

Metal-Mediated Transformation of a Triazinephenanthridinium Ligand Leading to a {Pd₅} Coordination Complex Observed Crystallographically and by Cryospray Mass Spectrometry

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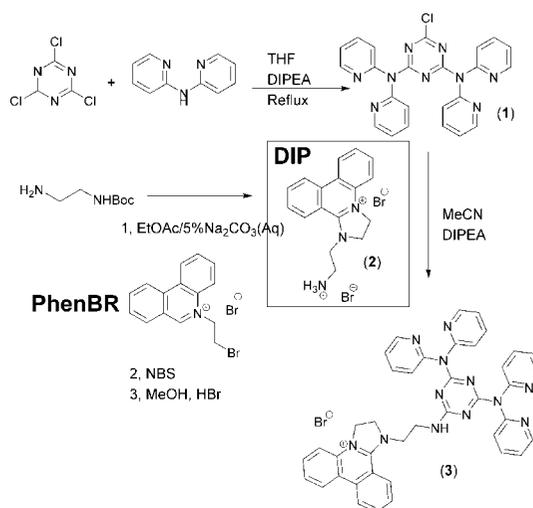
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The formation of a pentanuclear palladium(II) complex with a phenanthridinonetriazine-based ligand system, which itself is formed by a metal-mediated rearrangement of a triazinephenanthridinium proligand, is described.

Triazine-based compounds are widely used, with applications ranging from medicinal chemistry,¹ herbicides,² catalysis³ and polymer chemistry.⁴ *s*-Triazine derivatives have recently shown to be of great interest in supramolecular chemistry, because of the ease with which the successive chloride substitution of 2,4,6-trichloro-1,3,5-triazine can be achieved under controlled conditions, yielding trisubstituted ligands for the construction of multinuclear coordination frameworks.⁵ We are interested in combining the flexibility of the triazine-based ligand design with a novel heterocyclic system that forms upon reaction between a primary amine⁶ and (2-bromoethyl)phenanthridinium bromide (PhenBR), which leads to the formation of a dihydroimidazophenanthridinium (DIP) heterocyclic cation (Scheme 1).^{6a}

DIPs are interesting because they exhibit tunable structures^{6b} and biological activity and have affinity for DNA as well as resistance to reduction and hydrolysis.⁷ It has been shown that the cationic nature of the phenanthridinium is

Scheme 1. Synthesis of Compound 3^a



^a Compound 2 was isolated in 90% yield and compound 3 in a 58% yield.
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vital to its efficacy as a potential anticancer molecule.⁸ Metal complexes of ligands that contain DNA-intercalating properties/phenanthridinium moieties have been used as DNA sensors⁹ and as possible chemotherapeutic agents.¹⁰

Herein, we describe a new ligand design approach that exploits the versatile, “modular” reactivity of 2,4,6-trichloro-1,3,5-triazine to integrate the DIP moiety, producing a ligand that could form multinuclear coordination complexes that integrate pendent-delocalized aromatic frameworks. By using this strategy as a basis, we design complexes that display interesting properties such as supramolecular self-assembly or that act as potential multivalent DNA binding agents;

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(1) Ronchi, S.; Prosperi, D.; Compostella, F.; Panza, L. *Synth. Lett.* **2004**, 6, 1007.

(2) Oliva, J. M.; Azenha, E. M. D. G.; Burrows, H. D.; Coimbra, R.; de Melo, J. S. S.; Canle, M. L.; Fernandez, M. I.; Santaballa, J. A.; Serrano-Andres, L. *ChemPhysChem* **2005**, 6, 306.

(3) Hu, X. P.; Chen, H. L.; Zheng, Z. *Adv. Synth. Catal.* **2005**, 347, 541.

(4) Pedroso, L. M.; Castro, M. M. C. A.; Simoes, P.; Portugal, A. *Polymer* **2005**, 46, 1766.

(5) Gamez, P.; Reedijk, J. *Eur. J. Inorg. Chem.*, **2006**, 1, 29.

(6) (a) Parenty, A. D. C.; Smith, L. V.; Pickering, A. L.; Long, D. L.; Cronin, L. *J. Org. Chem.* **2004**, 69, 5934. (b) Parenty, A. D. C.; Smith, L. V.; Guthrie, K. M.; Long, D. L.; Plumb, J.; Brown, R.; Cronin, L. *J. Med. Chem.* **2005**, 48, 4504.

(7) Nakanishi, T.; Masuda, A.; Suwa, M.; Akiyama, Y.; Hoshino-Abe, N.; Suzuki, M. *Bioorg. Med. Chem. Lett.* **2000**, 10, 2321.

(8) Zee-Cheng, R. K. Y.; Yan, S. J.; Cheng, C. C. *J. Med. Chem.* **1978**, 21, 199.

(9) Mullins, S. T.; Sammes, P. G.; West, R. M.; Yahioğlu, G. *J. Chem. Soc., Perkin Trans.* **1996**, 1, 75.

(10) Whittaker, J.; McFayden, W. D.; Baguley, B. C.; Murray, V. *Anti-Cancer Drug Des.* **2001**, 16, 81.

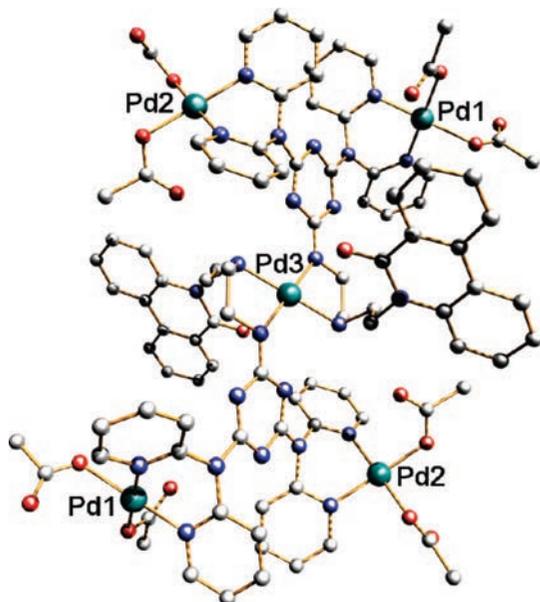
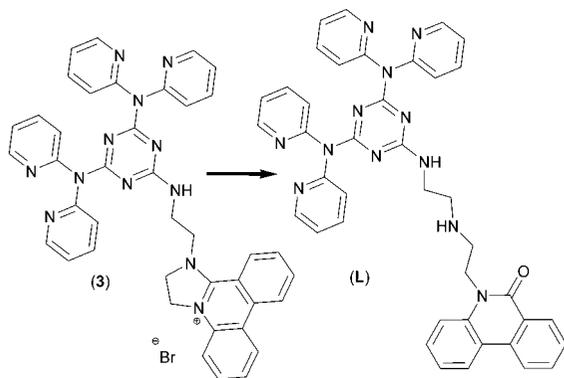


Figure 1. Ball-and-stick representation of $[\text{Pd}_5(\text{L})_2(\text{OAc})_8]^{2+}$. The solvent and anions of crystallization, as well as the H atoms, are omitted for clarity: C, gray; N, blue; O, red; Pd, green. Pd3 rests on an inversion center.

Scheme 2. Transformation of **3** into **L** upon Coordination to $\text{Pd}(\text{OAc})_2$ in DCM via a Ring-Opening Process, Occurring in a 33% Yield



therefore, a new ligand, compound **3**, was designed and synthesized. This compound integrates one DIP moiety along with two bidentate binding sites (Scheme 1). As shown in Scheme 1, 2-chloro[4,6-(dipyridin-2-ylamino)]-1,3,5-triazine¹¹ was coupled with ethylenediaminedihydroimidazophenanthridinium by nucleophilic substitution on the 2 position of the triazine; as a result, compound **3** is obtained with a good yield. The reaction of 2 equiv of palladium(II) acetate with 1 equiv of compound **3** in dichloromethane (DCM) yields light-yellow, needle-shaped single crystals of compound **4** after 2 weeks, whose crystal structure reveals that the initial compound **3** has been hydrolyzed upon coordination to give a new ligand, **L** (Scheme 2).

The structure of compound **4**, which crystallizes in the space group $P\bar{1}$, can be formulated as a pentanuclear Pd^{II} complex containing two of the new ligands, **L**, with a formula of $[\text{Pd}_5(\text{L})_2(\text{OAc})_8](\text{Br})_2$, and the structure is shown in Figure 1. The structure contains three different Pd^{II} ion positions identified as Pd1, Pd2, and Pd3. The coordination

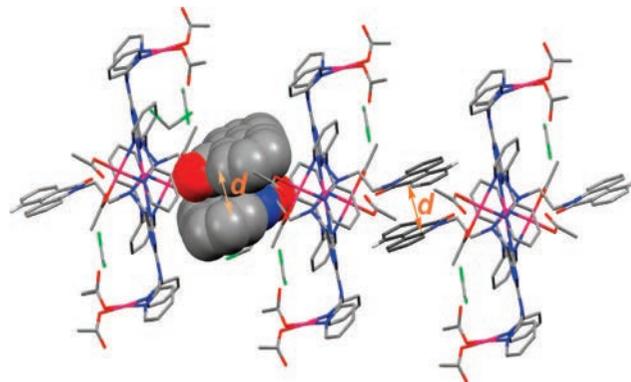


Figure 2. Perspective view showing the one-dimensional supramolecular chains assembled by means of π - π stacking interactions. The mean distance d between the two phenanthridine planes amounts to 3.391 Å.

geometries around all Pd atoms are square-planar, typical for d^8 Pd^{II} centers. Pd1 and Pd2 both have a N_2O_2 donor set resulting from the coordination of two pyridine units and two acetato ligands but with minor deviations. The structure is well-defined, but there is some disorder relating to the position of the two bromide anions that compensate for the charge of the cationic species (Figure 1). In addition, complex **4** crystallizes with water and DCM molecules in the crystal lattice.

The Pd-N and Pd-O bond lengths are in normal ranges, as compared with analogous complexes.¹² Pd3 is coordinated by four amine N atoms, belonging to two different **L** ligands, thus connecting two Pd1/Pd2 entities and generating the title pentanuclear compound (Figure 1). The coordinating ethylenediamine moieties are formed through the alteration of the original compound **3** upon reaction with palladium(II) acetate. The Pd-N bond distances are typical for a square-planar $\text{Pd}(\text{N}_{\text{amine}})_4$ coordination environment involving bidentate amine ligands.¹³ The angles around the Pd^{II} ion reflect a significant distortion from the ideal square-planar geometry, most likely as the result of the small bite angle of the chelating diethylenediamine group ($\text{N}_4\text{-Pd}_3\text{-N}_8 = 80.21^\circ$), combined with steric hindrance due to the phenanthridines.

The crystal packing of **4** shows interesting supramolecular features. The pentanuclear units are connected to two neighbors via π - π stacking interactions (the distance between the aromatic rings amounts to ca. 3.4 Å), giving rise to a one-dimensional chain (Figure 2). These supramolecular chains are further stabilized through $\text{C-H}\cdots\pi$ binding contacts ($d_{\text{H-arene centroid}} = 2.694$ Å), between phenanthridine H atoms and the triazine rings of adjacent pentanuclear complexes. Such $\text{C-H}\cdots\pi$ interactions with the *s*-triazine ring have been reported.¹⁴ It is interesting to note that these electron-deficient arenes appear to be interacting with the

(11) de Hoog, P.; Gamez, P.; Driessen, W. L.; Reedijk, J. *Tetrahedron Lett.* **2002**, *43*, 6783.

(12) (a) Seward, C.; Jia, W. L.; Wang, R. Y.; Wang, S. *Inorg. Chem.*, **2004**, *43*, 978. (b) Okabe, N.; Mizubayashi, Y.; Odoko, M. *Acta Crystallogr., Sect. E* **2006**, *62*, 2747.

(13) (a) Macdougall, J. J.; Nelson, J. H.; Fultz, W. C.; Burmeister, J. L.; Holt, E. M.; Alcock, N. W. *Inorg. Chim. Acta* **1982**, *63*, 75. (b) Newkome, G. R.; Frere, Y. A.; Fronczek, F. R.; Gupta, V. K. *Inorg. Chem.* **1985**, *24*, 1001.

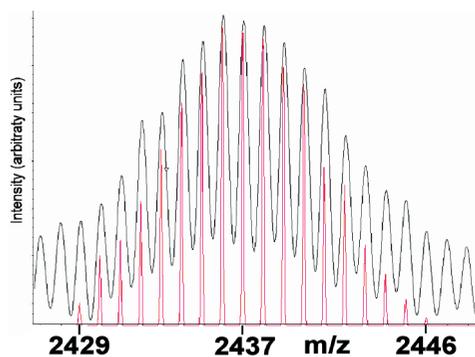


Figure 3. Cryospray mass spectrum (negative ion mode) of compound **4** in a DCM/MeCN (1:1) mixture at $-40\text{ }^{\circ}\text{C}$ shown in black. The simulated spectrum for $[\text{Pd}_5(\text{C}_{40}\text{H}_{34}\text{N}_{12}\text{O})_2(\text{CH}_3\text{CO}_2)_5\text{Cl}_6]^-$ is shown in red.

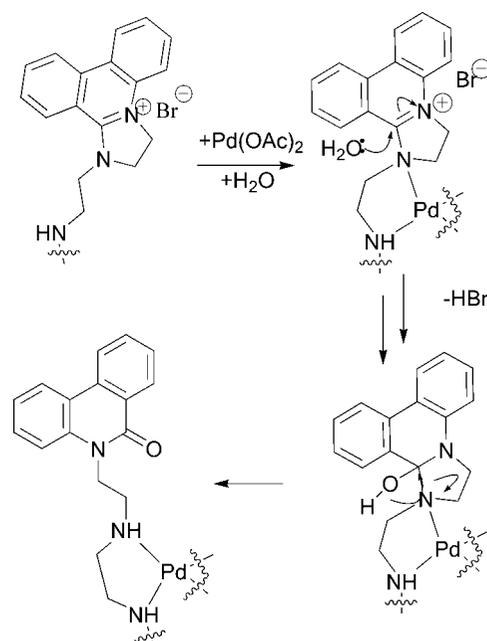
chlorine lone pairs¹⁵ ($d_{\text{Cl-arene centroid}} = 3.503\text{ \AA}$) from the DCM solvent (lp), which can be formulated as a type of $\text{C-H}\cdots\pi\cdots\text{lp}$ motif; although this is only a crystallographic observation, a search of CSD indicates that this observation is unique. Furthermore, the interplay between cation- π , π - π , and anion- π interactions^{14c} has been clearly demonstrated by density functional theory calculations, which have predicted that such interactions could exist.^{14b} Therefore, we tentatively suggest that the present system corresponds to the first crystallographic example of a $\text{C-H}\cdots\pi\cdots\text{lp}$ (which can also be symbolized as a $\delta+\cdots\pi\cdots\delta-$ supramolecular complex, corroborating the recent results of Quinonero et al.¹⁶

Solution investigations of **4** show that the Pd_5L_2 core of compound **4** can be observed using cryospray mass spectrometry as the $[\text{Pd}_5(\text{C}_{40}\text{H}_{34}\text{N}_{12}\text{O})_2(\text{CH}_3\text{CO}_2)_5\text{Cl}_6]^-$ anion, where the chloride anions originate from NaCl added to the solvent mixture (see Figure 3).

L forms from compound **3** (Scheme 2) via a ring-opening process with the introduction of a carbonyl group to give the ligand observed in the crystal structure upon coordination to $\text{Pd}(\text{OAc})_2$. While the precise mechanism of this ligand transformation has to await detailed experimental and theoretical investigation, one's first thought turns to a hydrolytic process during coordination, as shown in Scheme 3.

It is proposed that the Pd^{II} cation acts as a Lewis acid, which, upon coordination to the DIP N atom, activates the α position of the phenanthridinium moiety to nucleophilic attack from ambient water molecules in the reaction solvents. Elimination of HBr from this intermediate results in the formation of a neutral hydroxydihydroimidazophenanthridinium pseudobase molecule, which then undergoes a ring-opening rearrangement to form the crystallographically observed phenanthridinone moiety. This ring opening sig-

Scheme 3. Proposed Mechanism for the Ligand Transformation upon Coordination of Compound **3** by $\text{Pd}(\text{OAc})_2$



nificantly reduces the steric bulk around the Pd^{II} coordination environment, which may contribute to the driving force for this reaction. Preliminary NMR experiments (see the Supporting Information) show that the first step of this process is that compound **3** coordinates to Pd^{II} ion, after which hydrolysis by water completes the transformation.

In conclusion, a new triazine-based building block linked by a phenanthridinone molecule through an ethylenediamine unit has been designed and synthesized successfully. A novel pentanuclear Pd^{II} complex has been obtained by the reaction of compound **3** with $\text{Pd}(\text{OAc})_2$, in which a Pd^{II} -mediated ligand transformation from compound **3** to a phenanthridinone-based ligand in compound **4** has been observed. This observation represents the potential for the development of a new route to the synthesis of N-derivatized phenanthridinone moieties under mild conditions. The possible observation of a $\text{C-H}\cdots\pi\cdots\text{lp}$ interaction is interesting,¹⁷ and we will investigate this further with both theoretical and other experiments to gather further evidence giving insight into the nature of this interaction.

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Supporting Information Available: Full synthetic information and characterization of compounds **1–3** and complex **4**, CIF file of compound **4**, along with mass spectra and initial NMR experiments on ligand transformation. This material is available free of charge via the Internet at <http://pubs.acs.org>.

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- (14) (a) Thalladi, V. R.; Boese, R.; Brasselet, S.; Ledoux, I.; Zyss, J.; Jetli, R. K.; Desiraju, G. R. *Chem. Commun.* **1999**, 17, 1639. (b) Gamez, P.; Mooibroek, T. J.; Teat, S. J.; Reedijk, J. *Acc. Chem. Res.* **2007**, *40*, 435. (c) Frontera, A.; Quiñero, D.; Costa, A.; Ballester, P.; Deyà, P. M. *New J. Chem.* **2007**, *4*, 556.
- (15) Lu, Z.; Gamez, P.; Mutikainen, I.; Turpeinen, U.; Reedijk, J. *Cryst. Growth Des.* **2007**, *7*, 1669–1671.
- (16) Quinonero, D.; Frontera, A.; Garau, C.; Ballester, P.; Costa, A.; Deyà, P. M. *ChemPhysChem.* **2006**, *7*, 2487.

- (17) DiLabio, G. A.; Johnson, E. R. *J. Am. Chem. Soc.* **2007**, *219*(19), 6199.