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Structure of the Antitumour Active Compound Tetrachloro(2,2-dimethyl-1,3-propanediamine)platinum(IV)

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Abstract. [PtCl₄(C₅H₁₄N₂)], *M_r* = 439.08, monoclinic, *P*2₁/*m*, *a* = 7.5618 (6), *b* = 9.1686 (10), *c* = 8.6113 (8) Å, β = 107.92 (7)°, *V* = 568.07 Å³, *Z* = 2, *D_x* = 2.57 g cm⁻³, λ(Mo *K*α) = 0.71073 Å, μ = 134 cm⁻¹, *F*(000) = 404.3, *T* = 295 K, *R* = 0.022 for 2365 significant reflections. Molecular symmetry *m* (*C_s*). An alternative refinement in *P*2₁ shows high correlations. The octahedral coordination around Pt shows no unusual bond lengths or angles [Pt–Cl 2.304 (1), 2.309 (1), 2.318 (1) Å, Pt–N 2.062 (2) Å; all angles within 3° of 90 or 180°]. The six-membered Pt–diamine ring adopts a chair-like conformation which is somewhat flattened at the Pt–N₂ end. The molecular geometry is compared with that of analogous compounds.

Introduction. A number of square-planar Pt^{II} and octahedral Pt^{IV} compounds with *cis*-coordinated neutral primary (or secondary) amines and moderately strongly bound anions, such as chloride, appear to possess antitumour activity (Marcelis & Reedijk, 1983; Lippard, 1982; Lippert & Beck, 1983).

Until recently, most attention was given to the structure and kinetics of the Pt^{II} drugs, whereas the kinetically inert Pt^{IV} drugs (Mason, 1972) were barely studied. Recently, molecular structures of a few Pt^{IV}–amine compounds (Vollano, Blatter & Dabrowiak, 1984; Kuroda, Ismail & Sadler, 1984) as well as some mechanistic studies (Blatter, Vollano, Krishnan & Dabrowiak, 1984; van der Veer, Peters & Reedijk, 1985) have been reported, including the very promising

second-generation drug CHIP, [PtCl₂(OH)₂{HC–(CH₃)₂–NH₂}₂] (Harrap, 1984). Here we report the structure of the compound [Pt^{IV}Cl₄(dmdap)] (dmdap = 2,2-dimethyl-1,3-propanediamine). The synthesis of this compound has been published elsewhere (Van Kralingen, Reedijk & Spek, 1980).

Experimental. Crystal size approximately 0.17 × 0.21 × 0.15 mm. Cell constants from setting angles of 24 reflections (10 < θ < 12°) centred on an Enraf–Nonius CAD-4 diffractometer, graphite-monochromated Mo *K*α radiation, ω/θ scan, 2 < θ < 36°, *h*–12→12, *k* 0→15, *l*–15→15. Reflections corrected for Lorentz, polarization, absorption (de Graaff, 1973) and extinction effects (transmission coefficients 0.094–0.264). Three standard reflections, 3.1% intensity variation. 5640 reflections measured, 2828 independent, *R_{int}* = 0.075; 2365 reflections with *I* > 2σ(*I*) taken as observed.

Position of Pt derived from Patterson synthesis, other atoms from subsequent Fourier maps. *F* used in least-squares refinement. *R* = 0.0221, *wR* = 0.0266, *w* = 1/σ²(*F*), *S* = 1.053, Δ_{max}/σ < 0.01. Max. and min. Δρ excursions in final difference map 1.2 and –1.4 e Å⁻³ (close to Pt). Least-squares refinement; anisotropic thermal parameters for non-H atoms; H positions could be located in the difference-Fourier maps; however, H positions calculated (C–H: 0.96 Å) and only isotropic temperature factors refined. Scattering factors and anomalous-dispersion corrections taken from *International Tables for X-ray Crystallography* (1974). Leiden University Computer (Amdahl V7B); programs written or modified by Mrs E. W. Rutten-Ceulemans and Dr R. A. G. de Graaff.

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Discussion. The atomic coordinates and equivalent isotropic thermal parameters are listed in Table 1;* bond lengths and angles are given in Table 2. An ORTEP drawing of the molecular geometry with the atomic numbering is shown in Fig. 1. The bond angles in the octahedral geometry at Pt are very close to 90°, and the Pt–N and mean Pt–Cl distances of 2.06 and 2.31 Å are normal, although the axial Pt–Cl bonds are slightly shorter than those in the equatorial plane [Cl(2), Cl(2'), N(1) and N(1')]. The Pt atom lies 0.0187 (1) Å out of this plane. The six-membered ring,

* Lists of structure amplitudes, anisotropic thermal parameters and H-atom coordinates have been deposited with the British Library Lending Division as Supplementary Publication No. SUP 42699 (15 pp.). Copies may be obtained through The Executive Secretary, International Union of Crystallography, 5 Abbey Square, Chester CH1 2HU, England.

Table 1. Fractional atomic coordinates ($\times 10^5$) and equivalent isotropic thermal parameters ($\text{Å}^2 \times 10^3$) with e.s.d.'s in parentheses

$$B_{\text{eq}} = \frac{2}{3} \pi^2 \text{trace } \bar{U}$$

	x	y	z	B_{eq}
Pt	17829 (1)	25000	42980 (1)	1853 (5)
Cl(1)	-10256 (13)	25000	48246 (16)	295 (2)
Cl(2)	750 (1)	671 (1)	2373 (1)	3057 (14)
Cl(3)	46323 (13)	25000	38358 (14)	284 (2)
N(1)	2665 (3)	884 (2)	6030 (3)	235 (4)
C(1)	4416 (4)	1127 (3)	7386 (4)	263 (6)
C(3)	44211 (58)	25000	83754 (49)	264 (8)
C(31)	28267 (83)	25000	91265 (63)	358 (11)
C(32)	63113 (78)	25000	97583 (70)	399 (12)

Table 2. Bond distances (Å) and angles (°)

Pt–Cl(1)	2.304 (1)	N(1)–C(1)	1.489 (4)
Pt–Cl(2)	2.318 (1)	C(1)–C(3)	1.519 (4)
Pt–Cl(3)	2.309 (1)	C(3)–C(31)	1.534 (7)
Pt–N(1)	2.062 (2)	C(3)–C(32)	1.554 (6)
N(1)–Pt–Cl(2')	178.94 (7)	Cl(1)–Pt–Cl(3)	178.65 (4)
Cl(1)–Pt–Cl(2)	90.72 (3)	Pt–N(1)–C(1)	118.13 (17)
Cl(3)–Pt–N(1)	90.78 (7)	N(1)–C(1)–C(3)	114.33 (25)
Cl(2)–Pt–N(1)	87.72 (7)	C(1)–C(3)–C(1')	111.90 (34)
N(1)–Pt–N(1')	91.86 (13)	C(1)–C(3)–C(31)	111.71 (23)
Cl(1)–Pt–N(1)	88.29 (7)	C(1)–C(3)–C(32)	105.82 (24)
Cl(2)–Pt–Cl(3)	90.21 (3)	C(31)–C(3)–C(32)	109.51 (40)
Cl(2)–Pt–Cl(2')	92.68 (4)		

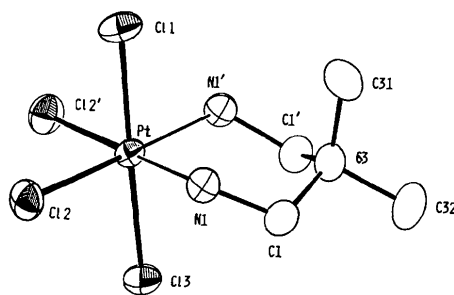


Fig. 1. ORTEP representation (Johnson, 1965) of $[\text{PtCl}_4(\text{dmdap})]$. H atoms have been omitted for clarity.

formed by the coordination of the bidentate dmdap to Pt, shows a symmetrical chair conformation, which is somewhat flattened at the Pt–N(1)–N(1') end. The dihedral angle between the planes through Pt–N(1)–N(1') and N(1)–N(1')–C(1)–C(1') is 32.6 (1)°. This angle is much larger than the 2.4° found in the comparable Pt^{II} compound [Pt(malonate)(dmdap)] (Van Kralingen *et al.*, 1980), but less than the expected value of 60° for an ideal chair conformation. In another Pt^{II} dmdap compound (Kleiböhmer, Krebs, Marcelis, Reedijk & van der Veer, 1983), no flattening at the Pt–N(1)–N(1') end of the ring occurs. The dihedral angle between N(1)–N(1')–C(1)–C(1') and C(1)–C(1')–C(3) is 58.7 (3)°, which is exactly the same value as has been found in [Pt(malonate)(dmdap)] (Van Kralingen *et al.*, 1980) and is also very close to the expected value of 60°. The present Pt^{IV} compound is of additional interest as it shows significant activity against leukaemia L1210 in mice (Van Kralingen & Reedijk, 1980). A special feature of this compound is its solubility, which is approximately twice that of the well known *cis*-[PtCl₂(NH₃)₂] (*cis*-platin). Good solubility is a prerequisite for these types of tumour drugs, since administration is much easier in such cases.

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