The First Reported Structure of a Platinum(IV) Complex containing Deprotonated Amide Ligands—A Model for Platinum(IV)–Peptide/Protein Interactions

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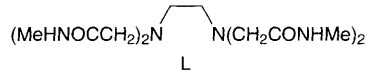
Reaction of 1,2-diaminoethane-*N,N,N',N'*-tetra(*N*-methylacetamide) L with $K_2[PtCl_4]$ in aqueous solution gave $H_2L[PtCl_4]$ and the unexpected product *cis*-$Pt(LH_{-2})Cl_2$ which is the first reported structure of a platinum(IV) complex containing deprotonated amide ligands and a model for platinum(IV)–peptide/protein interactions.

The synthesis of cisplatin analogues for testing as anticancer drugs is an area of active research and several second-generation analogues are now in clinical use or undergoing evaluation.[1] Recently some platinum(IV) complexes were found to be antitumour active,[2] and whether the activity of these involves reduction to platinum(II) or interaction with cellular targets, especially DNA, without prior reduction is contentious.[3] Whichever is the case platinum–protein interactions are likely to play a role in the uptake and activity of the complexes.[3] Despite the extensive literature which exists on metal–peptide complexes,[4] and on the coordination chemistry of platinum(IV),[5] surprisingly there are no reports to date on platinum(IV)–peptide interactions. Herein we report on the unexpected formation and structure of a platinum(IV) complex which contains deprotonated amide ligands, the first such structure to be reported and a model for platinum(IV)–peptide interactions.

The addition of an aqueous solution of L,[6] to an equimolar aqueous solution of $K_2[PtCl_4]$ produced on standing for 2–3 d red crystals of $H_2L[PtCl_4]$.† Removal of several crops of this compound eventually produced a yellow filtrate from which yellow crystals of the complex $Pt(LH_{-2})Cl_2$ were obtained. The structure,‡ Fig. 1, shows that it is a complex of platinum(IV)



L

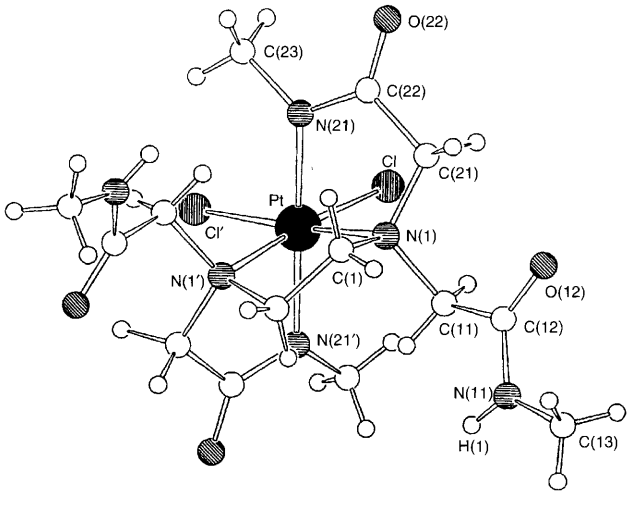


Fig. 1 Molecular structure of $Pt(LH_{-2})Cl_2$. Key interatomic distances (Å) and angles (°): Pt–Cl 2.307(3), Pt–N(1) 2.089(7), Pt–N(21) 2.030(6), N(21)–C(22) 1.31(1), N(21)–C(23) 1.47(1), C(22)–O(22) 1.245(9), N(11)–C(12) 1.32(2), N(11)–C(13) 1.48(1), C(12)–O(12) 1.22(1); Cl–Pt–Cl' 90.31(9), Cl–Pt–N(1) 92.1(3), Cl–Pt–N(1') 174.7(2), N(1)–Pt–N(1') 85.9(3), Cl–Pt–N(21) 86.0(2), Cl–Pt–N(21') 96.0(2), C(22)–N(21)–C(23) 118.9(7), C(12)–N(11)–C(13) 121.8(7). Intermolecular hydrogen bond; N(11)···O(22[a]) 2.86(1), N(11)–H(1)···O(22[a]) 165.3(6), where symmetry code *a* is 0.5 + *x*, −*y*, 0.5 + *z*.

containing LH_{-2} as a tetradentate ligand coordinated to the metal through the amino groups and two deprotonated amide groups. The complex is octahedral, typical of platinum(IV),[5] with the Cl^- ligands *cis* and the deprotonated amide groups *trans* to each other. The Pt–N (deprotonated amide) bond distance is shorter, albeit not greatly so, than the Pt–N (amine) distance, consistent with the fact that it is a better σ donor.[7]

The method of formation and structure of this platinum(IV) complex are both novel. It appears that the presence of the deprotonated amide groups results in facile oxidation of platinum(II) to platinum(IV) in the presence of air, a reaction that normally requires the addition of oxidising agents such as hydrogen peroxide or chlorine.[5] Also, although no base was added during the preparation, the crystallisation of $H_2L[PtCl_4]$ containing doubly protonated L resulted in the solution becoming sufficiently basic to allow formation of the deprotonated amide complex.

The known ligands most closely related to the tetraamide described in this paper are amino acid amides and peptides. Although complexes of platinum(II) with ligands of this type in solution and to a lesser extent in the solid state have been widely investigated,[8] there is no report in the literature of analogous complexes of platinum(IV). The facile formation of platinum(IV) complexes from the corresponding platinum(II) systems even in situations where two or more deprotonated amide groups are present has not previously been observed.

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Footnotes

† Yield 18%. Characterised by microanalysis, spectroscopy and X-ray crystallography.

‡ Yield 10%. A satisfactory microanalysis was obtained. IR(KBr), ν/cm^{-1}: 3290, 3100 ν(NH), 1670 (amide 1), 1600 ν(CO) deprotonated amide. *Crystal data*: $C_{14}H_{26}Cl_2N_6O_4Pt$, M = 608.40, monoclinic, space group $P2/n$, a = 11.764(4), b = 7.840(1), c = 11.829(2) Å, β = 104.09(2); U = 1058.1(6) Å^3, Z = 2, $F(000)$ = 592, D_c = 1.909 g cm^{-3}, yellow prismatic crystal, dimensions 0.15 × 0.30 × 0.40 mm, μ(Mo-Kα) = 6.984 mm^{-1}. 3125 reflections were collected at 20 °C on an Enraf Nonius CAD-4 diffractometer using the ω–2θ scan mode, λ(Mo-Kα) = 0.71073 Å. The structure was solved by direct methods and refined by full-matrix least-squares analysis using 2468 unique reflections with $I > 3\sigma(I)$. Absorption correction was applied by DIFABS.[9] Non-hydrogen atoms were refined anisotropically. Hydrogen atoms were introduced in the calculation, but not refined. Final R and R_w factors 0.048 and 0.056 respectively, maximum residual peak near Pt atom 3.683 e Å^{-3}. Calculations were performed on a DEC Microvax II computer using SHELX 86,[10] and SCHAKAL.[11] Atomic coordinates, bond lengths and angles, and thermal parameters have been deposited at the Cambridge Crystallographic Data Centre. See Information for Authors, Issue No. 1.

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