrahedral fashion by three histidine imidazoles; the fourth ligand site is said to be occupied by a coordinated $H_2O$ or $OH^-$ group, which may be important for the catalytic process. This special environment around the metal is manifested in extremely powerful catalysis, the turnover numbers for CA being among the highest known.

Model work on CA has centred on the design of chelating ligands that approximate to the distorted four-coordinate active site, and one way of obtaining functional model compounds of this type is the use of tridentate ligands providing an appropriate set of donor atoms and a favourable stereochemical disposition.[3] Brown *et al.*[4] have successfully applied this concept to the modelling of CA with zinc complexes of substituted imidazolyl phosphine. In this paper, we report the synthesis and crystal structure of the title compound, which appeared from molecular models to be a reasonable mimic for the active site in CA.

## EXPERIMENTAL

### *Preparation and analyses of the complex*

All chemicals were reagent grade. The ligand potassium hydrotris(3-phenylpyrazol-1-yl)borate [KHB(3-Phpz)$_3$] was prepared according to the published procedure.[5] Zinc bromide (8 mmol) was added to 50 cm$^3$ of methanol, and to this stirred solution was added all at once a THF solution of the crude ligand (8 mmol), with separation of some white solid material. Water (0.1 dm$^3$) was added to yield a white precipitate, which was collected by filtration and washed thoroughly with hot water and then with methanol. The white solid was recrystallized from toluene–heptane, and dried in a vacuum desiccator. Found: C, 55.3; H, 3.8; N, 14.3. Calc. for $C_{27}H_{22}BBrN_6Zn$($M_r$ 586.6): C, 55.2; H, 3.8; N, 14.3%. IR: $\nu$(B—H) 2510 cm$^{-1}$. $^1$H NMR (ppm): 12.81 (s, 1H), 7.8–7.6 (m, 2H), 7.43 (d, 1H), 7.3–7.1 (m, 3H), 6.50 (d, 1H).

### *Crystal structure determination*

Crystals of the title compound were obtained by slowly cooling a hot toluene–heptane solution to

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*Author to whom correspondence should be addressed.

Table 1. Crystallographic data of [$\eta^3$-HB(3-Phpz)$_3$]ZnBr

| | |
|---|---|
| Compound | [$\eta^3$-HB(3-Phpz)$_3$]ZnBr |
| Chemical formula | $C_{27}H_{22}BBrN_6Zn$ |
| Formula weight | 586.6 |
| Crystal size (mm) | 0.30 × 0.30 × 0.25 |
| Crystal class | Trigonal |
| Space group | $P\bar{3}$ |
| $T$ (°C) | 25 |
| $a$ (Å) | 11.482(2) |
| $c$ (Å) | 11.557(2) |
| $V$ (Å$^3$) | 1318.7(5) |
| $Z$ | 2 |
| $\lambda$ (Å) | 0.71073 |
| $D_c$ (g cm$^{-3}$) | 1.477 |
| $\mu$ (mm$^{-1}$) | 2.480 |
| $R$ | 0.0390 |
| $R_w$ | 0.0378 |

Table 2. Bond lengths (Å) for [$\eta$-HB(3-Phpz)$_3$]ZnBr

| | | | |
|---|---|---|---|
| Br—Zn | 2.280(1) | Zn—N(1) | 2.043(4) |
| Zn—N(1A) | 2.043(3) | Zn—N(1B) | 2.044(2) |
| B—N(2) | 1.536(5) | B—N(2A) | 1.537(4) |
| B—N(2B) | 1.537(3) | N(1)—N(2) | 1.378(2) |
| N(1)—C(5) | 1.347(6) | N(2)—C(3) | 1.329(6) |
| C(3)—C(4) | 1.368(7) | C(4)—C(5) | 1.398(6) |
| C(5)—C(6) | 1.480(6) | C(6)—C(7) | 1.380(7) |
| C(6)—C(11) | 1.401(8) | C(7)—C(8) | 1.390(7) |
| C(8)—C(9) | 1.370(11) | C(9)—C(10) | 1.362(9) |
| C(10)—C(11) | 1.383(8) | | |

room temperature, and a colourless platelet of size 0.30 × 0.30 × 0.25 mm was chosen for the measurement. All crystallographic data were obtained with a Siemens R3m/V diffractometer using Mo-$K_\alpha$ radiation ($\lambda = 0.71073$ Å). Of the 2023 reflections obtained with the $\omega$–$2\theta$ technique in the range $+h+k\pm l$ for $2\theta = 3.0$–$52.0°$, 1745 reflections were independent, and 1196 reflections with $F_0 > 4.0\sigma(F_0)$ were used for the calculations after an empirical absorption correction based on $\psi$ scans. The Siemens SHELXTL PLUS program system was used to solve the structure with direct methods and for the full matrix least-squares refinement. Anisotropic temperature factors were applied for all atoms.

## RESULTS AND DISCUSSION

The title compound [$\eta^3$-HB(3-Phpz)$_3$]ZnBr was characterized both by spectroscopy and also by an X-ray crystal structure determination. The crystallographic data are listed in Table 1, and bond distances and angles are listed in Tables 2 and 3. An ORTEP plot and unit cell packing diagram are presented in Figs 1 and 2, respectively.

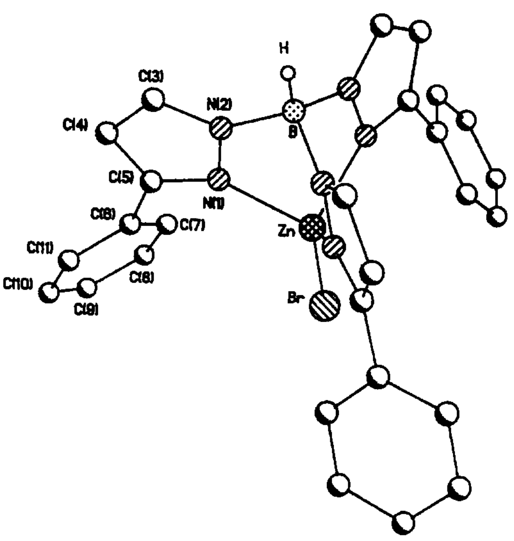

Fig. 1. The structure of [$\eta^3$-HB(3-Phpz)$_3$]ZnBr.

Table 3. Bond angles (°) in [$\eta^3$-HB(3-Phpz)$_3$]ZnBr

| | | | |
|---|---|---|---|
| Br—Zn—N(1) | 122.8(1) | Br—Zn—N(1A) | 122.8(1) |
| N(1)—Zn—N(1A) | 93.4(1) | Br—Zn—N(1B) | 122.8(1) |
| N(1)—Zn—N(1B) | 93.4(1) | N(1A)—Zn—N(1B) | 93.4(1) |
| N(2)—B—N(2A) | 109.4(3) | N(2)—B—N(2B) | 109.3(3) |
| N(2A)—B—N(2B) | 109.3(3) | Zn—N(1)—N(2) | 111.5(3) |
| Zn—N(1)—C(5) | 142.0(3) | N(2)—N(1)—C(5) | 106.2(3) |
| B—N(2)—N(1) | 120.8(4) | B—N(2)—C(3) | 129.6(4) |
| N(1)—N(2)—C(3) | 109.5(4) | N(2)—C(3)—C(4) | 109.3(4) |
| C(3)—C(4)—C(5) | 105.3(5) | N(1)—C(5)—C(4) | 109.6(4) |
| N(1)—C(5)—C(6) | 122.8(4) | C(4)—C(5)—C(6) | 127.5(5) |
| C(5)—C(6)—C(7) | 121.4(5) | C(5)—C(6)—C(11) | 119.9(4) |
| C(7)—C(6)—C(11) | 118.6(4) | C(6)—C(7)—C(8) | 120.7(6) |
| C(7)—C(8)—C(9) | 119.4(5) | C(8)—C(9)—C(10) | 121.2(6) |
| C(9)—C(10)—C(11) | 119.9(7) | C(6)—C(11)—C(10) | 120.2(5) |

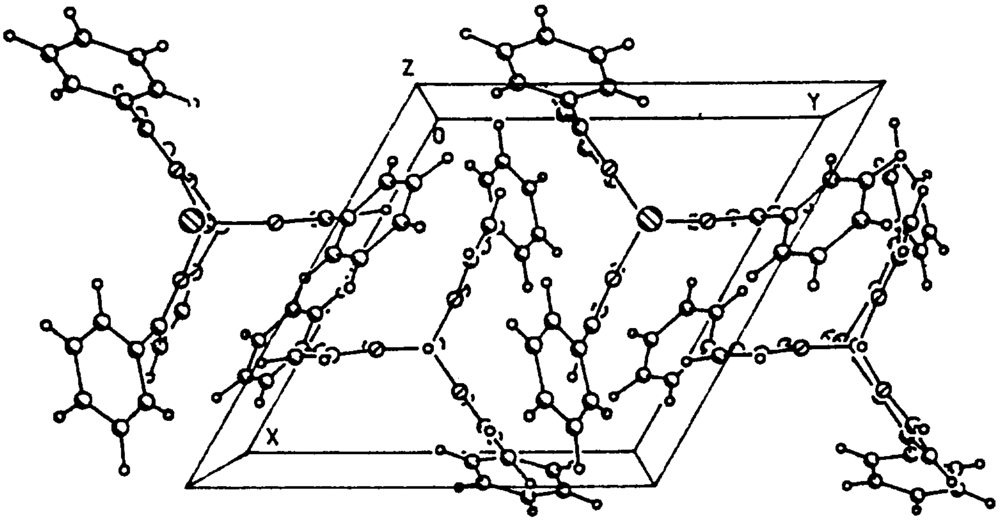

Fig. 2. Unit cell packing diagram for [$\eta^3$-HB(3-Phpz)$_3$]ZnBr.

The zinc ion is coordinated by three nitrogen atoms and the coordination environment about the zinc centre is trigonally distorted tetrahedral, as evidenced by the three small N—Zn—N [93.4(1)°] bond angles, and three accordingly large N—Zn—Br [122.8(1)°] bond angles. The remainder of the tris(pyrazolyl)hydroborato ligand has normal bond lengths and angles.[6] The Zn—Br bond length [2.280(1) Å] is larger than those of some other zinc complexes, [(Bu$^t$pz)$_3$Zn($\mu$-OH) Zn(Bu$^t$pz)$_3$](ClO$_4$)$_3$ (Zn—O = 1.901, 1.914 Å),[7] [$\eta^3$-HB(3-Phpz)$_3$]Zn(CH$_3$) (Zn—C = 1.97 Å)[8] and [$\eta^3$-HB(3-Phpz)$_3$Zn(SC$_2$H$_5$)] (Zn—S = 2.21 Å).[9] The Zn—N bond length [2.043(3) Å] may be compared with that of [$\eta^3$-HB(3-Bu$^t$-5-Mepz)$_3$]ZnOH (Zn—N = 2.052 Å).[10] The coordination environment of [$\eta^3$-HB(3-Phpz)$_3$] ZnBr also compares reasonably well with a theoretical calculation for the active site of CA, with bond lengths and angles of Zn—O = 1.96 Å, Zn—N = 2.10 Å and O—Zn—N = 117.6°.[11]

## REFERENCES

1. Y. Pocker and S. Sarkanen, in *Advances in Enzymology* (Edited by A. Meister), Vol. 47, pp. 149–274. Wiley, New York (1978).
2. A. Liljas, P.-C. Bergsten, K. K. Kannan, I. Waara, K. Fridborg, B. Strandberg, U. Carlbom, L. Jarup, S. Lovgren and M. Petef, *Nature New Biol.* 1972, **235**, 131.
3. R. H. Prince, *Adv. Inorg. Chem. Radiochem.* 1979, **22**, 349.
4. H. Slebocka-Tilk, J. L. Cocho, Z. Frakman and R. S. Brown, *J. Am. Chem. Soc.* 1984, **106**, 2421.
5. S. Trofimenko, *Inorg. Synth.* 1970, **12**, 99.
6. S. Trofimenko, *Prog. Inorg. Chem.* 1986, **34**, 115.
7. E. Dubler, G. Hanggi and H. Schmalle, *Inorg. Chem.* 1990, **29**, 2518.
8. I. B. Gorreu, A. Looney and G. Parkin, *J. Chem. Soc., Chem. Commun.* 1990, 220.
9. D. T. Corwin and S. A. Koch, *Inorg. Chem.* 1988, **27**, 493.
10. R. Alsfasser, S. Trofimenko, A. Looney, G. Parark and H. Vahrenkamp, *Inorg. Chem.* 1991, **30**, 4098.
11. M. M. Kenneth, R. Hoffman and M. J. S. Dewar, *J. Am. Chem. Soc.* 1989, **111**, 5636.