

Synthesis and X-ray Crystal Structure Determination of the First Transition Metal Complexes of the Tetracycles Formed by Tetraazamacrocycle–Glyoxal Condensation: PdL*Cl₂ (L = Cyclam–Glyoxal Condensate (1), Cyclen–Glyoxal Condensate (2))

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Tetraazamacrocycles are famously prolific ligands for transition and other metal ions, adopting numerous geometries and binding modes. Countless derivatizations of the monocyclic macrocycles cyclam (1,4,8,11-tetraazacyclotetradecane) and cyclen (1,4,7,10-tetraazacyclododecane) alone have produced pendant arm, bicyclic, tricyclic, tetracyclic, and linked forms of these workhorse ligands and their corresponding metal complexes.^{1–3} Surprisingly, the ability to complex with transition metal ions has not been demonstrated for one well-known type of derivative:^{4–7} the glyoxal condensation products of the parent tetraazamacrocycles synthesized according to Scheme 1.⁶ We now report the synthesis and crystal structure determination of two novel Pd^{II} complexes of the general formula PdLCl₂ where L is either variant **1** or **2** of the tetraazamacrocycle–glyoxal condensation products (**1** = *cis*-decahydro-1*H*,6*H*-3*a*,5*a*,8*a*,10*a*-tetraazapyrene, and **2** = *cis*-decahydro-2*a*,4*a*,6*a*,8*a*-tetraazacyclopent[*fg*]acenaphthylene), derived from cyclam and cyclen, respectively.

The tetracyclic condensation products of glyoxal and tetraazamacrocycles have been known for over twenty years.^{4–9} These interesting organic molecules are formed when each aldehyde functional group reacts with two secondary amines of the macrocycle, completing an aminal group and closing a tetracyclic, panel-like molecule. Under most reaction conditions, the methine hydrogens of the two-carbon central bridge in the resulting tetracyclic structures are located *cis* to each other, giving a folded system of four fused rings.^{5,6} The *trans* isomer can be obtained only under certain conditions and gives a more

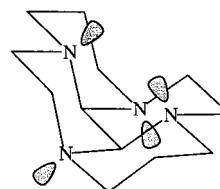
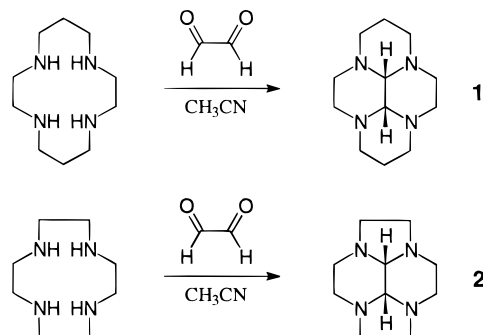


Figure 1. Location of nitrogen lone pairs in *cis*-fused **1**; adjacent pairs are directed to opposite sides of the molecular plane, resulting in two donors directed into and two away from the cleft.

Scheme 1. Condensation of Glyoxal with Tetraazamacrocycles to Give Tetracyclic Tetraamines; Ligand **1** Is the Cyclam Derivative, and Ligand **2** Is the Cyclen Derivative



nearly flat structure.¹⁰ Both kinetic⁵ and thermodynamic⁹ arguments have been offered to explain the preference for the *cis* structure.

As a result of the *cis* configuration, the lone pairs of the potential nitrogen donors are not all oriented toward the same side of the macrocycle plane. In fact, adjacent nitrogens direct their electron pairs to opposite sides of the macrocycle plane, resulting in a ligand with two nonadjacent nitrogen lone pairs directed into the concave fold while the other two nonadjacent nitrogen lone pairs point out from the convex side (Figure 1). It has been suggested that this arrangement might interfere with coordination to metal ions by these rigid tetracyclic molecules.⁵ However, we predicted, on the basis of molecular modeling studies, that the two nitrogens with lone pairs converging inside the concave fold could bind transition metals in a didentate fashion, if an adequate match in size and geometry was made with the metal ion. We were encouraged in this belief by the crystal structure of the diprotonated salt of **1**, in which both protons are found inside the cleft and bound to the two inward-facing nitrogens.¹¹ Replacement of these two protons by a single transition metal ion appeared plausible. Pd^{II}, a relatively large ion, with a preference for a square planar geometry was chosen to attempt such a complexation.

The [1+1] condensations of cyclam and cyclen with glyoxal were achieved by literature methods.⁶ Complexation with Pd^{II} was carried out by reacting the tetracyclic ligands with 1 equiv of PdCl₂ in acetonitrile at 40–50 °C for 20 h under nitrogen (Scheme 2). Filtration yielded the crude products as green, finely divided solids, which were then dissolved in methylene chloride and filtered through Celite to remove traces of black solids.

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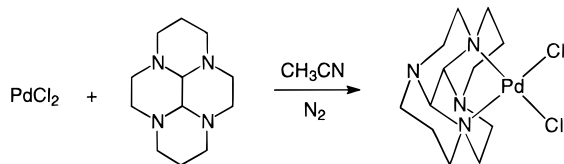
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Scheme 2. Reaction of PdCl₂ with the Tetracyclic Tetraamine **1**, Forming the Novel Pd^{II} Complex in Which the Ligand Is Bound in a Bidentate Manner; Not Shown Is the Corresponding Reaction with **2**



The orange filtrates were then either evaporated or precipitated with ether to give the pure yellow-orange solid products in 57–60% yield. Orange-red crystalline blocks of both complexes were grown by the slow evaporation of methylene chloride.

The molecular structures of Pd(1)Cl₂ and Pd(2)Cl₂ were determined crystallographically as tetracoordinate PdLCl₂ (Figure 2). Both structures have Pd^{II} in its usual square planar geometry, bound to the two concave-directed nitrogens of the tetraazatetracycle and to two chloride ligands in a cis arrangement. The tetracycles show the folded cis geometries characteristic of the free base; the cis structure has been determined for **1**¹⁰ and predicted for **2**.^{6,7} The structure of Pd(2)Cl₂ is the first crystallographic characterization of the folded nature of **2** and confirms that the smaller tetracyclic system behaves like the more fully characterized **1**. The Pd^{II} ion fits nicely into the clefts formed by the ligand folds, exhibiting normal bond angles and lengths. For Pd(1)Cl₂: Pd–N = 2.099(2) Å and 2.114(2) Å, Pd–Cl = 2.3001(5) Å and 2.3121(5) Å, N–Pd–N = 84.65(6)°, N–Pd–Cl(cis) = 91.32(5)° and 91.60(4)°, Cl–Pd–Cl = 92.48(2)°. For Pd(2)Cl₂: Pd–N = 2.086(3) Å and 2.079(3) Å, Pd–Cl = 2.2953(9) Å and 2.2973(9) Å, N–Pd–N = 83.61(13)°, N–Pd–Cl(cis) = 91.22(9)° and 92.62(10)°, Cl–Pd–Cl = 92.55(4)°. Spectroscopic results for the complexes are consistent with square planar Pd^{II} structures and include ¹H and ¹³C NMR, IR, and UV–vis experiments. Cyclic voltammetry of the complexes showed no reversible oxidations or reductions.

An interesting comparison between these complexes and the few complexes of a related pentacyclic hexamine “tetraaminal” can be drawn. The ligand used in those studies is a [2+2] condensation product of glyoxal and diethylenetriamine (Figure 3) and has been found to coordinate to Cd²⁺ and Mn²⁺ in a tetradentate fashion.^{12–14} Synthesized from two linear triamines, this pentacycle is much more elongated than our “modular” tetracyclic ligands. This characteristic, along with the presence of six potential nitrogen donors, four of which direct their lone pairs into the much wider and deeper cleft formed in the coordinated ligand (and allowing tetracoordination reminiscent of 2,5-diaminopiperazine), demonstrate the greater flexibility of this ligand as compared to our more constrained, more rigid tetracycle. In fact, isomerization from the centrosymmetric free ligand structure to the axially symmetric coordinated configuration is necessary and may occur through a sequence of reactions, such as solvent addition—configurational change—solvent elimination, in the methanol solvent used for formation of the complexes.¹² The smaller tetracyclic tetraamines of our complexes show none of this facile configuration change and appear much more rigid and configurationally stable, although capable of only bidentate coordination.

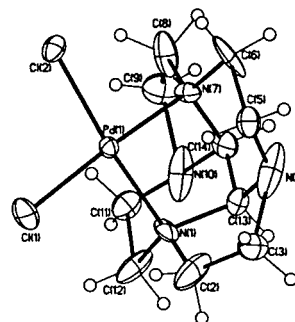
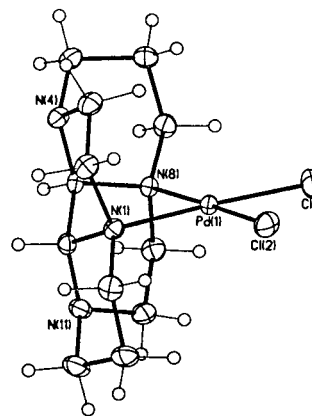


Figure 2. Molecular structures of Pd(1)Cl₂ (top) and Pd(2)Cl₂.

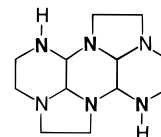


Figure 3. Structure of a pentacyclic hexamine related to the tetracycles **1** and **2**. This ligand coordinates Cd²⁺ and Mn²⁺ in a tetradentate manner (donor nitrogens in bold).

The synthesis of Pd(1)Cl₂ and Pd(2)Cl₂ introduces a novel class of tetraazatetracycle complexes, having ligands composed of four fused 5- or six-membered rings based on the condensation products of simple tetraazamacrocycles and glyoxal. These ligands can bind transition metal ions in a bidentate manner, if care is taken to choose an appropriate metal ion with respect to size and preferred coordination geometry. Investigations are ongoing to expand the range of metal ions for these ligands and explore the reactivity of their complexes. Initial findings suggest that metal size and preferred geometry are in fact important, as numerous attempted syntheses with the other most closely related Group 10 ions, Ni^{II} and Pt^{II}, have been unsuccessful. However, preliminary results show that Cu^I and Cu^{II} form complexes with **1** and **2**.¹¹ These ligands might find applications whenever rigid bidentate ligands are indicated. They also might be useful in supramolecular syntheses as *divergent turns*, i.e., ligands in which reactive functional groups (the two noncoordinated nitrogens) are directed away from the organizing metal ion *anchor*.¹⁵

Experimental Section

Materials. Solvents and reagents were the highest grade available and were found to be sufficiently pure for use as supplied. Where necessary, solvents were dried by prescribed techniques.

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Physical Techniques. Mass spectra (fast atom bombardment) were obtained using a VG ZAB HS spectrometer equipped with a xenon gun; an NBA (nitrobenzyl alcohol) matrix was used. Electrochemical experiments were performed on a Princeton Applied Research model 175 programmer and model 173 potentiostat using a homemade cell. A button Pt or glassy carbon electrode was used as the working electrode with a Pt-wire counter electrode and a Ag-wire pseudo-reference electrode. All electrochemical measurements were carried out under N₂ in dry, oxygen-free CH₃CN solutions which contained 0.1 M tetrabutylammonium hexafluorophosphate as the supporting electrolyte. The potentials vs SHE were determined using ferrocene as an internal reference. ¹H and ¹³C NMR spectra were recorded with Bruker DRX400 spectrometer. IR spectra were recorded as KBr disks using a Perkin-Elmer 1600 FTIR spectrometer. Electronic spectra were recorded using a Cary 3 spectrophotometer controlled by a Dell Dimension XPS P133s computer.

Synthesis of Ligands. The ligands **1** and **2** were synthesized according to literature procedures.⁶

Synthesis and Characterization of [Pd(1)Cl₂]. To 0.222 g (0.001 mol) of **1** dissolved in 15 mL of acetonitrile, under nitrogen, was added 0.176 g (0.001 mol) of PdCl₂ with stirring. The mixture was allowed to stir for 20 h at 40–50 °C before it was cooled and filtered to give the crude product, a dark green solid. This crude product was allowed to dry in the air overnight, then dissolved in 100 mL of methylene chloride and filtered through Celite to remove traces of black solids. Evaporation of the solvent yielded 0.228 g, or 57%, of the pure orange-yellow crystalline product. The FAB⁺ mass spectrum in methylene chloride (NBA matrix) exhibited a small peak at *m/z* 363 (Pd(1)Cl⁺). Elem. Anal. Calcd for Pd(1)Cl₂: C, 36.06; H, 5.55; N, 14.02. Found: C, 36.00; H, 5.60; N, 13.68. ¹H NMR (400 MHz, CD₂Cl₂): δ 1.29 (dd, 2H); 1.85 (td, 2H); 2.19 (td, 2H); 2.88 (m, 8H); 3.06 (s, 2H); 3.29 (dd, 2H); 3.67 (d, 2H); 5.62 (td, 2H). ¹³C NMR (400 MHz, CD₂Cl₂): δ 17.33, 46.36, 51.16, 57.79, 58.21, 81.90. IR (KBr cm⁻¹): 3443, 2950, 2877, 1458, 1297, 1145, 1113, 1090, 822, 772. UV-vis: λ_{max} = 398 nm (ε = 248 M⁻¹ cm⁻¹). Crystals suitable for X-ray diffraction were grown by the slow evaporation of a CH₂Cl₂ solution.

Synthesis and Characterization of [Pd(2)Cl₂]. To 0.194 g (0.001 mol) of **2** dissolved in 15 mL of acetonitrile, under nitrogen, was added 0.176 g (0.001 mol) PdCl₂ with stirring. The mixture was allowed to stir for 20 h at 40–50° before it was cooled and filtered to give the crude product, a dark green solid. This crude product was allowed to air-dry overnight, then dissolved in 100 mL of methylene chloride and filtered through Celite to remove traces of black solids. Precipitation by 1000 mL of ether resulted in a fine, orange-yellow solid which was filtered, yielding 0.223 g, or 60%, of pure product. The FAB⁺ mass spectrum in methylene chloride (NBA matrix) exhibited a small peak at *m/z* 371 (Pd(2)Cl₂⁺). Elem. Anal. Calcd for Pd(1)Cl₂: C, 32.32; H, 4.88; N, 15.08. Found: C, 32.70; H, 4.70; N, 14.83. ¹H NMR (400 MHz, CD₂Cl₂): δ 1.55 (br s, 2H); 2.31(m, 4H); 3.16 (s, 2H); 3.47 (m, 4H); 3.62 (dd, 2H); 3.73 (dd, 2H); 4.19 (m, 2H). ¹³C NMR (400 MHz, CDCl₃): δ 52.98, 53.80, 54.92, 55.22, 84.11. IR (KBr cm⁻¹): 3433, 2888, 1463, 1266, 1112, 1070, 845, 791. UV-vis: λ_{max} = 402 nm (ε = 241 M⁻¹ cm⁻¹). Crystals suitable for X-ray diffraction were grown by the slow evaporation of a CH₂Cl₂ solution.

X-ray Crystallography. Crystal Data for Pd(1)Cl₂. C₁₂H₂₂Cl₂N₄-Pd, *M* = 399.64, monoclinic, space group *P2(1)/n*, *a* = 7.3380(1) Å, *b* = 15.594(1) Å, *c* = 12.688(1) Å, β = 92.02°, *U* = 1450.93(4) Å³ (by least-squares refinement on 7407 reflection positions), *T* = 180(2) K, λ = 0.710 73 Å, *Z* = 4, *D*(cal) = 1.829 Mg/m³, *F*(000) = 808, μ(Mo Kα) = 1.639 mm⁻¹. Crystal character: red plates. Crystal dimensions 0.46 × 0.22 × 0.14 mm.

Crystal Data for Pd(2)Cl₂. C₁₀H₁₈Cl₂N₄Pd, *M* = 371.58, orthorhombic, space group *Pn2₁a*, *a* = 13.3071(2) Å, *b* = 11.5723(2) Å, *c* = 8.2846(2) Å, *U* = 1275.78(4) Å³ (by least-squares refinement on 5389 reflection positions), *T* = 180(2) K, λ = 0.710 73 Å, *Z* = 4, *D*(cal) = 1.935 Mg/m³, *F*(000) = 744, μ(Mo Kα) = 1.856 mm⁻¹. Crystal character: orange blocks. Crystal dimensions 0.3 × 0.2 × 0.2 mm.

Data Collection and Processing. Siemens SMART¹⁶ three-circle system with CCD area detector. Both crystals were held at 180(2) K with the Oxford Cryosystem Cryostream Cooler;¹⁷ maximum theta was 28.54°.

Pd(1)Cl₂. *hkl* ranges -9/5, -20/19, -16/17. of 8461 reflections measured, 3363 were unique [*R*(int) = 0.0308]. Absorption correction by ψ scan; minimum and maximum transmission factors: 0.73; 0.86.

Pd(2)Cl₂. *hkl* ranges -17/17, -11/15, -10/10. of 7158 reflections measured, 2505 were unique [*R*(int) = 0.0189]. Absorption correction by ψ scan; minimum and maximum transmission factors: 0.81; 0.93.

Structure Analysis and Refinement. The structures were solved by direct methods using SHELXS (TREF)¹⁸ with additional light atoms found by Fourier methods. Hydrogen atoms were added at calculated positions and refined using a riding model. Anisotropic displacement parameters were used for all non-H atoms; H-atoms were given isotropic displacement parameters equal to 1.2 times the equivalent isotropic displacement parameter of the atom to which the H-atom is attached. The weighting scheme was calculated as $w = 1/[s^2(F_o^2) + (aP)^2 + bP]$ where $P = (F_o^2 + 2F_c^2)/3$. Refinement used SHELXL96.¹⁹

Pd(1)Cl₂. Systematic absences indicated space group *P2(1)/n*. *a*(weight) = 0.0243; *b*(weight) = 0; goodness-of-fit on *F*² was 0.953, *R*1[for 2924 reflections with *I* > 2σ(*I*)] = 0.0210, *wR*2 = 0.0502. Data/parameters 3363/173. Extinction coefficient 0.0053(3). Largest difference Fourier peak and hole 0.380 and -0.609 eÅ⁻³.

Pd(2)Cl₂. Systematic absences indicated either space group *Pnma* or *Pn2₁a* (nonstandard setting of *Pna2₁*, chosen to allow ready comparison with the alternative of *Pnma*). The initial solution was in *Pnma*, but showed disorder in the ligand framework. It was found that an ordered ligand could be found in the noncentrosymmetric space group, although with extensive racemic twinning. This refined to a considerably better *R* value than in *Pnma*, where *R* = 0.040 was the best that could be achieved, with the ligand totally disordered across the mirror plane containing Pd, two Cl, and two N. The ultimate distinction is between disorder on a cell level, with nearby cells containing the alternative forms, and disorder on a domain level, with noncentric crystallites arranged randomly. The forms of the displacement ellipsoids shows that some residual rotational or mirror disorder is still present. Refinement of a delta-*f*^{''} multiplier showed the crystal to be a racemic twin, absolute structure parameter *x* = 0.54(7); *a*(weight) = 0.016; *b*(weight) = 4.38; goodness-of-fit on *F*² was 1.045, *R*1[for 2070 reflections with *I* > 2σ(*I*)] = 0.0277, *wR*2 = 0.0653. Data/restraints/parameters 2505/ 7/ 156. Extinction coefficient 0.00222(19). Largest difference Fourier peak and hole 0.912 and -0.657 eÅ⁻³.

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Supporting Information Available: Electronic spectra, cyclic voltammograms; tables of atomic coordinates and equivalent isotropic displacement parameters, bond distances and angles, anisotropic displacement parameters, hydrogen coordinates, and isotropic displacement parameters for Pd(1)Cl₂ and Pd(2)Cl₂ (9 pages). Ordering information is given on any current masthead page.

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