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Tetra-μ-benzoato-κ^8O:O'-bis({1-[(3,4-dimethoxyphenyl)methyl]-6,7-dimethoxyisoquinoline-κN}zinc(II)): the first crystal structure with papaverine as a ligand

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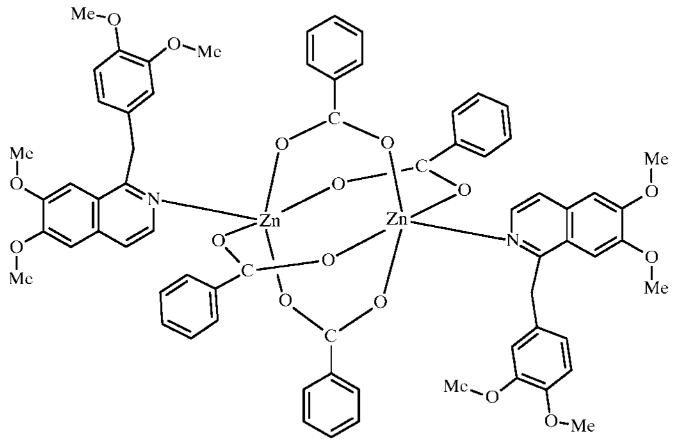
The title complex, $[Zn_2(C_7H_5O_2)_4(C_{20}H_{21}NO_4)_2]$, forms dimers of the paddle-wheel cage type located at crystallographic inversion centres. The two Zn atoms [Zn···Zn = 3.0533 (4) Å] are connected by four *syn–syn* benzoate ligands. The apical positions of the square-pyramidal zinc coordination polyhedra are occupied by the N atoms of the papaverine ligand. Upon coordination, the mutual orientation of the phenyl and isoquinoline rings in papaverine is changed compared with that in the uncoordinated ligand.

Comment

Papaverine, or 1-[(3,4-dimethoxyphenyl)methyl]-6,7-dimethoxyisoquinoline, is an alkaloid that is used as a vasodilator in cardiac and kidney surgery (Ali *et al.*, 1997; Zacherl *et al.*, 2002). When applied to human organisms, it can interact with a number of metal ions present in the body. One way to understand these metal–drug interactions is to study structures of metal complexes containing the drug as a ligand. There are a number of examples of such structural studies (Cini, 2000), although reports dealing with properties of metal complexes of papaverine are scarce (*e.g.* Sabirov *et al.*, 1994; Melník *et al.*, 1996; Györyová *et al.*, 2002; Williams *et al.*, 2003). The crystal structures of papaverine and its hydrochloride salt have already been described (Marek *et al.*, 1996; Reynolds *et al.*, 1974). Moreover, the papaverinium cation as the counterion in a cobalt-containing complex has been structurally characterized (Sabirov *et al.*, 1994). However, the Cambridge Structural Database (Allen, 2002) does not contain an entry of a crystal structure with papaverine as a ligand. The present study fills this gap; we describe here the structure of a zinc(II) benzoate complex, (I), of papaverine.

The molecular structure of (I) (Fig. 1) consists of discrete centrosymmetric $[Zn_2(C_6H_5COO)_4(C_{20}H_{21}NO_4)_2]$ dimers of the paddle-wheel cage type, with an inversion centre located at the mid-point of the Zn···Zn vector. This structure type was first described in 1953 for copper acetate monohydrate (van Nieker & Schoening, 1953) and has since been observed for a variety of transition metals (Mehrotra & Bohra, 1983). In the structure of (I), the pair of Zn^{II} atoms is bridged by four *syn–syn* benzoate ligands. The O atoms of these ligands are positioned in the basal plane of a tetragonal pyramid around each Zn^{II} atom ($\tau = 0.0$; Addison *et al.*, 1984), while the apical position is occupied by the N atom of the papaverine molecule. The Zn atom is shifted 0.412 (1) Å from the basal plane toward the apical position. Among Zn^{II}–carboxylate complexes, a similar coordination type was found in some aliphatic carboxylates, for example, acetate (Singh *et al.*, 1997) and crotonate (Clegg *et al.*, 1986, 1995).



(I)

The average Zn—O bond length [2.048 (8) Å; Table 1] is slightly longer than those observed for structurally characterized paddle-wheel zinc(II) complexes of formula $[Zn_2(RCOO)_4L_2]$, with average values of 2.043 Å (where *R*COO is crotonate and *L* is quinoline; Clegg *et al.*, 1986), 2.037 Å (where *R*COO is crotonate and *L* is 4-cyanopyridine; Clegg *et al.*, 1995), 2.038 and 2.041 Å (where *R*COO is acetate and *L* is pyridine; Singh *et al.*, 1997), and 2.034, 2.039 or 2.042 Å (where *R*COO is indomethacin and *L* is 1-methylpyrrolidinone, pyridine or dimethylacetamide; Zhou *et al.*, 2000). As a consequence, the Zn···Zn separation [3.0533 (4) Å] in (I) is longer than those in the above-mentioned complexes, which exhibit Zn···Zn separations of less than 3 Å.

The geometric parameters in the papaverine ligand are close to those observed for the free base (Marek *et al.*, 1996). The most remarkable differences were observed in the O5—C31 [1.384 (3) Å] and O6—C32 [1.381 (4) Å] bond lengths, which are shorter than the respective values in free papaverine [1.415 (5) Å (2×); Marek *et al.*, 1996]. This difference may be due to the strongly anisotropic displacement parameters within the peripheral groups. Moreover, as a result of the

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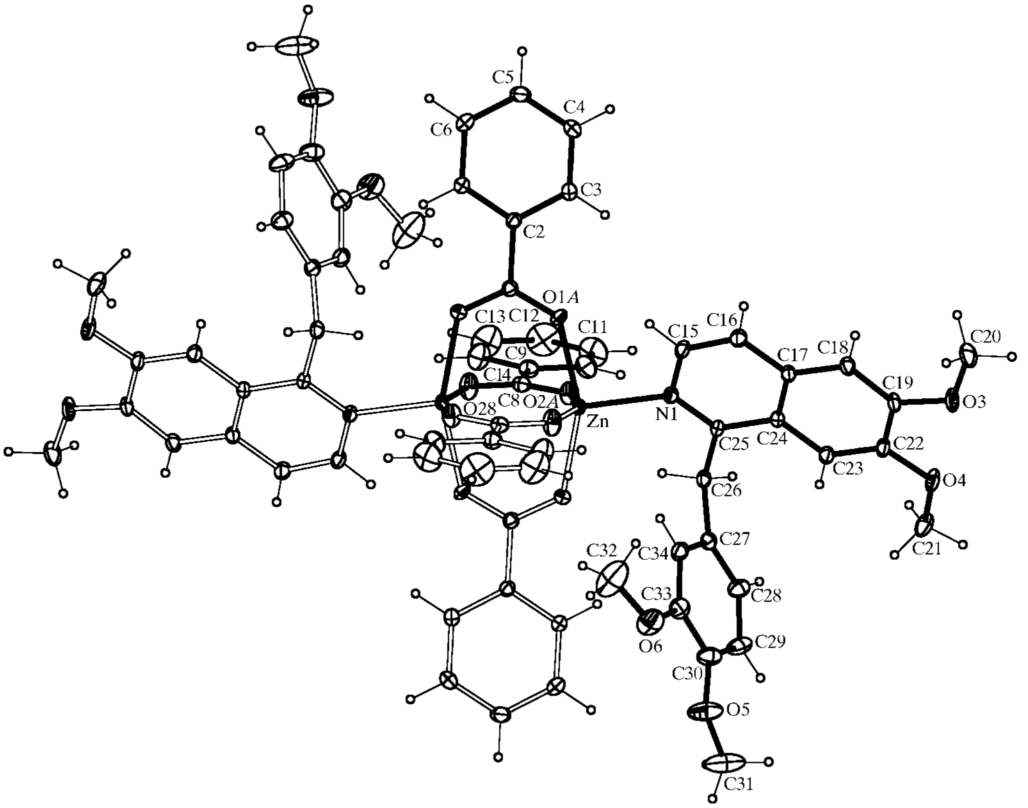

Figure 1
A view of the title centrosymmetric dimer, with the atom-labelling scheme. Displacement ellipsoids are drawn at the 30% probability level and H atoms are shown as spheres of arbitrary radii.

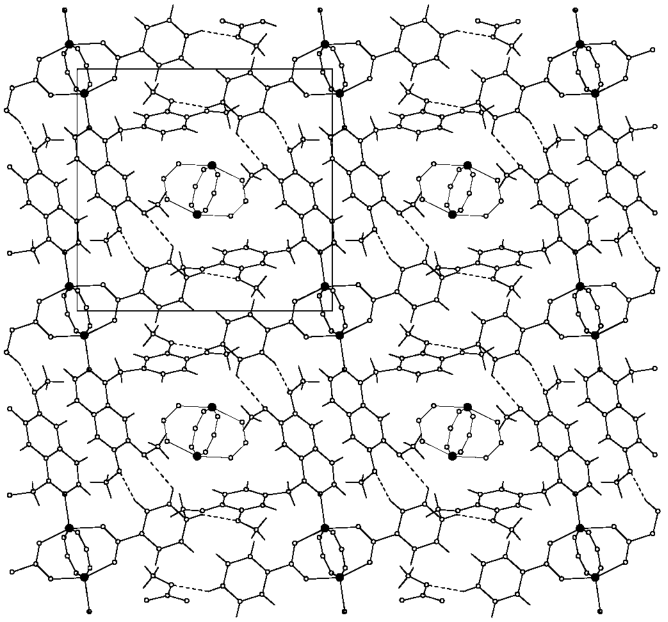

Figure 2
A view along the *a* axis, showing the intermolecular C—H···O contacts (dashed lines) in the planes parallel to *bc*. One such plane is displayed fully. For the adjacent plane, only the dimeric cages (grey) are shown for the sake of clarity. Benzoate ligands not involved in the contacts have also been omitted.

coordination of papaverine, a change in the orientation of the phenyl and isochinoline rings is observed. The C25—C26—C27 angle [112.2 (1)°] changes only slightly [115.2 (3)° in the free base, 112.2° in the hydrochloride and 113.8 (8)° in the cobalt complex containing the papaverinium cation]. More important changes are observed in the torsion angles. The C28—C27—C26—C25 torsion angle in (I) is −134.1 (2)°, while the angles in free papaverine and papaverine hydrochloride are 117.9 (4) and 80.5°, respectively (Marek *et al.*, 1996; Reynolds *et al.*, 1974). The value of this torsion angle in the cobalt complex containing the papaverinium cation is 63 (1)° (Sabirov *et al.*, 1994). Similarly, a difference was observed in the C27—C26—C25—N1 torsion angle [−106.6 (2)°, *c.f.* 112.7 (3)° in the free base, 84.8° in the hydrochloride salt and −112.8 (9)° in the cation in the cobalt complex]. This change in the mutual orientation of the rings may be a result of both steric hindrance of benzoate ligands and non-bonding interactions.

From the composition of complex (I), it is obvious that no conventional hydrogen bonds can be expected in the structure. The molecules are held together only by C—H···O and van der Waals interactions. The most important C—H···O intermolecular contacts shorter than the sum of the van der Waals radii are shown in Fig. 2 and listed in Table 2. These C—H···O intermolecular interactions connect the dimers into sheets parallel to the *bc* plane.

Experimental

In a typical procedure, papaverine hydrochloride (5 g, 13.30 mmol) was dissolved in water (150 ml). To this solution, an equimolar amount of sodium hydroxide (0.532 g) dissolved in water (25 ml) was added dropwise with vigorous stirring. The precipitated white papaverine powder was filtered off, washed with water and dried. Sodium benzoate (0.5 g, 3.47 mmol) dissolved in absolute ethanol (25 ml) was mixed with an ethanol solution (25 ml) of zinc chloride (0.236 g, 1.73 mmol). After the solution had been stirred for 30 min, it was filtered and an ethanol solution (30 ml) of papaverine (1.178 g, 3.47 mmol) was added to the filtrate. The reaction mixture was stirred for 1 h, and then filtered and left to stand at room temperature. Within a week, colourless crystals appeared. Recrystallization from ethanol gave crystals suitable for X-ray diffraction.

Crystal data

$[Zn_2(C_7H_5O_2)_4(C_{20}H_{21}NO_4)_2]$
$M_r = 1293.98$
Monoclinic, $P2_1/n$
$a = 14.1780\ (9)$ Å
$b = 14.4118\ (6)$ Å
$c = 15.5442\ (11)$ Å
$\beta = 101.799\ (8)°$
$V = 3109.0\ (3)$ Å^3
$Z = 2$
$D_x = 1.382$ Mg m^{-3}
Mo $K\alpha$ radiation
Cell parameters from 8002 reflections
$\theta = 3.0$–$30.3°$
$\mu = 0.84$ mm^{-1}
$T = 193\ (1)$ K
Block, colourless
$0.60 \times 0.45 \times 0.38$ mm

Data collection

Stoe IPDS diffractometer
φ scans
Absorption correction: multi-scan (*XPREP* in *SHELXTL*; Sheldrick, 1996)
$T_{\min} = 0.659$, $T_{\max} = 0.737$
45 411 measured reflections
8890 independent reflections
5836 reflections with $I > 2\sigma(I)$
$R_{\rm int} = 0.057$
$\theta_{\max} = 30.4°$
$h = -20 \rightarrow 20$
$k = -19 \rightarrow 18$
$l = -22 \rightarrow 22$

Refinement

Refinement on F^2
$R[F^2 > 2\sigma(F^2)] = 0.036$
$wR(F^2) = 0.088$
$S = 0.91$
8890 reflections
402 parameters
H-atom parameters constrained
$w = 1/[\sigma^2(F_o^2) + (0.05P)^2]$ where $P = (F_o^2 + 2F_c^2)/3$
$(\Delta/\sigma)_{\max} < 0.001$
$\Delta\rho_{\max} = 0.60$ e Å^{-3}
$\Delta\rho_{\min} = -0.69$ e Å^{-3}

155 reflections are missing from the data set [up to $\sin(\theta)/\lambda = 0.6$] as a result of the use of an IPDS one-circle imaging-plate diffractometer system. All H atoms were found in a difference map and then treated as riding, with $U_{\rm iso}$(H) values equal to $1.2U_{\rm eq}$(C) [or $1.5U_{\rm eq}$(C) for the methyl groups].

Data collection: *EXPOSE* (Stoe & Cie, 1999); cell refinement: *CELL* (Stoe & Cie, 1999); data reduction: *INTEGRATE* (Stoe & Cie, 1999); program(s) used to solve structure: *SHELXS*97 (Sheldrick, 1997); program(s) used to refine structure: *SHELXL*97 (Sheldrick, 1997); molecular graphics: *DIAMOND* (Brandenburg, 2000); software used to prepare material for publication: *SHELXL*97 and *enCIFer* (Smith & Johnson, 2002).

Supplementary data for this paper are available from the IUCr electronic archives (Reference: SK1689). Services for accessing these data are described at the back of the journal.

Table 1
Selected geometric parameters (Å, °).

Zn—O2*A*	2.0404 (12)	Zn—O2*B*$^{\rm i}$	2.0562 (13)
Zn—O1*A*	2.0470 (13)	Zn—N1	2.0812 (16)
Zn—O1*B*$^{\rm i}$	2.0494 (14)	Zn···Zn$^{\rm i}$	3.0533 (4)
O2*A*—Zn—O1*A*	87.17 (6)	O1*A*—Zn—N1	93.79 (6)
O2*A*—Zn—O1*B*$^{\rm i}$	87.24 (6)	O1*B*$^{\rm i}$—Zn—N1	109.50 (6)
O1*A*—Zn—O1*B*$^{\rm i}$	156.69 (6)	O2*B*$^{\rm i}$—Zn—N1	96.86 (6)
O2*A*—Zn—O2*B*$^{\rm i}$	156.84 (6)	O1*B*—C1—O1*A*	125.01 (17)
O1*A*—Zn—O2*B*$^{\rm i}$	89.17 (7)	O2*B*—C8—O2*A*	125.90 (16)
O2*A*—Zn—N1	106.20 (6)	C25—C26—C27	112.22 (13)

Symmetry code: (i) $-x, -y, -z$.

Table 2
Short intermolecular C—H···O contacts (Å) and angles (°) for compound (I).

D—H···*A*	*D*—H	H···*A*	*D*···*A*	*D*—H···*A*
C3—H3···O3$^{\rm ii}$	0.95	2.53	3.364 (2)	147
C4—H4···O4$^{\rm ii}$	0.95	2.68	3.312 (2)	125
C5—H5···O6$^{\rm iii}$	0.95	2.70	3.454 (2)	137

Symmetry codes: (ii) $-x, 1-y, -z$; (iii) $x, y, z-1$.

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