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(*N*-{[4-(1,3-Benzothiazol-2-yl)-anilino]carbonylmethyl-κO}iminodiacetato-$\kappa^3 O,N,O'$)(1,10-phenanthroline-$\kappa^2 N,N'$)cobalt(II) pentahydrate

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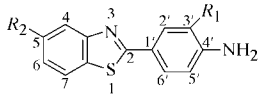
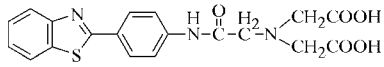
The title compound, $[Co(C_{19}H_{15}N_3O_5S)(C_{12}H_8N_2)]\cdot 5H_2O$, has a moderately distorted octahedral coordination environment composed of two N atoms of a 1,10-phenanthroline ligand and one N and three O atoms of an *N*-{[4-(1,3-benzothiazol-2-yl)anilino]carbonylmethyl}iminodiacetate (ZL-5^{2-}) ligand. The ring systems of the phenanthroline and ZL-5^{2-} ligands are coplanar and the complexes pack in layers parallel to the *ab* plane with the rings of adjacent complexes facing one another. The layers stack along the *c* axis and are linked by hydrogen bonds involving the five water solvent molecules in the asymmetric unit and O atoms of the acetate groups of the ZL-5^{2-} ligand. This is believed to be the first crystal structure of a complex of a 2-(4-aminophenyl)benzothiazole ligand.

Comment

In recent years, much effort has been directed towards the identification and characterization of novel potent and selective anticancer ligand molecules. 2-(4-Aminophenyl)benzothiazole (CJM 126) is an intriguing compound which emanated from a drug discovery programme initially aimed at developing tyrosine kinase inhibitors (Stevens *et al.*, 1994). Novel 2-(4-aminophenyl)benzothiazoles possess remarkably selective antitumour properties (Bradshaw, Wrigley *et al.*, 1998; Bradshaw, Shi *et al.*, 1998) and represent a mechanistic class distinct from clinically used chemotherapeutic agents. The original (unsubstituted) member of this series, namely 2-(4-aminophenyl)benzothiazole, was found to exhibit potent and selective activity against certain breast carcinoma cell lines *in vitro* (*e.g.* MCF-7 and MDA 468, $IC_{50} < 1$ n*M*) (Bradshaw *et al.*, 2002) irrespective of oestrogen receptor status and with an unusual biphasic dose–response relationship (Shi *et al.*, 1996). Derivatives such as 2-(4-amino-3-methylphenyl)benzothiazole (DF203, NSC 67449) and 2-(4-amino-3-methylphenyl)-5-fluorobenzothiazole (5F203, NSC 703786) were selected as lead candidates for further development on the basis of superior *in vivo* activity (Bradshaw, Wrigley *et al.*, 1998; Bradshaw, Shi *et al.*, 1998; Bradshaw *et al.*, 2001). In selective cytotoxicity experiments on various tumour cell lines, *N*-{[4-(1,3-benzothiazol-2-yl)anilino]carbonylmethyl}iminodiacetic acid (ZL-5) shows obvious inhibition activity on MCF-7 breast tumour cells.

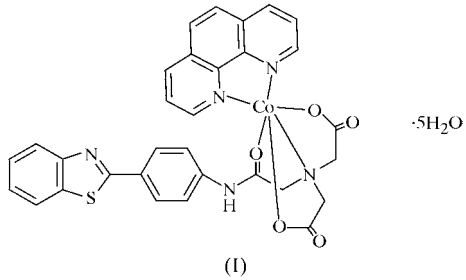


CJM216: R_1=H, R_2=H
DF203: R_1=Me, R_2=H
5F203: R_1=Me, R_2=F



ZL-5

Our interest has focused on the coordination chemistry of 2-(4-aminophenyl)benzothiazole with metals *via* linking to other groups such as iminodiacetic acid. We successfully synthesized ZL-5 and its complex with Co^{II}, (I). As far as we know, this is the first crystal structure of a 2-(4-aminophenyl)benzothiazole complex. There are a few reports of structures involving benzothiazole derivatives, for example, 2-(2-hydroxyphenyl)benzothiazole (Yu *et al.*, 2003; Tong *et al.*, 2005), 2-phenylbenzothiazole (Churchill *et al.*, 1980; Laskar *et al.*, 2005), 2-mercaptobenzothiazole (Brandenburg *et al.*, 1987; Cheng *et al.*, 1995) and 2-(pyridin-2-yl)benzothiazole (Hu *et al.*, 1990; He *et al.*, 2004). These compounds vary mainly in the group at the 2-position of the benzothiazole and they are different from ZL-5, where 2-(4-aminophenyl)benzothiazole is conjugated to iminodiacetic acid though a $-CH_2CO-$ group. Moreover, in their complexes they all coordinate to the metals through one N atom and other atoms from the benzothiazole moiety (Churchill *et al.*, 1980; Laskar *et al.*, 2005; Duatti *et al.*, 1988; Pyrz *et al.*, 1991). By contrast, the Co^{II} atom in (I) does not coordinate to ZL-5 through the 2-(4-aminophenyl)-benzothiazole group, but rather through one N and two O atoms of the iminodiacetate, and one amide O atom.



(I)

Compound (I) contains a [Co(ZL-5)(phen)] complex (phen is 1,10-phenanthroline) and five water molecules in the asymmetric unit (Fig. 1). Each Co^{II} ion is bonded to two pyridine N atoms of the bidentate phen ligand, and one iminodiacetate N atom and three O atoms from the tetradentate ZL-5^{2-} ligand. This ligand set generates a slightly distorted octahedral geometry, with three N atoms and one amide O atom occupying the equatorial plane, and two carboxylate O atoms from iminodiacetate occupying the axial positions. Bond angles in the coordination sphere that differ

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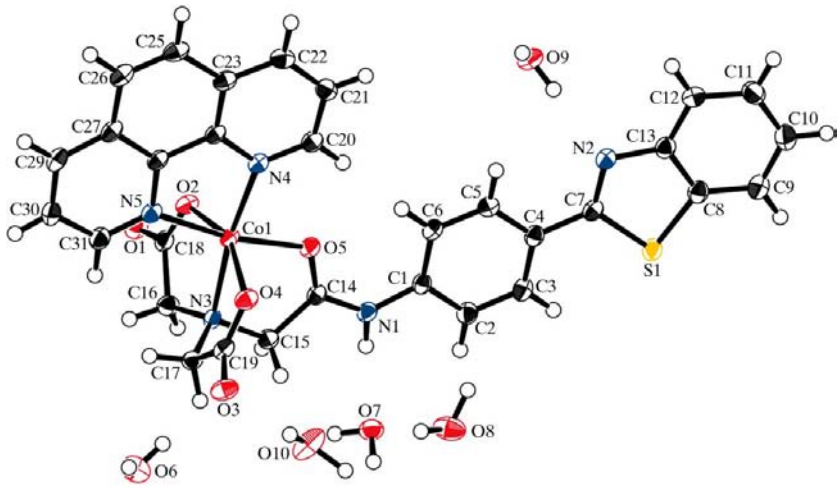

Figure 1
A view of (I), showing the atom-numbering scheme. Displacement ellipsoids are drawn at the 50% probability level and H atoms are shown as small spheres of arbitrary radii.

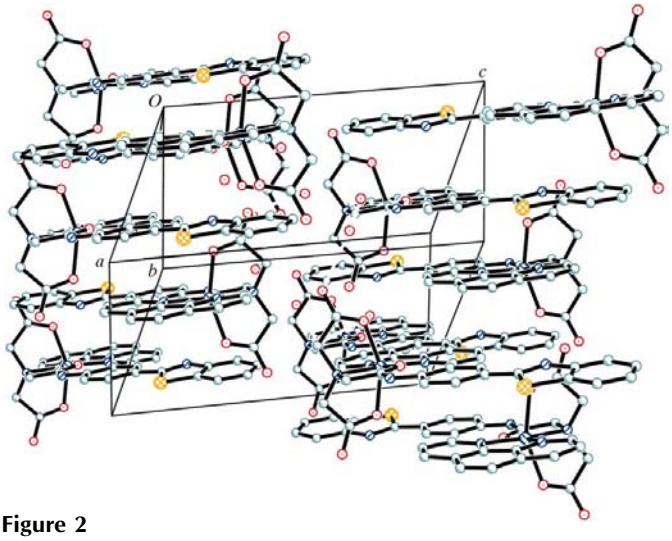

Figure 2
A packing diagram for (I), showing the π–π interactions along the *b* direction.

from ideal values by more than 10° are given in Table 1. This is the first structure in which iminodiacetic acid is linked with benzothiazole by a –CH_2CO– group, allowing ZL-5^{2-} to act as a tetradentate ligand. This is a rare coordination mode for an *N*-(*N*′-substituted acetamide)iminodiacetic acid compound compared with reported examples (Kanamori *et al.*, 2001; Radanović *et al.*, 2003). The presence of the –CH_2CO– spacer introduces sufficient flexibility to permit a coplanar arrangement of the planes of the phen and ZL-5^{2-} ligands [dihedral angle = 3.293 (2)°].

In the crystal structure of (I), adjacent complexes are packed into layers in the *ab* plane so as to afford face-to-face π–π interactions between the benzothiazole plane of one molecule and the phen plane of an adjacent molecule along the *b* direction (Fig. 2). The observed stacking in these molecules, with an interplanar distance of about 3.343 (2) Å, is similar to those encountered in the base stacking of DNA. Thus, the whole structure may easily bind to DNA in an intercalative mode. The layers stack in the *c* direction and are held together by a network of hydrogen bonds involving the five solvent water molecules in the asymmetric unit and the O and N atoms of the ZL-5^{2-} ligand molecules (Table 2).

A prominent feature of the title complex is the presence of an iminodiacetate group on the parent heterocyclic ring in ZL-5^{2-}. When bonded to the Co^{II} ion, it readily makes the metal coordination environment saturated without much steric hindrance, and each carboxyl group is deprotonated to form a charge-neutral complex. Charge neutrality is an important characteristic for biological activity, allowing mobilization of intracellular metal ions through the cell membrane. Furthermore, the solubility of the complex is improved compared with that of 2-(4-aminophenyl)benzothiazole (CJM 126) by the introduction of the hydrophilic iminodiacetate group.

Experimental

In a 250 ml round-bottomed flask equipped with a magnetic stirrer and a condenser were placed 2-(4-chloroacetamidophenyl)benzothiazole (5 g, 0.0165 mol), iminodiacetic acid (2.42 g, 0.0182 mol), sodium carbonate (3.0 g, 0.028 mol) and 75% ethanol solution (200 ml). The stirred mixture was heated under reflux for 12 h, after which the solid was precipitated at pH 2.5 with 5% HCl. The crude product was collected by filtration, washed with water and ethanol, and crystallized from absolute ethanol to afford ZL-5 (6.1 g, 0.015 mol, 91%) as a green powder. Orange platelet crystals of (I) were obtained by slow evaporation of a dimethylformamide solution of ZL-5, 1,10-phenanthroline and $CoCl_2·6H_2O$ (molar ratio 1:1:1) at room temperature.

Crystal data

$[Co(C_{19}H_{15}N_3O_5S)(C_{12}H_8N_2)]·5H_2O$	β = 102.770 (2)°
M_r = 726.62	γ = 97.389 (2)°
Triclinic, $P\overline{1}$	V = 1559.39 (17) Å^3
a = 8.9990 (7) Å	Z = 2
b = 12.7766 (7) Å	Mo $K\alpha$ radiation
c = 14.0652 (8) Å	μ = 0.69 mm^{-1}
α = 92.661 (2)°	T = 123.1 K
	0.50 × 0.50 × 0.20 mm

Data collection

Rigaku R-AXIS RAPID diffractometer
Absorption correction: multi-scan (*ABSCOR*; Higashi, 1995)
T_{min} = 0.703, T_{max} = 0.872
15300 measured reflections
7094 independent reflections
6151 reflections with $F^2 > 2\sigma(F^2)$
R_{int} = 0.030

Refinement

$R[F^2 > 2\sigma(F^2)]$ = 0.041
$wR(F^2)$ = 0.117
S = 1.12
7094 reflections
434 parameters
H atoms treated by a mixture of independent and constrained refinement
$\Delta\rho_{max}$ = 0.56 e Å^{-3}
$\Delta\rho_{min}$ = −0.83 e Å^{-3}

Table 1
Selected geometric parameters (Å, °).

Co1—O2	2.0728 (11)	Co1—N3	2.1973 (16)
Co1—O4	2.0577 (13)	Co1—N4	2.1007 (16)
Co1—O5	2.0943 (14)	Co1—N5	2.1680 (16)
O2—Co1—O4	154.50 (5)	O4—Co1—N3	78.63 (5)
O2—Co1—N3	79.77 (5)	N3—Co1—N5	109.17 (5)
O2—Co1—N4	104.18 (5)	N4—Co1—N5	78.15 (6)

Table 2
Hydrogen-bond geometry (Å, °).

D—H···A	D—H	H···A	D···A	D—H···A
O6—H6A···O8^{i}	0.90	1.87	2.763 (2)	170
O6—H6B···O3	0.87	1.88	2.739 (2)	170
O7—H7A···O1^{ii}	0.92	1.91	2.810 (2)	168
O7—H7B···O6^{iii}	0.92	1.80	2.699 (2)	164
O8—H8A···O7	0.92	2.00	2.906 (2)	168
O8—H8B···O9^{iv}	0.98	1.84	2.764 (2)	156
O9—H9A···O3^{v}	0.88	1.88	2.752 (2)	172
O9—H9B···N2	0.88	2.01	2.879 (2)	172
O10—H10A···O3	1.02	2.02	2.905 (2)	144
O10—H10B···O2^{ii}	1.03	1.94	2.957 (2)	169
N1—H1···O7	0.88	2.02	2.882 (2)	168

Symmetry codes: (i) $x, y-1, z$; (ii) $x-1, y, z$; (iii) $-x+1, -y+1, -z+1$; (iv) $-x+1, -y+2, -z$; (v) $-x+1, -y+1, -z$.

The positional parameters of the water and imine H atoms were calculated on the basis of the positions of their parent atoms, with U_{iso}(H) = 1.5U_{eq}(O,N). All other H atoms were located in difference Fourier maps and then regenerated at ideal positions and treated as riding, with aromatic C—H = 0.95 Å and alkyl C—H = 0.99 Å, and with U_{iso}(H) = 1.2U_{eq}(C).

Data collection: *PROCESS-AUTO* (Rigaku, 1998); cell refinement: *PROCESS-AUTO*; data reduction: *CrystalStructure* (Rigaku/MSC, 2006); program(s) used to solve structure: *SIR97* (Altomare *et al.*, 1999); program(s) used to refine structure: *SHELXL97* (Sheldrick, 2008); molecular graphics: *ORTEP-3* (Farrugia, 1997); software used to prepare material for publication: *CrystalStructure*.

Supplementary data for this paper are available from the IUCr electronic archives (Reference: SQ3122). Services for accessing these data are described at the back of the journal.

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