The First *X*-Ray Crystal Structures of the Platinum(II)-in and -out Complexes with Dioxocyclams

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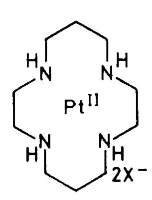
X-Ray studies of the two macrocyclic tetra-amine complexes $[Pt(H_{-2}L')]^0$. $5H_2O$ (**3b**) and $[PtLCl_2]^0$. $2H_2O$ (**4a**), where L = dioxocyclam and L′ = 6-methyldioxocyclam, show the first platinum(II)-in and -out structures, respectively.

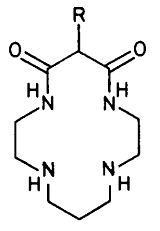
Among the well-documented square-planer Pt^{II}-tetra-amine (*e.g.*, $4NH_3$, 2en, *etc.*) complexes,[1] the complex with cyclam (1,4,8,11-tetra-azacyclotetradecane) (**1**) remains unknown. This is quite puzzling in view of the fact that the size (effective ionic radii of four-co-ordinate, square-planer M^{II} ion)[2] of Pt^{II} (74 pm) is similar to those of Cu^{II} (71 pm),[3a] Ni^{II} (63 pm),[3b] or Pd^{II} (78 pm),[3c] all of which comfortably stay in the cyclam N_4 cavity. The recent finding[4] that dioxocyclam (5,7-dioxo-1,4,8,11-tetra-azacyclotetradecane) (**2a**) with the same 14- membered N_4 ring can form a stable complex $[Pt^{II}(H_{-2}L)]^0$ (**3a**), where $H_{-2}L$ denotes doubly deprotonated (**2a**), was therefore significant. The dioxocyclam (**2**) was designed as a hybrid ligand of oligopeptides and cyclam.[5] A lipophilic dioxocylam (**2**) ($R = C_{16}H_{33}$) was proved to be a selective Pt^{II}-sequesting agent.[4] Since this is the first reported Pt^{II} macrocyclic N_4 complex, we wished to monitor the stereochemical features of the 14-membered macrocyclic N_4 environment around Pt^{II}.

A good crystalline dioxocyclam complex (**3b**) [$\nu_{C=O}$ 1580 cm^{-1}, λ_{max} 245 nm (ε 9000)] was isolated from derivatized dioxocyclam (5,7-dioxo-6-methyl-1,4,8,11-tetra-azacyclotetradecane) (**2b**)[6] and K_2PtCl_4 (1:1) in pH 6 (final pH)



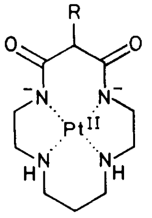
Pt^{II}– cyclam

(1)

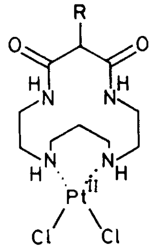


dioxocyclam

(2)



(3)



(4)

a; R = H b; R = CH_3

nonbuffered aqueous solution at room temperature, and its *X*-ray structure analysis was undertaken.†

The structure of (**3b**) is shown in Figure 1. The Pt atom sits in a square-planar array of four nitrogens, as previously assigned (**3b**). This also represents the first *X*-ray structure of the dioxocyclam complexes $[M^{II}(H_{-2}L)]^0$.[5] The co-ordinate bond lengths Pt^{II}–N^- (average 1.98 Å) and Pt^{II}–NH (average 2.05 Å) are close to those of the Pt^{II}–dipeptide (Gly–Met) complex, which has Pt^{II}–N^- (1.98 Å) and Pt^{II}–NH_2 (2.07 Å).[8] Five H_2O molecules provide hydrogen bondings with macrocyclic carbonyl oxygens and amines, but do not interact with Pt^{II}. The macrocyclic co-ordinate geometry is nothing unusual, with little by way of constraints seen around Pt^{II}. Taken together with similar bond parameters for Cu^{II}–,[3a] Ni^{II}–,[3b] and Pd^{II}–cyclam complexes,[3c] the present result suggests that the hypothetical square-planar Pt^{II}–cyclam complex (**1**) is stereochemically feasible.

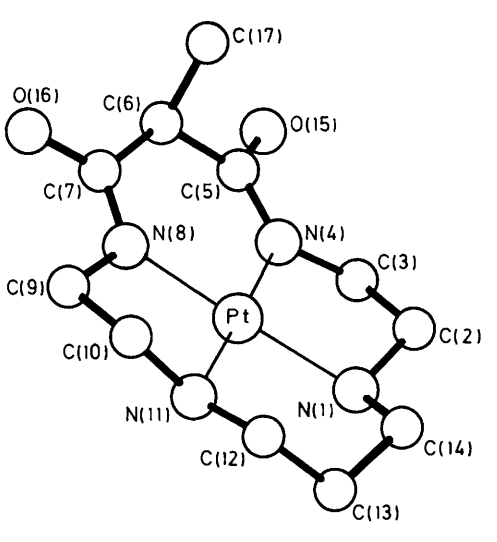


Figure 1. The structure of $[Pt(H_{-2}L')]^0$ (L′ = **2b**). Important bond lengths (Å) and bond angles (°) are as follows; Pt–N(1) 2.06(1), Pt–N(4) 1.98 (1), Pt–N(8) 1.98(1), Pt–N(11) 2.05(1), N(4)–C(5) 1.30(2), C(5)–O(15) 1.27(2), C(7)–N(8) 1.31(2), C(7)–O(16) 1.27(2); N(1)–Pt–N(4) 83.9(5), N(4)–Pt–N(8) 95.2(5), N(8)–Pt–N(11) 83.8(5), N(1)–Pt–N(11) 97.1(4), N(1)–Pt–N(8) 178.8(5), N(4)–Pt–N(11) 178.9(5), N(4)–C(5)–O(15) 123.7(12), N(8)–C(7)–O(16) 122.3(13).

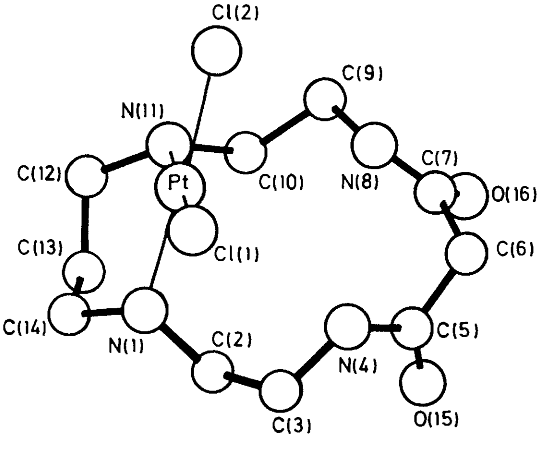


Figure 2. The structure of $[PtLCl_2]^0$ (L = **2a**). Important bond lengths (Å) and bond angles (°) are as follows; Pt–Cl(1) 2.316(3), Pt–Cl(2) 2.310(2), Pt–N(1) 2.051(7), Pt–N(11) 2.058(8), N(4)–C(5) 1.31(1), C(5)–O(15) 1.23(1), C(7)–N(8) 1.33(1), C(7)–O(16) 1.20(1); Cl(1)–Pt–Cl(2) 91.3(1), Cl(1)–Pt–N(1) 87.0(2), Cl(2)–Pt–N(11) 86.3(2), N(1)–Pt–N(11) 95.3(3), Cl(1)–Pt–N(11) 177.4(2), Cl(2)–Pt–N(1) 177.1(2), N(4)–C(5)–O(15) 123.9(10), N(8)–C(7)–O(16) 123.7(10).

Since the deprotonated amide nitrogen has been shown to stabilize high oxidation states of metals (*e.g.*, Cu^{3+}, Ni^{3+})[5c,9] and, moreover, it is a much stronger σ-donor than cyanide ion,[10] oxidation of (**3**) or the relevant oxopolyamine complexes[8b] might provide a new type of one-dimensional complex with Pt–Pt bonds, by analogy with $[Pt(CN)_4]^{2-}$.[11]

From a mixture of free dioxocyclam (**2a**) and $K_2Pt^{II}Cl_4$ (1:1) kept in pH 7 (starting pH) nonbuffered aqueous solution for 6 h, we have isolated yellow crystals (**4a**) (minor) in addition to the colourless crystals (**3a**) (major), which were separated by hand picking. The structure of (**4a**) [$\nu_{C=O}$ 1660 cm^{-1}, λ_{max} 272 nm (ε 200)] has been established by an *X*-ray study.

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† *Crystal data* for (**3b**): $C_{11}H_{22}N_4O_2Pt.5H_2O$, M = 527.5, monoclinic, space group *Cc*, a = 19.873(3), b = 5.906(1), c = 17.717(4) Å, β = 117.30(1)°, U = 1847.9(7) Å^3, Z = 4, D_c = 1.895 g cm^{-3}. Intensities of 1563 unique reflections in the region of $2\theta < 130°$ were measured on a Rigaku AFC-5 diffractometer using Cu-K_α radiation, and used with absorption corrections for spherical crystals (μR = 1.5).[7] The structure was solved by the heavy-atom method and refined by a block-diagonal least-squares technique to R and R_w = 0.043 and 0.057, respectively, for 1537 observed reflections with $|F_o| > 3\sigma(F_o)$.

Crystal data for (**4a**): $C_{10}H_{20}N_4O_2Cl_2Pt.2H_2O$, M = 530.3, triclinic, space group $P\bar{1}$, a = 8.974(2), b = 13.052(3), c = 8.532(2) Å, α = 92.99(3), β = 116.38(2), γ = 103.52(2)°, U = 839.1(4) Å^3, Z = 2, D_c = 2.099 g cm^{-3}. Intensities of 2497 unique reflections in the region of $2\theta < 120°$ were measured on a Rigaku AFC-5 diffractometer using Cu-K_α radiation, and corrected for absorption effects by use of North's method.[12] The structure was solved by the heavy-atom method and refined by a block-diagonal least-squares technique to R and R_w = 0.056 and 0.074, respectively, for 2412 observed reflections with $|F_o| > 3\sigma(F_o)$. Atomic co-ordinates, bond lengths and angles, and thermal parameters for (**3b**) and (**4a**) have been deposited at the Cambridge Crystallographic Data Centre. See Notice to Authors, Issue No. 1.

The structure of (**4a**) is shown in Figure 2, which clearly demonstrates the dioxocyclam serving as a bidentate ligand. The bond length Pt^{II}–NH (average 2.06 Å) here is almost the same as that for the platinum-in complex (**3b**). The Pt^{II}–Cl bond distance (2.31 Å) is similar to that (2.33 Å) found previously in *cis*-$[Pt^{II}(NH_3)_2Cl_2]$.[13] The platinum-out complex (**4a**) upon dissolution in phosphate buffer solution (pH = 7) gradually ($\tau_{1/2}$ = 6 h) turned to the platinum-in species (**3a**), which was monitored by silica gel thin-layer chromatography (Kieselgel 60 F_{254}, eluent: MeOH) or h.p.l.c. on a weak cation-exchange column (eluent; 0.10 M KH_2PO_4 aq. solution, detection by u.v. at 243 nm). A study of the anticancer activity of (**4a**) is in progress.

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