References

Chen, X.-M. & Mak, T. C. W. (1993). *Acta Cryst.* A**49**, C-220.
Chen, X.-M., Wang, R.-Q. & Yu, X.-L. (1995). *Acta Cryst.* C**51**. In the press.
Figgis, B. N., Skelton, B. W. & White, A. H. (1978). *Aust. J. Chem.* **31**, 57–64.
Johnson, C. K. (1965). *ORTEP*. Report ORNL-3794. Oak Ridge National Laboratory, Tennessee, USA.
Sheldrick, G. M. (1990*a*). *SHELXTL/PC User's Manual*. Siemens Analytical X-ray Instruments Inc, Madison, Wisconsin, USA.
Sheldrick, G. M. (1990*b*). *SHELXTL-Plus. An Integrated System for Solving, Refining and Displaying Crystal Structures from Diffraction Data*. Univ. of Göttingen, Germany.
Wada, A., Katayama, C. & Tanaka, J. (1976). *Acta Cryst.* B**32**, 3194–3199.
Yanagi, K., Ohashi, Y., Sasada, Y., Kaizu, Y. & Kobayashi, H. (1981). *Bull. Chem. Soc. Jpn*, **54**, 118–126.

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Bis(acetato)amminedichloro(cyclohexylamine)platinum(IV), an Orally Active Anticancer Drug

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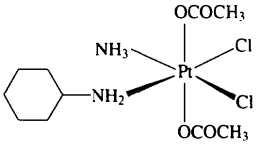
Abstract

The structure of the anticancer drug bis(acetato)-amminedichloro(cyclohexylamine)platinum(IV), $[PtCl_2(C_2H_3O_2)_2(C_6H_{13}N)(NH_3)]$, is reported. The acetato groups are axial to the square plane composed of the chlorine and amine substituents. The cyclohexane ring may sterically hinder one of the acetato groups for metabolic attack. The amine groups are hydrogen bonded to the carbonyl O atoms of the acetato groups.

Comment

The platinum(II) complex cisplatin (*cis*-diamminedichloroplatinum) is an established and effective drug in the treatment of certain cancers, especially testicular and ovarian cancer (Horwich, 1989). However, because of its severe nephrotoxicity, relatively narrow spectrum of activity and lack of activity in tumours with acquired resistance, there has been a continuing search for new platinum compounds that circumvent these problems (Kelland, 1993). It has been found that platinum(IV) alkylamines with axial carboxylate groups show selective cytotoxicity to cisplatin-resistant human tumour cell lines (Kelland *et al.*, 1992). This biological response is due mainly to the lipophilicity of the axial groups combined with activation of the complex *via* reduction to the platinum(II) species. The title compound, JM216, an outstandingly active member of the series (Kelland *et al.*, 1993), is currently being evaluated in clinical trials. Its crystal structure has been determined as part of a study relating structural features to possible patterns of metabolism.



JM216

The title complex has standard octahedral coordination around the Pt^{IV} atom. The two Cl atoms, the ammine group and the cyclohexylamine group are in a square-planar arrangement around the Pt atom. The two acetato groups are axial to this plane (Fig. 1) and the cyclohexane ring adopts a chair conformation. The angle N1—Pt—N2 is significantly greater than 90°.

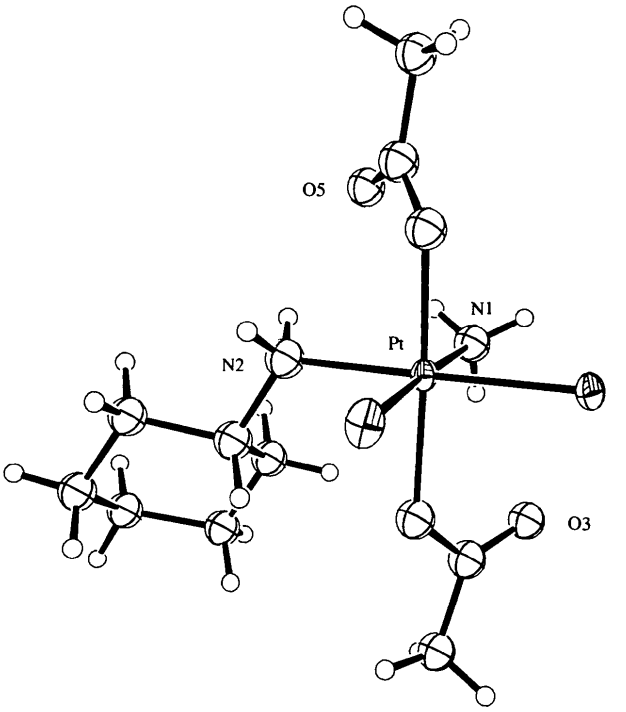


Fig. 1. View of the title molecule (*ORTEX*; McArdle, 1993) showing 50% displacement ellipsoids for the Pt and Cl atoms and the numbering scheme for selected non-H atoms. H atoms are plotted as spheres of arbitrary size.

The two amine ligands, together with the two carbonyl O atoms, are involved in intramolecular hydrogen bonding, which may be responsible for the particular conformations adopted by the acetato groups with respect to the groups in the square plane around the Pt atom. The distances N1···O3 [2.78 (3) Å], N1···O5 [2.84 (3) Å] and N2···O5 [2.86 (3) Å] are all within standard hydrogen-bonding ranges. The carbonyl O5 atom is thus approximately equidistant from the two amine N atoms and the projection of the C3—O5 bond onto the square plane bisects the N1—Pt—N2 angle. The orientation of the cyclohexane ring is asymmetric with respect to the two acetato groups, so that the one below the plane may be more hindered to metabolic attack than the other (Fig. 1). An analogous orientation effect has been noted in the interactions of the Pt^{II} metabolite of JM216 to DNA (Hartwig & Lippard, 1992).

Experimental

Crystals of the title compound were obtained by aqueous dilution of a solution of the complex in *N,N*-dimethylacetamide.

Crystal data

$[PtCl_2(C_2H_3O_2)_2(C_6H_{13}N)(NH_3)]$
$M_r = 500.29$
Monoclinic
$P2_1/a$
$a = 13.588\ (2)$ Å
$b = 8.2860\ (10)$ Å
$c = 14.683\ (2)$ Å
$\beta = 110.510\ (10)°$
$V = 1548.4\ (4)$ Å^3
$Z = 4$
$D_x = 2.146$ Mg m^{-3}
Cu $K\alpha$ radiation
$\lambda = 1.54051$ Å
Cell parameters from 25 reflections
$\theta = 1.5$–$22°$
$\mu = 20.518$ mm^{-1}
$T = 293\ (2)$ K
Plate
0.04 × 0.03 × 0.01 mm
Light yellow

Data collection

Enraf–Nonius CAD-4T diffractometer
$\omega/2\theta$ scans
Absorption correction: refined from ΔF (*DIFABS*; Walker & Stuart, 1983)
$T_{min} = 0.78$, $T_{max} = 0.91$
2063 measured reflections
2063 independent reflections
972 observed reflections [$I > 2\sigma(I)$]
$\theta_{max} = 64.83°$
$h = -11 \rightarrow 11$
$k = 0 \rightarrow 9$
$l = 0 \rightarrow 16$
3 standard reflections
frequency: 60 min
intensity decay: none

Refinement

Refinement on F^2
$R(F) = 0.037$
$wR(F^2) = 0.111$
$S = 0.981$
2063 reflections
92 parameters
$w = 1/[\sigma^2(F_o^2) + (0.1000P)^2]$ where $P = (F_o^2 + 2F_c^2)/3$
$(\Delta/\sigma)_{max} = -0.004$
$\Delta\rho_{max} = 0.547$ e Å^{-3}
$\Delta\rho_{min} = -0.854$ e Å^{-3}
Atomic scattering factors from *International Tables for Crystallography* (1992, Vol. C, Tables 4.2.6.8 and 6.1.1.4)

Table 1. *Fractional atomic coordinates and equivalent isotropic displacement parameters* (Å^2)

U_{iso} for O, N and C; $U_{eq} = (1/3)\Sigma_i\Sigma_j U_{ij} a_i^* a_j^* \mathbf{a}_i.\mathbf{a}_j$ for Pt and Cl.

	x	y	z	U_{eq}/U_{iso}
Pt1	0.11762 (5)	0.17580 (5)	0.17340 (4)	0.0216 (5)
Cl1	0.0599 (3)	−0.0847 (3)	0.1302 (2)	0.028 (2)
Cl2	0.2789 (3)	0.0794 (3)	0.2735 (3)	0.034 (2)
O1	0.0730 (11)	0.1677 (9)	0.2934 (9)	0.029 (2)
O3	−0.0953 (9)	0.1033 (11)	0.2233 (8)	0.039 (2)
O4	0.1750 (11)	0.1814 (9)	0.0645 (9)	0.034 (2)
O5	0.1026 (10)	0.4192 (11)	0.0033 (8)	0.042 (2)
N1	−0.0297 (11)	0.2505 (13)	0.0838 (8)	0.029 (2)
N2	0.1734 (11)	0.4082 (12)	0.2113 (9)	0.030 (2)
C1	−0.0185 (16)	0.1342 (16)	0.2960 (13)	0.030 (3)
C2	−0.0181 (18)	0.1466 (18)	0.3948 (15)	0.046 (4)
C3	0.1556 (14)	0.2945 (15)	−0.0007 (11)	0.029 (3)
C4	0.1949 (18)	0.2656 (20)	−0.0790 (14)	0.048 (4)
C5	0.1673 (13)	0.4863 (14)	0.3000 (11)	0.027 (3)
C6	0.2425 (14)	0.6331 (16)	0.3273 (11)	0.033 (3)
C7	0.2390 (16)	0.7165 (17)	0.4152 (13)	0.039 (3)
C8	0.1314 (17)	0.7659 (20)	0.4028 (14)	0.050 (4)
C9	0.0535 (20)	0.6218 (25)	0.3706 (18)	0.068 (5)
C10	0.0575 (15)	0.5441 (16)	0.2829 (12)	0.037 (3)

Table 2. *Selected geometric parameters* (Å, °)

Pt1—O4	2.01 (2)	Pt1—N2	2.073 (13)
Pt1—O1	2.06 (2)	Pt1—Cl1	2.308 (2)
Pt1—N1	2.067 (13)	Pt1—Cl2	2.312 (3)
O4—Pt1—O1	174.7 (3)	N1—Pt1—Cl1	86.9 (3)
O4—Pt1—N1	92.6 (6)	N2—Pt1—Cl1	178.3 (5)
O1—Pt1—N1	92.6 (6)	O4—Pt1—Cl2	88.2 (3)
O4—Pt1—N2	89.1 (6)	O1—Pt1—Cl2	86.7 (3)
O1—Pt1—N2	89.4 (6)	N1—Pt1—Cl2	177.1 (3)
N1—Pt1—N2	94.3 (4)	N2—Pt1—Cl2	88.5 (3)
O4—Pt1—Cl1	89.5 (3)	Cl1—Pt1—Cl2	90.39 (10)
O1—Pt1—Cl1	91.8 (2)		

The structure was solved by initial location of the Pt atom by direct methods using *SHELXS*86 (Sheldrick, 1990), followed by location of the light atoms from difference electron-density maps. H atoms were placed in calculated positions and refined with a riding model.

Data collection: *CAD-4 Operations Manual* (Enraf–Nonius, 1977). Cell refinement: *CAD-4 Operations Manual*. Data reduction: *MolEN* (Fair, 1990). Program(s) used to solve structure: *SHELXS*86. Program(s) used to refine structure: *SHELXL*93 (Sheldrick, 1993). Molecular graphics: *ORTEX* (McArdle, 1993).

This work was supported by the Cancer Research Campaign. We are grateful to Professor K. R. Harrap for suggesting this problem and to both him and Dr Lloyd Kelland for useful discussions.

Lists of structure factors, anisotropic displacement parameters, H-atom coordinates and complete geometry have been deposited with the IUCr (Reference: CR1156). Copies may be obtained through The Managing Editor, International Union of Crystallography, 5 Abbey Square, Chester CH1 2HU, England.

References

Enraf–Nonius (1977). *CAD-4 Operations Manual*. Enraf–Nonius, Delft, The Netherlands.

Fair, C. K. (1990). *MolEN. An Interactive Intelligent System for Crystal Structure Analysis*. Enraf–Nonius, Delft, The Netherlands.

Hartwig, J. F. & Lippard, S. J. (1992). *J. Am. Chem. Soc.* **114**, 5646–5654.
Horwich, A. (1989). *Br. J. Cancer*, **59**, 156–159.
Kelland, L. R. (1993). *Crit. Rev. Oncol. Hematol.* **15**, 191–219.
Kelland, L. R., Abel, G., McKeage, M. J., Jones, M., Goddard, P. M., Valenti, M., Murrer, B. A. & Harrap, K. R. (1993). *Cancer Res.* **53**, 2581–2586.
Kelland, L. R., Murrer, B. A., Abel, G., Giandomenico, C. M., Mistry, P. & Harrap, K. R. (1992). *Cancer Res.* **52**, 822–828.
McArdle, P. (1993). *J. Appl. Cryst.* **26**, 752.
Sheldrick, G. M. (1990). *Acta Cryst.* A**46**, 467–473.
Sheldrick, G. M. (1993). *SHELXL93. Program for the Refinement of Crystal Structures*. Univ. of Göttingen, Germany.
Walker, N. & Stuart, D. (1983). *Acta Cryst.* A**39**, 158–166.

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Tetrachloropentakis(dimethyl sulfoxide)-diruthenium(II)

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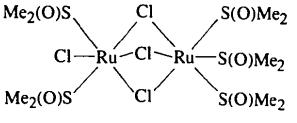
Abstract

Tri-μ-chloro-chloropentakis(dimethyl sulfoxide)diruthenium(II), $[Ru_2Cl\{(CH_3)_2SO\}_5(\mu\text{-}Cl)_3]$ has a face-sharing bioctahedral structure with the common face constructed by three bridging Cl atoms. The metal atoms are separated by 3.245 (2) Å.

Comment

The chemistry of halogen–dimethyl sulfoxide–ruthenium(II) complexes is of considerable current interest because of their antitumour activities (Allesio *et al.*, 1988, 1991). A number of such complexes of Ru^{II} and Ru^{III}, including the title complex, have been reported, but all the structurally characterized species are limited to mononuclear complexes only (Allesio *et al.*, 1991; Davies, Einstein, Farell, James & McMillan, 1978).

Herein we report the first crystal structure of a binuclear complex of this category, namely $[Ru_2Cl(Me_2SO)_5(\mu\text{-}Cl)_3]$, (I), whose ^1H NMR and IR spectra are known (Heath, Lindsay & Stephenson, 1982; Hudali, Kingston & Tayim, 1979).



(I)

All the Me_2SO ligands are bonded terminally to the metal through sulfur. The two metal atoms are bridged by three Cl atoms, leading to a face-sharing bioctahedral structure. The bridging atoms have a staggered conformation with respect to the terminal donor atoms, which in turn are mutually eclipsed when viewed down the Ru(1)–Ru(2) axis. The average Ru—Cl(bridging) bond length [2.461 (3) Å] is longer than the Ru—Cl(terminal) bond length [2.394 (4) Å]. The average Ru(1)—S bond length [2.233 (3) Å] is shorter than the average Ru(2)—S bond length [2.275 (3) Å], indicating greater π back bonding in the former which possibly arises from greater σ donation from the terminal Cl atom.

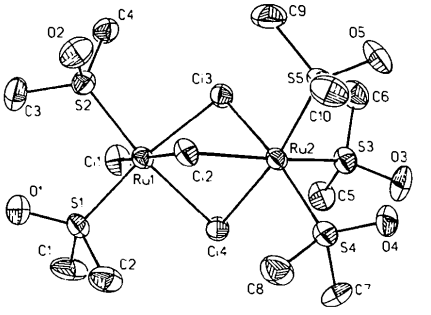


Fig. 1. Molecular structure showing 50% probability displacement ellipsoids. H atoms are omitted for clarity.

Experimental

Synthesis was performed by literature method (Heath, Lindsay & Stephenson, 1982). Single crystals were grown by diffusion of a dichloromethane solution of the complex into *n*-hexane.

Crystal data

$[Ru_2Cl_4(C_2H_6OS)_5]$
M_r = 734.6
Monoclinic
$P2_1/n$
a = 11.095 (7) Å
b = 15.692 (8) Å
c = 15.173 (7) Å
β = 109.83 (4)°
V = 2485 (2) Å^3
Z = 4
D_x = 1.963 Mg m^{-3}
Mo $K\alpha$ radiation
λ = 0.71073 Å
Cell parameters from 35 reflections
θ = 8–16°
μ = 2.084 mm^{-1}
T = 295 K
Parallelepiped
0.33 × 0.24 × 0.18 mm
Red

Data collection

Siemens *R3m/V* diffractometer
ω scans
Absorption correction: empirical
T_{min} = 0.89, T_{max} = 1.00
5045 measured reflections
4278 independent reflections
3016 observed reflections [$F > 6\sigma(F)$]
R_{int} = 0.0430
θ_{max} = 25°
$h = -13 \rightarrow 12$
$k = 0 \rightarrow 18$
$l = 0 \rightarrow 18$
2 standard reflections monitored every 98 reflections
intensity decay: 3%