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# Pd(II) complexes of aliphatic polyamine ligands in aqueous solution: thermodynamic and structural features

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## Abstract

This review collects the stability constants of Pd(II) complexes with amines determined in aqueous solution. The 23 ligands considered herein, span ammonia to acyclic and macrocyclic polyamines. Also the few enthalpy and entropy changes available for such complexation reactions are reported. The thermodynamic data are discussed, taking into account the structural information given for these complexes by spectroscopic measurements (UV–vis, NMR) in solution and X-ray analyses in the solid state. The effects due to nitrogen alkylation of the ligands, as well as the characteristics determined by the ligand structures (acyclic, macrocyclic) are considered. © 1999 Elsevier Science S.A. All rights reserved.

*Keywords:* Palladium; Palladium complexes; Polyamines; Macrocycles; Complexation thermodynamics

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## 1. Introduction

Although Pd(II) has been studied as a Pt(II) substitute in amine complexes which exhibit antitumoral properties, thermodynamic data for the binding of Pd(II) in aqueous solution by amine ligands are rare. This is mostly due to experimental difficulties concerned with the nature of such complexation reactions and the stability of Pd(II) aqueous solutions. As a soft metal ion, Pd(II) forms stronger bonds with nitrogen donors than with oxygen donors; for this reason water molecules in the $[Pd(H_2O)_4]^{2+}$ aqua ion are favorably replaced by amine ligands, forming complexes with very high stability constants, too high in many cases to be determined by direct conventional methods. Furthermore, the complexation reactions may be fairly slow, especially with polydentate and macrocyclic polyamines. To complicate this picture, the Pd(II) aqua ion is stable only in very acidic aqueous solutions, since it undergoes hydrolysis at $pH > 1$, and precipitation of $Pd(OH)_2$ occurs in less acidic media due to its low solubility. For these reasons, in order to reduce the magnitude of the stability constants to be determined and protect the metal ion, solutions containing $PdX_4^{2-}$ complexes with halide or pseudo-halide ligands, instead of the aqua ion, have been largely employed.

In the present review we collect the thermodynamic data [1–13] for the complexation reactions of Pd(II) with polyamine ligands in aqueous solution. When possible the thermodynamic information has been integrated with structural details of the complexes in solution and in the solid state.

## 2. Pd(II) complexes with acyclic amine ligands

Thermodynamic data for the formation of the Pd(II) complexes considered in this review are listed in Table 1.

Ammonia reacts with the aqua ion $[Pd(H_2O)_4]^{2+}$ in successive steps giving rise to the formation of the four complexed species $[Pd(NH_3)(H_2O)_3]^{2+}$, $[Pd(NH_3)_2(H_2O)_2]^{2+}$, $[Pd(NH_3)_3(H_2O)]^{2+}$ and $[Pd(NH_3)_4]^{2+}$. The stability constants of these complexes were determined by Rasmussen and Jørgensen following the dissociation equilibria of $[Pd(NH_3)_4]^{2+}$ in solutions of increasing acidity [1]. Up to 40 min was necessary to reach the equilibrium corresponding to the dissociation of the first two $NH_3$ molecules, while the release of the remaining $NH_3$ molecules took many hours.

The square $[Pd(NH_3)_4]^{2+}$ complex is strictly planar in the solid state, as shown by the crystal structure [14] reported in Fig. 1. On the other hand, loss of the center of inversion is suggested by the absorption spectra of the complex in solution [1].

Based on kinetic evidence, Rasmussen and Jørgensen suggested that two $NH_3$ in *cis* position are the first two ligand molecules leaving $[Pd(NH_3)_4]^{2+}$ upon acid catalyzed dissociation of the complex [1]. Consequently, *cis*-$[Pd(NH_3)_2(H_2O)_2]^{2+}$ is the main isomeric form of the $[Pd(NH_3)_2(H_2O)_2]^{2+}$ complex formed in the experiments performed by these authors for the determination of the stability constants [1], and hence such stability constants (Table 1) should be referred only to equilibria

Table 1
Log *K* values for the formation of Pd(II) complexes with acyclic amines in aqueous solution[a]

Ammonia ($NH_3$) $NH_3$

| Reaction | Log *K* | Method | *T* (°C) | Medium (mol $dm^{-3}$) | Ref. |
|---|---|---|---|---|---|
| $Pd^{2+} + L = PdL^{2+}$ | 9.6 | Pot | 25.0 | 1.0 $NaClO_4$ | [1] |
| $PdL^{2+} + L = PdL_2^{2+}$ | 8.9 | Pot | 25.0 | 1.0 $NaClO_4$ | [1] |
| $PdL_2^{2+} + L = PdL_3^{2+}$ | 7.5 | Pot | 25.0 | 1.0 $NaClO_4$ | [1] |
| $PdL_3^{2+} + L = PdL_4^{2+}$ | 6.8 | Pot | 25.0 | 1.0 $NaClO_4$ | [1] |
| $Pd^{2+} + 4L = PdL_4^{2+}$ | 29.6 | Pot (ISE) | 25.0 | 0.5 | [2] |
| $Pd^{2+} + L = PdL^{2+}$ | 6.06 | Pot | 25.0 | $KNO_3$ | [3] |

1,2-Diaminoethane, ethylenediamine (en)

| Reaction | Log *K* | Method | *T* (°C) | Medium (mol $dm^{-3}$) | Ref. |
|---|---|---|---|---|---|
| $Pd^{2+} + L = PdL^{2+}$ | $>20$ | Pot | 25.0 | 1.0 $NaClO_4$ | [1] |
| $PdL_2^{2+} + L = PdL_2^{2+}$ | 18.4 | Pot | 25.0 | 1.0 $NaClO_4$ | [1] |
| $Pd^{2+} + L = PdL^{2+}$ | 23.6 | Pot | 25.0 | 1.0 $NaClO_4$ | [1] |
| $PdL_2^{2+} + L = PdL_2^{2+}$ | 18.6 | Pot | 25.0 | 1.0 $NaClO_4$ | [4] |

1,3,5-Triazaheptane, diethylenetriamine (den)

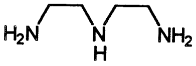
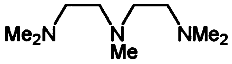


Table 1 (Continued)

| Ammonia ($NH_3$) | $NH_3$ | | | | |
|---|---|---|---|---|---|
| Reaction | Log *K* | Method | *T* (°C) | Medium (mol $dm^{-3}$) | Ref. |
| $Pd^{2+} + L = PdL^{2+}$ | 34 | Pot | 25.0 | 1.0 $NaClO_3$ | [5] |
| $Pd^{2+} + L = PdL^{2+}$ | 32.6 | Pot | 25.0 | 1.0 $NaClO_4$ | [4] |
| $Pd^{2+} + L = PdL_2^{2+}$ | 7.8 | Pot | 25.0 | 1.0 $NaClO_4$ | [4] |
| $PdL^{2+} + NH_3 = PdL(NH_3)^{2+}$ | 6.9 | Pot | 25.0 | 1.0 $NaNO_3$ | [5] |
| $PdL^{2+} + H_2O = PdL(OH)^{+} + H^{+}$ | −7.589 | Pot | 25.0 | 0.5 $NaClO_4$ | [6] |
| $PdL^{2+} + PdL(OH)^{+} = Pd_2L_2(OH)^{3+}$ | 2.19 | Pot | 25.0 | 0.5 $NaClO_4$ | [6] |
| $PdL^{2+} + H_2O = PdL(OH)^{+} + H^{+}$ | −7.243 | Pot | 25.0 | 0.5 $NaNO_3$ | [6] |
| $PdL^{2+} + PdL(OH)^{+} = Pd_2L_2(OH)^{3+}$ | 2.10 | Pot | 25.0 | 0.5 $NaNO_3$ | [6] |

2,5,8-Trimethyl-2,5,8-triazanonane ($Me_5$den)



| Reaction | Log *K* | Method | *T* (°C) | Medium (mol $dm^{-3}$) | Ref. |
|---|---|---|---|---|---|
| $Pd^{2+} + L + Cl^{-} = PdLCP^{+}$ | 24.9 | Pot | 25.0 | 1.0 $NMe_4Cl$ | [7] |
| $Pd^{2+} + L + H_2O = PdL(OH)^{+} + H^{+}$ | 14.1 | Pot | 25.0 | 1.0 $NMe_4Cl$ | [7] |
| $PdL^{2+} + H_2O = PdL(OH)^{+} + H^{+}$ | −7.293 | Pot | 25.0 | 0.5 $NaClO_4$ | [6] |
| $PdL^{2+} + PdL(OH)^{+} = Pd_2L_2(OH)^{3+}$ | 1.08 | Pot | 25.0 | 0.5 $NaClO_4$ | [6] |
| $PdL^{2+} + H_2O = PdL(OH)^{+} + H^{+}$ | −7.241 | Pot | 25.0 | 0.5 $NaNO_3$ | [6] |
| $PdL^{2+} + PdL(OH)^{+} = Pd_2L_2(OH)^{3+}$ | 0.07 | Pot | 25.0 | 0.5 $NaNO_3$ | [6] |

*N*,*N*,*N''*,*N''*-tetraethyl-diethylenetriamine ($Et_4$den)

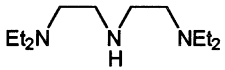
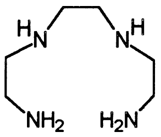


Table 1 (Continued)

| Ammonia ($NH_3$) | $NH_3$ | | | | |
|---|---|---|---|---|---|
| Reaction | Log *K* | Method | *T* (°C) | Medium (mol $dm^{-3}$) | Ref. |
| $PdL^{2+} + H_2O = PdL(OH)^+ + H^+$ | −7.688 | Pot | 25.0 | 0.5 $NaClO_4$ | [6] |
| $PdL^{2+} + PdL(OH)^+ = Pd_2L_2(OH)^{3+}$ | 0.09 | Pot | 25.0 | 0.5 $NaClO_4$ | [6] |
| $PdL^{2+} + H_2O = PdL(OH)^+ + H^+$ | −7.677 | Pot | 25.0 | 0.5 $NaNO_3$ | [6] |
| $PdL^{2+} + PdL(OH)^+ = Pd_2L_2(OH)^{3+}$ | 0.05 | Pot | 25.0 | 0.5 $NaNO_3$ | [6] |

1,4,7,10-Tetraazadecane, triethylenetetraamine, trien (2,2,2-tet)



| Reaction | Log *K* | Method | *T* (°C) | Medium (mol $dm^{-3}$) | Ref. |
|---|---|---|---|---|---|
| $Pd^{2+} + L = PdL^{2+}$ | 40.1 | Pot | 25.0 | 1.0 $NaClO_4$ | [8] |
| $PdL^{2+} + H^+ = Pd(LH)^{3+}$ | 0.84 | Pot/sp | 25.0 | 1.0 $NaClO_4$ | [8] |
| $Pd^{2+} + 2L = PdL_2^{2+}$ | 41.4 | Sp | 20 | 0.1 | [9] |

2,5,8,11-Tetramethyl-2,5,8,11-tetraazadodecane, $Me_6$trien ($Me_6$(2,2,2-tet))

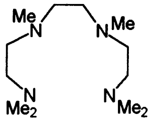
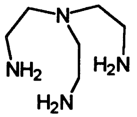


Table 1 (Continued)

Ammonia ($NH_3$) $NH_3$

| Reaction | Log *K* | Method | *T* (°C) | Medium (mol $dm^{-3}$) | Ref. |
|---|---|---|---|---|---|
| $Pd^{2+} + L = PdL^{2+}$ | 23.38 | Pot | 25.0 | 0.1 $NMe_4Cl$ | [7] |
| $PdL^{2+} + Cl^- + H^+ = Pd(HL)Cl^{2+}$ | 6.85 | Pot | 25.0 | 0.1 $NMe_4Cl$ | [7] |
| $PdL^{2+} + OH^- = PdL(OH)^+$ | 4.3 | Pot | 25.0 | 0.1 $NMe_4Cl$ | [7] |

2,2′,2″-Triaminotriethylamine (tren)



| Reaction | Log *K* | Method | *T* (°C) | Medium (mol $dm^{-3}$) | Ref. |
|---|---|---|---|---|---|
| $2Pd^{2+} + 2L = Pd_2L_2^{4+}$ | 77.4 | Pot | 25.0 | 1.0 $KNO_3$ | [4] |

Tris[2-(dimethylamino)ethyl] amine ($Me_6$tren)

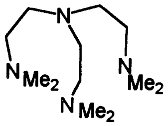
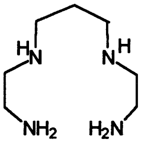


Table 1 (Continued)

Ammonia ($NH_3$) $NH_3$

| Reaction | Log *K* | Method | *T* (°C) | Medium (mol $dm^{-3}$) | Ref. |
|---|---|---|---|---|---|
| $Pd^{2+} + L = PdL^{2+}$ | 30.5 | Pot | 25.0 | 1.0 NaCl | [10] |
| $Pd^{2+} + L = PdL^{2+}$ | 30.8 | Pot | 25.0 | 1.0 NaBr | [10] |
| $PdL^{2+} + H^{+} = Pd(HL)^{3+}$ | 6.58 | Pot | 25.0 | 1.0 NaCl | [10] |
| $PdL^{2+} + H_2O = PdL(OH)^{+} + H^{+}$ | −7.60 | Pot | 25.0 | 1.0 NaCl | [10] |

1,4,8,11-Tetazaundecane (2,3,2-tet)



| Reaction | Log *K* | Method | *T* (°C) | Medium (mol $dm^{-3}$) | Ref. |
|---|---|---|---|---|---|
| $Pd^{2+} + L = PdL^{2+}$ | 46.3 | Pot | 25.0 | 1.0 $NaClO_4$ | [8] |

2,5,9,12-Tetraazamethyl-2,5,9,12-tetraazatridecane ($Me_6$(2,3,2-tet))

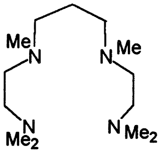
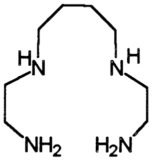


Table 1 (Continued)

Ammonia ($NH_3$) $NH_3$

| Reaction | Log *K* | Method | *T* (°C) | Medium (mol $dm^{-3}$) | Ref. |
|---|---|---|---|---|---|
| $Pd^{2+} + L = PdL^{2+}$ | 28.3 | Pot | 25.0 | 0.1 $NMe_4Cl$ | [7] |
| $PdL^{2+} + Cl^- + H^+ = Pd(HL)Cl^{2+}$ | 3.6 | Pot | 25.0 | 0.1 $NMe_4Cl$ | [7] |
| $PdL^{2+} + OH^- = PdL(OH)^+$ | 2.4 | Pot | 25.0 | 0.1 $NMe_4Cl$ | [7] |

1,4,9,12-Tetraazadodecane (2,4,2-tet)



| Reaction | Log *K* | Method | *T* (°C) | Medium (mol $dm^{-3}$) | Ref. |
|---|---|---|---|---|---|
| $Pd^{2+} + L = PdL^{2+}$ | 42.0 | Pot | 25.0 | 1.0 $NaClO_4$ | [8] |

1,4,10,13-Tetraazatridecane (2,5,2 tet)

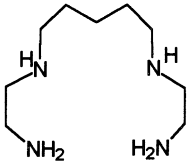
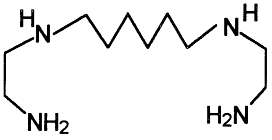


Table 1 (Continued)

Ammonia ($NH_3$) $NH_3$

| Reaction | Log *K* | Method | *T* (°C) | Medium (mol $dm^{-3}$) | Ref. |
|---|---|---|---|---|---|
| $Pd^{2+} + L = PdL^{2+}$ | 37.9 | Pot | 25.0 | 1.0 $KNO_3$ | [8] |

1,4,11,14-Tetraazatetradecane (2,6,2 tet)



| Reaction | Log *K* | Method | *T* (°C) | Medium (mol $dm^{-3}$) | Ref. |
|---|---|---|---|---|---|
| $Pd^{2+} + L = PdL^{2+}$ | 38.14 | Pot | 25.0 | 1.0 $KNO_3$ | [8] |

2,6,9,13-Tetramethyl-2,6,9,13-tetraazatetradecane ($Me_6$(3,2,3 tet))

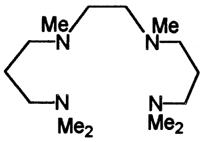
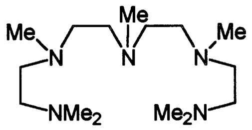


Table 1 (Continued)

| Ammonia ($NH_3$) | $NH_3$ | | | | |
|---|---|---|---|---|---|
| Reaction | Log *K* | Method | *T* (°C) | Medium (mol $dm^{-3}$) | Ref. |
| $Pd^{2+} + L = PdL^{2+}$ | 22.95 | Pot | 25.0 | 0.1 $NMe_4Cl$ | [7] |
| $PdL^{2+} + Cl^- + H^+ = Pd(HL)Cl^{2+}$ | 9.30 | Pot | 25.0 | 0.1 $NMe_4Cl$ | [7] |
| $Pd(HL)Cl^{2+} + Cl^- + H^+ = Pd(H_2L)Cl_2^{2+}$ | 4.52 | Pot | 25.0 | 0.1 $NMe_4Cl$ | [7] |
| $PdL^{2+} + OH^- = PdL(OH)^+$ | 4.84 | Pot | 25.0 | 0.1 $NMe_4Cl$ | [7] |

2,5,8,11,14-Pentamethyl-2,5,8,11,14-pentaazapentadecane ($Me_7$(2,2,2,2-pent))



| Reaction | Log *K* | Method | *T* (°C) | Medium (mol $dm^{-3}$) | Ref. |
|---|---|---|---|---|---|
| $Pd^{2+} + L = PdL^{2+}$ | 21.41 | Pot | 25.0 | 0.1 $NMe_4Cl$ | [7] |
| $PdL^{2+} + H^+ = Pd(HL)^{3+}$ | 8.68 | Pot | 25.0 | 0.1 $NMe_4Cl$ | [7] |
| $Pd(HL)^{3+} + H^+ + Cl^- = Pd(H_2L)Cl^{3+}$ | 5.76 | Pot | 25.0 | 0.1 $NMe_4Cl$ | [7] |
| $PdL^{2+} + OH = PdL(OH)^+$ | 3.41 | Pot | 25.0 | 0.1 $NMe_4Cl$ | [7] |

2,5,8,11,14,17-Hexamethyl-2,5,8,11,14,17-hexaazaoctadecane ($Me_8$(2,2,2,2,2-hexa))

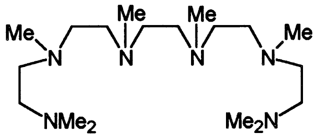
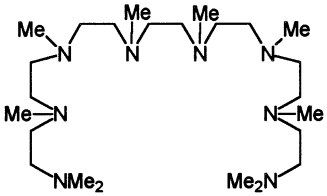


Table 1 (Continued)

Ammonia ($NH_3$) $NH_3$

| Reaction | Log *K* | Method | *T* (°C) | Medium (mol $dm^{-3}$) | Ref. |
|---|---|---|---|---|---|
| $Pd^{2+} + L + H^+ = Pd(HL)^{3+}$ | 30.83 | Pot | 25.0 | 0.1 $NMe_4Cl$ | [7] |
| $Pd(HL)^{3+} + H^+ = Pd(H_2L)^{4+}$ | 7.16 | Pot | 25.0 | 0.1 $NMe_4Cl$ | [7] |
| $PdL^{2+} + H_2O = PdL(OH)^+ + H^+$ | 10.75 | Pot | 25.0 | 0.1 $NMe_4Cl$ | [7] |
| $2Pd^{2+} + L + 2Cl^- = Pd_2LCl_2^{2+}$ | 44.0 | Pot | 25.0 | 0.1 $NMe_4Cl$ | [7] |
| $Pd_2LCl_2^{2+} + H^+ + Cl^- = Pd_2(HL)Cl_3^{2+}$ | 5.8 | Pot | 25.0 | 0.1 $NMe_4Cl$ | [7] |
| $2Pd^{2+} + L + Cl^- + H_2O = Pd_2L(OH)Cl^{2+} + H^+$ | 33.9 | Pot | 25.0 | 0.1 $NMe_4Cl$ | [7] |

2,5,8,11,14,17,20,23-Octamethyl-2,5,8,11,14,17,20,23-octaazatetracosane ($Me_{10}$(2,2,2,2,2,2,2 octa))



| Reaction | Log *K* | Method | *T* (°C) | Medium (mol $dm^{-3}$) | Ref. |
|---|---|---|---|---|---|
| $Pd^{2+} + L = PdL^{2+}$ | 22.85 | Pot | 25.0 | 0.1 $NMe_4Cl$ | [7] |
| $PdL^{2+} + 3H^+ = Pd(H_3L)^{5+}$ | 22.68 | Pot | 25.0 | 0.1 $NMe_4Cl$ | [7] |
| $2Pd^{2+} + L = Pd_2L^{4+}$ | 44.7 | Pot | 25.0 | 0.1 $NMe_4Cl$ | [7] |
| $Pd_2L^{4+} + H^+ + Cl^- = Pd_2(HL)Cl^{4+}$ | 6.5 | Pot | 25.0 | 0.1 $NMe_4Cl$ | [7] |
| $Pd_2(HL)Cl^{4+} + H^+ + Cl^- = Pd_2(H_2L)Cl_2^{4+}$ | 5.8 | Pot | 25.0 | 0.1 $NMe_4Cl$ | [7] |
| $Pd_2L^{4+} + 2OH^- = Pd_2L(OH)_2^{2+}$ | 8.8 | Pot | 25.0 | 0.1 $NMe_4Cl$ | [7] |

[a] Methods are abbreviated as follows: potentiometric, pot; spectrophotometric, sp; calorimetric, cal.

involving the *cis* isomer. As a matter of fact, treatment of a solution containing $[Pd(NH_3)_4]^{2+}$ with excess perchloric acid, followed, after several hours, by the addition of a concentrated NaX (X = Cl, Br, I) solution, results in the precipitation of *cis*-$[Pd(NH_3)_2X_2]$ [15]. The chloro and bromo complexes are stable in the solid state while the iodo complex undergoes isomerization in about 1 year. The *cis* isomers can only be obtained under controlled conditions, while the *trans* isomers (or mixtures of isomers) are normally obtained according to the *trans*-directing influence [16] of the ligands.

Regarding the equilibrium constants for the addition of successive $NH_3$ molecules to the Pd(II) aqua ion, while the ratio between the first and second constants, as well as the ratio between the third and the fourth ones, can be accounted for on the basis of statistical considerations, the ratio between the second and the third stepwise complexation constants is significantly larger than predicted by statistics.

Other values for the overall equilibrium constants for the addition of four $NH_3$ to Pd(II) [2] and the equilibrium constant for the addition of the first $NH_3$ molecule [3] were reported by different authors who however, did not furnish complete information regarding the medium employed in their measurements.

Ethylendiamine (en) forms the two complexes $[Pd(en)(H_2O)_2]^{2+}$ and $[Pd(en)_2]^{2+}$ with Pd(II). In an early study performed by means of pH-metric and spectrophotometric techniques, Rasmussen and Jørgensen concluded that the equilibrium constant for the formation of $[Pd(en)(H_2O)_2]^{2+}$ is greater than $10^{20}$ [1]. In the same study these authors determined the equilibrium constant for the addition of the second en molecule ($\log K = 18.4$) by using two samples, equilibrated at 25°C during some days, prepared by adding different amounts of $H_2en^{2+}$ to solutions of the metal ion.

More recently, employing $Br^-$ as an auxiliary ligand, Anderegg performed an accurate determination of the stability constants of $[Pd(en)(H_2O)_2]^{2+}$ ($\log K = 23.6$) and $[Pd(en)_2]^{2+}$ ($\log K = 18.6$ for $[Pd(en)(H_2O)_2]^{2+} + en = [Pd(en)_2]^{2+} + 2H_2O$) indicating that estimation of the equilibrium constant corresponding to the second complexation step carried out by Rasmussen and Jørgensen [1] was in very good agreement with his value [4].

Anderegg noted that comparison between the stability constants of complexes with en and those with ammonia shows a larger chelate effect for Pd(II) than for 3d divalent cations. Since the entropic gain for chelation is expected to be similar

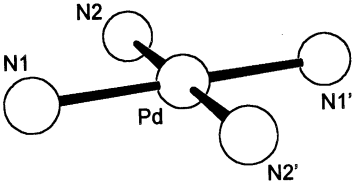


Fig. 1. Crystal structure of $[Pd(NH_3)_4]^{2+}$. Selected bond distances (Å) and angles (°): Pd–N1 2.039, Pd–N2 2.026; N1–Pd–N2 90.3 [14].

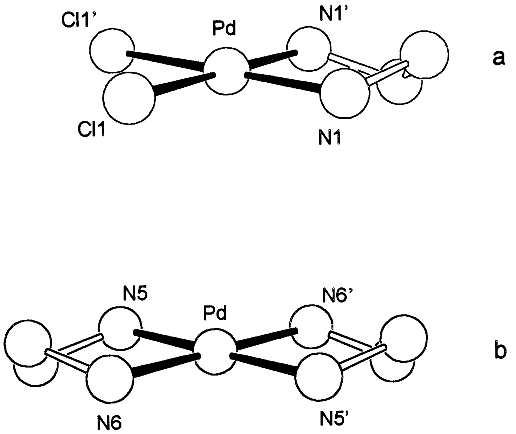


Fig. 2. Crystal structures of (a) *cis*-$[Pd(en)Cl_2]$ and (b) $[Pd(en)_2]^{2+}$. Selected bond distances (Å) and angles (°) for (a): Pd–Cl1 2.309, Pd–N1 1.978; N1–Pd–Cl1 90.8, Cl1–Pd–Cl1′ 96.4, N1–Pd–N1′ 83 [19]. Selected bond distances (Å) and angles (°) for (b): Pd–N1 2.030, Pd–N2 2.043; N1–Pd–N2 83.6, N1–Pd–N2′ 96.5 [20].

for all cations, this larger chelate effect was ascribed to a larger ligand field stabilization [4].

Mellor and Maley also determined these constants, but they reported incorrect values as they neglected the effect on the studied equilibria of chloride present in their samples [17].

Actually chloride displays good coordination ability towards Pd(II), as demonstrated by the equilibrium constants for the successive complexation steps leading to the formation of $[PdCl_4]^{2-}$ ($\log K_1 = 3.48$, $\log K_2 = 6.27$, $\log K_3 = 8.62$, $\log K_4 = 9.72$ [18]). For this reason, when the ligands employed for Pd(II) complexation do not complete the metal ion coordination sphere, mixed-ligand complexes are normally formed in the presence of chloride, and these can be isolated as solid compounds. This is the case, for instance, with the complex $[Pd(en)Cl_2]$ whose crystal structure is shown in Fig. 2a, [19].

As indicated by this structure, although the chelate nature of en favors its complexation with respect to monodentate ligands such as ammonia, en does not present the optimal binding bite for square coordination, the N–Pd–N bond angle (83°) being significantly smaller than the ideal value (90°). Similar features are also observed in the crystal structure of the $[Pd(en)_2]Cl_2$ complex (Fig. 2b), [20].

Rasmussen and Jørgensen [5] reported that when an acidic solution containing $[Pd(H_2O)_4]_2^{2+}$ is added to an acidic solution containing the triprotonated form of diethylentriamine (den) $H_3den^{3+}$, metal ion complexation takes place via two distinct reactions: the first one characterized by a first-order kinetics with half time of 35 min in which the intermediate complex $[Pd(Hden)]^{3+}$ is likely to be formed, and the second one leading in a few days to the final equilibrium corresponding to the formation of $[Pd(den)H_2O]^{2+}$. The stability constant of the last complex was estimated at $\log K = 34$. $[Pd(den_2)H_2O]^{2+}$ displayed an unexpected ability to bind half an equivalent of $OH^-$ suggesting the formation of a hydroxo-bridged binuclear complex. The stability constant of $[Pd(den)_2]^{2+}$ was not determined, although it was observed that the complex undergoes protonation in acidic solution forming $[Pd(Hden)den]^{3+}$ and $[Pd(Hden)_2]^{4+}$. Log $K_1 = 6.1$ and log $K_2 = 2.5$ (1 mol dm$^{-3}$ $NaClO_4$, 25°C) were determined for the two successive protonation reactions [5].

The stability constants of both $[Pd(den)H_2O]^{2+}$ and $[Pd(den)_2]^{2+}$ were later determined by Anderegg, who employed $Br^-$ as a competing ligand [4]. The difference between the equilibrium constants (log $K_1 = 32.6$, log $K_2 = 7.8$, Table 1) for the successive coordination of den molecules is consistent with the presence in $[Pd(den)H_2O]^{2+}$ of only one free coordination site on the metal ion. Actually log $K_2 = 7.8$ is comparable with the equilibrium constants for the addition of one $NH_3$ molecule to $[Pd(den)H_2O]^{2+}$ (log $K = 6.9$) [5] to form the complex $[Pd(den)NH_3]^{2+}$.

Fig. 3 shows the crystal structure of a Pd(II) complex with den where a $NO_2^-$ anion completes the coordination environment of the metal ion [21]. Also in this case the bond angles (Fig. 3) show that the ethylenic chains connecting the amine groups in den are too short to furnish optimal binding bites of the ligand in a square coordination environment.

The equilibria involving coordination of simple anions such as $Cl^-$, $Br^-$, $I^-$, $SCN^-$, and $OH^-$ to $[Pd(L)H_2O]^{2+}$ (L = den, $Me_5$den, $Et_4$den) were investigated by Giacomelli et al. [6]. In the presence of $OH^-$ the species formed are $[Pd(L)OH]^+$ and $[Pd_2(L)_2OH]^{3+}$, whose stability constants (Table 1) were accurately determined. The higher acidity of $[Pd(Me_5den)H_2O]^{2+}$, with respect to the analogous complexes with den and $Et_4$den, was ascribed to a lower ability of $Me_5$den in reducing the effective positive charge of the metal ions owing to the lower inductive effect of methyl groups, compared with the ethyl ones, and also the presence of only tertiary nitrogen atoms, which are less basic than primary and secondary ones. Further effects must arise from the different solvation around the coordinated water molecule, due to the hydrophobic action of the alkyl groups.

From a structural point of view, no important effects on Pd(II) coordination seem to be brought about in the solid state by nitrogen alkylation of den as this is indicated by the crystal structure of the $[Pd(Et_4den)NCS]PF_6$ compound [22] in which the complex cation $[Pd(Et_4den)NCS]^+$ (Fig. 4) does not show significant

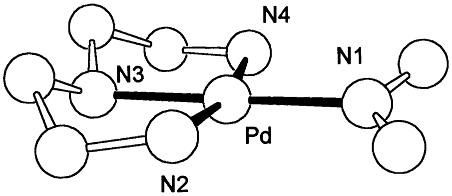


Fig. 3. Crystal structure of $[Pd(den)NO_2]^+$. Selected bond distances (Å) and angles (°): Pd–N2 2.041, Pd–N3 2.047, Pd–N4 2.048, Pd–N1 2.028; N1–Pd–N2 95.1, N1–Pd–N4 95.9, N2–Pd–N3 85.3, N3–Pd–N4 83.6, N1–Pd–N3 179.4, N2–Pd–N4 167.2 [21].

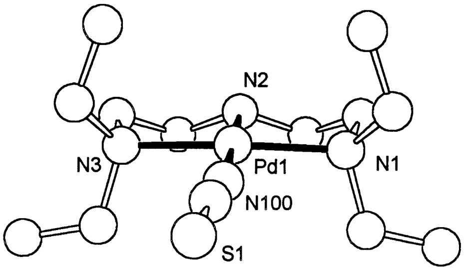


Fig. 4. Crystal structure of $[Pd(Et_4den)NCS]^+$. Selected bond distances (Å) and angles (°): Pd1–N1 2.077, Pd1–N2 1.998, Pd1–N3 2.099, Pd1–N100 2.019; N1–Pd1–N2 84.80, N2–Pd1–N3 85.45, N3–Pd1–N100 94.16, N1–Pd1–N100 95.69, N1–Pd–N3 168.2, N2–Pd–N100 179.1 [22].

differences in ligand binding properties, in terms of ligand conformation, bond distances and bond angles, with respect to those displayed by den in $[Pd(den)NO_2]^+$ (Fig. 3).

The effect of nitrogen methylation on the complexation properties of polyamine ligands towards Pd(II) has been extensively analyzed, both in solution and in the solid state, by Bazzicalupi et al. [7] which we will deal with later on in this review.

The formation of Pd(II) complexes with tetraamines of the type $H_2N–(CH_2)_2–NH–(CH_2)_n–NH–(CH_2)_2–NH_2$ ($n = 2–6$), hereafter indicated as 2,*n*,2-tet, were studied by Yan and Anderegg, using pH-metric and spectrophotometric techniques [8]. The stability constants (Table 1) of the complexes formed were determined in the presence of $Br^-$ or $SCN^-$ or 2,2′-bipyridyl as auxiliary ligands. Equilibration times ranging from several minutes to several days were necessary depending on the ligands and solution pH.

In contrast with a previous work [9], in which the formation of $[Pd(2,2,2\text{-tet})_2]^{2+}$ was reported and the relevant equilibrium constant (Table 1) determined by means of a metal indicator method employing Arsenazo I at a fixed pH value (pH 4), Yan and Anderegg found only 1:1 complexes with their 2,*n*,2-tet ($n = 2–6$) ligands.

Tetraamines 2,3,2-tet and 2,4,2-tet form more stable Pd(II) complexes than 2,2,2-tet, while complexes with 2,5,2-tet and 2,6,2-tet have lower stability. The

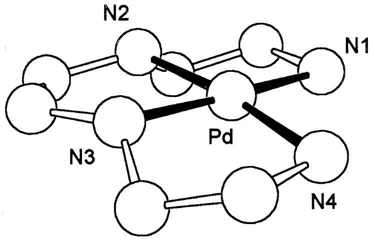


Fig. 5. Crystal structure of $[Pd(trien)]^{2+}$. Selected bond distances (Å) and angles (°): Pd–N1 2.07, Pd–N2 2.00, Pd–N3 1.94, Pd–N4 2.09; N1–Pd–N2 85.5, N2–Pd–N3 85.7, N3–Pd–N4 84.3, N1–Pd–N4 104.4, N2–Pd–N4 169.8, N1–Pd–N3 170.6 [23].

crystal structure of $[Pd(2,2,2\text{-tet})]^{2+}$ (Fig. 5) [23] indicates that, as already observed for en and den (Figs. 2 and 3), the ethylenic chains connecting the amine groups are too short to furnish optimal binding bites of the ligand in a square coordination environment, the N–Pd–N binding angles showing significant deviations from the ideal value (90°). Replacement of the central ethylenic chain in 2,2,2-tet by a longer propylenic chain is expected to produce larger chelate rings, more suitable for square coordination. This is most likely to be the reason why 2,3,2-tet forms a more stable Pd(II) complex than 2,2,2-tet. On the other hand, further prolongation of such a hydrocarbon chain gives rise to the formation of larger and larger chelate rings and produces a destabilization of the complex. A compromise between these two opposite effects would determine the stability trend of the Pd(II) complexes with 2,*n*,2-tet ligands: 2,3,2-tet > 2,4,2-tet > 2,2,2-tet > 2,5,2-tet = 2,6,2-tet.

As anticipated above, Bazzicalupi et al. have reported very recently [7] a solution and solid state study on Pd(II) coordination by a series of fully nitrogen-methylated polyamines including $Me_5$den, $Me_6$(2,2,2-tet), $Me_6$(2,3,2-tet), $Me_6$(3,2,3-tet), $Me_7$(2,2,2,2-pent), $Me_8$(2,2,2,2,2-hexa) and $Me_{10}$(2,2,2,2,2,2,2-octa). The equilibrium constants for the complexes formed (Table 1) were determined by means of pH-metric titrations in a wide pH range (2–11) employing $Cl^-$ as an auxiliary ligand. In the case of $Me_6$(2,3,2-tet), due to the very high stability of its complex, $Me_6$(2,2,2-tet) was employed as a further competing ligand. The rather slow complexation reactions required long equilibration times ( > 10 min) between successive titrant ($OH^-$) additions to ensure the attainment of the equilibrium.

Ligands containing up to five amine groups were found to form only mononuclear complexes while the hexaamine $Me_8$(2,2,2,2,2-hexa) and the octaamine $Me_{10}$(2,2,2,2,2,2,2-octa) form both mono- and bi-nuclear complexes. Spectral data indicate square planar coordination environments for all Pd(II) complexes of these ligands.

Complexes with methylated ligands are largely less stable than the corresponding species with the unmethylated analogues (Table 1). The reduced stability of such complexes, which is accompanied by a red shift of their charge-transfer absorption bands, was ascribed [7] to a lower solvation of the complexes with tertiary amines and to the poorer donating ability of these amines in comparison with secondary and primary ones. The effect of nitrogen-methylation on the donating properties of the non-bonding electron pair of the nitrogen atoms was attributed to two main factors: (i) the influence of the M–N–H···O(water) hydrogen bonds to the solvent (absent in tertiary amines) which increase such donating properties, and (ii) the steric hindrance of the methyl groups which may cause elongation of the M–N bonds as well as distortion of the coordination sphere around Pd(II).

As already observed for the corresponding unmethylated ligands, replacement of the central ethylenic chain in $Me_6$(2,2,2-tet) by a propylenic one, to give $Me_6$(2,3,2-tet), produces a more stable Pd(II) complex. Conversely the stability of the complex with $Me_6$(3,2,3-tet), containing two propylenic chains, is very similar to that of the complex with $Me_6$(2,2,2-tet).

The reduced thermodynamic stability of the Pd(II) complexes with tertiary amines remarkably affects their acid–base behavior in solution. The equilibrium

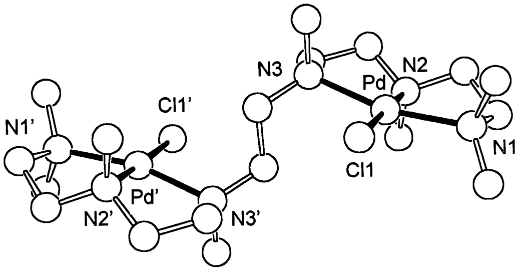


Fig. 6. Crystal structure of $[Pd_2(Me_8(2,2,2,2,2\text{-hexa}))Cl_2]^{2+}$. Selected bond distances (Å) and angles (°): Pd–Cl1 2.306, Pd–N1 2.063, Pd–N2 2.049, Pd–N3 2.074; N2–Pd–N3 86.6, N1–Pd–N2 86.0, Cl1–Pd–N3 93.5, Cl1–Pd–N1 94.4, N2–Pd–Cl1 177.4, N1–Pd–N3 165.6 [7].

data reported in Table 1 indicate that the metal complexes with methylated ligands display a higher tendency to protonation than do the corresponding unmethylated ones. Actually, while the Pd(II) complexes with den, 2,2,2-tet and 2,3,2-tet bind protons only at very acidic pH, protonated species of the analogous complexes with the corresponding methylated ligands are formed in neutral or slightly acidic solutions. Protonation of Pd(II) complexes with ligands having four or less amine groups implies detachment of a nitrogen donor and coordination of a solvent molecule or of an anionic species from the medium ($Cl^-$ in the present case). On the other hand, complexes with $Me_8$(2,2,2,2,2-hexa) and $Me_{10}$(2,2,2,2,2,2,2-octa) contain uncoordinated amine groups which can be easily protonated [7].

The Pd(II) complexes with methylated ligands form hydroxylated species in alkaline solutions, while similar species with unmethylated ligands were found only for den. The ability to bind $OH^-$, exhibited by complexes of methylated ligands containing four or more amine groups was again ascribed to the weakening of the N–Pd(II) bonds, since binding of $OH^-$ seems to involve detachment of a coordinated nitrogen atom.

As noted above the hexaamine $Me_8$(2,2,2,2,2-hexa) and the octaamine $Me_{10}$(2,2,2,2,2,2,2-octa) are able to form binuclear Pd(II) complexes in which the ligands act as if they were composed of two identical, almost independent binding units. This is clearly shown by the crystal structures [7] reported in Figs. 6 and 7.

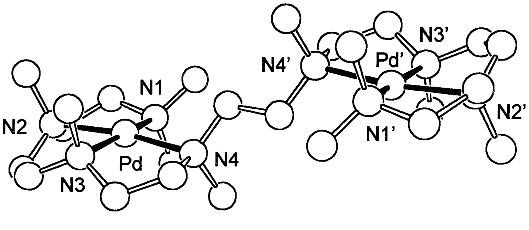


Fig. 7. Crystal structure of $[Pd_2(Me_{10}(2,2,2,2,2,2,2\text{-octa}))]^{4+}$. Selected bond distances (Å) and angles (°): Pd–N1 2.14, Pd–N2 2.04, Pd–N3 2.05, Pd–N4 2.12; N2–Pd–N3 84.8, N1–Pd–N2 85.3, N4–Pd–N3 85.2, N4–Pd–N1 105.0, N2–Pd–N4 168.4, N1–Pd–N3 167.9 [7].

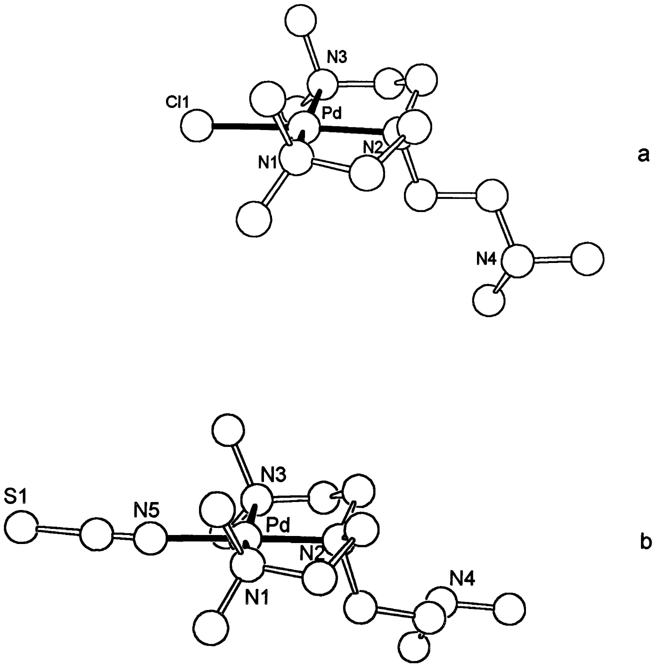


Fig. 8. Crystal structures of (a) $[Pd(HMe_6tren)Cl]^{2+}$ and (b) $[Pd(Me_6tren)NCS]^{+}$. Selected bond distances (Å) and angles (°) for (a): Pd–Cl1 2.315, Pd–N1 2.062, Pd–N2 2.039, Pd–N3 2.079; N1–Pd–Cl1 94.2, N1–Pd–N2 86.5, N2–Pd–N3 86.0, N3–Pd–Cl1 93.8, N2–Pd–Cl1 177.2, N1–Pd–N3 166.2 [24]. Selected bond distances (Å) and angles (°) for (b): Pd–N1 2.054, Pd–N2 1.985, Pd–N3 2.055, Pd–N5 1.987; N1–Pd–N5 92.6, N1–Pd–N2 87.3, N2–Pd–N3 84.1, N3–Pd–N5 96.3, N1–Pd–N3 167.2, N2–Pd–N5 178.3 [25].

The hexadentate ligand $Me_8$(2,2,2,2,2-hexa) does not contain enough donor atoms to fulfill the coordination environment of the two Pd(II) ions inducing the binding of other species from the medium.

As shown in Table 1, these binuclear complexes form both protonated and hydroxylated species. Analogous arguments were put forward to account for the formation of such species and the protonated and hydroxylated mononuclear complexes discussed above.

Complexation of Pd(II) by the tripodal ligands 2,2′,2″-triaminotriethylamine (tren) and tris[2-(dimethylamino)ethyl]amine ($Me_6$tren) was studied by Anderegg and Melichar using pH-metric, spectrophotometric and NMR techniques [4,10]. The two ligands display peculiar binding properties towards Pd(II). Both ligands bind the metal ion in acidic solutions forming monoprotonated complexes $[Pd(HL)]^{3+}$ (L = tren, $Me_6$tren) in which Pd(II) is coordinated by three nitrogen atoms of the ligands and a water molecule, which can be easily replaced by coordinating anions, such as halides or $NCS^-$, to form $[Pd(HL)X]^{2+}$ species. The crystal structure of the $[Pd(HMe_6tren)Cl]^{2+}$ complex [24] is shown in Fig. 8a, which displays the metal ion in a slightly distorted square planar coordination environment. Base addition causes deprotonation of the ammonium group which, in the case of tren, coordinates to the metal center of another complex cation forming the very stable dimeric species $[Pd_2(tren)_2]^{4+}$, containing two square planar $PdN_4$ chromophores [4,10]. In the case of $Me_6$tren, probably due to steric reasons, a similar dimerization does not take place, and upon further addition of base the unprotonated complex undergoes deprotonation of the coordinated water molecules, giving rise to the formation of the hydroxylated species $[Pd(Me_6tren)OH]^+$. Fig. 8b shows the crystal structure of $[Pd(Me_6tren)NCS]^+$ [25] in which a nitrogen atom of the ligand is not involved in the coordination. The stability constants determined for such complexes are reported in Table 1.

## 3. Pd(II) complexes with macrocyclic polyamines

Few macrocyclic polyamines have been considered to study complexation equilibria with Pd(II) [11–13], three of them, 1,4,7,10,13,16-hexaazacyclooctadecane ([18]ane$N_6$), 1,4,7,10,13,16,19-heptaazacyclohenicosane ([21]ane$N_7$) and 1,4,7,10,13,16,19,22-octaazacyclotetracosane ([24]ane$N_8$) are saturated cyclic polyamines, while the others, 1,4,7,16,19,22-hexamethyl-1,4,7,16,19,22-hexaaza-[9.9]-*p*-cyclophane ($Ph_2N_6$) and 1,4,7-trimethyl-19,22,28,31-tetraoxa-1,4,7,14,23-pentaaza[9.5]-*p*-cyclophane ($Ph_2N_5O_4$), are cyclophanes containing two benzene spacers. The equilibrium data for the formation of Pd(II) complexes with these ligands are listed in Table 2.

In spite of their cyclic nature, these ligands compared with the acyclic ones, are not particularly sluggish in binding Pd(II) in solution, and hence the stability constants of the species formed were determined by conventional pH-metric titrations, although equilibration times of at least 10 min were necessary between successive titrant ($OH^-$) additions to ensure the attainment of the equilibrium. On the other hand the stability constants of such complexes are very high and consequently $Cl^-$ was employed as an auxiliary ligand [11–13].

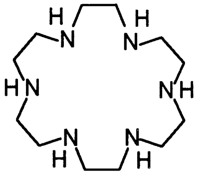
Studying [18]ane$N_6$ and [21]ane$N_7$ the formation of both mono- and binuclear Pd(II) complexes was observed [11]. The ability of these macrocycles to form mononuclear complexes decreases with increasing number of donor atoms in the ligands, while the stability of the binuclear complexes increases. Accordingly with these results, just the formation of a binuclear Pd(II) complex was found with [24]ane$N_8$, but its stability was too high to be accurately determined [12].

Crystal structures of the $[Pd_2([18]aneN_6)Cl_2]^{2+}$ [11] and $[Pd_2([24]aneN_8)]^{4+}$ [12] cations are shown in Fig. 9. In $[Pd_2([18]aneN_6)Cl_2]^{2+}$ the two palladium ions, 3.04 Å apart from each other, are coordinated by three nitrogen atoms and a chloride anion in a distorted square geometry, while in $[Pd_2([24]aneN_8)]^{4+}$ the two metal ions (Pd–Pd distance 5.447 Å) involve only donor atoms of the ligand adopting a distorted square planar coordination. Another crystal structure containing $[Pd_2([18]aneN_6)Br_2]^{2+}$ displayed a quite similar conformation of the complex cation [26]. $^1$H- and $^{13}$C-NMR spectra demonstrated that the structures observed in the solid state for $[Pd_2([18]aneN_6)Cl_2]^{2+}$ and $[Pd_2([24]aneN_8)]^{4+}$ are maintained in solution [12].

Table 2

Log $K$ and $\Delta H°$ (kcal $mol^{-1}$) values for the formation of Pd(II) complexes with macrocyclic polyamines in aqueous solution[a]

1,4,7,10,13,16-Heptaazacyclooctadecane ([18]ane$N_6$)



| Reaction | Log $K$ | Method | $\Delta H°$ (kcal $mol^{-1}$) | $T$ (°C) | Medium (mol $dm^{-3}$) | Ref. |
|---|---|---|---|---|---|---|
| $Pd^{2+} + L = PdL^{2+}$ | 29.2 | Pot | | 25.0 | 0.5 NaCl | [11] |
| $PdL^{2+} + H^{+} = Pd(HL)^{3+}$ | 8.3 | Pot | | 25.0 | 0.5 NaCl | [11] |
| $Pd(HL)^{3+} + H^{+} = Pd(H_2L)^{4+}$ | 4.9 | Pot | | 25.0 | 0.5 NaCl | [11] |
| $2Pd^{2+} + L + 2Cl^{-} = Pd_2LCl_2^{2+}$ | 51.8 | Pot, cal | 49.7 | 25.0 | 0.5 NaCl | [11,12] |

1,4,7,10,13,16,19-Hexaazacyclohenicosane ([21]ane$N_7$)

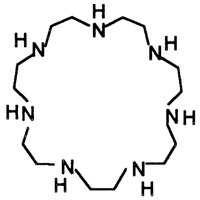
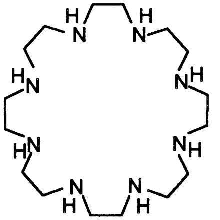


Table 2 (Continued)

| Reaction | Log K | Method | ΔH° (kcal $mol^{-1}$) | T (°C) | Medium (mol $dm^{-3}$) | Ref. |
|---|---|---|---|---|---|---|
| $Pd^{2+} + L = PdL^{2+}$ | 24.55 | Pot | | 25.0 | 0.5 NaCl | [11] |
| $PdL^{2+} + H^{+} = Pd(HL)^{3+}$ | 10.0 | Pot | | 25.0 | 0.5 NaCl | [11] |
| $Pd(HL)^{3+} + H^{+} = Pd(H_2L)^{4+}$ | 8.1 | Pot | | 25.0 | 0.5 NaCl | [11] |
| $Pd(H_2L)^{4+} + H^{+} = Pd(H_3L)^{5+}$ | 4.5 | Pot | | 25.0 | 0.5 NaCl | [11] |
| $2Pd^{2+} + L + Cl^{-} = Pd_2LCl^{3+}$ | $>52$ | Pot, cal | 51.7 | 25.0 | 0.5 NaCl | [11,12] |

1,4,7,10,13,16,19,22-Octaazacyclotetracosane ([24]ane$N_8$)



| Reaction | Log K | Method | ΔH° (kcal $mol^{-1}$) | T (°C) | Medium (mol $dm^{-3}$) | Ref. |
|---|---|---|---|---|---|---|
| $Pd^{2+} + L = PdL^{2+}$ | | Cal | 51.6 | 25.0 | 0.5 NaCl | [12] |

1,4,7,16,19,22-Hexamethyl-1,4,7,16,19,22-hexaaza[9.9]-*p*-cyclophane ($Ph_2N_6$)

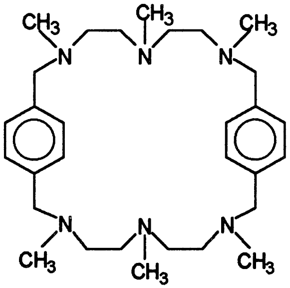
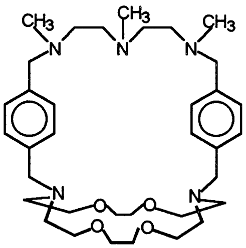


Table 2 (Continued)

| Reaction | Log *K* | Method | $\Delta H°$ (kcal mol$^{-1}$) | *T* (°C) | Medium (mol dm$^{-3}$) | Ref. |
|---|---|---|---|---|---|---|
| $Pd^{2+} + L + Cl^- + 2H^+ = Pd(H_2L)Cl^{3+}$ | 37.44 | Pot | | 25.0 | 0.1 $NMe_4Cl$ | [13] |
| $2\ Pd^{2+} + L + 2Cl^- = Pd_2LCl_2^{2+}$ | 42.9 | Pot | | 25.0 | 0.1 $NMe_4Cl$ | [13] |
| $2\ Pd^{2+} + L + 3Cl^- + H^+ = Pd_2(HL)Cl_3^{2+}$ | 43.7 | Pot | | 25.0 | 0.1 $NMe_4Cl$ | [13] |

1,4,7-Trimethyl-19,22,28,31-tetraoxa-1,4,7,14,23-pentaza[9.5]-*p*-cyclophane ($Ph_2N_5O_4$)



| Reaction | Log *K* | Method | $\Delta H°$ (kcal mol$^{-1}$) | *T* (°C) | Medium (mol dm$^{-3}$) | Ref. |
|---|---|---|---|---|---|---|
| $Pd^{2+} + L + Cl^- = PdLCl^+$ | 23.7 | Pot | | 25.0 | 0.1 $NMe_4Cl$ | [13] |
| $Pd^{2+} + L + Cl^- + H^+ = Pd(HL)Cl^{2+}$ | 31.1 | Pot | | 25.0 | 0.1 $NMe_4Cl$ | [13] |
| $Pd^{2+} + L + Cl^- + 2H^+ = Pd(H_2L)Cl^{3+}$ | 36.7 | Pot | | 25.0 | 0.1 $NMe_4Cl$ | [13] |
| $PdLCl^+ + H^+ = Pd(HL)Cl^{2+}$ | 7.4 | Pot | | 25.0 | 0.1 $NMe_4Cl$ | [13] |
| $Pd(HL)Cl^{2+} + H^+ = Pd(H_2L)Cl^{3+}$ | 5.6 | Pot | | 25.0 | 0.1 $NMe_4Cl$ | [13] |

[a] Methods are abbreviated as follows: potentiometric, pot; calorimetric, cal.

The binuclear complex of [21]ane$N_7$ can react with a further Pd(II) giving rise to a trinuclear species, whose formation is accompanied by the release of one equivalent of $H^+$. From solutions containing this complex, the compound $[Pd_3([21]aneN_7)Cl_3](ClO_4)_2 \cdot H_2O$ was isolated. X-ray analysis revealed the presence in $[Pd_3([21]aneN_7)Cl_3]^{2+}$ (Fig. 10) of a deprotonated nitrogen atom of the ligand bridging two metal cations. Three chloride anions, one of which bridges two Pd(II) ions, complete the rather distorted square planar coordination environments of the three metal ions.

The electronic spectra of the solid trinuclear complex and of its aqueous solutions suggested that the structure of $[Pd_3([21]aneN_7)Cl_3]^{2+}$, observed in the solid state, is likely to be maintained in solution. This hypothesis was also confirmed by $^{13}C$-NMR spectra [12]. The assembly of three bipositive metal centers in the macrocyclic cavity leads to a rather unusual deprotonation of an amine group in aqueous solution.

The enthalpy changes for the formation of the complexes $[Pd_2([18]aneN_6)Cl_2]^{2+}$, $[Pd_2([21]aneN_7)Cl]^{3+}$ and $[Pd_2([24]aneN_8)]^{4+}$ in solution were determined by direct microcalorimetry [12]; these are, so far, the only enthalpy changes reported for the complexation of Pd(II) with polyamine ligands (Table 2). As can be seen, the

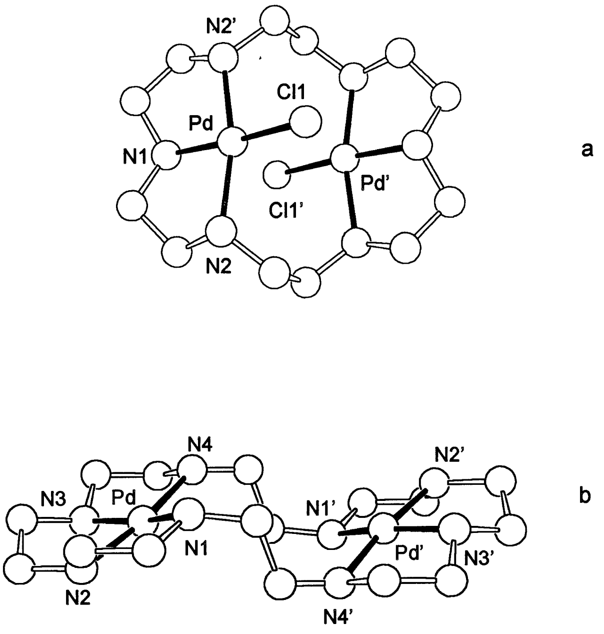


Fig. 9. Crystal structures of (a) $[Pd_2([18]aneN_6)Cl_2]^{2+}$ and (b) $[Pd_2([24]aneN_8)]^{4+}$. Selected bond distances (Å) and angles (°) for (a): Pd–N1 1.99, Pd–N2 2.049, Pd–Cl1 2.301, Pd–Pd′ 3.04; N1–Pd–N2 83.9, Cl1–Pd–N2 95.6, N2–Pd–N2′ 166.5, N1–Pd–Cl1 171.4 [11]. Selected bond distances (Å) and angles (°) for (b): Pd–N1 2.10, Pd–N2 1.98, Pd–N3 1.99, Pd–N4 2.04, Pd–Pd′ 5.447; N3–Pd–N4 86.7, N2–Pd–N4 171.4, N2–Pd–N3 85.4, N1–Pd–N4 164.4, N1–Pd–N3 164.4, N1–Pd–N2 84.0, N1–Pd–N3 179.4, N2–Pd–N4 167.2 [12].

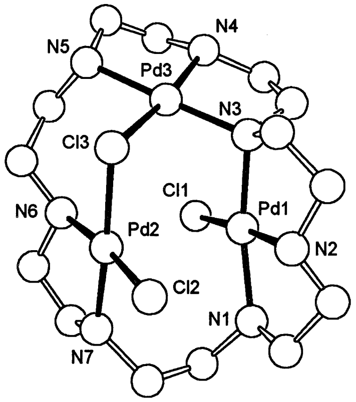


Fig. 10. Crystal structure of $[Pd_3([21]aneN_7)Cl_3]^{2+}$ in which the ligand is present in deprotonated form. Selected bond distances (Å) and angles (°): Pd1–Cl1 2.356, Pd1–N1 2.02, Pd1–N2 2.01, Pd1–N3 2.07, Pd2–N6 2.04, Pd2–N7 1.99, Pd2–Cl2 2.276, Pd2–Cl3 2.306, Pd3–Cl3 2.341, Pd3–N3 1.95, Pd3–N4 1.98, Pd3–N5 2.09, Pd1–Pd2 3.057, Pd1–Pd3 3.232, Pd2–Pd3 3.478; N2–Pd1–N3 88, N1–Pd1–N2 81, Cl1–Pd1–N3 98.0, Cl1–Pd1–N1 93.1, Cl1–Pd1–N2 173,4, N1–Pd1–N3 168, N6–Pd2–N7 84, Cl3–Pd2–N6 93.7, Cl2–Pd2–N7 92.8, Cl2–Pd2–Cl3 83.1, Cl2–Pd2–N6, 173.0, Cl3–Pd2–N7 176.6, N4–Pd3–N5 82, N3–Pd3–N4 89, Cl3–Pd3–N5 94.6, Cl3–Pd3–N3 95.4 [11].

increasing stability observed for the binuclear complexes of $[18]aneN_6$ and $[21]aneN_7$ is followed by an increasing enthalpic contribution. On the other hand, the enthalpy changes for the formation of the binuclear complexes $[Pd_2([21]aneN_7)Cl]^{3+}$ and $[Pd_2([24]aneN_8)]^{4+}$ are equal within experimental error. Namely, from an enthalpic point of view, the eight nitrogens of $[24]aneN_8$ and the seven donors of $[21]aneN_7$ plus a chloride anion make similar contributions to the stability of the above complexes, while a lower enthalpic contribution to the formation of $[Pd_2([18]aneN_6)Cl_2]^{2+}$ is made by the six donors of $[18]aneN_6$ plus two chloride anions. Along with the favorable enthalpic contribution, the entropic one, at least in the case of $[18]aneN_6$ ($T\Delta S° = 21$ kcal $mol^{-1}$ for $2Pd^{2+} + [18]aneN_6 + 2Cl^- = [Pd_2([18]aneN_6)Cl_2]^{2+}$), is of great importance in determining the very high stability of these complexes [12].

The ligational properties of the two cyclophanes $Ph_2N_6$ and $Ph_2N_5O_4$ towards Pd(II) have been studied recently by Bencini et al. by means of pH-metric and NMR methods [13]. The cyclophane $Ph_2N_6$ is composed of two triamine moieties connected by two benzene spacers. According to its ditopic nature, $Ph_2N_6$ presents a marked tendency to form binuclear Pd(II) complexes (Table 2). Only in acidic solutions (containing $Cl^-$) and for low ligand:Pd(II) molar ratios, does the formation of the mononuclear complex $[Pd(H_2Ph_2N_6)Cl]^{3+}$ compete with the formation of a binuclear species [13]. This is the unique mononuclear Pd(II) complex of $Ph_2N_6$ found in solution. The absence of unprotonated species of the type $[Pd(Ph_2N_6)Cl]^+$ suggests that, due to the ligand rigidity determined by the aromatic spacers, Pd(II) is coordinated by a single triamine moiety, the other one remaining available for protonation. The metal ion completes its coordination environment through the binding of a solvent molecule or another coordinating species present in solution, such as $Cl^-$ in the present case.

Such a coordination environment is observed for both metal ions in $[Pd_2(Ph_2N_6)Cl_2]^{2+}$, as shown by the crystal structure [13] reported in Fig. 11. An accurate $^1$H- and $^{13}$C-NMR study demonstrated that the structure of $[Pd_2(Ph_2N_6)Cl_2]^{2+}$ found in the solid state is maintained in solution. This is the principal consequence of the matching between a ligand displaying considerable molecular rigidity and a metal ion which imposes a strict coordination environment.

This binuclear complex is characterized by high thermodynamic stability ($\log K = 42.9$ for $2Pd^{2+} + Ph_2N_6 + 2Cl^- = [Pd_2(Ph_2N_6)Cl_2]^{2+}$, Table 2) although the presence of tertiary amine groups, and perhaps the presence of the bulky benzene spacers, give rise to a considerably lower stability with respect to the analogous complex $[Pd_2([18]aneN_6)Cl_2]^{2+}$ ($\log K = 51.8$ for $2Pd^{2+} + [18]aneN_6 + 2\ C1^- = [Pd_2([18]aneN_6)Cl_2]^{2+}$, Table 2) in which the metal ions have quite similar coordination environments.

Concerning $Ph_2N_5O_4$, its molecular architecture is similar to that of $Ph_2N_6$, a triamine moiety of the last ligand being replaced by an $N_2O_4$ unit. Due to the poor binding properties of such a unit towards Pd(II), $Ph_2N_5O_4$ forms only mononuclear Pd(II) complexes in which the triamine moiety is the binding site for the metal ion. The $N_2O_4$ unit is not involved in the coordination, giving rise to protonated species in acidic solutions. Such characteristics have been clearly described by NMR measurements in solution and by the crystal structure of $\{[Pd(H_2Ph_2N_5O_4)Cl]H_2O\}(ClO_4)_3$ (Fig. 12) in the solid state, showing a marked similarity between the binding properties of $Ph_2N_5O_4$ and $Ph_2N_6$ in the formation of mononuclear complexes [13]. However, due to the modest basicity of the $N_5O_2$ unit, the diprotonated dinuclear complex of $Ph_2N_5O_4$ is easily deprotonated, via two successive steps, up to the formation of the $[Pd(Ph_2N_5O_4)Cl]^+$ species (Table

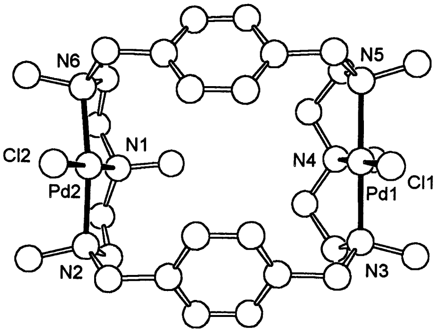


Fig. 11. Crystal structure of $[Pd_2(Ph_2N_6)Cl_2]^{2+}$. Selected bond distances (Å) and angles (°): Pd1–N4 2.001, Pd1–N5 2.089, Pd1–N3 2.099, Pd1–C11 2.301, Pd2–N1 2.005, Pd2–N6 2.072, Pd2–N2 2.082, Pd2–C12 2.295, Pd1–Pd2 7.08; N1–Pd2–N6 86.6, N1–Pd2–N2 84.2, N6–Pd2–N2 165.9, N1–Pd2–C12 178.5, N6–Pd2–C12 94.2, N2–Pd2–C12 95.3, N4–Pd1–N5 85.3, N4–Pd1–N3 84.6, N5–Pd1–N3 169.2, N4–Pd1–C11 178.7, N5–Pd1–C11 95.6, N3–Pd1–Cl1, 94.5 [13].

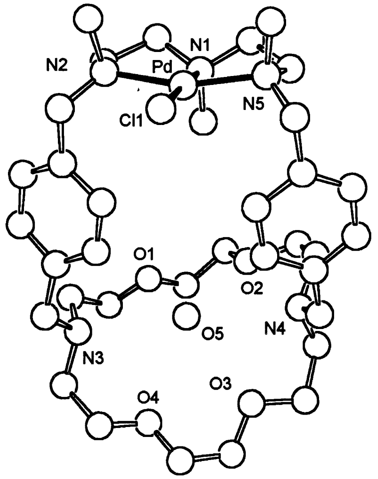


Fig. 12. Crystal structure of $\{[Pd(H_2Ph_2N_5O_4)Cl]H_2O\}^{3+}$. Selected bond distances (Å) and angles (°) around Pd: Pd1–N1 2.017, Pd1–N2 2.046, Pd1–N5 2.082, Pd1–Cl 2.316; N1–Pd1–N2 86.4, N1–Pd1–N5 86.3, N2–Pd1–N5 163.4, N1–Pd1–Cl1 176.4, N2–Pd1–Cl1 93.2, N5–Pd1–Cl1 95.0. A water molecule (O5) is hydrogen bounded to the protonated N3 and N4 atoms [13].

1). As already stated, a similar unprotonated mononuclear complex was not found with $Ph_2N_6$.

## 4. Concluding remarks

In spite of the large interest always shown in the coordination properties of polyamine ligands and the attention paid in recent years to the possible involvement of Pd(II) complexes in anti-cancer therapies, studies dealing with formation equilibria of Pd(II) polyamine complexes are still very rare. On the contrary a greater deal of research directed towards the formation equilibria of new similar complexes with anti-cancer activity and low cytotoxicity would be greatly desirable.

The thermodynamic stability of these complexes is very high; in most of cases it is larger by several orders of magnitude than that of the most stable complexes of other M(II) transition metal ions with the same ligands. This very high thermodynamic stability coupled with the observed slowness of the complexation reactions make the complexes greatly inert towards dissociation. Such thermodynamic and kinetic properties are favorable conditions for the in vivo application of these compounds, since due to these characteristics they oppose metal ion release and transmetallation processes.

In a few cases the enthalpy changes for the complexation reactions of Pd(II) with polyamines in solution have been measured, showing that the high stability of the complexes is determined by largely favorable enthalpic and entropic contributions.

The Pd(II) coordination environments in the polyamine complexes so far considered are strictly square and commonly slightly distorted, depending on the nature of the ligands. For instance it has been previously observed that polyamines only bearing ethylenic chains do not present the optimal binding bites for square coordination, the N–Pd–N bond angles in the complexes being significantly smaller than the ideal value (90°). Replacement of ethylenic chains for longer propylenic ones produces more regular square coordination geometries around Pd(II) which, at least in the case of $[Pd(2,3,2\text{-tet})]^{2+}$ and $[Pd(Me_6(2,3,2\text{-tet}))]^{2+}$, is accompanied by a greater thermodynamic stability.

The presence of alkyl substituents, such as methyl and ethyl groups, on the nitrogen donor atoms does not significantly affect the coordination characteristics of the ligands in the solid state, in terms of bond distances and angles, as shown by the several crystal structures reported herein. Conversely, in solution the presence of alkyl groups on donor atoms reduces considerably the thermodynamic stability of the complexes. Taking into account the solid state information, the observed reduced donating properties of alkylated ligands seem to be mostly ascribable to solvation effects, such as the absence of M–N–H···O(water) hydrogen bonds to the solvent which enhance such donating properties.

Finally, the complex structures found in the solid state are generally maintained in solution; this applies strictly for complexes with rigid ligands such as macrocyclic polyamines. This is a useful characteristic, commonly not observed for other metal ions, which allows one to extend rather confidently the structural information obtained in solution to the solid state and vice versa.

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