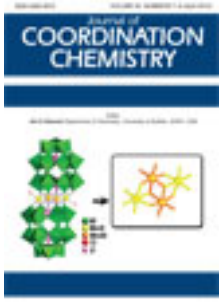

Journal of Coordination Chemistry
Publication details, including instructions for authors and subscription information:
http://www.tandfonline.com/loi/gcoo20

Binuclear cyclopalladated compounds with antitubercular activity: synthesis and characterization of [{Pd(C^2,N-dmba)(X)}$_2$(μ-bpp)] (X=Cl, Br, NCO, N_3; bpp=1,3-bis(4-pyridyl)propane)

Antonio C. Moro [a] , Ana C. Urbaczek [b] , Eduardo T. De Almeida [c] , Fernando R. Pavan [d] , Clarice Q.F. Leite [d] , Adelino V.G. Netto [a] & Antonio E. Mauro [a]

[a] Departamento de Química Geral e Inorgânica , Instituto de Química, UNESP , CEP 14801-970, Araraquara , SP , Brazil

[b] Departamento de Análises Clínicas, Faculdade de Ciências Farmacêuticas , UNESP , CEP 14801-902, Araraquara , SP , Brazil

[c] Departamento de Ciências Exatas , UNIFAL , CEP 31130-000, Alfenas , MG , Brazil

[d] Departamento de Ciências Biológicas, Faculdade de Ciências Farmacêuticas , UNESP , CEP 14800-900, Araraquara , SP , Brazil

Published online: 30 Mar 2012.

Journal of Coordination Chemistry
Vol. 65, No. 8, 20 April 2012, 1434–1442

Binuclear cyclopalladated compounds with antitubercular activity: synthesis and characterization of $[\{Pd(C^2,N\text{-dmba})(X)\}_2(\mu\text{-bpp})]$ (X = Cl, Br, NCO, N_3; bpp = 1,3-bis(4-pyridyl)propane)

ANTONIO C. MORO†, ANA C. URBACZEK‡, EDUARDO T. DE ALMEIDA§, FERNANDO R. PAVAN¶, CLARICE Q.F. LEITE¶, ADELINO V.G. NETTO† and ANTONIO E. MAURO*†

†Departamento de Química Geral e Inorgânica, Instituto de Química, UNESP, CEP 14801-970, Araraquara, SP, Brazil
‡Departamento de Análises Clínicas, Faculdade de Ciências Farmacêuticas, UNESP, CEP 14801-902, Araraquara, SP, Brazil
§Departamento de Ciências Exatas, UNIFAL, CEP 31130-000, Alfenas, MG, Brazil
¶Departamento de Ciências Biológicas, Faculdade de Ciências Farmacêuticas, UNESP, CEP 14800-900, Araraquara, SP, Brazil

(*Received 15 November 2011; in final form 8 February 2012*)

Reactions between $[Pd(C^2,N\text{-dmba})(\mu\text{-X})]_2$ (Hdmba = *N*,*N*-dimethylbenzylamine; X = Cl, Br, NCO, N_3) and 1,3-bis(4-pyridyl)propane (bpp) in 1 : 1 molar ratio at room temperature resulted in the binuclear compounds $[\{Pd(C^2,N\text{-dmba})(X)\}_2(\mu\text{-bpp})]$ (X = Cl (**1**), Br (**2**), NCO (**3**), N_3 (**4**)), which were characterized by elemental analyses, infrared (IR), ^{1}H- and $^{13}C\{^1H\}$-NMR spectroscopies, and thermogravimetric analysis. The IR and NMR data of **1**–**4** were consistent with the presence of bridging bpp. The thermal stability order of the complexes was **4** > **3** > **2** > **1**. Compounds **1**–**4** and bpp were tested against *Mycobacterium tuberculosis* and their MIC values were determined.

Keywords: Cyclopalladated; bpp; Spectroscopy; Tuberculosis; Antimycobacterial agents

1. Introduction

In developing countries, tuberculosis (TB) is a leading cause of morbidity and mortality. Its coinfection with the human immunodeficiency virus has been responsible for changes in the TB epidemiologic situation and also corroborates the urgency for the development of drugs able to act against multidrug resistant (MDR) strains of *Mycobacterium tuberculosis* [1–4]. Treatment against TB involves three or four different kinds of antibacterial drugs given in combination over 6–9 months. These are isoniazid, pyrazinamide, ethambutol, and rifampicin. Multiple combinations are necessary to prevent the emergence of MDR strains, which would lead to treatment failure [1–4].

*Corresponding author. Email: mauro@iq.unesp.br

ISSN 0095-8972 print/ISSN 1029-0389 online © 2012 Taylor & Francis
http://dx.doi.org/10.1080/00958972.2012.673718

Complexes of metals such as Ag, Cu, Fe, and Ru have attracted much attention because they show higher activity than free ligands and corresponding metal salts. In some cases metal complexes containing drugs as ligands can overcome resistance developed by bacteria to drug alone [5, 6]. The antimycobacterial activity of palladium(II) complexes has not been studied as exhaustively but can be exemplified with some literature reports [2, 7]. For instance, Pd(II) complexes with fluoroquinolones and thiosemicarbazones have shown prominent antitubercular activity [7, 8]. *trans*-$[Pd(N_3)_2(isn)_2]$ (isn = isonicotinamide) was effective against *M. tuberculosis* [4]. Particularly, studies on the antimycobacterial activity toward TB involving cyclopalladated compounds are very rare. Cyclopalladated complexes $[Pd(C^2,N\text{-dmba})(X)(tu)]$ (X = Cl, Br; tu = thiourea) are the only examples of compounds with interesting activity [2] *in vitro* against *M. tuberculosis* virulent strain $H_{37}Rv$ described in the literature.

The choice of using 1,3-bis(4-pyridyl)propane (bpp) as ligand was motivated by its ability to join two metallic centers affording in this way polymetallic complexes [9, 10]. Additionally, bpp has a carbon chain that is able to penetrate into the lipid-rich hydrophobic cell wall of *M. tuberculosis*. Therefore, Pd(II) derivatives bearing bpp can be attractive in both coordination chemistry and medicinal areas. Despite the fact that antibacterial properties of palladium(II) compounds have been the subject of many reports [11, 12], studies on the antitubercular activity of 1,3-bis(4-pyridyl)propane-based Pd(II) complexes remain unknown.

Focusing our interest on cyclometallated and coordination chemistry of palladium-based compounds [13–20], we describe herein the syntheses, spectroscopic characterizations, and thermal behaviors of $[\{Pd(C^2,N\text{-dmba})(X)\}_2(\mu\text{-bpp})]$ (Hdmba = *N*,*N*-dimethylbenzylamine; X = Cl (**1**), Br (**2**), NCO (**3**), N_3 (**4**)). This work also evaluated the minimum inhibitory concentration (MIC) values of **1**–**4** against the *M. tuberculosis*.

2. Experimental

2.1. *General methods*

The syntheses were performed at room temperature. Commercial reagents and solvents were employed without purification. The starting materials $[Pd(C^2,N\text{-dmba})(\mu\text{-X})]_2$ (X = Cl, Br, NCO, N_3) were prepared as previously described [21–24].

2.2. *Preparation of 1–4*

A solution of 0.18 mmol (0.036 g) of 1,3-bis(4-pyridyl)propane (bpp) in 5 cm^3 of acetone was added to a 10 cm^3 chloroform solution of 0.18 mmol of $[Pd(C^2,N\text{-dmba})(\mu\text{-X})]_2$ (0.10 g of $[Pd(C^2,N\text{-dmba})(\mu\text{-Cl})]_2$; 0.12 g of $[Pd(C^2,N\text{-dmba})(\mu\text{-Br})]_2$; 0.10 g of $[Pd(C^2,N\text{-dmba})(\mu\text{-NCO})]_2$ or 0.10 g of $[Pd(C^2,N\text{-dmba})(\mu\text{-N}_3)]_2$). The mixtures were stirred for 1 h, solvent was removed under reduced pressure and the yellow (**1** and **2**) and white (**3** and **4**) solids obtained were washed with acetone and pentane and dried in vacuum. The yield was 70% in each case. Anal. Calcd for $C_{31}Cl_2H_{38}N_4Pd_2$, **1** (%): C, 49.61; H, 5.11; N, 7.47. Found (%): C, 49.12; H, 5.11; N, 7.11. Anal. Calcd for $Br_2C_{31}H_{38}N_4Pd_2$, **2** (%): C, 44.36; H, 4.57; N, 6.68. Found (%): C, 44.40; H, 4.50; N, 6.54. Anal. Calcd for $C_{33}H_{38}N_6O_2Pd_2$, **3** (%): C, 51.90; H, 5.03; N, 11.01. Found (%): C,

51.65; H, 5.09; N, 11.48. Anal. Calcd for $C_{31}H_{38}N_{10}Pd_2$, **4** (%): C, 48.75; H, 5.03; N, 18.35. Found (%): C, 48.00; H, 5.05; N, 17.71.

2.3. *Physical measurements*

Carbon, nitrogen, and hydrogen analyses were performed on an EA1110–CHNS–O microanalyzer from CE-Instruments. Middle and far infrared (IR) spectra were recorded on a Nicolet Impact 400 spectrophotometer from 4000 to 400 cm^{-1} (KBr pellets) and on a Perkin Elmer Spectrum 2000 spectrophotometer from 700 to 100 cm^{-1} (CsI pellets), respectively. ^{1}H- and $^{13}C\{^1H\}$-NMR spectra were obtained as $CDCl_3$ solutions and referred to $Si(CH_3)_4$ on a Varian INOVA 500 spectrometer. Thermogravimetry (TG) and differential thermal analyses (DTA) were carried out using a TA Instruments model SDQ 600, under flow of dry synthetic air (50 mL min^{-1}), temperature to 900°C and heating rate of 20°C min^{-1} in α-alumina sample holders. The reference substance was pure α-alumina in DTA measurements. X-ray powder diffraction patterns were measured on a Siemens D-5000 X-ray diffractometer using Cu-Kα radiation ($\lambda = 1.541$ Å) and setting of 34 kV and 20 mA. The peaks were identified using ICDD bases [25].

2.4. *Antimycobacterial assay*

The activity of the tested compounds against *M. tuberculosis* H_{37}Rv ATCC 27294 was determined *in vitro* by Resazurin Microtiter Assay (REMA) [26]. The MIC defined as the lowest concentration resulting in 90% inhibition of growth of *M. tuberculosis* was determined by incorporating decreasing concentrations of the tested compounds dissolved in DMSO in Middlebrook 7H9 agar medium. The tested compounds concentrations ranged from 0.15 to 250 μg mL^{-1} and the isoniazid from 0.015 to 1.0 μg mL^{-1}. As a standard control, the MIC value of isoniazid was determined on each microplate [27]. MIC values represent mean of three separate experiments.

3. Results and discussion

Elemental analyses for the compounds are in agreement with the proposed formulae. In acetone/chloroform (1 : 2) solutions, reactions between $[Pd(C^2,N\text{-dmba})(\mu\text{-}X)]_2$ (X = Cl, Br, NCO, N_3) and 1,3-bis(4-pyridyl)propane (bpp) in 1 : 1 molar ratio occurred readily, leading to $[\{Pd(C^2,N\text{-dmba})(X)\}_2(\mu\text{-bpp})]$ [X = Cl (**1**), Br (**2**), NCO (**3**), N_3 (**4**)]. These complexes are soluble in DMSO and chloroform. The IR and NMR spectra and thermogravimetric data of **1**–**4** are reported below.

3.1. *IR and NMR spectra*

IR spectra of **1**–**4** allowed us to gain some insight about the molecular structure of these cyclopalladated species. For dmba, the characteristic bands of the chelating C^2,N-dmba [23, 24] were observed at 3047–3049 cm^{-1} (νCH_{ring}), 2910–2975 cm^{-1}

(νCH_3), and 2783–2856 cm^{-1} (νCH_2) in **1**–**4**. The existence of terminally coordinated halides was evidenced in the IR spectra of **1** and **2** by the presence of bands at 298 cm^{-1} (**1**) and 195 cm^{-1} (**2**), assigned to ν(Pd–Cl) and ν(Pd–Br) [22] modes, respectively. For pseudohalides, the presence of terminal N-cyanate in **3** was evidenced by $\nu_{as}NCO$ at 2204 cm^{-1} whereas the terminal azide in **4** was inferred from $\nu_{as}N_3$ at 2028 cm^{-1} [28]. The bridging coordination mode of 1,3-bis(4-pyridyl)propane through pyridinic nitrogen atoms was inferred by the shift of the absorptions attributed to $\nu_{CC/CN}$ pyridine ring stretching modes to higher frequencies (1618 cm^{-1} and 1429 cm^{-1}) in **1**–**4** when compared to those of the free ligand (1604 cm^{-1} and 1413 cm^{-1}) [10].

^{1}H-NMR spectra of **1**–**4** (table 1) show formation of symmetric dinuclear complexes with two [Pd(C^2,N-dmba)(X)] units bridged by one 1,3-bis(4-pyridyl)propane, since only one set of signals appeared for cyclometallated ring and bpp. The ^{1}H-NMR spectrum of **1** is depicted in figure 1. The signals were sharp and showed no indication of restricted rotation about the Pd–N_{bpp} bond at room temperature. With regard to [Pd(C^2,N-dmba)], the $N(CH_3)_2$ groups appeared as a singlet at *ca* 2.92 ppm and CH_2 as a singlet at ~3.94 ppm [2, 23, 24], implying the existence of a plane of symmetry in the palladium coordination plane. The doublet assigned to H_6 experienced an upfield shift

Table 1. ^{1}H-NMR data (ppm) for bpp and [{Pd(C^2,N-dmba)(X)}$_2$(μ-bpp)] (X = Cl (**1**), Br (**2**), NCO (**3**), N_3 (**4**)) complexes (500 MHz) at 298 K, in $CDCl_3$, given as ppm, multiplicity, assignment, J (Hz), [integration].

	^{1}H-NMR	
Compounds	dmba	bpp
bpp	–	2.60 t, –CH_2–py, 7.6 Hz, [2H] 1.95 q, –CH_2–, 7.6 Hz, [1H] 7.06 d, H_β, 5.6 Hz, [2H] 8.47 d, H_α, 5.6 Hz, [2H]
1	2.94 s, $N(CH_3)_2$, [6H] 3.98 s, –CH_2–, [2H] 6.05 d, H_6, 7.5 Hz, [1H] 6.79 m, H_4, [1H] 7.00 m, $H_3 + H_5$, [2H]	2.75 t, –CH_2–py, 7.9 Hz, [2H] 2.05 q, –CH_2–, 7.9 Hz, [1H] 7.20 d, H_β, 6.5 Hz, [2H] 8.80 d, H_α, 6.5 Hz, [2H]
2	2.92 s, $N(CH_3)_2$, [6H] 3.92 s, –CH_2–, [2H] 5.85 d, H_6, 7.2 Hz, [1H] 6.71 m, H_4, [1H] 6.93 m, $H_3 + H_5$, [2H]	2.68 t, –CH_2–py, 7.9 Hz, [2H] 1.98 q, –CH_2–, 7.9 Hz, [1H] 7.14 d, H_β, 6.5 Hz, [2H] 8.72 br, H_α, [2H]
3	2.79 s, $N(CH_3)_2$, [6H] 3.88 s, –CH_2–, [2H] 6.05 d, H_6, 7.3 Hz, [1H] 6.73 pseudot, H_4, [1H] 6.92 pseudod, $H_3 + H_5$, [2H]	2.70 t, –CH_2–py, 7.8 Hz, [2H] 2.02 q, –CH_2–, 7.8 Hz, [1H] 7.17 d, H_β, 6.6 Hz, [2H] 8.63 d, H_α, 6.6 Hz, [2H]
4	2.85 s, $N(CH_3)_2$, [6H] 3.97 s, –CH_2–, [2H] 6.16 d, H_6, 8.0 Hz, [1H] 6.81 pseudot, H_4, [1H] 7.01 m, $H_3 + H_5$, [2H]	2.78 t, –CH_2–py, 7.8 Hz, [2H] 2.10 m, –CH_2–, [1H] 7.30 br, H_β, [2H] 8.74 d, H_α, 6.4 Hz, [2H]

Abbreviations: s = singlet; d = doublet; t = triplet; q = quintet; pseudod = pseudodoublet; pseudot = pseudotriplet; m = multiplet; br = broadened.

to *ca* 6.0 ppm due to anisotropic shielding from the ring current of the adjacent pyridine [29], indicating that N_{dmba} and N_{bpp} are *trans*.

^{1}H-NMR spectroscopy showed only one set of signals from the α- and β-protons of 1,3-bis(4-pyridyl)propane, as proof of the symmetric nature of the complexes. Also diagnostic were the significant downfield shifts of H_α/H'_α and H_β/H'_β pyridyl signals (*ca* 0.2 ppm), associated with loss in electron density upon coordination by the nitrogen lone pair to palladium. Integration of the proton signals was in accord with the requirements for **1**–**4**.

^{13}C{^{1}H}-NMR spectra of **1**–**4** (table 2) exhibited characteristic signals [23, 24] of the ortho-metallated ring at ~152 ppm (C_{ar}–Pd), 149.0–121.6 ppm (C_{ar}), ~74 ppm (−N–CH_2−), and *ca* 53 ppm [−N(CH_3)$_2$]. The ^{13}C{^{1}H}-NMR spectrum of **1** is illustrated by figure 2. Typical ^{13}C signals of the bridging bpp ligand were observed at 153–125 ppm (pyridine ring), ~35 ppm (−CH_2–Py), and *ca* 30 ppm (−CH_2−).

Taking into account the IR and NMR data, the two remaining coordination sites of the *cis*-protected fragment [Pd(C^2,N-dmba)] are occupied by one terminal anionic group (X = Cl, Br, NCO, N_3) and one 4-pyridyl ring from bidentate bpp which acts as a bridge between two metallic centers. The suggested molecular structures for [{Pd(C^2,N-dmba)(X)}$_2$(μ-bpp)] [X = Cl (**1**), Br (**2**), NCO (**3**), N_3 (**4**)] are shown in figure 3.

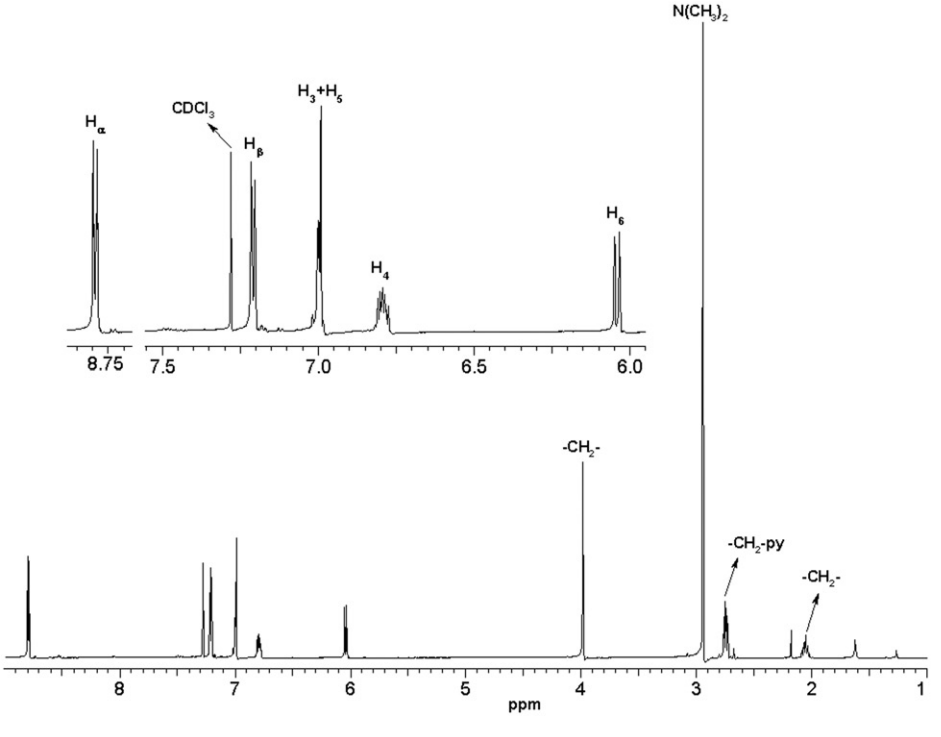

Figure 1. ^{1}H-NMR spectrum of [{Pd(C^2,N-dmba)(Cl)}$_2$(μ-bpp)] (**1**) in $CDCl_3$.

Table 2. $^{13}C\{^1H\}$-NMR data (ppm) for **1**–**4** (125 MHz) at 298 K, in $CDCl_3$.

	Compounds			
	1	**2**	**3**	**4**
dmba				
C_1	152.55	152.54	153.07	[a]
C_2	132.18	131.73	132.98	132.75
C_3	121.55	121.63	121.70	121.60
C_4	124.48	124.60	124.63	124.54
C_5	125.31	125.29	125.50	125.40
C_6	147.55	147.51	148.35	147.79
$–N–CH_2$	74.04	73.93	74.06	73.83
$–N(CH_3)_2$	52.71	53.50	52.75	51.92
bpp				
C_α	153.32	153.47	153.32	152.65
C_β	125.05	125.06	125.42	125.62
C_γ	148.89	150.04	149.18	149.97
$–CH_2–py$	34.47	34.49	34.74	34.35
$–CH_2–$	29.63	29.60	29.90	[a]

[a]Not detected.

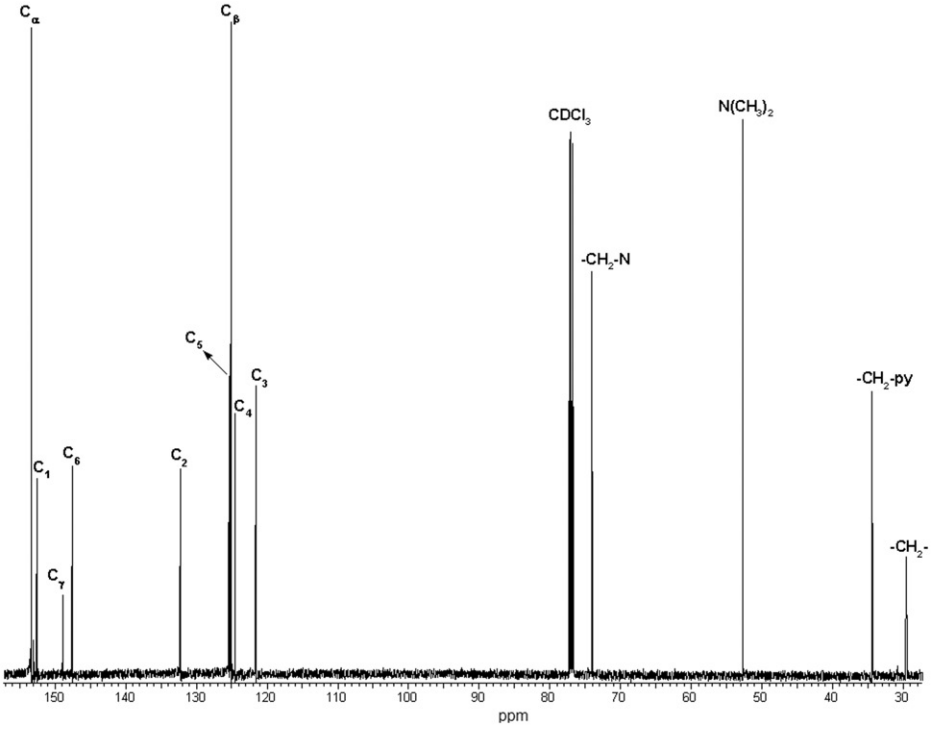

Figure 2. $^{13}C\{^1H\}$-NMR spectrum of **1** in $CDCl_3$.

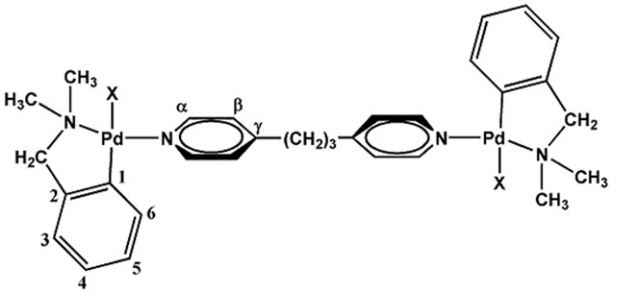

Figure 3. Proposed structure for [{Pd(C^2,N-dmba)(X)}$_2$(μ-bpp)] (X = Cl (**1**), Br (**2**), NCO (**3**), N_3 (**4**)).

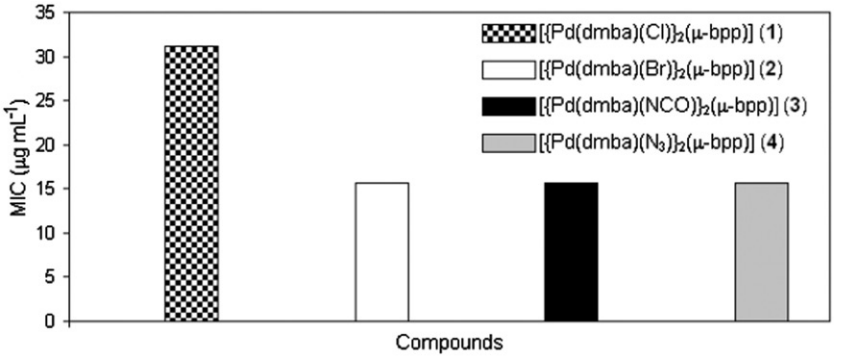

Figure 4. MIC values ($\mu g\,mL^{-1}$) for Pd(II) complexes, determined by REMA.

3.2. *Thermogravimetric analysis*

Compounds **1**, **2**, **3**, and **4** start to decompose at 132°C, 134°C, 166°C, and 173°C, respectively. DTA curves of the synthesized compounds exhibit an intense exothermic peak at 213–558°C which is attributed to pyrolysis of the ligands [28, 30]. In addition, the DTA curves show an endothermic peak corresponding to thermal decomposition of PdO to Pd° at 818–828°C [28, 30]. X-ray powder diffraction patterns of the thermal decomposition residues were compared with those obtained from the ASTM powder diffraction files of the Joint Committee on Powder Diffraction Standards (JCPDS). All the final residues were identified as palladium(0) (ICDD 05-0681) due to the appearance of its characteristic peak at $2\theta = 40.1$. The TG-DTA curves of **1** are depicted in "Supplementary material."

3.3. *Antimycobacterial activities*

The MIC values for cyclopalladated complexes **1**–**4** against *M. tuberculosis* are shown in figure 4. Isoniazid, employed extensively for TB treatment [26, 27], was used as standard antitubercular drug. The MIC values of the cyclopalladated complexes **1**–**4** varied from 15.6 $\mu g\,mL^{-1}$ to 31.2 $\mu g\,mL^{-1}$. The lower antimycobacterial activity of **1**

can be reasonably explained by the presence of labile Pd–Cl bonds as a result of an interaction between a soft Lewis acid and a hard Lewis base. The same inhibitory activities of **2**–**4** could be associated with the ability of soft Lewis bases to reduce the lability of the Pd(II) complexes. These results suggest that replacement of Cl by X (X = Br, NCO, N_3) increased the activity of the palladium(II) compound against *M. tuberculosis*, as observed for other screening of antitubercular agents [2, 4]. Such replacement is expected to decrease the substitution rates for Br, NCO, and N_3 compared with Cl ligands which may contribute to stabilization and biological activity of these Pd(II) species [2, 4].

These complexes show higher antitubercular activity than Hdmba and bpp ligands (MIC $\geq 250.0\,\mu g\,mL^{-1}$). Previous investigations explain this as a result of the polarity reduction of the complex molecule as a whole, when compared with the free complexing agents, by partial sharing of their charges within the coordination compounds, favoring their permeation through the lipid layer of the cell membrane, hence resulting in a better cell uptake of the active species [8].

Complexes **1**–**4** possess higher inhibitory activity than pyrazinamide (MIC value of $50–100\,\mu g\,mL^{-1}$), used for TB treatment [31]. On the other hand, none of the synthesized complexes was more active than isoniazid (MIC value of $0.030\,\mu g\,mL^{-1}$), one of the first-line antitubercular drugs [27].

4. Conclusion

Synthesis, spectroscopic characterization, and investigation on the thermal behavior of [{Pd(C^2,N-dmba)(X)}$_2$(μ-bpp)] [X = Cl (**1**), Br (**2**), NCO (**3**), N_3 (**4**)] have been described in this work. For **1**–**4** the halide and pseudohalide groups are coordinated to palladium in terminal mode, with 1,3-bis(4-pyridyl)propane acting as bridging ligand. The thermoanalytical data showed that the thermal stabilities of **1**–**4** are **4** > **3** > **2** > **1**. Biological evaluation of the cyclopalladated compounds bearing bpp suggest that the Pd(II) complexes display interesting antimycobacterial activity against *M. tuberculosis*, showing that the change of Cl for Br, NCO, or N_3 improved the biological activity. A similar trend of bioactivity was also observed on comparing the MIC values of **1** and **2** to those previously reported for the mononuclear cyclopalladated [Pd(C^2,N-dmba)(thiourea)(X)] species (X = Cl, $31\,\mu g\,mL^{-1}$, X = Br, $23\,\mu g\,mL^{-1}$) [2]. These results are consistent with the strength of the Pd–X bond as being important for anti-TB activity. A literature survey showed that other Pd(II) compounds, such as *trans*-[Pd(N_3)$_2$(isonicotinamide)$_2$], MIC = $15.6\,\mu g\,mL^{-1}$ [4] and [Pd(2-acetylpyridine-thiosemicarbazone)(PPh_3)](NO_3) · H_2O, MIC = $12.5\,\mu g\,mL^{-1}$ [8] displayed an antimycobacterial activity comparable to **2**, **3**, and **4** described in this work.

Acknowledgments

This research was supported by FAPESP, CNPq, Capes, and FAPEMIG.

References

[1] J. van den Boogaard, G.S. Kibiki, E.R. Kisanga, M.J. Boeree, R.E. Aarnoutse. *Antimicrob. Agents Chemother*., **53**, 849 (2009).
[2] A.C. Moro, A.E. Mauro, A.V.G. Netto, S.R. Ananias, M.B. Quilles, I.Z. Carlos, F.R. Pavan, C.Q.F. Leite, M. Hörner. *Eur. J. Med. Chem*., **44**, 4611 (2009).
[3] L.A. Basso, C.Z. Schneider, A.J.A.B. Santos, A.A. Santos Jr, M.M. Campos, A.A. Souto, D.S. Santos. *J. Braz. Chem. Soc*., **21**, 1384 (2010).
[4] R.A. Souza, A. Stevanato, O. Treu-Filho, A.V.G. Netto, A.E. Mauro, E.E. Castellano, I.Z. Carlos, F.R. Pavan, C.Q.F. Leite. *Eur. J. Med. Chem*., **45**, 4863 (2010).
[5] F.B. Nascimento, G.V. Poelhsitz, F.R. Pavan, D.N. Sato, C.Q.F. Leite, H.S.S. Araújo, J. Ellena, E.E. Castellano, V.M. Deflon, A.A. Batista. *J. Inorg. Biochem*., **102**, 1783 (2008).
[6] F.R. Pavan, G. Von Poelhsitz, F.B. Nascimento, S.R.A. Leite, A.A. Batista, V.M. Deflon, D.N. Sato, S.G. Franzblau, C.Q.F. Leite. *Eur. J. Med. Chem*., **45**, 598 (2010).
[7] L.M.M. Vieira, M.V. Almeida, M.C.S. Lourenço, F.A.F.M. Bezerra, A.P.S. Fontes. *Eur. J. Med. Chem*., **44**, 4107 (2009).
[8] P.I.S. Maia, A. Graminha, F.R. Pavan, C.Q.F. Leite, A.A. Batista, D.F. Back, E.S. Lang, J. Ellena, S.S. Lemos, H.S.S. Araujo, V.M. Deflon. *J. Braz. Chem. Soc*., **21**, 1177 (2010).
[9] E.-C. Yang, X.-J. Shi, Z.-Y. Liu, X.-J. Zhao. *Inorg. Chem. Commun*., **13**, 733 (2010).
[10] R.A. Farani, W.M. Teles, C.B. Pinheiro, K.J. Guedes, K. Krambrock, M.I. Yoshida, L.F.C. Oliveira, F.C. Machado. *Inorg. Chim. Acta*, **361**, 2045 (2008).
[11] A.A. El-Sherif. *J. Coord. Chem*., **64**, 2035 (2011).
[12] F.R.G. Bergamini, C. Abbehausen, A. Magalhães, W.R. Lustri, A.F. Gomes, F.C. Gozzo, P.P. Corbi. *J. Coord. Chem*., **64**, 3092 (2011).
[13] K. Tomita, A.C.F. Caires, V.A.D. Neto, A.E. Mauro. *Acta Crystallogr. C, Cryst. Struct. Commun*., **50**, 1872 (1994).
[14] A.V.G. Netto, R.C.G. Frem, A.E. Mauro. *Polyhedron*, **24**, 1086 (2005).
[15] S.R. Ananias, A.E. Mauro, K. Zutin, C.M.C. Picchi, R.H.A. Santos. *Trans. Met. Chem*., **29**, 284 (2004).
[16] A.C.F. Caires, A.E. Mauro, R.H.A. Santos, M.T.P. Gambardella, J.R. Lechat. *Gazz. Chim. Ital*., **123**, 495 (1993).
[17] A.M. Santana, A.E. Mauro, A.V.G. Netto, S.I. Klein, R.H.A. Santos, J.R. Zóia. *J. Coord. Chem*., **53**, 163 (2001).
[18] A.E. Mauro, A.C.F. Caires, R.H.A. Santos, M.T.P. Gambardella. *J. Coord. Chem*., **48**, 521 (1999).
[19] A.V.G. Netto, A.E. Mauro, R.C.G. Frem, A.M. Santana, R.H.A. Santos, J.R. Zóia. *J. Coord. Chem*., **54**, 129 (2001).
[20] A.M. Santana, J.G. Ferreira, A.C. Moro, S.C. Lemos, A.E. Mauro, A.V.G. Netto, R.C.G. Frem, R.H.A. Santos. *Inorg. Chem. Commun*., **14**, 83 (2011).
[21] A.C. Cope, E.C. Friedrich. *J. Am. Chem. Soc*., **90**, 909 (1968).
[22] B. Crociani, T. Boschi, R. Pietropaolo, U. Belluco. *J. Chem. Soc. (A)*, 531 (1970).
[23] E.T. de Almeida, A.E. Mauro, A.M. Santana, S.R. Ananias, A.V.G. Netto, J.G. Ferreira, R.H.A. Santos. *Inorg. Chem. Commun*., **10**, 1394 (2007).
[24] V.A. de Lucca Neto, A.E. Mauro, A.C.F. Caires, S.R. Ananias, E.T. de Almeida. *Polyhedron*, **18**, 413 (1998).
[25] International Center of Diffraction Data. Powder diffraction file: release. New Square (1999). PDF no. 05-0681.
[26] J.C. Palomino, A. Martin, M. Camacho, H. Guerra, J. Swings, F. Portaels. *Antimicrob. Agents Chemother*., **46**, 2720 (2002).
[27] L.A. Collins, S.G. Franzblau. *Antimicrob. Agents Chemother*., **41**, 1004 (1997).
[28] E.T. de Almeida, A.M. Santana, A.V.G. Netto, C. Torres, A.E. Mauro. *J. Therm. Anal. Cal*., **82**, 361 (2005).
[29] A.J. Deeming, I.P. Rothwell, M.B. Hursthouse, L. New. *J. Chem. Soc., Dalton Trans*., 1490 (1978).
[30] A.C. Moro, A.E. Mauro, S.R. Ananias, A. Stevanato, A.O. Legendre. *J. Therm. Anal. Cal*., **87**, 721 (2007).
[31] A. Somoskovi, M.M. Wade, Z. Sun, Y. Zhang. *J. Antimicrob. Chemother*., **53**, 192 (2004).