

SYNTHESIS AND CHARACTERISATION OF A NOVEL PHOSPHONATE LIGAND AND ITS PALLADIUM(II) COORDINATION COMPOUND

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Abstract. The novel N-(methylene-2-pyridine)-N,N-bis(diethoxyphosphorylmethyl)amine ligand (L) was obtained through a double Kabachnik-Fields reaction, starting from 2-(aminomethyl)pyridine (2-picolylamine). Based on the L ligand, a new palladium(II) coordination compound $[Pd(L)_2Cl_2]$ has been synthesized and comprehensively characterized by spectroscopic methods (1H NMR, UV-Vis), ESI mass spectrometry and X-ray crystallography.

Keywords: palladium, coordination compounds, phosphonate ligands, X-ray characterisation.

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Introduction

Phosphonates and phosphonic metal complexes represent an interesting class of coordination compounds which have been described and widely studied for several decades. Their syntheses, structures and potential applications have been reviewed in detail [1-4].

Phosphonate ligands are considered to be a significant class of molecules which possess a high activity in the medical treatment of bone diseases [5] or contrast agents for magnetic resonance imaging [6]. Moreover the pharmacological use of phosphonates in the prevention of various types of skeletal problems enhances the importance of the requirement of a high oral absorption of these compounds. Also, it was determined that the antiresorptive potency of phosphonates can be magnified due to the presence of nitrogen atoms by 10 - 10000 times in comparison to non-containing nitrogen phosphonates [7].

From the point of view of coordination chemistry, after the group of carboxylate ligands, the phosphonates are considered to be the biggest class of ligands which can generate a variety of complexes due to their multiple coordination sites. The possible coordination pathway for phosphonate ligands $[RPO_3]^{2-}$ is shown elsewhere [2]. The coordination through multiple sites usually contributes to the formation of polymeric coordination compounds or metal-organic frameworks, which are usually insoluble or possess a poor solubility in both organic solvents and aqueous solutions. These complexes may find

application in biomedical studies [6,8], and this can be related to the fact that some bisphosphonates may also act as ligands for metals, thus leading them to be employed in the treatment therapy for metal intoxication [9].

It was shown that aminophosphonate ligands easily lead to the formation of metal complexes, which either possess biomedical potential [8], or show thermoluminescent properties [10]. On the other hand, the use of bisphosphonic esters as ligands for metals has been described a lot less [11-14]. Another interest raised by this kind of ligands is that the presence of bisphosphonate function may influence the solubility of the corresponding complexes in water, therefore allowing the possibility to use such compounds as catalysts in water mediated reactions.

The chemical properties of the 8th group metal complexes are multilateral, versatile and have a large area of applications. Nevertheless, the chemistry of phosphonate ligands with 8th group metals is not well studied yet, and there are known only a few examples of palladium based phosphonates.

From another point of view, palladium chemistry is a wide-ranged research area which mediates a big variety of catalytic reactions. Although the design of renewable palladium catalysts for aerobic oxidation is a quite new research area in the field of palladium chemistry. Mekmouche *et al.* reported a completely new bimolecular system consisting of a redox enzyme – laccase and a water soluble palladium complex

that is able to perform the reaction of alcohol oxidation into the corresponding aldehyde in an aqueous solution at ambient temperature [15].

In order to synthesize a new potential molecular palladium based catalyst with a high solubility in water, we turned out towards the synthesis of a new aminobisphosphonate ligand, namely pyridylbisphosphonate, since this ligand may modify the electronic density around the metal and therefore its reactivity, with the aim of preparing the palladium coordination compound for catalytic studies, and/or for biochemical experiments.

In the perspective of developing new catalysts for clean water mediated reactions, herein we report the synthesis of both a novel phosphonate ligand (L) and a new palladium(II) coordination compound [Pd(L)₂Cl₂]. The crystallographic characterization of the [Pd(L)₂Cl₂] complex is also described.

Experimental

Chemicals

All chemicals were purchased from commercial sources and used as received unless otherwise stated. Basic solvents for synthesis were dried using literature methods. Solvents for spectroscopic investigations were of the highest purity available.

Synthesis of *N*-(methylene-2-pyridine)-*N,N*-bis(diethoxyphosphorylmethyl)amine (L)

A mixture of diethyl phosphite (3 g, 22 mmol), 2-(aminomethyl)pyridine (0.94 g, 9 mmol) and paraformaldehyde (0.62 g, 21 mmol) was stirred under reflux at 100°C for 3 h. After cooling, 20 mL diethyl ether and K₂CO₃ (2 g, 15 mmol) were added and stirred another 2 h at room temperature. The organic reddish solution was separated from the brown solid by decantation and the solvent was removed at 700 mBar at 40°C. Purification by flash chromatography using ethylacetate/methanol (4:1) afforded the desired compound L (3 g, 85% yield) as orange oil.

UV-Vis (CH₃CN): λ_{\max} , nm (ϵ , 10³ L mol⁻¹ cm⁻¹) = 260 (7.7).

¹H-NMR (400 MHz, CDCl₃, ppm): δ 8.45 (d, 1H, CH, 4.28 Hz), 7.65 (t, 1H, 7.59 Hz, 7.66 Hz), 7.56 (d, 1H, CH, 7.79 Hz), 7.14 (t, 1H, CH, 5.36 Hz, 6.04 Hz), 4.07 (d, 8H, CH₂, 6.87 Hz) 4.03 (s, 2H, CH₂), 3.18 (d, 4H, CH₂, 9.70 Hz), 1.25 (t, 12H, CH₃, 7.07 Hz, 7.07 Hz).

³¹P-NMR (162 MHz, CDCl₃, ppm): δ 24.36 (s).

ESI-MS (CH₂Cl₂): m/z 408.16 [M+H]⁺.

Synthesis of palladium complex [Pd(L)₂Cl₂]

To a solution of PdCl₂ (0.1985 g, 1.119 mmol) in CH₃CN was added dropwise a solution of L in CH₂Cl₂ (0.8756 g, 2.144 mmol), and the mixture was stirred at room temperature. The pale yellow precipitate was recrystallized from DMSO and in 1 year we obtained a yellow monocrystalline compound. Yield: 11.5%, 0.2536 g, 0.246 mmol.

UV-Vis (CH₃CN): λ_{\max} , nm (ϵ , 10³ L mol⁻¹ cm⁻¹) = 230 (25.3), 260 (sh), 400 (0.2).

¹H-NMR (400 MHz, CDCl₃, ppm): δ 9.05 (d, 2H, CH, 5.44 Hz), 8.06 (t, 2H, 9.27 Hz, 8.34 Hz), 7.81 (t, 2H, CH, 7.63 Hz, 7.82 Hz), 7.33 (t, 2H, CH, 6.08 Hz, 7.30 Hz), 5.40 (s, 4H, CH₂), 4.19 (m, 16H, CH₂), 3.46 (d, 8H, CH₂, 9.21 Hz), 1.36 (t, 24H, CH₃, 7.02 Hz, 6.93 Hz).

³¹P-NMR (162 MHz, CDCl₃, ppm): δ 24.32 (s).

ESI-MS (CH₂Cl₂): m/z 1017.15 [M+Na]⁺.

Characterisation

The ¹H, and ³¹P NMR spectra were recorded at 25°C on Bruker Avance III nanobay – 400 MHz spectrometer. Chemical shifts were reported in parts per million (ppm) referenced to residual solvent peak. The spectra were recorded using CDCl₃ as deuterated solvent.

UV-Vis spectra were recorded on a Varian Cary 50 spectrophotometer from 200-800 nm with samples in 1.0 path length quartz cuvette. Electronic spectra were recorded for solutions of different concentrations in order to be able to calculate the extinction coefficient.

Suitable crystals for single crystal X-ray diffraction study of [Pd(L)₂Cl₂] complex were grown by slow evaporation of DMSO solution. The intensity data were collected at 293 K on a Rigaku Oxford Diffraction SuperNova diffractometer using MoK α radiation (λ = 0.71073 Å). Data collection, cell refinement and data reduction were performed with CrysAlisPro (Rigaku Oxford Diffraction). The structures were solved with ShelXT [18] and ShelXL [19] was used for full matrix least squares refinement in all cases. Crystallographic data for [Pd(L)₂Cl₂] complex, CCDC-1518527 can be obtained free of charge from The Cambridge Crystallographic Data Centre *via*: www.ccdc.cam.ac.uk/data_request/cif.

Results and discussion

Synthesis and characterisation of the phosphonate ligand

The new *N*-(methylene-2-pyridine)-*N,N*-bis(diethoxyphosphorylmethyl)amine ligand (L) was obtained through a double Kabachnik-Fields

reaction, by adaptation of a known procedure, [16] starting from 2-aminomethyl pyridine (2-picolylamine) and diethyl phosphite in presence of paraformaldehyde (Figure 1).

We should mention that the reaction was performed in absence of any solvent. This gave the ligand L – an orange oil with a 85% yield after purification, which was fully characterized using the common spectroscopic techniques.

NMR spectra (Figure 2) were performed in CDCl_3 at room temperature. The ^{31}P NMR (Figure 2, insertion) displays a single peak at 24.4 ppm, whereas the ^1H spectrum is in accordance with the structure. The ^1H NMR spectrum (Figure 2) of L includes eight signals. Four signals in the aromatic region of the spectrum

(8.45 – 7.14 ppm) are assigned to four protons of the pyridine ring and four signals in the aliphatic region of the spectrum (4.07 – 1.25 ppm) are assigned to the protons from CH_2 and CH_3 groups. High resolution mass spectroscopy performed in CH_2Cl_2 shows a molecular peak at 408.16 Da, which matches with the required mass.

The UV-Vis spectra for the L ligand, recorded in acetonitrile at different concentrations, are shown in Figure 3. The electronic absorption spectra for the ligand invariably show the presence of a characteristic band in the ultraviolet domain at 260 nm (Figure 3). The extinction coefficient value is $7700 \text{ L mol}^{-1} \text{ cm}^{-1}$, which corresponds to the energy of 460 kJ/mol.

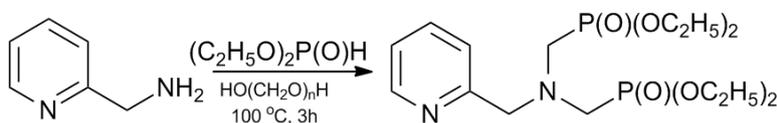


Figure 1. Synthesis of the *N*-(methylene-2-pyridine)-*N,N*-bis(diethoxyphosphorylmethyl)amine (L) ligand.

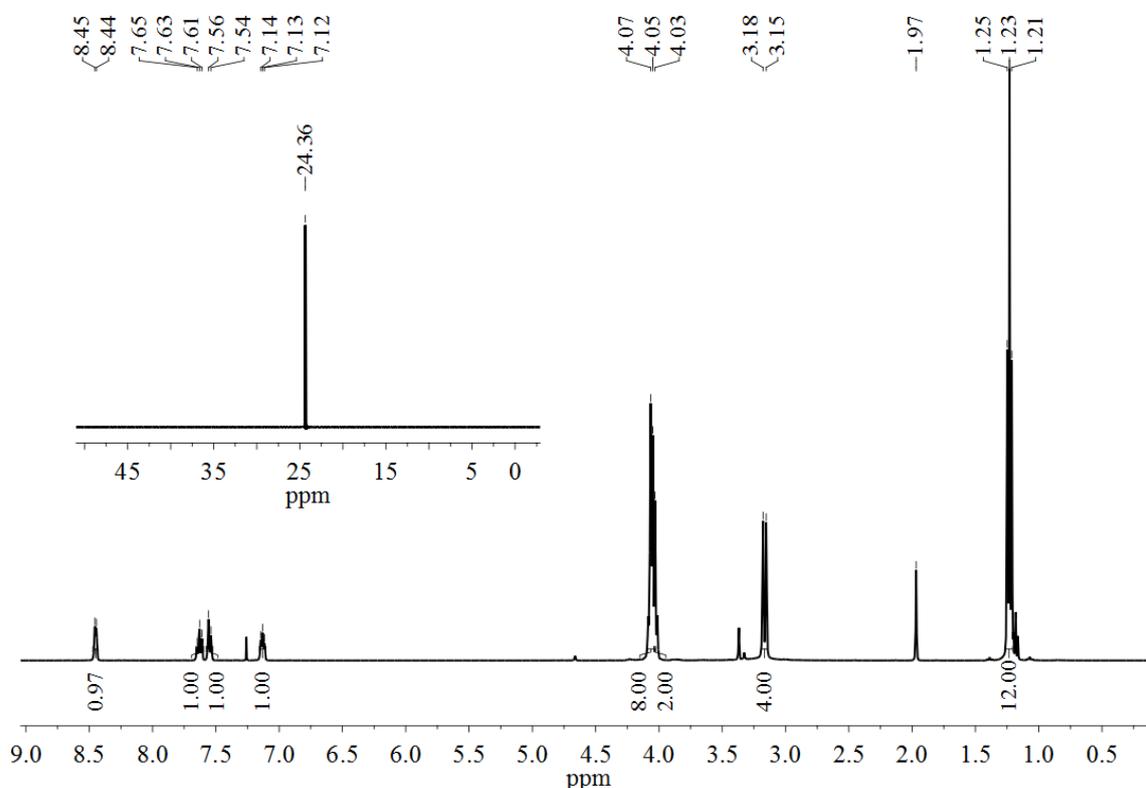


Figure 2. ^1H and ^{31}P (insertion) NMR spectra of L recorded in CDCl_3 .

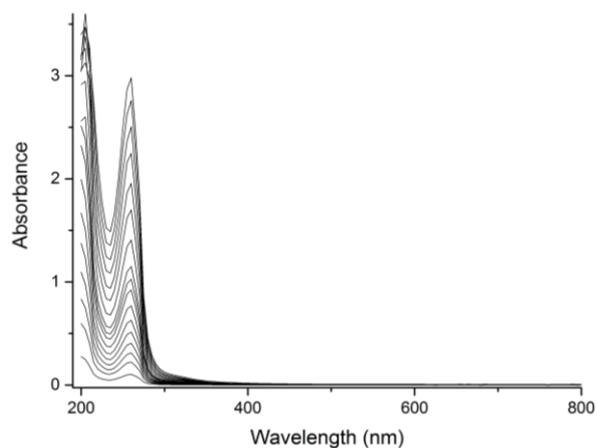


Figure 3. Electronic absorption spectra for L in CH_3CN at different concentrations (15 – 476 μM).

Synthesis and characterisation of the palladium(II) coordination compound

The palladium(II) complex $[\text{Pd}(\text{L})_2\text{Cl}_2]$ was easily formed by mixing and stirring a solution of

palladium chloride in acetonitrile with a solution of ligand in dichloromethane, at room temperature (Figure 4). Crystals suitable for single X-ray diffraction analysis were grown from a DMSO solution (after one year).

The NMR spectra for the palladium complex (Figure 5) are quite similar to those of the free ligand (Figure 2). ^{31}P NMR displays a peak at 24.3 ppm. The ^1H NMR spectrum of $[\text{Pd}(\text{L})_2\text{Cl}_2]$ contains nine signals. Four signals in the aromatic region of the spectrum (9.05 – 7.29 ppm) are assigned to four protons of the pyridine ring and five signals in the aliphatic region of the spectrum (5.40 – 1.36 ppm): four of which are assigned to the protons from CH_2 and CH_3 groups and one signal to protons from water molecules. In addition, the mass spectrum of this complex leads to the conclusion that a compound with a formula $\text{C}_{32}\text{H}_{60}\text{O}_{12}\text{P}_4\text{PdCl}_2$ is present, corresponding to an exact mass of 994.16 Da.

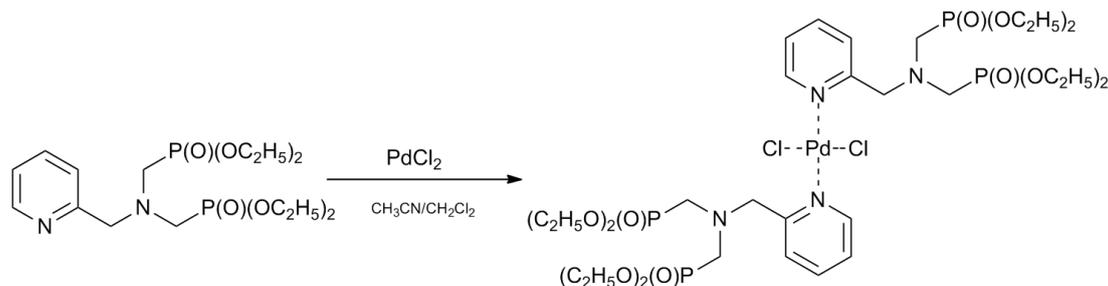


Figure 4. Synthesis of the $[\text{Pd}(\text{L})_2\text{Cl}_2]$ complex.

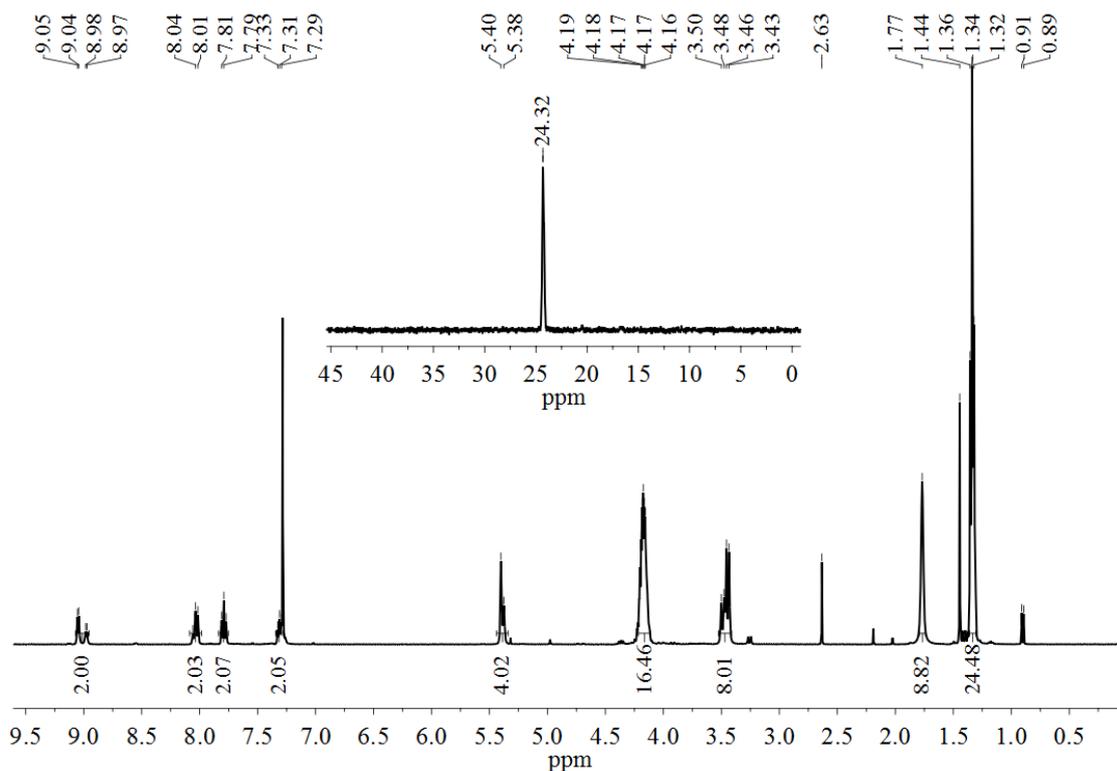


Figure 5. ^1H and ^{31}P (insertion) NMR spectra of $[\text{Pd}(\text{L})_2\text{Cl}_2]$ recorded in CDCl_3 .

The electronic absorption spectra for the complex in acetonitrile (Figure 6) display bands in both the ultraviolet region (190 – 380 nm) and the visible region of the spectrum (380 – 750 nm). The additional band at 400 nm is characteristic for the metal – ligand charge transfer and is indicating towards the coordination of the ligand to the palladium atom. However the extinction coefficient for this band is rather low: $200 \text{ L mol}^{-1} \text{ cm}^{-1}$ and the corresponding energy is 299 kJ/mol.

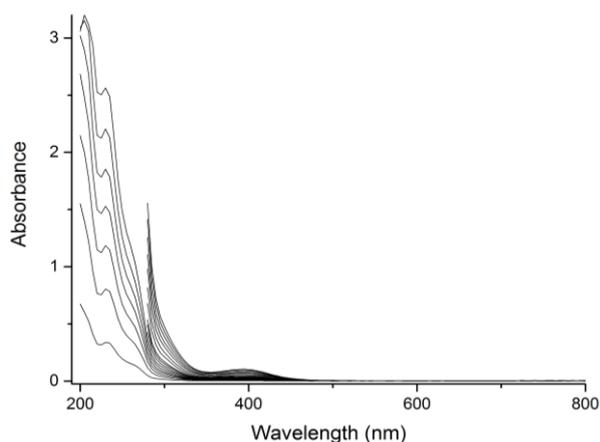


Figure 6. Electronic absorption spectra for $[\text{Pd}(\text{L})_2\text{Cl}_2]$ in CH_3CN at different concentrations (15 – 476 μM).

Structural characterization of palladium(II) coordination compound

The crystallographic structure of the complex $[\text{Pd}(\text{L})_2\text{Cl}_2]$ could be seen in Figure 7 and a fragment of the crystal packing in the molecule in Figure 8. Compound $[\text{Pd}(\text{L})_2\text{Cl}_2]$ has a molecular structure in the crystal.

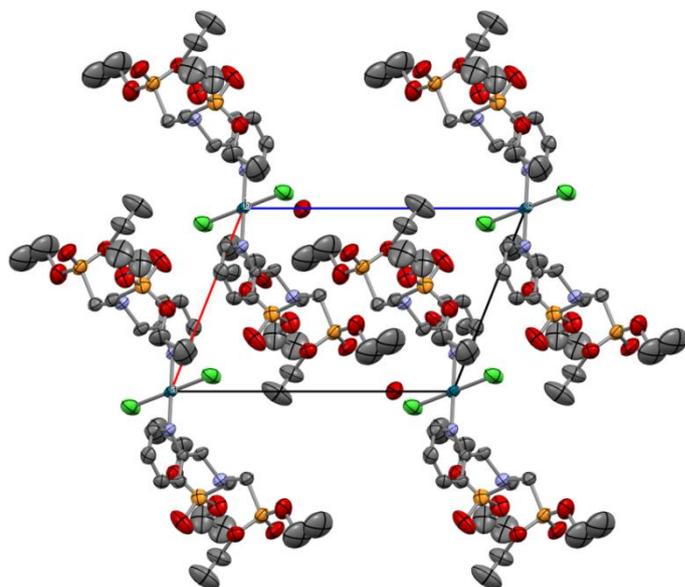


Figure 8. A fragment of crystal packing in the molecule $[\text{Pd}(\text{L})_2\text{Cl}_2]$. Hydrogen atoms were omitted for clarity.

The asymmetric unit consists of a palladium atom with one coordinated L ligand molecule, one coordinated chlorine atom, and one cocrystallized water molecule.

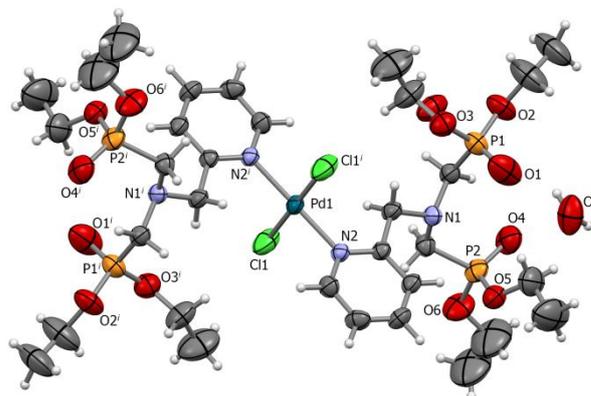


Figure 7. View of the molecule $[\text{Pd}(\text{L})_2\text{Cl}_2]$. Symmetry code: (i) $-x -y -z$. Thermal ellipsoids are drawn at 50 % probability level.

The $[\text{Pd}(\text{L})_2\text{Cl}_2]$ complex crystallizes in the triclinic centrosymmetric space group P-1. The palladium has a square planar coordination sphere provided by two nitrogen and two chlorine atoms in a *trans* arrangement. The pyridine rings are situated perpendicular to the plane formed by the central metal and its coordination sphere.

The crystallographic data containing the structural parameters and unit cell characteristics are shown in Table 1. CCDC 1518527 contains the supplementary crystallographic data for this paper. The data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/structures.

Table 1

Crystallographic data for palladium phosphonate complex [Pd(L) ₂ Cl ₂].	
Parameter	Value
Empirical formula	C ₃₂ H ₆₄ Cl ₂ N ₄ O ₁₄ P ₄ Pd
Formula weight (g/mol)	1030.05
Crystal system	Triclinic
Space group	P-1
<i>a</i> (Å)	9.09726(18)
<i>b</i> (Å)	11.7041(3)
<i>c</i> (Å)	13.2219(3)
α (°)	109.521(2)
β (°)	104.3024(19)
γ (°)	104.788(2)
Volume (Å ³)	1194.60(5)
<i>Z</i>	1
λ (Å)	0.71073
ρ_{calc} (g/cm ³)	1.432
Crystal size (mm ³)	0.24 × 0.12 × 0.04
Colour	Brown needle
Temperature (K)	293
μ (mm ⁻¹)	0.695
Unique data, parameters, restraints	5792, 277, 2
<i>R</i> ₁ ^(a)	0.0489
<i>wR</i> ₂ ^(b)	0.1616
GOF ^(c)	1.263

$$^a R_1 = \frac{\sum ||F_o| - |F_c||}{\sum |F_o|};$$

$$^b wR_2 = \left\{ \frac{\sum [w(F_o^2 - F_c^2)^2]}{\sum [w(F_o^2)]} \right\}^{1/2};$$

$$^c GOF = \left\{ \frac{\sum [w(F_o^2 - F_c^2)^2]}{(n - p)} \right\}^{1/2},$$

where *n* is the number of reflections and *p* is the total number of parameters refined.

The presented data reveals that palladium is coordinated only to the two nitrogen atoms from the two pyridine rings, and is not bound to the phosphonate moiety. This structure is in contrast with the complex described by Jordan *et al.* [17] in which palladium is bound to the phosphine, and to the oxygen atom of the phosphoryl bond.

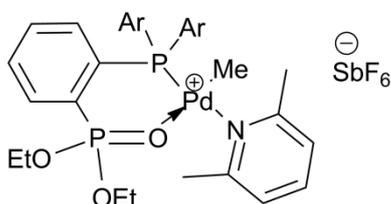


Figure 9. Palladium-phosphonate complex described by Jordan *et al.* [17].

Conclusions

In this work, it is described the synthesis of a palladium(II) complex from an aminobisphosphonate ligand incorporating an aminopyridine moiety. This is the first time that such a bisphosphonate is used as a ligand.

The complex was fully characterized by the usual spectroscopic techniques. In the palladium complex, the metal has a square planar coordination sphere and the ligand is bound to the pyridine nitrogen atom only. The use of this catalyst in different organic reactions is under evaluation.

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