Phosphate Ester Cleavage with a Zinc Hydroxide Complex. Formation and Crystal Structure of a Dinuclear Zinc Complex Bridged with a Phosphate Monoester

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The P–O bond in tris- or bis-phosphate ester is cleaved by a hydroxo zinc(II) complex to give a dinuclear μ-phosphate monoester complex **3**, monomeric phosphate diester complex **4** and phenoxo complex **5**.

Hydrolysis of phosphate esters catalysed by zinc-containing enzymes is an important biochemical process. For example, alkaline phosphatase[1] catalyses non-specific hydrolysis of phosphate monoesters and Klenow fragment of *Escherichia coli* DNA polymerase I[2] which is responsible for hydrolytic cleavage of the phosphodiester backbone of DNA. The catalytic role of zinc is ascribed to the binding and activation of substrates, whereas deprotonation of coordinated water to produce a nucleophilic zinc hydroxide is also proposed as an essential catalytic function. Although several synthetic model studies on hydrolysis of phosphate esters have been reported,[3] most of these have been accomplished with metals such as Co^{3+} and Cu^{2+}; few of the structural and reaction aspects of zinc hydroxide species toward binding and activation of phosphate esters are known.

Treatment of $Zn(OAc)_2{\cdot}2H_2O$ with KL[4] [L denotes hydrotris(3,5-diisopropyl-1-pyrazolyl)borate] in CH_2Cl_2 gave LZn(OAc) **1** almost quantitatively. Subsequent treatment of **1** with NaOH (aq.; 0.1 mol dm^{-3}) in diethyl ether under argon afforded LZn(OH) **2**. Although the crystal structure of **2** could not be determined because of its extremely high solubility, we infer that **2** is monomeric on the basis that an analogous hydroxo zinc complex with a hindered tris(pyrazolyl)borate ligand is monomeric as was recently reported by Parkin and coworkers.[5]

Treatment of **2** with 0.5 equiv. of mono(*p*-nitrophenyl)-phosphate in Et_2O under argon quantitatively yielded a novel μ-phosphate complex LZn[OP(O)($OC_6H_4NO_2$)O]ZnL **3**.† The crystal structure of **3** is presented in Fig. 1. Both zinc(II) ions in **3** adopt a slightly distorted tetrahedral coordination environment with the phosphate group bridging in a *syn–anti* mode. Although several other metal complexes[6] containing a bridging phosphate group are known, **3** is the first dinuclear zinc complex solely bridged with a phosphate. A similar structure is known for the dinuclear zinc site in *E. coli* alkaline phosphatase;[1] while the coordination mode of the phosphate is *syn–syn*. Accordingly, the Zn–Zn separation is considerably shorter than that found in **3** (3.9 *vs.* 5.1 Å). The phosphate monoester bound in **3** is quite stable, being ineffective for further hydrolytic reaction with **2**.

The treatment of **2** with 1 equiv. of bis(*p*-nitrophenyl)-phosphate gave a monomeric phosphate complex LZn[OP(O)($OC_6H_4NO_2$)$_2$] **4** as a sole product. In the presence of an excess of **2**, however, initially produced **4** reacts further with **2**, resulting in formation of LZn($OC_6H_4NO_2$) **5** and **3**. The X-ray analysis of **5** established its monomeric structure; the coordination structure is best described as distorted tetrahedral with a N_3O ligand donor set. The reaction of tris(*p*-nitrophenyl)phosphate with **2** also causes facile hydrolytic P–O bond cleavage, affording a kinetic mixture of **3**, **4** and **5**. For instance, the treatment of the tris-phosphate ester with 5 equiv. of **2** in MeCN at room temperature for 40 h gave a mixture of **3** (12.5), **4** (25) and **5** (62.5%). The formation of **3**, **4** and **5** from the tris- or bis-phosphate ester is explained in terms of the consecutive reactions illustrated in Scheme 1. Here, the P–O bond cleavage of the tris-phosphate with **2** is much faster than the

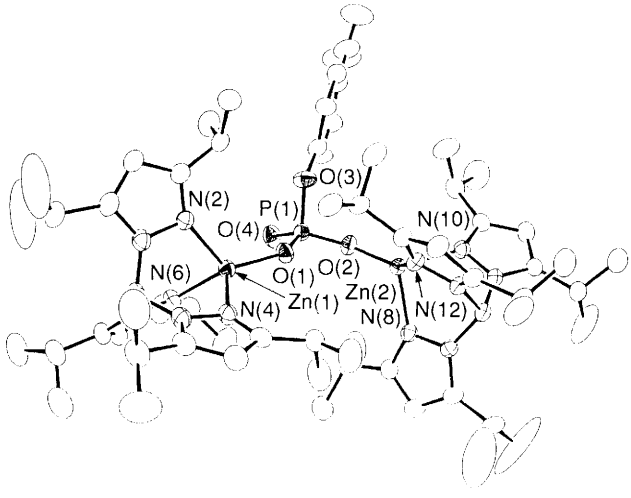
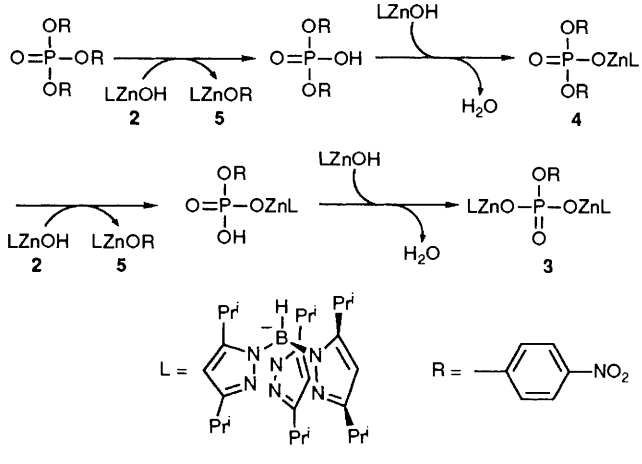


Fig. 1 ORTEP drawing of LZn[OP(O)($OC_6H_4NO_2$)O]ZnL **3**. The selected bond distances (Å) and angles (°) are: Zn(1)–O(1), 1.871(5); Zn(1)–N(2), 2.046(6); Zn(1)–N(4), 2.016(4); Zn(1)–N(6), 2.028(6); Zn(2)–O(2), 1.868(5); Zn(2)–N(8), 2.011(5); Zn(2)–N(10), 2.031(6); Zn(2)–N(12), 2.027(5); P(1)–O(1), 1.519(4); P(1)–O(2), 1.510(6); P(1)–O(3) 1.643(4); P(1)–O(4), 1.454(5); Zn(1)···Zn(2), 5.137(2); Zn(1)–O(1)–P(1), 138.3(3); Zn(2)–O(2)–P(1), 134.9(3); O(1)–P(1)–O(2), 110.8(3).



† *Spectroscopic and crystallographic data* for **3** ($C_{60}H_{96}N_{13}O_6B_2Zn_2P$): IR (KBr, ν/$cm^{-1}$): 2552 (BH), 1604 (Ph–C=C), 1593 (NO), 1342(NO), 1236 (PO). ^{1}H NMR (270 MHz, $CDCl_3$) δ 1.11 (d *J* 7.0 Hz, 36H, $CHMe_2$), 1.23 (d, *J* 7.0 Hz, 36H, $CHMe_2$), 3.38 (m, *J* 7.0 Hz, 12H, $CHMe_2$), 5.79 (s, 6H, *pz-4*), 7.65 (d, *J* 9.2 Hz, 2H, *Ph*) 8.16 (d, *J* 9.2 Hz, 2H, *Ph*). ^{13}C NMR (67 MHz, $CDCl_3$) δ 23.3 ($CHMe_2$), 23.5 ($CHMe_2$), 26.1 ($CHMe_2$), 26.9 ($CHMe_2$), 97.2 (pz–*C*–H), 119.7 (Ph–*2,6–C*) 125.1 (Ph–*3,5–C*), 141.4 (Ph–*4–C*), 156.2 (pz–C=N), 160.5 (pz–C=N), 161.2 (Ph–*1–C*). ^{31}P NMR [40 MHz, $CDCl_3$ (reference 85%-H_3PO_4)]: δ –4.7. FDMS (m/z): 1274 (**3**–4–H). **3** crystallized in the triclinic space groupe $P\bar{1}$ with a = 13.963(7) Å, b = 23.213(7) Å, c = 13.852(7) Å, α = 93.17(4)°, β = 118.39(4)°, γ = 104.64(3)°, V = 3739(3) Å^3, Z = 2, D_c = 1.16 g cm^{-3}. The structure was solved by the direct method, and refined with anisotropic thermal parameters for all non-hydrogen atoms. The final $R(R_W)$ value was 4.83 (7.64)% for 7009 reflections ($F_o \geq 6\sigma F_o$, $5° \leq 2\theta \leq 45°$).

Atomic coordinates, bond lengths and angles, and thermal parameters have been deposited at the Cambridge Crystallographic Data Centre. See Notice to Authors, Issue No. 1.

reaction between **4** and **2**. The slower rate of the P–O bond cleavage in **4**, as well as the inertness of **3**, indicates the critical role of the steric hindrance in these reactions. Thus, the present hydrolytic cleavage of the P–O bond by **2** seems to proceed within the zinc coordination sphere of **2**, presumably *via* a concerted mechanism.

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