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[*N,N*-Bis(2-chloroethyl)-1,2-ethanediamine-*N,N'*]bis(3-methyl-2,4-pentanedionato-*O,O'*)cobalt(III) Perchlorate: a Potential Hypoxia Selective Anticancer Agent

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Abstract

The crystal structure of the title complex, [Co(C₆H₉O₂)₂(C₆H₁₄Cl₂N₂)]ClO₄ or [Co(Meacac)₂(DCE)]ClO₄, has been determined by X-ray diffraction. The coordination geometry about cobalt is typical of an octahedral tris-chelate complex. The Co—N bond length involving the tertiary N atom of the DCE ligand [2.092 (4) Å] is significantly longer than that to the primary N atom [1.931 (4) Å].

Comment

We have been engaged in the synthesis of cobalt(III) complexes designed to act as selective anticancer drugs. A potent cytotoxin such as the nitrogen mustard DCE is inactive when coordinated to the inert cobalt(III) centre. In a hypoxic environment such as that found in solid tumors, net reduction to the more labile cobalt(II) complex results in release of the free mustard and thus selective delivery of the cytotoxin to the interior of the tumor. The lead compound, [Co(Meacac)₂(DCE)]ClO₄ or (I), has been found in biological assays to exhibit a 30-fold hypoxic selectivity in some cell lines (30 times more cell killing in the absence of air than in its presence). The synthesis, chemistry and biological activity of a series of related compounds have been described previously (Ware, Wilson, Denny & Rickard,

1991; Ware, Palmer, Wilson & Denny, 1993). As a result of widespread interest in this new class of potential anticancer drugs, we have determined the X-ray crystal structure of the lead compound.

The six-coordinate Co atom in the complex shows the expected octahedral coordination geometry, with bond angles in the range 86.8 (2)–94.4 (2) and 175.3 (2)–178.6 (2)°. The Co—O bond lengths to the Meacac O atoms range from 1.868 (3) to 1.877 (4) Å and are all in the lower quartile of the range observed for six-coordinate Co^{III}-pentanedionato complexes, although they are also all within 2σ of the mean (mean = 1.887 Å, σ = 0.013, n = 41; Orpen *et al.*, 1989). The DCE ligand [H₂NCH₂CH₂N(CH₂CH₂Cl)₂] contains both primary and tertiary nitrogen donors. The Co—N1 (primary) bond [1.931 (4) Å] is significantly shorter than the Co—N2 (tertiary) bond [2.092 (4) Å] which is indistinguishable from the longest Co^{III} tertiary N bond length on six-coordinate complexes reported to date. [A search of the Cambridge Structural Database (Allen & Kennard, 1993) revealed 125 structures containing 208 comparable bonds, of which only two, 2.11 (2) Å in ZACDEM (Baxter, Hanton, Simpson, Vincent & Blackman, 1995) and 2.10 (2) Å in PEACOD (Di Vaira, Meli & Sacconi, 1977), were nominally longer than that in the present complex, although the difference is less than 1σ]. These values can be compared with the Co—N bond lengths of 1.988 (14) and 1.961 (12) Å to secondary amines in the closely related compound [Co(Clacac)₂(BCE)]ClO₄, where Clacac is 3-chloro-2,4-pentanedionato and BCE is *N,N'*-bis(2-chloroethyl)-1,2-ethanediamine (Ware *et al.*, 1991).

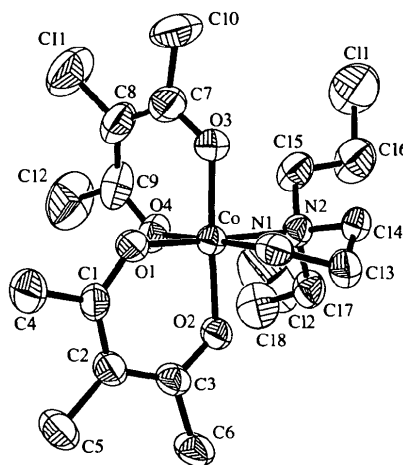
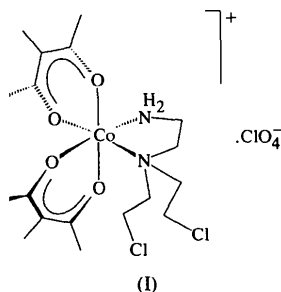


Fig. 1. Cation geometry and the atomic numbering scheme. Atoms are depicted as 50% probability ellipsoids. The Cl2 atom is shown in its position of greater occupancy.

Experimental

The complex as the perchlorate salt was prepared and purified as described in the literature (Ware *et al.*, 1993). Suitable

crystals were obtained by the slow evaporation of a solution of the complex in methanol/0.05 M NaClO₄.

Crystal data

[Co(C₆H₉O₂)₂(C₆H₁₄-Cl₂N₂)]ClO₄

M_r = 569.74

Monoclinic

*P*2₁/*c*

a = 17.229 (3) Å

b = 10.817 (5) Å

c = 14.851 (6) Å

β = 110.78 (3)°

V = 2587.7 (16) Å³

Z = 4

D_x = 1.462 Mg m⁻³

D_m not measured

Data collection

Enraf–Nonius CAD-4 diffractometer

2θ/ω scans

Absorption correction:

empirical via ψ scans

(North, Phillips &

Mathews, 1968)

T_{min} = 0.722, *T_{max}* = 0.859

4307 measured reflections

4049 independent reflections

Mo *K*α radiation

λ = 0.71069 Å

Cell parameters from 25

reflections

θ = 9.5–11.8°

μ = 1.016 mm⁻¹

T = 293 (2) K

Thin plate

0.32 × 0.18 × 0.15 mm

Green

2735 reflections with

I > 2σ(*I*)

R_{int} = 0.023

θ_{max} = 23.98°

h = 0 → 19

k = 0 → 12

l = -16 → 15

3 standard reflections

frequency: 60 min

maximum variation: ±3%

Refinement

Refinement on *F*²

R [*F*² > 2σ(*F*²)] = 0.050

wR (*F*²) = 0.160

S = 1.142

4049 reflections

299 parameters

H atoms riding

w = 1/[σ²(*F_o*²) + (0.0572*P*)² + 6.1844*P*]

where *P* = (*F_o*² + 2*F_c*²)/3

(Δ/σ)_{max} = 0.033

Δρ_{max} = 0.922 e Å⁻³

Δρ_{min} = -0.635 e Å⁻³

Extinction correction: none

Scattering factors from

International Tables for

Crystallography (Vol. C)

Disorder was apparent in the position of Cl2. It was therefore refined as two part-atoms, with occupancies summing to 1.0.

Data collection: *CAD-4 Software* (Enraf–Nonius, 1989). Cell refinement: *CAD-4 Software*. Data reduction: local program. Program(s) used to solve structure: *SHELXS86* (Sheldrick, 1990). Program(s) used to refine structure: *SHELXL93* (Sheldrick, 1993). Molecular graphics: *SHELXTL* (Sheldrick, 1995). Software used to prepare material for publication: *SHELXL93*.

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Supplementary data for this paper are available from the IUCr electronic archives (Reference: BS1025). Services for accessing these data are described at the back of the journal.

References

- Allen, F. H. & Kennard, O. (1993). *Chem. Des. Autom. News*, **8**, 1–31.
- Baxter, K. E., Hanton, L. R., Simpson, J., Vincent, B. R. & Blackman, A. G. (1995). *Inorg. Chem.* **34**, 2795–2796.
- Di Vaira, M., Meli, A. & Sacconi, L. (1977). *Cryst. Struct. Commun.* **6**, 727–731.
- Enraf–Nonius (1989). *CAD-4 Software*. Version 5.0. Enraf–Nonius, Delft, The Netherlands.
- North, A. C. T., Phillips, D. C. & Mathews, F. S. (1968). *Acta Cryst.* **A24**, 351–359.
- Orpen, A. G., Brammer, L., Allen, F. H., Kennard, O., Watson, D. G. & Taylor, R. (1989). *J. Chem. Soc. Dalton Trans.* pp. S1–83.
- Sheldrick, G. M. (1990). *Acta Cryst.* **A46**, 467–473.
- Sheldrick, G. M. (1993). *SHELXL93. Program for the Refinement of Crystal Structures*. University of Göttingen, Germany.
- Sheldrick, G. M. (1995). *SHELXTL*. Version 5. Siemens Analytical X-ray Instruments Inc., Madison, Wisconsin, USA.
- Ware, D. C., Palmer, B. D., Wilson, W. R. & Denny, W. A. (1993). *J. Med. Chem.* **36**, 1839–1846.
- Ware, D. C., Wilson, W. R., Denny, W. A. & Rickard, C. E. F. (1991). *J. Chem. Soc. Chem. Commun.* pp. 1171–1173.

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Bis[aqua(chlorodifluoroacetato-*O*)triphenyltin-1,10-phenanthroline]

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Abstract

The coordinated water molecule in the centrosymmetric title compound [Sn(C₂ClF₂O₂)(C₆H₅)₃(H₂O)]₂·2C₁₂H₈N₂, engages in hydrogen bonding with two heterocycles. The Sn atom shows *trans*-C₃SnO₂ trigonal bipyramidal coordination.

Comment

An earlier study (Ng, Kumar Das & Kennard, 1996) documented the 'outer-sphere coordination' of 1,10-phenanthroline in dimeric bis[aqua(trifluoroacetato)triphenyltin-1,10-phenanthroline]. Despite the difference in electron-withdrawing ability of the F and Cl atoms, the bis[aqua(chlorodifluoroacetato)triphenyltin-1,10-phenanthroline] analogue, (I), is isomorphous with bis[aqua(trifluoroacetato)triphenyltin-1,10-phenanthroline], both compounds crystallizing with matching unit-cell dimensions. The latter compound displays a somewhat longer Sn···H₂O interaction [2.335 (4) Å] but its two hydrogen bonds [2.809 (6) and 2.814 (6) Å] are of the same length as those [2.799 (6) and 2.846 (6) Å] of the