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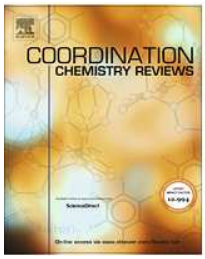

Palladium(II) Coordination with Polyazacycloalkanes

Nathalie Le Bris[a,*], Julie Pineau[a], Luís M. P. Lima[b], and Raphaël Tripier[a,*]

[a] Univ Brest, UMR-CNRS 6521 CEMCA, 6 avenue Victor Le Gorgeu, 29200 Brest, France.
[b] Instituto de Tecnologia Química e Biológica António Xavier, Universidade Nova de Lisboa, Avenida da República, 2780-157 Oeiras, Portugal.

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ABSTRACT

In view of the growing interest of palladium(II) for medical applications and the important role of polyamines in exploiting its properties, this review combines the published literature on the coordination of Pd(II) with small polyazacycloalkanes (three and four nitrogen atoms), such as 1,4,7-triazacyclononane, 1,5,9-triazacyclododecane, cyclen, cyclam, as well as their derivatives or close scaffolds such as pyclen. Finally, the rare examples of the use of aza-ligands with ^{103}Pd and ^{109}Pd radioisotopes for therapeutic purposes are also presented. The coordination of the Pd(II) ion is mainly square planar, often slightly distorted depending on the nature of the ligand. A few rare five-coordinated complexes with square pyramidal or trigonal bipyramidal geometries have been described in cases where the steric or topological requirements of the ligand outweigh the loss of stabilization due to geometric distortion. Considering the marked structural preference of Pd(II) for square planar coordination, this review allows us to propose hypotheses on the nature of new Pd(II) complexes whose properties could be exploited, especially in nuclear medicine.

Contents

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1. Introduction

Palladium is a metal widely explored in chemistry, especially for applications in catalysis, radiochemistry, and medicine. Since the discovery, in the 1960s, of antitumor properties of platinum(II) compounds such as the commercially available cisplatin $[Pt(NH_3)_2Cl_2]$ and its derivatives, palladium(II) anticancer analogues have also been strongly studied due to the similarity of their coordination chemistry behavior. Pd(II) is, according to the HSAB (Hard and Soft Acids and Bases) Pearson classification, a soft Lewis acid of d^8 electronic configuration showing a higher affinity for soft bases such as sulfur, phosphorus, or nitrogen donors than with hard bases such as oxygen donors.

In 1979, Graham and Williams were among the first to report numerous Pd(II) complexes exhibiting anticancer, antiviral, antifungal, and antimicrobial activities [1]. Thirty-five years later, Kapdi and Fairlamb published a well-documented review listing Pd(II) complexes of mono- or multidentate ligands based on sulfur, phosphorus and nitrogen as potential anticancer agents [2].

For *in vivo* medical applications, the development of efficient ligands suitable for Pd(II) requires an in-depth knowledge of their coordination chemistry. The challenge lies in the design of the coordinating agents, which must fulfill several criteria such as fast complexation, high thermodynamic stability and kinetic inertness.

Ligands containing *N*-donor atoms are of high interest for Pd(II) coordination and the use of polyamine-based ligand complexes appears to be particularly attractive, especially in the medical field. This is notably the case for naturally occurring polyamines such as spermidine and spermine that lead to complexes recognized as anticancer agents [3,4]. One also have to mention Tookad® Soluble which is, to our knowledge, the only Pd(II) complex accepted for medical purposes. This Pd-bacteriopheophorbide-based species is a useful reagent for targeted photodynamic therapy (PDT) in localized prostate cancer treatment [5].

Pd(II) complexes with ammonia [6] and polyamine ligands have been reported, including diamines [6-10], linear triamines [11-13], linear tetraamines [14], tripodal tetraamines [15,16] and linear octaamines, as well as large polyazamacrocycles such as [18]aneN$_6$, [21]aneN$_7$, [24]aneN$_8$ and other derivatives [17-19].

Bianchi and co-workers published a review in 1999 collecting thermodynamic data from studies in aqueous solution and structural features of a series of Pd(II) complexes with ammonia and aliphatic polyamines. The presence of alkyl substituents on the nitrogen atoms of the ligands does not affect the coordination of Pd(II) in the solid state but reduces considerably the thermodynamic stability of the complexes in solution. In most cases, this stability is larger by several orders of magnitude than that of the most stable complexes of other transition divalent metal ions with the same ligands. For example, for the complexes of the linear tetraamine *N,N'*-bis(2-aminoethyl)-1,3-propanediamine with Pd(II) and Cu(II), complexation constants (log K_{ML}) are respectively 30.5 and 20.1. The Pd(II) complexes are also particularly inert towards dissociation. The high thermodynamic stability of the complexes coupled to their kinetic inertness are therefore favorable for *in vivo* applications, which explains the interest in Pd(II) complexes for medicine [20].

Gianguzza and coll. described the behavior in aqueous solution of the Pd(II) complexes of a series of acyclic aminopolycarboxylic ligands such as nitrilotriacetic acid (NTA), ethylenediamine tetraacetic acid (EDTA), diethylenetriamine pentaacetic acid (DTPA), and triethylenetetramine hexaacetic acid (TTHA). The thermodynamic stability constants were determined by means of potentiometric titrations, with log K_{PdL} values ranging from 17.8 for NTA to 37.0 for TTHA. While the stability of such Pd(II) complexes is a function of the number of binding groups (-NH and -COO$^-$) present in the ligand, the dependence is not linear [21].

Although Pd(II) complexes of cyclic and acyclic polyamines have been investigated, thermodynamic data for coordination of Pd(II) with polyazacycloalkanes in aqueous solution are rather rare. To our knowledge, very few original papers and even fewer reviews have been published reporting ligands suitable for Pd(II) complexation and the physicochemical data in terms of stability and inertness.

In view of the growing interest in the use of Pd(II), particularly in the field of health, and the great utility of polyamines to take advantage of its properties, it is timely to examine the body of knowledge relating cyclic polyamines with Pd(II). This paper aims to review the published literature on the Pd(II) coordination with small polyazacycloalkanes (three and four nitrogen atoms), such as 1,4,7-triazacyclononane, 1,5,9-triazacyclododecane, cyclen and cyclam, as well as their *N*-alkylated (or *N*-functionalized), reinforced or oxo-derivatives. Considering their similarity to cyclen, pyclen complexes will also be described. Next, the synthesis of Pd(II) complexes of *C*-alkylated cyclams and larger tetraazamacrocycles, called "swollen", obtained by a template effect from complexes of diamines or linear tetramines will be discussed. Finally, in the last part, some rare examples of the use of two radioisotopes of palladium, ^{103}Pd and ^{109}Pd, for therapeutic purposes with aza-ligands will also be presented.

2. Palladium(II) coordination with polyazacycloalkanes

2.1. Triazacycloalkanes

2.1.1. 1,4,7-triazacyclononane (tacn)

The formation of a Pd(II) complex with 1,4,7-triazacyclononane (tacn) was easily obtained in a 1:2 metal/ligand ratio leading to various distinct spatial arrangements and geometries. Two configurational isomers were reported in the literature in which Pd(II) is coordinated by two *N*-donor atoms of each macrocycle with a square planar coordination geometry. The two non-bonding nitrogen atoms lie either on opposite sides (*anti* configuration) or on the same side (*syn* configuration) of the PdN_4 plane. Crystal structures including non-protonated, mono-protonated and di-protonated Pd(II) complexes have been reported.

McAuley and co-workers have described the structure of the non-protonated $[Pd(tacn)_2](PF_6)_2$ complex, which exhibits the *anti* configuration. This species was obtained by reaction of tacn (2.5 equiv) with $PdCl_2$ in water followed by addition of NH_4PF_6 leading to yellow single crystals suitable for X-ray diffraction. The complex has a perfect square plane around the Pd(II), which is dictated by the 2-fold axis through the metal ion. The average of Pd-N bonds distance is 2.057 Å and the N-Pd-N angles formed by the two 5-membered chelate rings are equal to 82.2°, which deviates from the ideal value of a square

plane (90°). The non-coordinated nitrogen atoms are directed away from the Pd(II) at a distance of 3.499 Å (**Fig. 1**) [22]. The UV-visible spectrum of the $[Pd(tacn)_2]^{2+}$ complex showed an absorption band of significant intensity at 296 nm (ε = 440 M^{-1} cm^{-1}) with a shoulder at 440 nm (ε = 30 M^{-1} cm^{-1}) [23]. This band is similar to that of $[Pd^{II}(en)_2](Cl)_2$ (en = ethylenediamine) with a λ_{max} at 286 nm (ε = 285 M^{-1} cm^{-1}), determined by Rasmussen and Jørgensen, suggesting that in $[Pd(tacn)_2]^{2+}$ the binding of Pd(II) is not significantly affected by the remaining ligand bridge in the solid state and that the environment around the Pd(II) center is a normal PdN_4 chromophore [24].

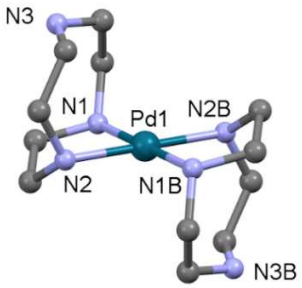


Fig. 1. Crystal structure of $[Pd(tacn)_2]^{2+}$ cation in $[Pd(tacn)_2](PF_6)_2$ with *anti* configuration. Selected bond distances (Å) and angles (°): Pd1-N1 2.067, Pd1-N2 2.050, Pd1-N3 3.499, N1-Pd1-N2 82.2, N1-Pd1-N2B 97.8.

The structure of a diprotonated $[Pd(Htacn)_2](ClO_4)_4{\cdot}H_2O$ complex, found in the solid state by Margulis and Zompa, revealed that the two unbound nitrogen atoms of each tacn are protonated and located on the opposite side in the *anti* configuration as in the example described above. The reported Pd-N distances are quite similar to those of the previous non-protonated complex with average values around 2.06 Å, as are the angles with the two N-Pd-N internal angles having values of approximately 81.0°. In this example, the two non-bonded protonated nitrogen atoms are slightly more distant from Pd(II) with a distance of about 3.66 Å than in the non-protonated complex. The acid dissociation constants of this diprotonated complex have been measured in 0.1 M ClO_4^- media. The first equilibrium, corresponding to the deprotonation of the $[Pd(Htacn)_2]^{4+}$ species, led to a pK_a value of 2.40, while the second equilibrium involving the loss of the remaining proton of $[Pd(Htacn)(tacn)]^{3+}$ gave a pK_a of 4.72. These values are not unusual since H_3tacn^{3+} is a strong acid [25] and a Pd(II) ion has less effect on the acid dissociation than a proton. Actually, $[Pd(Htacn)(tacn)]^{3+}$ has the same charge as the triprotonated ligand and is a moderately weak acid [26].

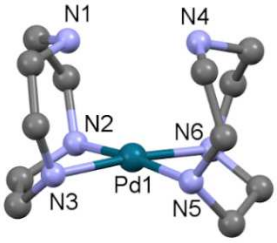


Fig. 2. Crystal structure of $[Pd(tacn)(Htacn)]^{3+}$ cation in $[Pd(tacn)(Htacn)](PF_6)_2(NO_3).H_2O$ with *syn* configuration. Selected bond distances (Å) and angles (°): Pd1-N1 2.983, Pd1-N2 2.017, Pd1-N3 2.087, Pd1-N4 3.079, Pd1-N5 2.051, Pd1-N6 2.067, N1-N4 2.954; N2-Pd1-N3 83.0, N3-Pd1-N5 97.2, N5-Pd1-N6 81.5, N2-Pd1-N6 97.7.

Schröder and coll. have obtained the monoprotonated $[Pd^{II}(tacn)(Htacn)](PF_6)_2(NO_3).H_2O$ complex in the *syn* configuration. They suggested that the stabilization of this species can be attributed to the formation of an extensive hydrogen bond between the Pd(II) ion, one NO_3^- ion and one water molecule. One can note that the Pd-N2 bond is significantly shorter than the other three (2.017 *vs* 2.087, 2.051 and 2.067 Å). The distances between the two uncoordinated nitrogen atoms and Pd(II) are around 3.0 Å, which is clearly shorter than on non-protonated or diprotonated species (**Fig. 2**) [27].

Temperature-dependence NMR studies on the $[Pd(tacn)_2]^{2+}$ complex have been performed by McAuley and Whitcombe in various deuterated solvents. ^{13}C NMR spectra recorded at ambient temperature showed surprisingly one single resonance peak at 52.6 ppm, whatever the solvent, which is in contrast to what was observed in the crystalline structure. The authors deduced the existence of a dynamic process rendering all of the carbon atoms equivalent on the NMR time scale. At low temperature (-90°C) in methanol-d4, the ^{13}C NMR spectrum showed two series of peaks corresponding respectively to the *anti* and *syn* structures in an approximate ratio of 2:1. The absence of the characteristic signals of the free tacn ligand suggested an intramolecular mechanism rather than a dissociative one (**Fig. 3**). These data display the fluxional behaviour of tacn for which coordinated and unbound nitrogen atoms can be easily exchanged. This was the first example of such a behaviour for a Pd(II)-amine complex. The authors also reported the value of the activation barrier ΔG_{298} = 10.2 ± 3.8 kcal mol^{-1}, determined from the NMR variable temperature study [28].

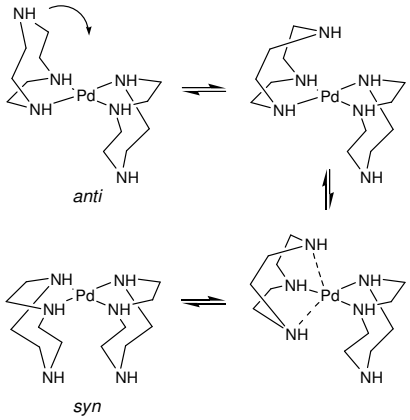


Fig. 3. Temperature-dependent dynamic process exchanging *anti* and *syn* configurations in $[Pd(tacn)_2]^{2+}$ complex *via* an intramolecular mechanism.

The redox chemistry of $[Pd(tacn)_2]^{2+}$ species was investigated under different experimental conditions. Schröder and coll. have studied its electrochemical behavior in MeCN (0.1 M Bu_4NPF_6). The cyclic voltammogram showed a first reversible oxidation peak at $E_{1/2}$ = +0.07 V *vs* Fc/Fc^+ which was assigned to the Pd(II)/Pd(III) couple followed by a second slower oxidation corresponding to the Pd(III)/Pd(IV) couple at $E_{1/2}$ = +0.45 V. McAuley and Whitcombe have reported the redox potential of $[Pd(tacn)_2]^{2+}$ in different electrolytes (1 M $LiClO_4$ or $LiNO_3$). The Pd(II)/Pd(III) oxidation

process appeared at $E_{1/2}$ = +0.37 *vs* NHE. The second oxidation current related to the Pd(III)/Pd(IV) couple was observed at $E_{1/2}$ = +0.64 V. The ligand shows an unusual fluxional behavior which facilitates the oxidation of Pd(II) to Pd(III) leading to the surprisingly very stable hexacoordinated $[Pd^{III}(tacn)_2]^{3+}$ complex (**Fig. 4**) [29].

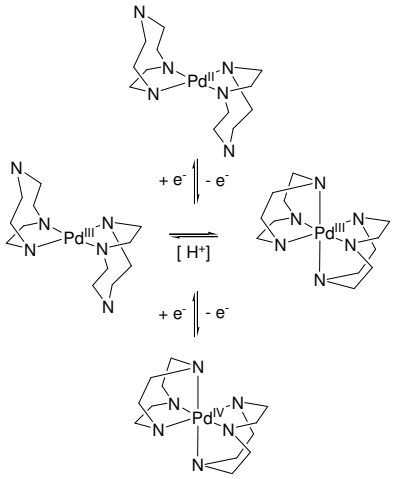


Fig. 4. Oxidative interconversion of $[Pd(tacn)_2]^{n+}$ species between square planar and octahedral geometries through the protonation of apical amines. Hydrogen atoms are omitted as in the original article.

Margulis and Zompa have obtained the $[Pd(Htacn)Br_2]^+$ complex by addition to $[Pd(tacn)_2]^{2+}$ of a large excess of bromide ions in acidic medium leading to the displacement of one tacn ligand. Crystallographic analysis revealed that Pd(II) is tetra-coordinated in a square planar geometry involving two nitrogen atoms of one tacn and two bromine atoms in *cis* position. The strain N-Pd-N angle of 82° is similar to that of the two previous complexes and Pd-N distances are 2.062 and 2.047 Å. The two Pd-Br bond length values are around 2.43 Å and the unbound protonated nitrogen atom lies at 3.517 Å to the metal center. This value is in the same range as the distance between Pd and unbound nitrogen atom in $[Pd(tacn)_2]^{2+}$ at 3.499 Å (**Fig. 5**) [30].

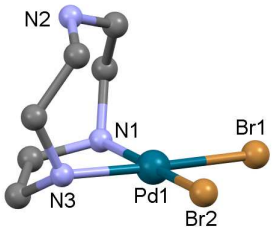


Fig. 5. Crystal structure of $[Pd(Htacn)Br_2]^+$ cation in $[Pd(Htacn)Br_2](ClO_4)\cdot H_2O$. Selected bond distances (Å) and angles (°): Pd1-N1 2.062, Pd1-N2 3.517, Pd1-N3 2.047, Pd1-Br1 2.439, Pd1-Br2 2.425, N1-Pd1-N3 82.0, N1-Pd1-Br1 91.2, N3-Pd1-Br2 91.6, Br1-Pd1-Br2 95.4.

Schröder and co-workers have obtained the chlorine analogue $[Pd(Htacn)Cl_2]^+$ of the previously described bromine complex, together with a binuclear species [31] . The treatment of tacn with $PdCl_2$ in the presence of NaOH (pH~8), followed by the addition of NH_4PF_6, led to yellow monocrystals. The crystallographic study showed the presence of two monomeric cations $[Pd(Htacn)Cl_2]^+$ and one binuclear cation $[Cl_2(Htacn)Pd\text{-}Pd(Htacn)Cl_2)]^{2+}$ within an extensive H-bonded network. The Pd(II) center of each monomer is bound to two chloro-ligands and to two *N*-donors of the monoprotonated ligand in a square plane. Furthermore, an apical interaction with one of the protons of the non-bonded protonated nitrogen atom is observed with an average distance Pd···$^+$H-NHR_2 of 2.400 Å (**Fig. 6**).

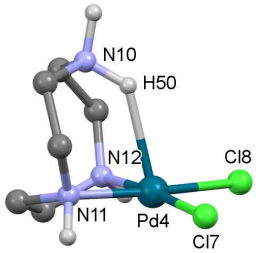


Fig. 6. Crystal structure of $[Pd(Htacn)Cl_2]^+$ cation in $[Pd(Htacn)Cl_2](PF_6)$. Selected bond distances (Å) and angles (°): Pd4-N11 2.065, Pd4-N12 2.008, Pd4-Cl7 2.322, Pd4-Cl8 2.300, Pd4-N10 3.223, Pd4-H50 2.400, N11-Pd4-N12 83.0, Cl7-Pd4-Cl8 94.3. Hydrogen atoms are omitted for clarity, except on nitrogen atoms.

In the dimer $[Cl_2(Htacn)Pd\text{-}Pd(Htacn)Cl_2)]^{2+}$ (**Fig. 7**), each Pd(II) ion is bound to two *N*-donors nitrogen atoms of a mono-protonated macrocycle and to two mutually *cis* Cl^- ligands with a Pd-Pd bond length of 3.311 Å. The two pairs of chloro-ligands are situated *trans* to one another with respect to the Pd-Pd axis. In this dimer, the two macrocycles adopt a different conformation. One macrocycle has its protonated nitrogen atom inclined toward the Pd1 with one of the protons forming an agostic interaction with the Pd(II) at a distance of Pd1-H2 of 2.297 Å, whereas the second macrocycle has its protonated nitrogen atom inclined away from the other Pd2 ion with a bond length Pd2-N4 of 3.472 Å. Finally, both structures, $[Pd(Htacn)Cl_2]^+$ and $[Cl_2(Htacn)Pd\text{-}Pd(Htacn)Cl_2)]^{2+}$, present Pd···H$^+$···$NHR_2$ interactions. Even though these examples are not formally electron-deficient, the authors rationalized the bonding *via* H^+ bridging between lone pairs on the nitrogen atom and Pd(II) d_z^2 orbital [31].

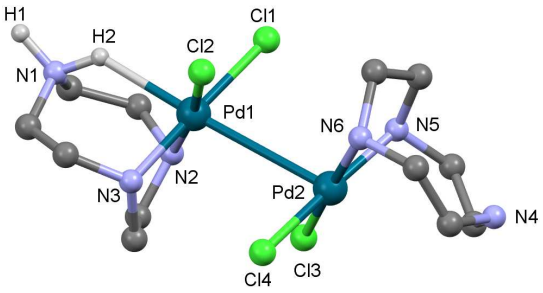


Fig. 7. Crystal structure of $[Cl_2(Htacn)Pd\text{-}Pd(Htacn)Cl_2)]^{2+}$ cation in $[Cl_2(Htacn)Pd\text{-}Pd(Htacn)Cl_2)](PF_6)_2$. Selected bond distances (Å) and angles (°): Pd1-N2 2.041, Pd1-N3 2.015, Pd1-N1 3.108, Pd1-Cl1 2.326, Pd1-Cl2 2.299, Pd1-H2 2.297, Pd1-Pd2 3.311, Pd2-N5 2.061, Pd2-N6 2.025, Pd2-N4, 3.472, Pd2-Cl3 2.293, Pd2-Cl4 2.307; N2-Pd1-N3 83.3, Cl1-Pd1-Cl2 94.3, N5-Pd2-N6 82.9, Cl3-Pd2-Cl4 94.7. Hydrogen atoms are omitted for clarity, except on N1.

2.1.2. 1,4,7-trimethyl-1,4,7-triazacyclononane (Me$_3$tacn)

Some Pd(II) complexes of 1,4,7-trimethyl-1,4,7-triazacyclononane (Me_3tacn) in a 1:1 stoichiometry have

been described in particular for catalytic applications such as C-C coupling or selective C_{sp2}-O bond formation. The use of different reaction conditions (Pd(II) salt, solvent...) has led to the observation of either tetra- or pentacoordinated complexes.

Among the few reported examples, $[Pd(Me_3tacn)(CH_3CN)_2]^{2+}$ complex was firstly synthesized by Schröder and coll. by reaction of Me_3tacn with $[Pd(CH_3CN)_4]^{2+}$ salt followed by the addition of NH_4PF_6. The crystal structure analysis of the purple complex showed that the Pd(II) ion is five-coordinated by the three *N*-donors of the macrocycle and two *N*-donors of CH_3CN ligands bound in the equatorial plane (**Fig. 8**). The Pd-N_{amine} bond distance involved in the basal plane showed values of 2.036 Å whereas the third *N*-donor interacts with Pd(II) at long range distance in an axial bond Pd-N_{amine} at 2.523 Å to give a distorted square-based pyramidal structure. The Pd-N_{CH_3CN} bond length values are 2.016 Å [31].

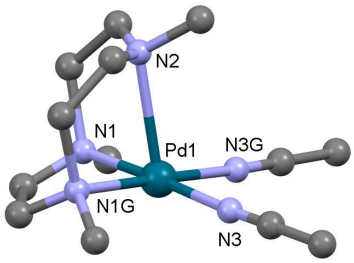


Fig. 8. Crystal structure of $[Pd(Me_3tacn)(CH_3CN)_2]^{2+}$ in $[Pd(Me_3tacn)(CH_3CN)_2](PF_6)_2$. Selected bond distances (Å) and angles (°): Pd1-N1 2.036, Pd1-N2 2.523, Pd1-N3 2.016; N1-Pd1-N1G 84.9, N1-Pd1-N3G 92.9, N1G-Pd1-N3 92.9, N3-Pd1-N3G 89.3.

Mirica and co-workers have synthesized the Pd(II) complexes $[Pd(Me_3tacn)X_2]$ (X = Cl, Br) through the reaction of Me_3tacn with $[Pd(CH_3CN)_2X_2]$ in dichloromethane [32]. The X-ray structure analysis of the yellow chlorinated complex showed a square-planar geometry around the metal center which is bound to two nitrogen atoms and two Cl^- while the remaining nitrogen atom of the ligand not involved in the coordination is at a distance of 3.364 Å from the Pd(II). The Pd-N_{amine} bond length values are around 2.08 Å and the Pd-Cl bond lengths are around 2.31 Å (**Fig. 9**). Proton NMR data recorded in CD_3CN showed a multiplet signal corresponding to the CH_2 α-N of the triazamacrocycle and only one singlet signal at 2.73 ppm characteristic to the three methyl that is due to the fluxional behavior of the ligand as seen above. UV-visible measurements of $[Pd(Me_3tacn)Cl_2]$ complex performed in acetonitrile showed three absorption bands at 396 nm ($\varepsilon = 270\ M^{-1}\ cm^{-1}$), 290 nm ($\varepsilon = 1300\ M^{-1}\ cm^{-1}$) and 232 nm ($\varepsilon = 23\,000\ M^{-1}\ cm^{-1}$). The cyclic voltammetry of this Pd(II) complex, performed in MeCN (0.1 M Bu_4NPF_6), exhibited two oxidation waves close to each other between 0.05 and 0.17 V *vs* Fc/Fc^+. The measurement of controlled potential electrolysis showed a value between 0.3-0.4 V attributed to one electron oxidation of the Pd(II) complex in a dinuclear Pd(III) complex.

No X-rays structure was reported for the bromine complex $[Pd(Me_3tacn)Br_2]$ but studies in solution (^1H NMR, UV-visible and electrochemistry data) are very similar to those described for the analogous chlorinated complex [32].

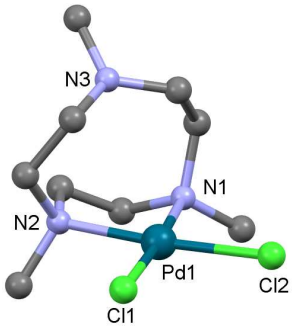


Fig. 9. Crystal structure of $[Pd(Me_3tacn)Cl_2]$. Selected bond distances (Å) and angles (°): Pd1-N1 2.074, Pd1-N2 2.088, Pd1-N3 3.364, Pd1-Cl1 2.307, Pd1-Cl2 2.321, N1-Pd1-N2 84.5, N1-Pd1-Cl2 93.6, N2-Pd1-Cl1 91.1, Cl1-Pd1-Cl2 90.7.

The addition of AgOTf (1 equiv) to the previously described $[Pd(Me_3tacn)Cl_2]$ complex led to the precipitation of AgCl and the formation of $[Pd(Me_3tacn)(CH_3CN)Cl]^+$ (**Fig 10**). The X-ray structure analysis of the dark purple crystals revealed a distorted square pyramidal geometry of the metal center. The five-coordinated geometry of Pd(II) involves the three nitrogen atoms of the ligand completed by one Cl^- and one CH_3CN ligand. The distances of Pd-N_{amine} in the basal plane are 2.079 and 2.061 Å whereas the third axial Pd-N_{amine} bond distance is 2.615 Å. Pd-N_{CH_3CN} and Pd-Cl bond lengths are respectively 2.001 Å and 2.302 Å. The proton NMR spectrum of the $[Pd(Me_3tacn)(CH_3CN)Cl]^+$ species, obtained in CD_3CN, consists of two multiplet signals in the range 2.80-3.20 ppm corresponding to hydrogen atoms of the methylene groups whereas the three methyl groups of Me_3tacn appear as a singlet at 2.86 ppm. The methyl signal of the acetonitrile ligand was not reported, which is in contradiction with the HRMS and elemental analysis showing the presence of $[Pd(Me_3tacn)(CH_3CN)Cl]^+$ complex. The UV-vis spectrum of this Pd(II) complex revealed three absorption bands at 534 nm ($\varepsilon = 50\ M^{-1}\ cm^{-1}$), 370 nm ($\varepsilon = 220\ M^{-1}\ cm^{-1}$), 230 nm ($\varepsilon = 27000\ M^{-1}\ cm^{-1}$) [32].

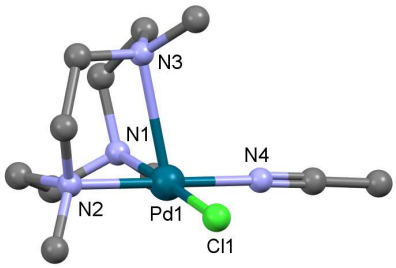


Fig. 10. Crystal structure of $[Pd(Me_3tacn)(CH_3CN)Cl]^+$ in $[Pd(Me_3tacn)(CH_3CN)Cl](ClO_4)$. Selected bond distances (Å) and angles (°): Pd1-N1 2.079, Pd1-N2 2.061, Pd1-N3 2.615, Pd1-N4 2.001, Pd1-Cl1 2.302, N1-Pd1-N2 84.0, N1-Pd1-N4 94.3, N4-Pd1-Cl1 88.2, N2-Pd1-Cl1 93.5, N2-Pd1-N4 178.0, N1-Pd1-Cl1 177.2.

Mirica and coll. have also described the formation of $[Pd(Me_3tacn)Me_2]$ complex through the reaction of $[Pd(COD)Me_2]$ with Me_3tacn (COD = cycloocta-1,5-

diene) [33]. X-ray analysis showed a square-planar geometry of the Pd(II) center, which is bound to two methyl groups and two nitrogen atoms of Me_3tacn. The third nitrogen atom of the ligand points away from the Pd(II). The structure is similar to that of [Pd(Me_3tacn)Cl_2] described above (**Fig. 11**). The Pd-Me bond lengths are about 2.03 Å, which are in accordance with those of other Pd(II)-dimethyl complexes of permethyldiamine ligands such as [Pd(tmeda)Me_2] (tmeda = tetramethylethylene diamine) [34,35]. The ^{1}H NMR spectrum of the complex exhibits only a singlet for the two methyl ligands whereas Me_3tacn shows a fluxional behavior with only one average singlet for the three methyl groups, even at low temperature, due to the exchange between the free and coordinated nitrogen atoms. The cyclic voltammogram performed in MeCN (0.1 M Bu_4NPF_6) shows an irreversible oxidation wave Pd^{II}/Pd^{III} at -0.71 V *vs* Fc^+/Fc, which is significantly lower than analogous "Pd-dimethyl" complexes with bidentate *N*-donor ligands. This was explained by the ability of the tridentate tacn-type ligand to stabilize the octahedral or distorted octahedral geometry of high-valent Pd centers [33].

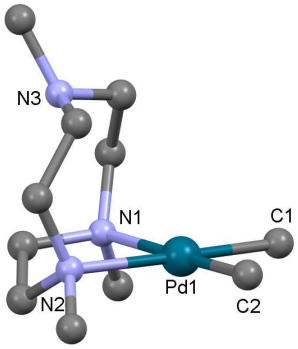


Fig. 11. Crystal structure of [Pd(Me_3tacn)Me_2] complex. Selected bond distances (Å) and angles (°): Pd1-N1 2.220, Pd1-N2 2.249, Pd1-N3 3.574, Pd1-C1 2.032, Pd1-C2 2.034, N1-Pd1-N2 80.7, N1-Pd1-C1 96.1, N2-Pd1-C2 95.6, C1-Pd1-C2 87.5.

2.1.3. 1,4,7-tris(2-pyridylmethyl)-1,4,7-triazacyclononane (Py_3tacn)

The addition of three coordinating 2-pyridylmethyl arms on the nitrogen atoms of tacn, forming 1,4,7-tris(2-pyridylmethyl)-1,4,7-triazacyclononane (Py_3tacn), led after reaction with Pd(II) acetate in methanol, and further addition of NH_4PF_6, to the formation of one single Pd(II) complex as red monocrystals. Wieghardt and coll. described the five coordinated Pd(II) species $[Pd(Py_3tacn)]^{2+}$ in which the metal ion exhibits a distorted square-based pyramidal environment of five-coordinated nitrogen atoms with two tertiary amines of the macrocycle and two pyridine nitrogen atoms in the basal plane. The last tertiary nitrogen atom of Py_3tacn completes the coordination sphere in apical position leaving one pendant pyridylmethyl arm uncoordinated. The average distances of Pd-N_{amine} and Pd-N_{Py} in the basal plane are respectively 2.03 Å and 2.04 Å whereas the axial bond distance is 2.580 Å (**Fig. 12**). The electronic spectra of $[Pd(Py_3tacn)]^{2+}$ in solution, as well as in the solid state, exhibit a weak absorption maximum at 453 nm ($\varepsilon = 76\ M^{-1}\ cm^{-1}$) assigned to a d-d transition of the low-spin, square-based PdN_5 chromophore. Electrochemical measurement in CH_3CN (0.1 M Bu_4NPF_6) showed that the complex was redox inactive in the studied potential range of +1.7 to -1.5 V *vs* Ag/AgCl [36].

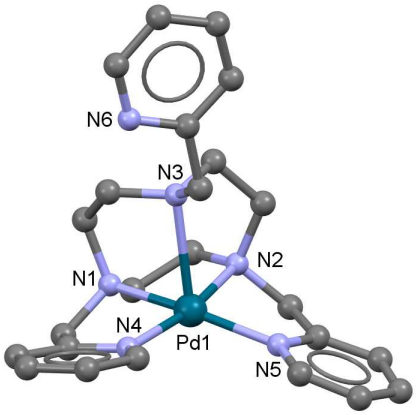


Fig. 12. Crystal structure of $[Pd(Py_3tacn)]^{2+}$ cation in $[Pd(Py_3tacn)](PF_6)_2$. Selected bond distances (Å) and angles (°): Pd1-N1 2.041, Pd1-N2 2.010, Pd1-N3 2.580, Pd1-N4 2.041, Pd1-N5 2.048; N1-Pd1-N2 86.2, N2-Pd1-N3 78.8, N3-Pd1-N5 112.4, N1-Pd1-N3 77.9, N1-Pd1-N4 83.0, N3-Pd1-N4 96.0, N2-Pd1-N5 83.2.

2.1.4. 1,5,9-tris(2-pyridylmethyl)-1,5,9-triazacyclododecane (Py_3tacd)

The reaction of 1,5,9-tris(2-pyridylmethyl)-1,5,9-triazacyclododecane (Py_3tacd) with $PdCl_2$ in methanol, followed by the addition of NH_4PF_6 leading to the $[Pd(Py_3tacd)]^{2+}$ complex, was performed by Zhang and Busch. No crystal structure has been reported but the electronic spectrum of the yellow complex indicates a maximum of absorption at 316 nm ($\varepsilon = 704\ M^{-1}\ cm^{-1}$). This value suggests a different coordination geometry from that found for $[Pd(Py_3tacn)]^{2+}$ described above in which Pd(II) ion was five-coordinated. The redox potential measured in acetonitrile (0.1 M Bu_4NBF_4) displays an irreversible oxidation peak of Pd(II) to Pd(III) at +1.27 V *vs* NHE. This complex is much more resistant to oxidation than $[Pd(Py_3tacn)]^{2+}$. An unexpected reversible reduction potential of Pd(II) to Pd(I) was also observed at -0.76 V *vs* NHE. The authors mentioned that the observation of Pd(I) complexes is rare in the absence of strong π-back-bonding donors such as phosphine or carbon monoxide [37].

2.2. Tetraazacycloalkanes

2.2.1. 1,4,7,10-tetraazacyclododecane (cyclen)

To our knowledge, no Pd(II) complex of "naked" cyclen (meaning cyclen without additional *N*-anchored functions) has been described. The rare existing examples are Pd(II) complexes of cyclen tri-*N*-functionalized by acetate derivative arms. A first example described by Tae and co-workers consists of a dinuclear Pd(II) complex of a tri-*tert*-butylacetate cyclen linked to a rhodamine-hydroxamate (**Fig. 13**) [38]. This species has been used as a Pd(II) specific fluorescent chemosensor since it binds specifically with Pd(II) ions to induce a strong fluorescence enhancement and color changes in aqueous solution and can discriminate Pd(II) over Pt(II). The authors proposed a 1:2 complex (**Fig. 13**), but the coordination scheme between the cyclen-based ligand and the cation was not confirmed.

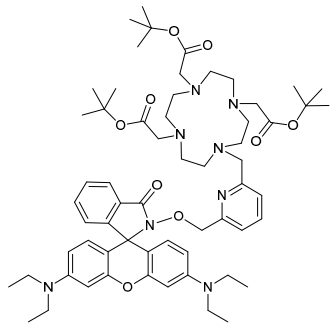


Fig. 13. Structure of the rhodamine hydroxamate-cyclen conjugate.

Grin and coll. have studied the complexation with Pd(II) of a conjugate of a natural chlorin with a cyclen moiety for applications in the development of contrast agents for diagnostics and therapy. The synthesis of the dinuclear Pd(II) species was not possible from the conjugate chlorin-cyclen even in the presence of an excess of Pd(II) acetate and the authors proved that the obtained monomeric Pd(II) complex corresponds to the incorporation of the Pd(II) into the chlorin (**Fig. 14**, structure **a**).

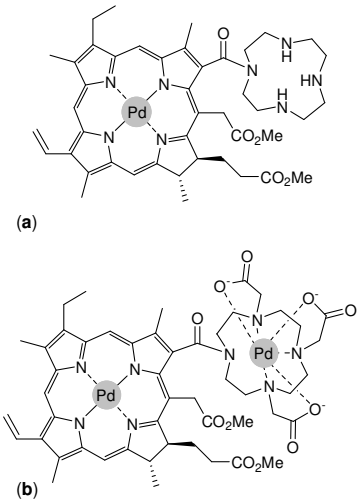


Fig. 14. Mononuclear (**a**) and dinuclear Pd(II) complexes (**b**) of chlorin-cyclen conjugates represented as in the original article.

The reaction was followed by spectrophotometric monitoring of the absorption band Q2 of the chlorin and the characteristic hypsochromic shift from 663 to 624 nm. The authors concluded that the introduction of a Pd(II) ion into a "naked" cyclen was unlikely due to the non-planarity of the macrocycle and the inability for the Pd(II) ion to adopt a square planar geometry. The addition of three acetate coordinating arms on cyclen was then necessary to obtain the dinuclear Pd(II) complex (**Fig. 14**, structure **b**). The introduction of a second Pd(II) into the triacetate-cyclen moiety was revealed by a hypsochromic shift of the Q2 band from 624 to 614 nm even though the coordination scheme of this second Pd(II) ion, as represented in Fig. 14, is not argued [39].

2.2.2. 1,4,8,11-tetraazacyclotetradecane (cyclam)

Ito and co-workers have reported the synthesis of $[Pd^{II}(cyclam)](ClO_4)_2$ complex by the reaction of cyclam with Pd(II) acetate in water and subsequent addition of $HClO_4$. The X-ray structure shows a square planar geometry in which Pd(II) is found in the plane of the four nitrogen atoms. In this four-coordinated complex, the two six-membered metallacycles adopt a chair conformation [40,41]. The hydrogen atoms of two successive amino functions separated by a propylene bridge lie on the same side of the midplane of the complex and opposite the other two hydrogen atoms giving the *trans*-III configuration according to the Bosnich nomenclature [42]. The average Pd–N bond length value is 2.051 Å (**Fig. 15**). These authors have also reported an unusual mixed-valence complex $[Pd^{II}(cyclam)][Pd^{IV}(cyclam)](Cl)_2(ClO_4)_4$ in which the four-coordinated Pd(II) and the six-coordinate Pd(IV) units (both of them being +2 charged) are stacked alternately in the direction of the apical axis, forming linear chains of ···Cl-Pd^{IV}-Cl···Pd^{II}··· segments. Neighboring Pd(II) and Pd(IV) units are connected by hydrogen bonds.

Sadler and coll. have synthesized the chloride Pd(II) complex of cyclam $[Pd^{II}(cyclam)](Cl)_2{\cdot}2CH_3OH$. The crystallographic study is in accordance with the one described by Ito et al. Two-dimensional NMR experiments performed with this complex showed that the *trans*-III configuration is the only one present in aqueous solution [43].

Hancock and co-workers have estimated the formation constant of $[Pd(cyclam)]^{2+}$ at log K = 56.9 by a linear free energy relationship (LFER) plot comparing the log K_{ML} values for a variety of metal complexes of cyclam and the related linear tetraamine 2,3,2-tet (1,4,8,11-tetraazaundecane), after an attempted competition experiment between $[Pd(cyclam)]^{2+}$ and cyanide failed for a presumable kinetic barrier. The equilibrium found to occur in this competition was actually $[Pd(cyclam)]^{2+} + 2\ CN^- \rightleftarrows [Pd^{II}(cyclam)(CN)_2]$, for which a formation constant of log K = 5.2 was obtained. NMR and IR studies suggested that such ternary complex species, once formed, is oxidized to Pd(IV) in $[Pd^{IV}(cyclam)(CN)_2]^{2+}$ followed by disproportionation to give back $[Pd(cyclam)]^{2+}$ and probably cyanogen $(CN)_2$ [44]. Comparing the log K value estimated for the formation constant of $[Pd(cyclam)]^{2+}$ (at 56.9) with corresponding values reported for the cyclam complexes of Cu(II) and Ni(II), at 28.09 [45] and 22.2 [46] respectively, one can see that the Pd(II) complex is hugely more stable that the one of Cu(II) and even more so than that of Ni(II). Such differences highlight the adequateness of the cyclam skeleton to achieve an outstanding stability in Pd(II) complexation.

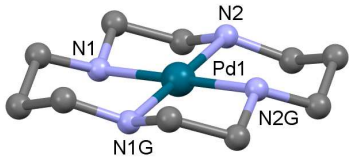


Fig. 15. Crystal structure of $[Pd(cyclam)]^{2+}$ cation in $[Pd(cyclam)](ClO_4)_2$. Selected bond distances (Å) and angles (°): Pd1-N1 2.054, Pd1-N2 2.048; N1-Pd1-N2 83.1, N1-Pd1-N1G 96.2. [40]

2.2.3. C-functionalized cyclam

A *C*-functionalized cyclam derivative, 6,13-dimethyl-1,4,8,11-tetra-azacyclotetradecane-6,13-diamine, bearing a NH_2 function and a methyl group on both carbon atoms in β-N position of the cyclam core, (noted cyclam$Me_2(NH_2)_2$) was investigated for Pd(II) complexation with K_2PdCl_4 in aqueous perchloric acid. Ivory colored crystals of the form [Pd(cyclam$Me_2(NH_3)_2$)]$(ClO_4)_4{\cdot}6H_2O$ showed that the complex adopts a square-planar geometry with the *trans*-III configuration. Both pendant primary amine groups are protonated and situated on opposite sides of the macrocyclic plane. The Pd-nitrogen atom distances Pd1-N2 and Pd1-N3 are respectively 2.044 and 2.036 Å, which is slightly shorter than in $[Pd(cyclam)]^{2+}$ (**Fig. 16**) [47].

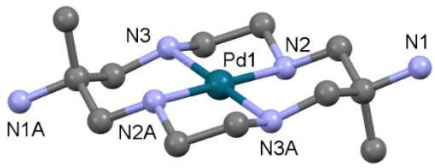


Fig. 16. Crystal structure of $[Pd(cyclamMe_2(NH_3)_2)]^{2+}$ cation in [Pd(cyclam$Me_2(NH_3)_2$)]$(ClO_4)_4{\cdot}6H_2O$. Selected bond distances (Å) and angles (°): Pd1-N2 2.044, Pd1-N3 2.036, N2-Pd1-N3 85.3, N2-Pd1-N3A 94.7.

2.2.4. N-Functionalized cyclams

- *N,N′,N″,N‴-tetramethylcyclam*

The addition of pendant arms on the nitrogen atoms of the cyclam core led to a modification of the geometry of the Pd(II) complexes. Thus, *N,N′,N″,N‴*-tetramethylcyclam (Me4cyclam) complex $[Pd(Me_4cyclam)]^{2+}$ adopts the favored *trans*-I configuration with the four substituents of the nitrogen atoms oriented on the same side of the mean plane. The average Pd-N bond distance is 2.059 Å and the metal ion is placed out of the plane of the four nitrogen atoms of the macrocycle by 0.082 Å giving a distorted square-planar structure (**Fig. 17**). The electrochemical studies indicated that the Pd(II)/Pd(I) reduction potential of -1.53 V *vs* Fc^+/Fc was 0.57 V more positive than for the cyclam complex $[Pd(cyclam)]^{2+}$ [48,49].

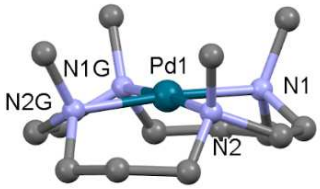


Fig. 17. Crystal structure of $[Pd(Me_4cyclam)]^{2+}$ cation in [Pd(Me4cyclam)]$(PF_6)_2{\cdot}CH_3NO_2$. Selected bond distances (Å) and angles (°): Pd1-N1 2.051, Pd1-N2 2.066, N1-Pd1-N2 88.0, N2-Pd1-N2G 91.0.

- *N,N′,N″,N‴-tetrabenzylcyclam*

In the case of *N,N′,N″,N‴*-tetrabenzylcyclam (Bn4cyclam), the $[Pd(Bn_4cyclam)]^{2+}$ complex adopts the *trans*-I configuration as well and exhibits a pyramidal distortion in which the metal ion is at almost 0.1 Å out of the plane and a tetrahedral distortion of the N_4-plane formed by the cyclam. The average bond distance Pd-N is 2.096 Å. The tetrahedral distortion was explained as the minimization of the steric effects between the four benzyl groups and the macrocycle (**Fig. 18**). In solution, the benzyl groups are found to be equivalent by NMR spectroscopy. In a parallel study, the Pd(I) complex of Bn4cyclam was isolated and structurally characterized (the reduction potential for Pd(II)/Pd(I) is -1.27 V *vs* Fc^+/Fc) [50].

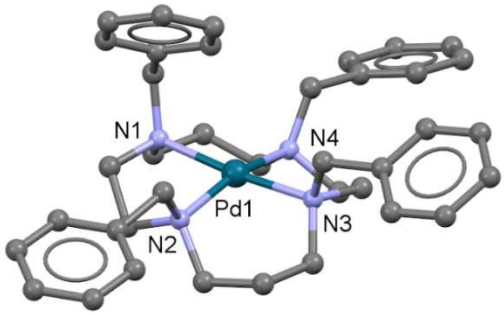


Fig. 18. Crystal structure of $[Pd(Bn_4cyclam)]^{2+}$ in [Pd(Bn4cyclam)]$(PF_6)_2{\cdot}0.4CH_3NO_2$. Selected bond distances (Å) and angles (°): Pd1-N1 2.105, Pd1-N2 2.078, Pd1-N3 2.098, Pd1-N4 2.104, N1-Pd1-N2 85.2, N2-Pd1-N3 94.5, N3-Pd1-N4 95.0, N1-Pd1-N4 95.0.

- *N,N′-dibenzylcyclams*

Lindoy and coll. have described the synthesis of a series of complexes of cyclam derivatives incorporating from one to three *N*-benzyl groups. The X-ray crystal structures of two dibenzylated cyclam (Bn2cyclam) complexes have been determined, respectively *N1,N2*-Bn2cyclam with the two benzyl groups separated by a propylene chain (**Fig. 19**) and *N1,N1A*- Bn2cyclam with the two benzyl moieties on two non-adjacent nitrogen atoms (**Fig. 20**). Both structures resemble that of the parent cyclam complex $[Pd(cyclam)]^{2+}$ and adopt the *trans*-III configuration. The Pd(II) ion occupies the N_4-plane of the respective macrocycles with only minimal distortion from a square planar arrangement, in contrast with the case of the previously described Bn4cyclam derivative that is also in the *trans*-I configuration [51].

For *N1,N2*-Bn2cyclam, the two benzyl moieties lie on the same side of the N_4 plane. There is a weak interaction involving the metal and two fluorine atoms of the hexafluorophosphate counter ions. The presence of the benzyl substituents on N1 and N2 atoms is reflected by a slightly longer Pd-N bond lengths involving these atoms with an average value of 2.087 Å, relative to those of the Pd-NH bonds around 2.052 Å. However, all four values are in accordance with the literature range for such Pd-N bond lengths in related complexes (**Fig. 19**).

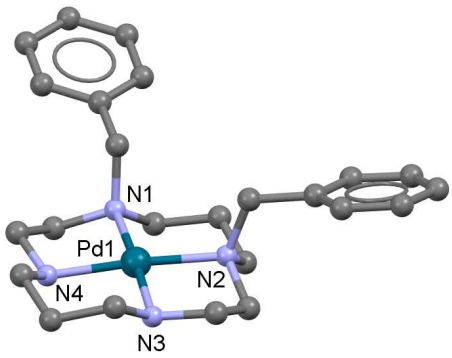


Fig. 19. Crystal structure of $[Pd(N1,N2\text{-}Bn_2cyclam)]^{2+}$ cation in $[Pd(N1,N2\text{-}Bn_2cyclam)](PF_6)_2{\cdot}CH_3COCH_3$. Selected bond distances (Å) and angles (°): Pd1-N1 2.094, Pd1-N2 2.080, Pd1-N3 2.047, Pd1-N4 2.058, N1-Pd1-N2 97.1, N2-Pd1-N3 85.4, N3-Pd1-N4 91.9, N1-Pd1-N4 85.5.

In the case of *N1,N1A*-Bn_2cyclam, the asymmetric unit contains two Pd(II) macrocyclic units, which are centered on inversion sites, four perchlorate counter ions and a water molecule. Here, the benzyl groups are orientated on either side of the coordination plane (**Fig. 20**).

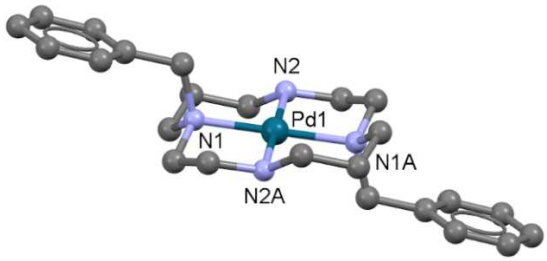


Fig. 20. Crystal structure of $[Pd(N1,N1A\text{-}Bn_2cyclam)]^{2+}$ in $[Pd(N1,N1A\text{-}Bn_2cyclam)](ClO_4)_2{\cdot}0.5H_2O$. Selected bond distances (Å) and angles (°): Pd1-N1 2.073, Pd1-N2 2.048, N1-Pd1-N2 94.5, N1-Pd1-N2A 85.5.

^1H and ^{13}C NMR spectra of both Pd(II) complexes, $[Pd(N1,N2\text{-}Bn_2cyclam)]^{2+}$ and $[Pd(N1,N1A\text{-}Bn_2cyclam)]^{2+}$, are much more convoluted than those of the respective free ligands and show additional resonances and splitting as well as a tendency of signal overlapping. This complexity may be attributed to the presence of a mixture of two or three of the six possible configurational isomers according to Bosnich nomenclature. This behavior has already been reported for Ni(II) or Zn(II) complexes of cyclam derivatives [51]. For example, Sadler and coll. have proved that the complex formed with the monobenzylcyclam (Bn_1cyclam) with Zn(II), $[Zn(Bn_1cyclam)]^{2+}$, that crystallized in the *trans-III* configuration, exists in solution as a mixture of three configurations *trans*-I, *trans*-II and *cis*-V [52].

• *N,N′,N″,N‴-tetra(2-hydroxyethyl)cyclam*

Hay, Perotti and Ungaretti reported in 1987 the complexation of *N,N′,N″,N‴*-tetra(2-hydroxyethyl) cyclam (HE_4cyclam) with Pd(II) comparatively with Cu(II) and Ni(II) [53]. The authors found that this cyclam derivative substituted with 2-hydroxyethyl pendant arms is able to form complexes very quickly with the studied metal ions, unlike what is usual for many cyclam derivatives. They attributed such behavior to the presumed participation of the coordinating arms as initial binding sites for metal coordination, upon which a transfer of the metal ion to the final macrocyclic ring site would then become a rapid intramolecular process. Equilibrium constants could be obtained by direct potentiometric titration for the complexation of Pd(II) in aqueous medium (0.1 M $NaClO_4$, 25 °C), determined at log K = 18.32 for the single $[Pd(HE_4cyclam)]^{2+}$ existing species. Such value is two orders of magnitude higher than for Cu(II) or many orders higher than for Ni(II), for which the respective log K values found were 16.20 and 7.45. But a value of 18.32 is also dramatically lower than that estimated for the Pd(II) complex of the parent macrocycle cyclam (at log K = 56.9), a fact that has been attributed to the steric hindrance caused by the *N*-(2-hydroxyethyl) pendants in HE_4cyclam [54]. Unfortunately, no structural data was obtained for the $[Pd(HE_4cyclam)]^{2+}$ complex, so no other discussion could be made.

2.2.5. CB-cyclam derivative

The complexation of a *N,N'*-dimethylcyclam derivative bearing a two-carbon bridge between two non-adjacent nitrogen atoms, named cross-bridged dimethylcyclam (CB-Me_2cyclam), has been studied. This constrained ligand reacts with Pd(II) to give dark blue crystals which exhibit a distorted five-coordinated square-pyramidal geometry with the *cis*-V configuration. This structure, usual for CB-cyclam derivatives, is due to the short ethylene cross-bridge which enforces a fold in the ligand that is conserved on binding to Pd(II), and does not allow the occupation of the four sites of a square plane. The metal ion is then coordinated by the four nitrogen atoms and one chloro ligand which completes the coordination sphere of Pd(II) allowing the retention of part of the advantage of a square-based geometry. The nitrogen atoms N1 and N8 occupy inequivalent sites in the square pyramidal geometry because N1 is on the base while N8 is at the apex. This is demonstrated by the difference of the corresponding Pd-N bond lengths: Pd1-N1 is 2.112 Å and Pd1-N3 is 2.461 Å. This latter value shows that the ligand topology imposes the coordination geometry of the complex rather than the electronic configuration of the Pd(II) ion (d^8), which predicts a square planar environment (**Fig. 21**) [55].

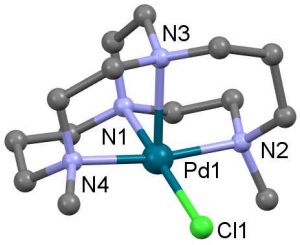


Fig. 21. Crystal structure of $[Pd(CB\text{-}Me_2cyclam)Cl]^+$ cation in $[Pd(CB\text{-}Me_2cyclam)Cl](Cl){\cdot}2H_2O$. Selected bond distances (Å) and angles (°): Pd1-N1 2.111, Pd1-N2 2.077, Pd1-N3 2.461, Pd1-N4 2.101, Pd1-Cl1 2.341, N1-Pd1-N2 85.1, N1-Pd1-N3 80.1, N1-Pd1-N4 91.0, N2-Pd1-Cl1 89.9, N4-Pd1-Cl1 95.1.

2.2.6. Dioxocyclam derivative

1,4,8,11-tetraazacyclotetradecane-5,7-dione, called dioxocyclam, is a cyclam derivative with two amide and two secondary amine groups. With divalent transition metals such as Pt(II) or Cu(II), dioxocyclam derivatives are known to act as tetradentate ligands to form doubly deprotonated complexes [56,57]. Pd(II) complexes of *N*-dialkylated dioxocyclam with 2-pyridylmethyl arms (Py_2dioxocyclam) have been described by Kimura and co-workers. In the solid state, two complexes have been isolated depending on the pH. The crystal structure of the complex $[Pd(Py_2dioxocyclam)]^{2+}$, isolated at pH 6, shows that Pd(II) is four-coordinated by two the tertiary amines of the macrocycle and the two pyridyl nitrogen atoms, giving a square-planar geometry, in which the two amide nitrogen groups remain protonated and do not take part in the coordination. The Pd-N bond lengths of the two tertiary amines and the two pyridyl amines exhibit similar values (average values are Pd-$N_{tertiary}$ 2.072 Å and Pd-N_{py} 2.077 Å). The Pd(II) ion is displaced by 0.062 Å above the four nitrogen atoms involved in the coordination (**Fig. 22**) [58].

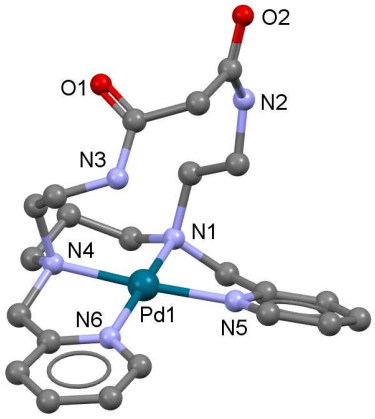


Fig. 22. Crystal structure of $[Pd(Py_2dioxocyclam)]^{2+}$ cation in $[Pd(Py_2dioxocyclam)](ClO_4)_2{\cdot}H_2O$ isolated at pH 6. Selected bond distances (Å) and angles (°): Pd1-N1 2.072, Pd1-N4 2.072, Pd1-N5 2.077, Pd1-N6 2.078, N1-Pd1-N4 95.9, N1-Pd1-N5 80.7, N4-Pd1-N6 85.4.

The X-rays structure of the complex isolated at pH 10 corresponds to the doubly deprotonated species $[Pd(Py_2dioxocyclamH_{-2})]$ that shows a square-planar geometry as well. But in these basic conditions, the Pd(II) ion is four-coordinated by the two deprotonated nitrogen atoms of the amide functions and the two tertiary amines of the macrocycle as previously described for non-alkylated dioxocyclam. Both 2-pyridylmethyl arms are located on the same side of the molecule, while the average Pd-N_{amide} bond length of 1.982 Å is shorter than the average Pd-$N_{tertiary}$ length of 2.079 Å. In this structure, Pd(II) is almost in the N_4-plane with a slight displacement of 0.022 Å (**Fig. 23**).

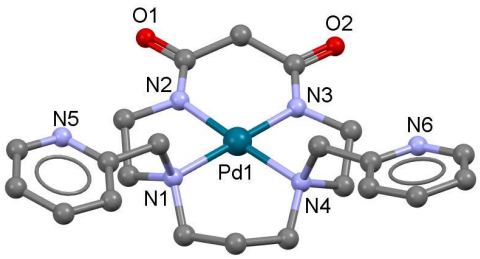


Fig. 23. Crystal structure of $[Pd(Py_2dioxocyclamH_{-2})]{\cdot}H_2O$ isolated at pH 10. Selected bond distances (Å) and angles (°): Pd1-N1 2.077, Pd1-N2 1.985, Pd1-N3 1.979, Pd1-N4 2.081, N1-Pd1-N2 83.4, N1-Pd1-N4 98.9, N2-Pd1-N3 94.1, N3-Pd1-N4 83.2.

Studies in solution showed the reversible interconversion between the complexes $[Pd(Py_2dioxocyclam)]^{2+}$ and $[Pd(Py_2dioxocyclam\text{-}H_{-2})]$, which easily occurs through a pH-dependent deprotonation of the amide groups (**Fig. 24**).

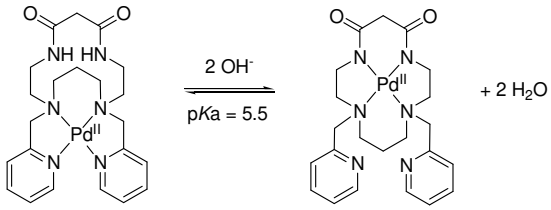


Fig. 24. Equilibrium between complex $[Pd(Py_2dioxocyclam)]^{2+}$ (left) and $[Pd(Py_2dioxocyclamH_{-2})]$ (right) depending on the pH.

2.3. Other tetraazamacrocycle: pyclen

Pyclen is a particular partially non-saturated tetraazamacrocycle that incorporates a pyridine moiety into the cyclic structure. One of the four nitrogen atoms is therefore sp^2 hybridized, which added to the rigidity of the pyridine ring confers different properties to those offered by the more common polyazacycloalkanes. In 2017 and 2018, Bianchi, García-España and López-Garzón described the synthesis and use of Pd(II) complexes of two pyclen derivatives, with pyrimidine moieties appended on the central nitrogen atom of the macrocycle, for the construction of nanostructured heterogeneous catalysts *via* non-covalent surface decoration of multi-walled carbon nanotubes. Determination of the equilibrium constants for the formation of both Pd(II) complexes was not possible because of the slowness of the complexation reactions. Nevertheless, once formed, these species proved to be highly stable, thus, protonation constants of the complexes have been determined by means of potentiometric titrations in aqueous solution (0.1 M Me_4NCl, 298.1 K).

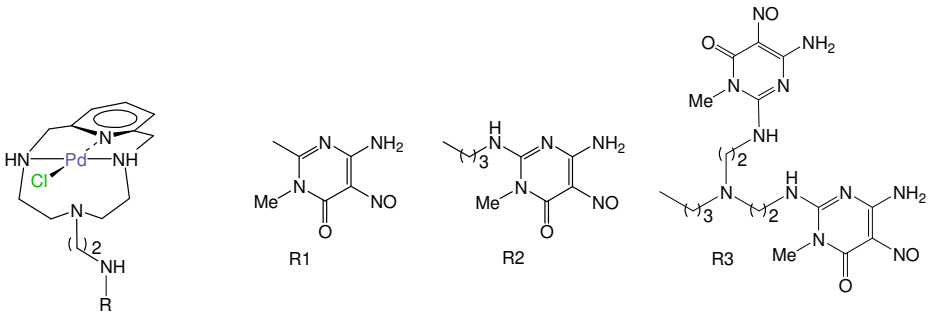


Fig. 25. Proposed mode of coordination for the Pd(II) complexes with mono-*N*-functionalized pyclen derivatives.

Two and three protonation constants were obtained for the complexes containing R1 and R2, respectively, with pK_a values of 9.46 and 2.2 in the first case, and of 10.19, 7.0 and 2.5 in the second case. The highest pK_a values in each case (pK_a > 5) are not consistent with protonation occurring on metal-bound amine groups, being assigned to the protonation of uncoordinated amines. These results, coupled with UV-visible spectrophotometry studies of the free ligands and their Pd(II) complexes, enabled the authors to conclude that in both cases the Pd(II) ion is coordinated to only three of the four macrocyclic nitrogen atoms and one chloride anion from the medium. There is no participation of the *N*-donor atom of the appended chain in metal coordination. This binding mode has been assessed by ion chromatography analysis of a solution containing equivalent molar quantities of ligand and $[PdCl_4]^{2-}$. After completion of the reaction, the concentration of free Cl^- was three times that of the original $[PdCl_4]^{2-}$ proving that one chloride anion remained coordinated to Pd(II) (**Fig. 25**) [59,60]. The same authors later described another Pd(II) complex of a pyclen derivative for the supramolecular decoration of graphene which contained two pyrimidine moieties appended on a diamino-alkyl pendant arm (R3). As above, only protonation constants of the complex could be determined from potentiometric titrations in aqueous solution (0.15 M NaCl, 298.1 K), with obtained pK_a values of 7.30, 5.1, 2.7 and 2.4. As in the previous cases, after resorting to UV-visible spectrophotometry and ion chromatography analysis, the authors found that Pd(II) is coordinated to only three of the four macrocyclic nitrogen atoms and one chloride anion from the medium, with the nitrogen atom where the pyrimidine-containing substituent is appended in pyclen being uncoordinated [61].

3. Palladium(II) as a versatile template for the synthesis of "swollen" tetraazacycloalkanes

Lawrance and co-workers have described a Pd(II)-directed template synthesis of *C*-functionalized 14-, 16- and 18-membered macrocyclic complexes, called "swollen" macrocycles, *via* a Mannich-type macrocyclization [62]. The reaction starts from Pd(II) complexes of diamines such as ethylenediamine [63], propane-1,3-diamine [64] and butane-1,4-diamine. These species, with a metal/ligand ratio of 1:2, have five-, six- and seven-membered chelate rings, respectively. They react with formaldehyde and nitroethane in basic conditions to yield the corresponding *C*-functionalized macrocyclic Pd(II) complexes (**Fig. 26**).

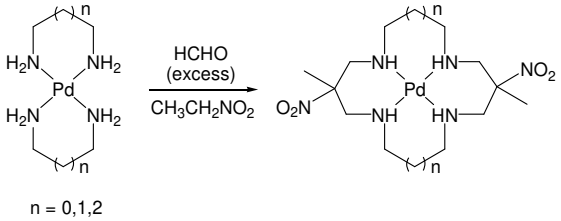


Fig. 26. Synthesis of *C*-functionalized 14-, 16- and 18-membered macrocyclic complexes (respectively n = 0, 1, 2) *via* a Mannich-type macrocyclization of Pd(II) complexes of diamines.

When n = 0, the obtained species is actually the *C*-functionalized cyclam Pd(II) complex [Pd(6,13-dimethyl-6,13-dinitro)1,4,8,11-tetraazacyclotetradecane]$^{2+}$ isolated in high yield. Colorless crystals of the perchlorate salt were suitable for X-ray analysis (**Fig. 27**). The molecule is symmetrical, the Pd(II) lies at the center of symmetry and this cation and the nitrogen atoms are coplanar. The species has a square-planar coordination and Pd(II) adopts the *trans*-III configuration such as $[Pd(cyclam)]^{2+}$. Nitro groups are on opposite sides of the macrocyclic plane with the *anti* configuration. Each nitro group is axial and each methyl group equatorial, attached to central carbon atoms of six-membered rings which adopt chair conformations. The electronic spectrum (in water) shows λ_{max} at 275 nm (ε = 508 M^{-1} cm^{-1}) and 220 nm (ε = 2200 M^{-1} cm^{-1}).

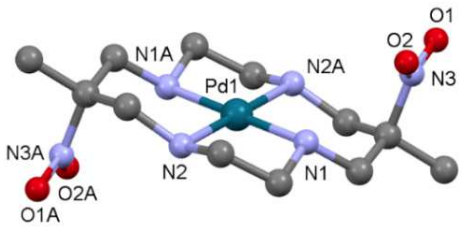


Fig. 27. Crystal structure of the [Pd(6,13-dimethyl-6,13-dinitro-1,4,8,11-tetraazacyclotetradecane]$^{2+}$ cation in [Pd(6,13-dimethyl-6,13-dinitro-1,4,8,11-tetraazacyclotetradecane]$(ClO_4)_2$. Selected bond distances (Å) and angles (°): Pd1-N1 2.034, Pd1-N2 2.040, N1-Pd1-N2A 94.8, N1-Pd1-N2 85.2.

In the species with n = 1 and n = 2, respectively for cations [Pd(3,11-dimethyl-3,11-dinitro-1,5,9,13-tetraazacyclohexadecane]$^{2+}$ and [Pd(3,12-dimethyl-3,12-dinitro-1,5,10,14-tetraazacyclooctadecane]$^{2+}$ cations, X-ray analysis showed that the dominant crystallized compounds

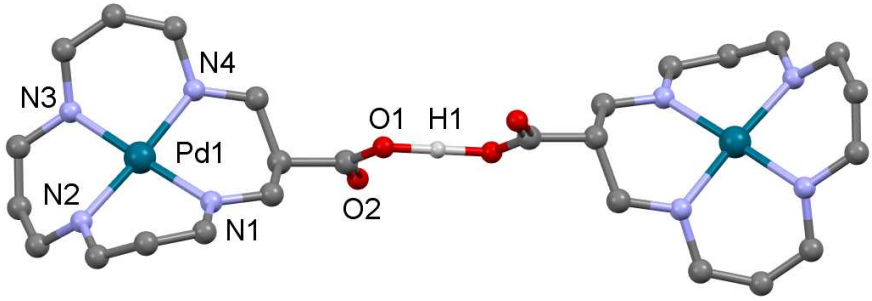
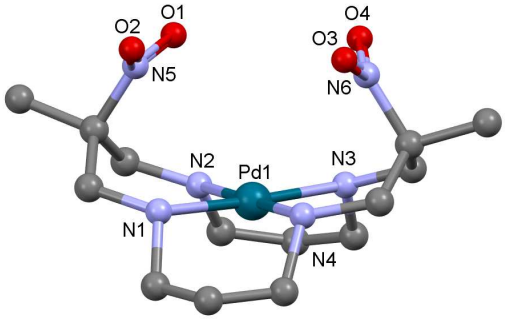
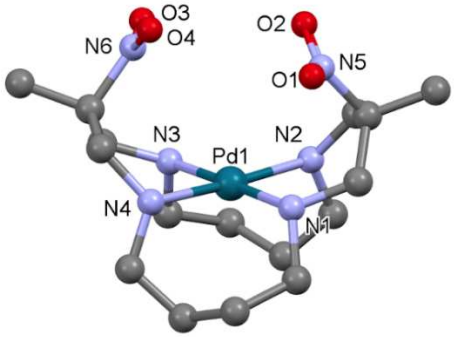


Fig. 31. Structure of the {[Pd(**5**)][Pd(**5**H$_{-1}$)]}$^{3+}$ cation in the {[Pd(**5**)[Pd(**5**H$_{-1}$)]}$(ClO_4)_2(PF_6)$ complex. Selected bond distances (Å) and angles (°): Pd1-N1 2.028, Pd1-N2 2.042, Pd1-N3 2.046, Pd1-N4 2.027; N1-Pd1-N2 91.2, N2-Pd1-N3 90.9, N3-Pd1-N4 86.5, N1-Pd1-N4 91.5.

(colorless crystals) are the *syn* isomers with nitro groups situated on the same side of the mean plane, although NMR spectroscopy proved that the reaction is stereoselective rather than stereospecific (**Fig. 28**, structures **a** and **b**).



(a)



(b)

Fig. 28. Structures of (**a**) [Pd(3,11-dimethyl-3,11-dinitro-1,5,9,13-tetraazacyclohexadecane]$^{2+}$ in [Pd(3,11-dimethyl-3,11-dinitro-1,5,9,13-tetraazacyclohexadecane]$(ClO_4)_2 \cdot H_2O$ and (**b**) [Pd(3,12-dimethyl-3,12-dinitro-1,5,10,14-tetraaza-cyclooctadecane]$^{2+}$ in [Pd(3,12-dimethyl-3,12-dinitro-1,5,10,14-tetraazacyclooctadecane]$(ClO_4)_2 \cdot 2H_2O$. Selected bond distances (Å) and angles (°): (**a**) Pd1-N1 2.067, Pd1-N2 2.039, Pd1-N3 2.059, Pd1-N4 2.060; N1-Pd1-N2 93.8, N2-Pd1-N3 85.8, N3-Pd1-N4 96.3, N1-Pd1-N4 84.1. (**b**) Pd1-N1 2.068, Pd1-N2 2.077, Pd1-N3 2.065, Pd1-N4 2.065, N1-Pd1-N2 90.1, N5-N6 4.204; N2-Pd1-N3 90.2, N3-Pd1-N4 90.0, N1-Pd1-N4 89.8.

Unlike the previous $[Pd(cyclamMe_2(NO_2)_2]^{2+}$ species, both complexes adopt what could be likened to the Bosnich *trans*-I configuration [42]. The electronic spectra of the complexes showed very similar absorption bands than for n=0; indeed, for [Pd(3,11-dimethyl-3,11-dinitro-1,5,9,13-tetraazacyclohexadecane]$^{2+}$, λ_{max} are 292 nm (ε = 577 M^{-1} cm^{-1}) and 225 nm (ε = 1790 M^{-1} cm^{-1}) while for [Pd(3,12-dimethyl-3,12-dinitro-1,5,10,14-tetraazacyclooctadecane]$^{2+}$ λ_{max} 291 nm (ε = 613 M^{-1} cm^{-1}) and 230 nm (ε = 3050 M^{-1} cm^{-1}) [62].

According to a similar Mannich-type cyclization, but starting from Pd(II) complexes of open chain tetraamines Lawrence and co-workers have described the synthesis of a series of *C*-functionalized macrocycle complexes including side-bridged reinforced structures (**Fig. 29**) [65].

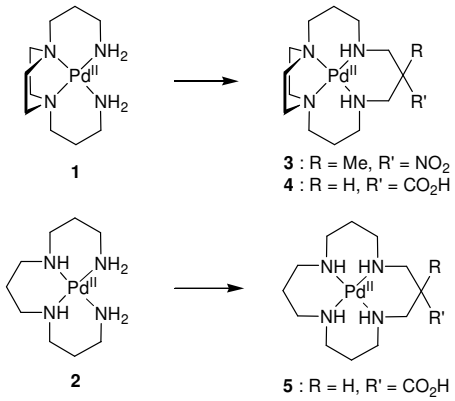


Fig. 29. Structures of the complexes **3**-**5** synthesized *via* the Pd(II)-directed template synthesis from open chain tetraamines Pd(II) complexes **1** and **2**.

Thus, the reaction of the bis(3-aminopropyl)piperazine Pd(II) complex **1** with formaldehyde and nitroethane, in basic aqueous solution, led to the side-bridged macrocycle 7-methyl-7-nitro-1,5,9,13-tetraazabicyclo[11.2.2] heptadecane as its Pd(II) complex **3**. The crystal structure shows that Pd(II) lies in a slightly tetrahedrally distorted square plane of four nitrogen donors. The average bond length of Pd-N$_{tertiary}$ is slightly shorter (2.059 Å) than those of the secondary amines (2.066 Å) (**Fig. 30**). The electronic spectrum (in water) shows an absorption band λ_{max} at 298 nm (ε = 586 M^{-1} cm^{-1}).

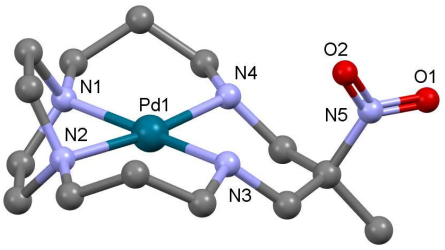


Fig. 30. Structure of the [Pd(7-methyl-7-nitro-1,5,9,13-tetraazabicyclo[11.2.2]heptadecane)]$^{2+}$ cation from [Pd(7-methyl-7-nitro-1,5,9,13-tetraazabicyclo[11.2.2] heptad ecane)]$(ClO_4)_2{\cdot}H_2O$. Selected bond distances (Å) and angles (°): Pd1-N1 2.063, Pd1-N2 2.056, Pd1-N3 2.072, Pd1-N4 2.060; N1-Pd1-N2 73.1, N2-Pd1-N3 99.5, N3-Pd1-N4 88.3, N1-Pd1-N4 98.7.

The reaction of the (4,8-diazaundecane-1,11-diamine) Pd(II) complex **2** with formaldehyde and diethyl malonate in basic aqueous solution, followed by subsequent ester hydrolysis and decarboxylation, led to the carboxylic pendant macrocycle 1,5,9,13-tetraazacyclohexadecane-3-carboxylic acid as its Pd(II) complex **5**. The crystal structure is composed of a hydrogen bonded dimer charged +3 where the pair of inversion related square-planar complexes share a single proton between their pendant carboxylate residues (**Fig. 31**). The shared proton is placed on the pivotal inversion site and the complex in the asymmetric unit is then formulated as a monomer. It is interesting to note that the Pd(II) ions adopt the quite unusual configuration with only three substituents of the nitrogen atoms facing on the same side of the N_4-plane as the substituted chelate ring (analogue of the *trans*-II configuration of cyclam-based complexes referring to the Bosnich nomenclature [42]). The Pd-N distances range from 2.027 to 2.046 Å and there is a tetrahedral distortion from square planar coordination with diagonally opposing pairs of nitrogen atoms located below (N1, N3 at -0.03, -0.03 Å) or above (N2, N4 at 0.04, 0.03 Å) of the ideal plane. The Pd(II) ion is also displaced 0.006 Å below it. The electronic spectrum (water) shows an absorption band λ_{max} at 295 nm (ε = 562 M^{-1} cm^{-1}).

In the same manner, the side-bridged reinforced 1,5,9,13-tetraazabicyclo[11.2.2]heptadecane-7-carboxylic acid Pd(II) complex **4** was obtained from the bis(3-aminopropyl) (piperazine) Pd(II) linear precursor **1**. One can note that in each case of this Pd(II)-directed template synthesis, a zinc/acid reduction of the Pd(II) complex led readily to the corresponding free polyamine [65].

4. Radioisotopes of palladium(II) for therapeutic purposes

Two Pd(II) radionuclides have found applications in the field of nuclear medicine for therapy. Metallic radioisotopes are indeed well prized for both diagnosis and therapy provided they can be strongly chelated to ensure safe use. Here, the kinetic and thermodynamic parameters are of primary interest. ^{103}Pd ($t_{1/2}$ = 17 days) decays by electron capture (100%) with the emission of Auger electrons and multiple low-abundance γ photons (average energy of 21 keV) to ^{103}Rh. ^{109}Pd ($t_{1/2}$ = 13.7 hours) decays by the emission of β^- particles (E_{max} = 1.12 MeV, 100%) to ^{109m}Ag ($t_{1/2}$ = 39.6 s) which, in turn, emit a photon (88 keV, 3.6%) accompanied by the emission of conversion and Auger electrons leading to stable ^{109}Ag [66].

4.1. Palladium-109

In the early 1970s, Fawwaz and co-workers described palladium-109 complexes of natural unsaturated polyazamacrocycles, i.e., porphyrin derivatives named hematoporphyrin and protoporphyrin, for the control of homograft rejection by lymphatic ablation [67-69]. They also described later a promising ^{109}Pd-DTPA-monoclonal antibody (DTPA: diethylenetriamine pentaacetic acid) for tumor therapy of human melanoma, but the mode of production of ^{109}Pd at the time of the study was not optimal as well as the methods of purification of antibodies giving incomplete results [70].

Banerjee and coll. have synthesized in 2008 and 2012 ^{109}Pd-labelled porphyrins derivatives containing different peripheral substituents in order to study the effect of lipophilicity on pharmacokinetic properties for optimal tumor uptake. Among the ligands evaluated, 5,10,15,20-tetrakis[4-carboxymethyleneoxyphenyl]porphyrin (PHBEPH) gave the most promising results in terms of radiolabeling with ^{109}Pd and biological behavior in small animal models (**Fig. 32**) [71,72].

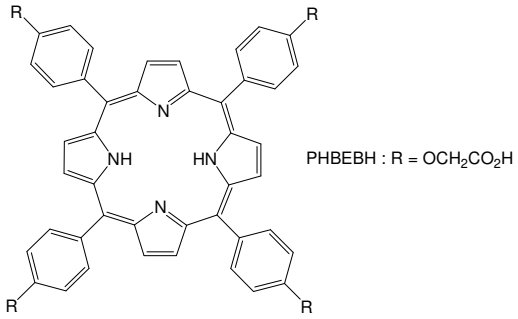


Fig. 32. Structure of 5,10,15,20-tetrakis[4-carboxymethyleneoxyphenyl]porphyrin (PHBEPH).

4.2. Palladium-103

Palladium-103 was introduced in 1987 as a radionuclide in radiotherapy procedure with the use of "seeds" for permanent interstitial implants, called brachytherapy, especially in the case of prostate cancer. ^{103}Pd has energy and safety characteristics similar to Iodine-125, used since the 1960s for the same purpose, but its initial peripheral dose rate is approximately three times greater which may provide improved control of rapidly proliferating tumors [73-75].

^{103}Pd complexes of bleomycin or thiosemicarbazone have also been evaluated by Jalilian and coll. as potential agents for tumor targeted therapy [76-78].

5. Conclusion and outlook

In this review, the Pd(II) complexes of a series of tri- and tetraazacycloalkanes have been listed, among which are triazacyclononane, triazacyclododecane, cyclen, cyclam and larger tetraazamacrocycles, as well as their reinforced and dioxo-analogues. Pyclen complexes were also described for their similarity to cyclen. The coordination of the Pd(II) ion is mainly square planar,

often slightly distorted depending on the nature of the ligands. This geometry is the most energetically favorable due to the stabilization of the crystal field. A few rare five-coordinated complexes with square pyramidal or trigonal bipyramidal geometries have been described in cases where the steric or topological requirements of the ligand outweigh the loss of stabilization due to geometric distortion.

Despite a persisting lack of thermodynamic stability data for most Pd(II) complexes herein described, certainly as a consequence of the generally very high stability expected for such complexes and the associated difficulty in studying their complexation equilibria, some general ideas in this regard can nonetheless be pointed out from the scarce available data. The extremely high stability constant for the complex of cyclam is remarkable, and the much lower stability of the complex of HE_4cyclam evidences a highly detrimental effect of substitution of the secondary amines of polyazacycloalkanes regarding the thermodynamic stability of their Pd(II) complexes, corroborating what was already described for acyclic polyamine ligands [20]. Taking into account that the structures of complexes of substituted and unsubstituted polyazacycloalkanes are not much different in the solid state, while generally showing similar geometries and bond distances, the explanation for such effect must be more related to the behavior in solution, where factors such as an increased steric hindrance or an increased solvation energy caused by amine substitution could play a crucial role. Conversely, it is known that amine substitution with pendant arms containing additional donor atoms may improve the kinetics of complexation of such ligands, which suggests that a limited substitution pattern on the polyamine ligands might be suitable to achieve a balance between high thermodynamic stability and fast complexation kinetics.

Note

Crystal structures have been obtained using CCDC files and Mercury software.

Acknowledgements

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References

[1] R. D. Graham, D. R. Williams, J. Inorg. Nucl. Chem. 41 (1979) 1245-1249.
[2] A. R. Kapdi, I. J. S. Fairlamb, Chem. Soc. Rev. 43 (2014) 4751-4777.
[3] M. P. M Marques, ISRN Spectrosc. (2013) 1-29.
[4] T. J. Carneiro, A. S. Martins, M. P. M. Marques, A. M. Gil, Front. Oncol. 10 (2020) 590970.
[5] Y. Vakrat-Haglili, L. Weiner, V. Brumfeld, A. Brandis, Y. Salomon, B. Mcllroy, B. C. Wilson, A. Pawlak, M. Rozanowska, T. Sarna, A. Scherz, J. Am. Chem. Soc. 127 (2005) 6487-6497.
[6] L. Rasmussen, C. K. Jørgensen, Acta Chem. Scand. 22 (1968) 2313-2323.
[7] J. R. Wiesner, E. C. Lingafelter, Inorg. Chem. 5 (1966) 1770-1775
[8] T. G. Appleton, J. R. Hall, Inorg. Chem. 9 (1970) 1800-1806.
[9] J. Iball, M. MacDougall, S. Scrimgeour, Acta Cryst. B31 (1975) 1672-1674.
[10] M. Rossignoli, C. C. Allen, T. W. Hambley, G. A. Lawrance, M. Maeder, Inorg. Chem. 35 (1996) 4961-4966.
[11] L. Rasmussen, C. K. Jørgensen, Inorg. Chim. Acta 3 (1969) 543-546.
[12] N. B. Pahor, M. Calligaris, L. Randaccio, J. Chem. Soc., Dalton Trans. (1976) 725-730.
[13] A. Giacomelli, M. Malatesta, M. Spinetti, Inorg. Chim. Acta 51 (1981) 55-60.
[14] Q. Y. Yan, G. Anderegg, Inorg. Chim. Acta 105 (1985) 121-128.
[15] C. V. Senoff, Inorg. Chem. 17 (1978) 2320-2322.
[16] S. N. Bhattacharya, C. V. Senoff, Inorg. Chem. 22 (1983) 1607-1610.
[17] A. Bencini, A. Bianchi, P. Dapporto, E. Garcia-Espana, M. Micheloni, P. Paoletti, P. Paoli, J. Chem. Soc., Chem. Commun. (1990) 1382-1384.
[18] A. Bencini, A. Bianchi, M. Micheloni, P. Paoletti, P. Dapporto, P. Paoli, E. Garcia-Espana, J. Incl. Phen. Mol. Rec. Chem. 12 (1992) 291-304.
[19] G. Yang, R. Miao, Y. Li, J. Hong, C. Zhao, Z. Guo, L. Zhu, Dalton Trans. (2005) 1613-1619.
[20] C. Bazzicalupi, A. Bencini, A. Bianchi, C. Giorgi, B. Valtancoli, Coord. Chem. Rev. 184 (1999) 243-270.
[21] C. De Stefano, A. Gianguzza, A. Pettignano, S. Sammartano, J. Chem. Eng. Data, 56 (2011) 4759-4771.
[22] G. Hunter, A. McAuley, T.W. Whitcombe, Inorg. Chem. 27 (1988) 2634-2639.
[23] A. McAuley, T.W. Whitcombe, Inorg. Chem. 27 (1988) 3090-3099.
[24] L. Rasmussen, C. K. Jørgensen, Acta Chem. Scand. 22 (1968) 2313-2323.
[25] L. J. Zompa, Inorg. Chem. 17 (1978) 2531-2536.
[26] T. N. Margulis, L. J. Zompa, Inorg. Chim. Acta 201 (1992) 61-67.
[27] A. J. Blake, L. M. Gordon, A. J. Holder, T. I. Hyde, G. Reid and M. Schröder, J. Chem. Soc., Chem. Commun. (1988) 1452-1454.
[28] G. Hunter, A. McAuley, T.W. Whitcombe, Inorg. Chem. 27 (1988) 2634-2639.
[29] A. McAuley, T.W. Whitcombe, Inorg. Chem. 27 (1988) 3090-3099.
[30] T. N. Margulis, L. J. Zompa, Inorg. Chim. Acta 201 (1992) 61-67.
[31] A. J. Blake, A. J. Holder, Y. V. Roberts, M. Schroder, J. Chem. Soc., Chem. Commun. (1993) 260-263.
[32] J. R. Khusnutdinova, N. P. Rath, L. M. Mirica, Angew. Chem. 123 (2011) 5646-5660.
[33] J. R. Khusnutdinova, F. Qu, Y. Zhang, N. P. Rath, L. M. Mirica, Organometallics 31 (2012) 4627-4630.
[34] W. de Graaf, J. Boersma, D. Grove, A. L. Spek, G. van Koten, Recl. Trav. Chim. Pays-Bas 107 (1988) 299-301.
[35] J. E. Bercaw, G. S. Chen, J. A. Labinger, B. -L. Lin, J. Am. Chem. Soc. 130 (2008) 17654-17655.
[36] K. Wieghardt, E. Schöffmann, B. Nuber, J. Weiss, Inorg. Chem. 25 (1986) 4877-4883.
[37] D. Zhang, D. H. Busch, Inorg. Chem. 33 (1994) 5138-5143.
[38] H. Hyemi, K. -S. Moon, S. Shim, J. Tae, Asian Chem J. 6 (2011) 1987-1991.
[39] M. A. Grin, S. S. Brusov, E. Y. Shchepelina, P. V. Ponomarev, M. K. Khrenova, A. S. Smirnov, V. S. Lebedeva, A. F. Mironov, Mendeleev Commun. 27 (2017) 338-340.
[40] M. Yamashita, H. Ito, K. Toriumi, T. Ito, Inorg. Chem. 10 (1983) 1566-1568.
[41] K. Toriumi, M. Yamashita, H. Ito, T. Ito, Acta Cryst. C42 (1986) 963-968.
[42] B. Bosnich, C. K. Poon, M. L. Tobe, Inorg. Chem. (1965)

1102-1108.
[43] T. M. Hunter, S. J. Paisey, Hye-seo Park, L. Cleghorn, A. Parkin, S. Parsons, P. J. Sadler, J. Inorg. Chem. 98 (2004) 713-719.
[44] J. M. Harrington, S. B. Jones, R. D. Hancock, Inorg. Chim. Acta 358 (2005) 4473-4480.
[45] R. J. Motekaitis B. E. Rogers, D. E. Reichert, A. E. Martell, M. J. Welch, Inorg. Chem. 35 (1996) 3821-3827
[46] F. P. Hinz, D. W. Margerum, Inorg. Chem. 13 (1974) 2941-2949.
[47] P. V. Bernhardt, G. A. Lawrance, W. C. Patalinghug, B. W. Skelton, A. H. White, N. F. Curtis, A. Siriwardena, J. Chem. Soc., Dalton Trans. (1990) 2853-2858.
[48] A. J. Blake, R. O. Gould, T. I. Hyde, M. Schröder, J. Chem. Soc., Chem. Commun. (1987) 431-433.
[49] E. K. Barefield, Coord. Chem. Rev. 254 (2010) 1607-1627.
[50] A.J. Blake, R. O. Gould, T. I. Hyde, M. Schröder, J. Chem. Soc., Chem. Commun. (1987) 1730-1732.
[51] Y. Dong, L. F. Lindoy, P. Turner, Aust. J. Chem. 58 (2005) 339-344.
[52] X. Liang, J. A. Parkinson, M. Weishaüpl, R. O. Gould, S. J. Paisey, H. -S. Park, T. M. Hunter, C. A. Blindauer. S. Parsons, P. J. Sadler, J. Am. Chem. Soc. 124 (2002) 9105-9112.
[53] R.W. Hay, M.P. Pujari, W.T. Moodie, S. Craig, D.T. Richens, A. Perotti, L. Ungaretti, J. Chem. Soc., Dalton Trans. (1987) 2605-2613.
[54] J. M. Harrington, S. B. Jones, R. D. Hancock, Inorg. Chim. Acta 358 (2005) 4473-4480.
[55] T. J. Hubin, N. W. Alcock, D. H. Busch, Acta Cryst. C55 (1999) 1404-1406.
[56] E. Kimura, S. Korenari, M. Shionoya, M. Shiro, J. Chem. Soc., Chem. Commun. (1988) 1166-1168.
[57] X. H. Bu, D. L. An, X. C. Cao, R. H. Zhang, T. Clifford, E. Kimura, J. Chem. Soc., Dalton Trans. (1998) 2247-2252.
[58] H. Kurosaki, H. Yoshida, A. Fujimoto, M. Goto, M. Shionoya, E. Kimura, E. Espinosa, J. -M. Barbe, R. Guilard, J. Chem. Soc., Dalton Trans. (2001) 898-901.
[59] M. Savastano, P. Arranz-Mascarós, C. Bazzicalupi, M. P. Clares, M. L. Godino-Salido, M. D. Gutiérrez-Valero, M. Inclán, A. Bianchi, E. García-España, R. Lopez-Garzón, J. Catal. 353 (2017) 239-249.
[60] M. Passaponti, M. Savastano, M. P. Clares, M. Inclán, A. Lavacchi, A. Bianchi, E. García-España, M. Innocenti, Inorg. Chem. 57 (2018) 14484-14488.
[61] M. Savastano, P. Arranz-Mascarós, M. P. Clares, R. Cuesta, M. L. Godino-Salido, L. Guijarro, M. D. Gutiérrez-Valero, M. Inclán, A. Bianchi, E. García-España, R. Lopez-Garzón, Molecules 24 (2019) 1-19.
[62] M. Rossignoli, C. C. Allen, T. W. Hambley, G. A. Lawrance, M. Maeder, Inorg. Chem. 35 (1996) 4961-4966.
[63] R. Wiesner, E. C. Lingafelter, Inorg. Chem. 5 (1966) 1770-1775.
[64] T. G. Appleton, J. R. Hall, Inorg. Chem. 9 (1970) 1800-1806.
[65] G. A. Lawrance, M. Maeder, M. Napitupulu, A. L. Nolan, M. Rossignoli, V. Tiwow, P. Turner, Inorg. Chim. Acta 358 (2005) 3227-3235.
[66] R. B. Firestone, Table of isotopes (V. S. Shirley, ed) 8th edition, John Wiley and Sons, Inc, New York (1996) 846-847.
[67] R. A. Fawwaz, W. Hemphill, H. S. Winchell, J. Nucl. Med. 12 (1971) 231-236.
[68] R. A. Fawwaz, F. Frye, W. D. Laughman, W. Hemphill, J. Nucl. Med. 15 (1974) 997-1102.
[69] J. D. Doi, D. K. Lavallee, S. C. Srivastava, T. Prach, P. Richards, R. A. Fawwaz, Int. J. Appl. Radiat. Isotopes 32 (1981) 877-880.
[70] R. A. Fawwaz, T. S. T. Wang, S. C. Srivastava, J. M. Rosen, S. Ferrone, M. A. Hardy, P. O. Alderson, J. Nucl. Med. (1984) 796-799.
[71] T. Das, S. Chakraborty, H. D. Sarma, S. Banerjee, Radiochim. Acta 96 (2008) 427-433.
[72] T. Das, S. Chakraborty, H. D. Sarma, S. Barnerjee, Curr. Radiopharm. 5 (2012) 340-347.
[73] M. S. Porrazzo, B. S. Hilaris, C. R. Moorthy, A. E. Tchelebi, C. A. Mastoras, L. L. Shih, L. Stabile, N. Salvaras, Int. J. Radiation Oncol. Biol. Phys. 23 (1992) 1033-1036.
[74] J. C. Blasko, P. D. Grimm, J. E. Sylvester, K. R. Badiozamani, D. Hoak, W. Cavanagh, Int. J. Radiation Oncology Biol. Phys. 46 (2000) 839-850.
[75] K. Wallner, G. Merrick, L. True, W. Cavanagh, C. Simpson, W. Butler, Cancer J. 8 (2000) 67-73.
[76] A. R. Jalilian, Y. Yari-Kamrani, M. Sadeghi, Nukleonika 51 (2006) 119-123.
[77] A. R. Jalilian, M. Sadeghi, Y. Yari-Kamrani, Radiochim. Acta 94 (2006) 865-869.
[78] A. R. Jalilian, M. Sadeghi, Y. Yari-Kamrani, M. R. Ensaf, J. Radioanal. Nucl. Chem. 268 (2006) 605-611.