

# Supplementary Information

## Antiprotozoal Activity of the Cyclopalladated Complexes Against *Leishmania amazonensis* and *Trypanosoma cruzi*

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### Spectroscopy data

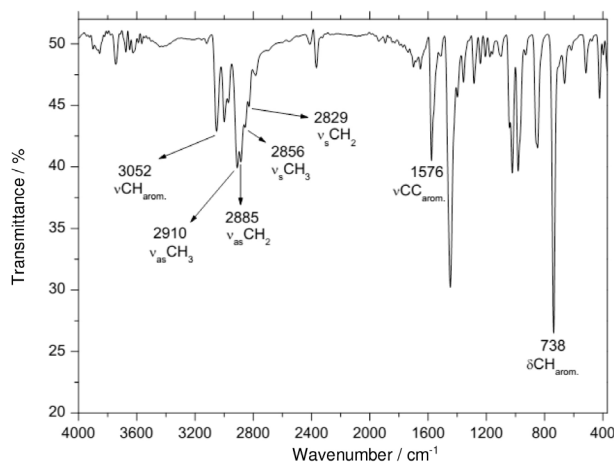


Figure S1. Infrared (IR) spectrum (KBr) of [Pd(dmab)(μ-Cl)]<sub>2</sub> (1).

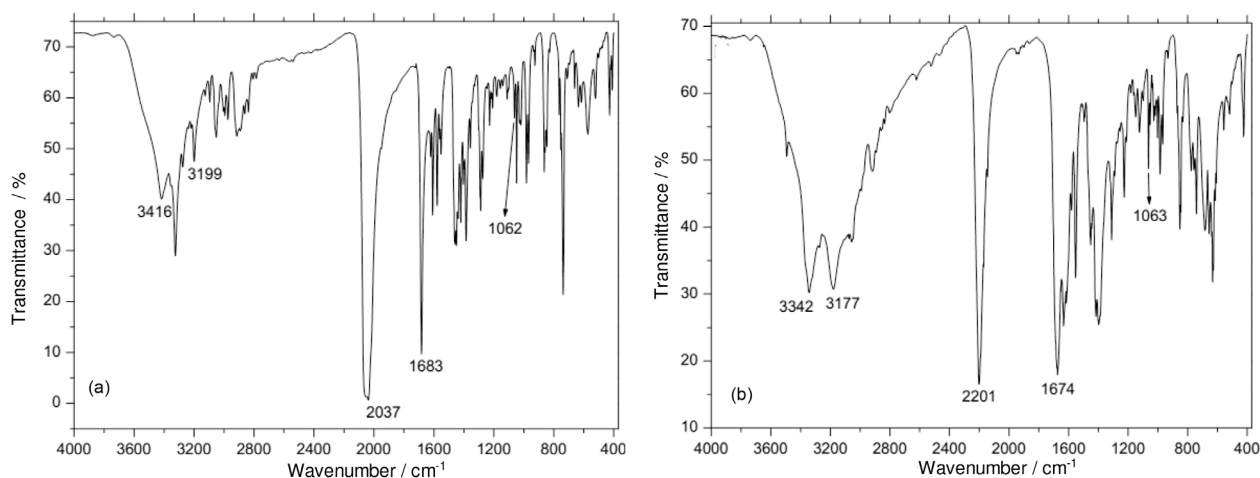
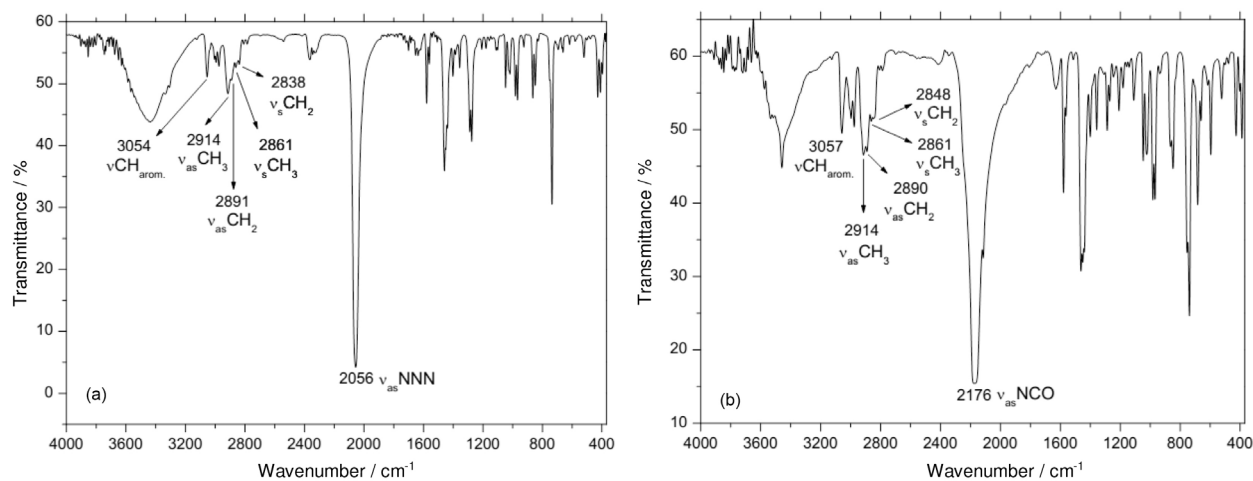
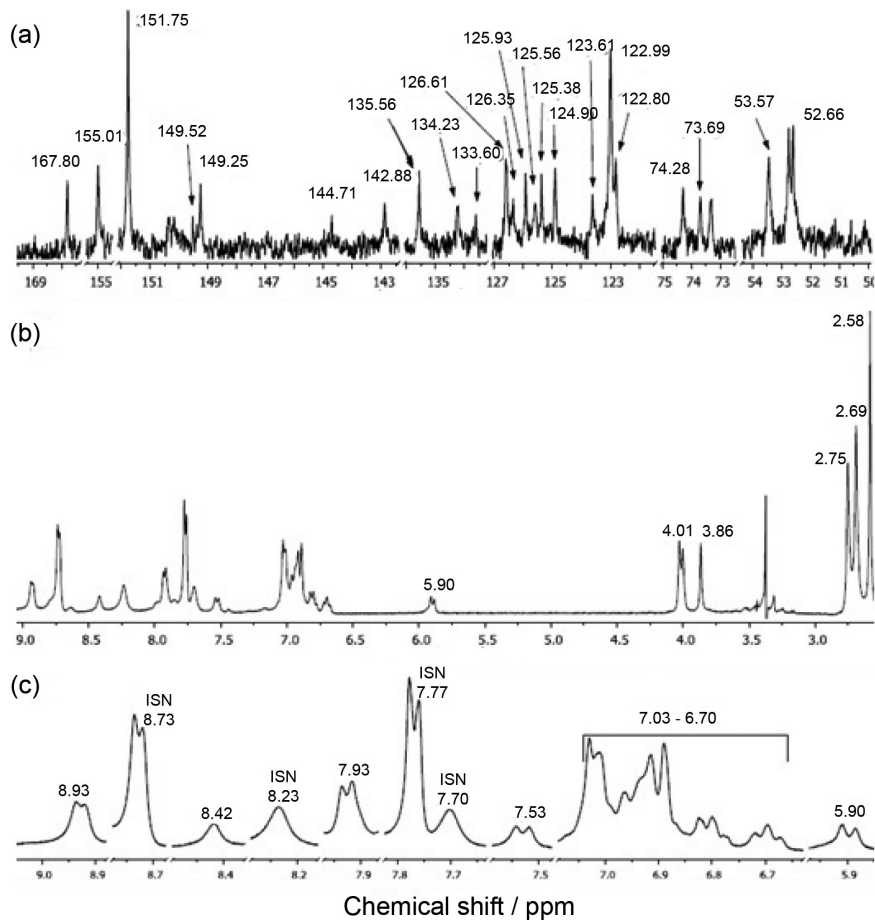


Figure S2. IR spectrum (KBr) of compounds (3) and (2): [Pd(dmab)X(isn)], (a) X = N<sub>3</sub>; (b) X = NCO; isn: isonicotinamide.

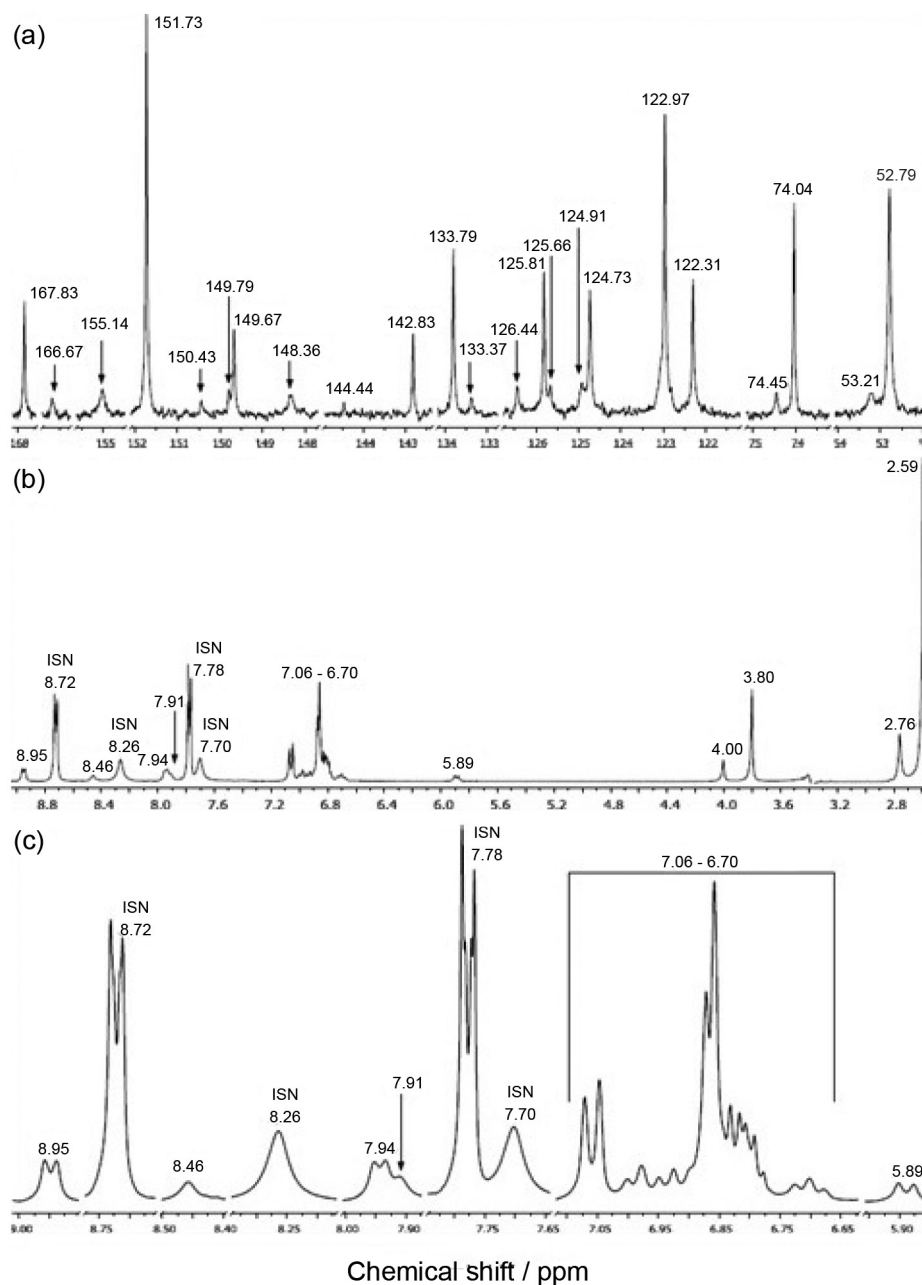
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**Figure S3.** IR spectrum (KBr) of (a)  $[\text{Pd}(\text{dmmba})(\mu\text{-N}_3)]_2 \cdot \text{H}_2\text{O}$ ; (b)  $[\text{Pd}(\text{dmmba})(\mu\text{-NCO})]_2$  (4).



**Figure S4.** Nuclear magnetic resonance (NMR) spectra of  $[\text{Pd}(\text{dmmba})\text{NCO}(\text{isn})]$  (2), 11.7 T and 28  $^{\circ}\text{C}$ . (a)  $^{13}\text{C}\{^1\text{H}\}$  spectrum (500 and 125 MHz,  $\text{DMSO-}d_6$ ); (b) and (c) expansion of spectral region between 9.05 to 5.85 ppm for  $^1\text{H}$  spectrum.



**Figure S5.** NMR spectra of  $[\text{Pd}(\text{dmab})\text{N}_3(\text{isn})]$  (**3**), 11.7 T and 28 °C. (a)  $^{13}\text{C}$   $\{^1\text{H}\}$  spectrum (500 and 125 MHz,  $\text{DMSO}-d_6$ ), (b) and (c) expansion of spectral region between 9.05 to 5.85 ppm for  $^1\text{H}$  spectrum.

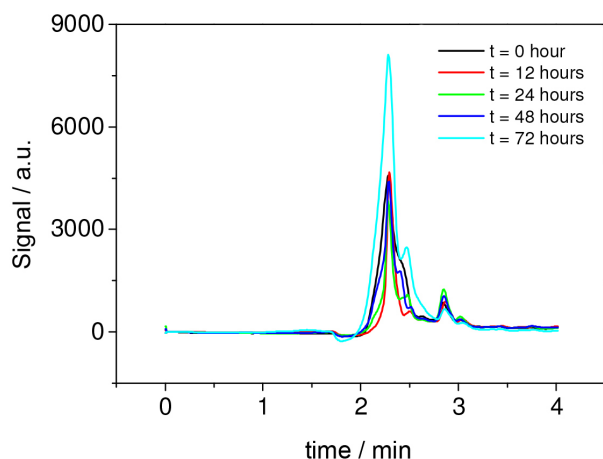
Figure S4 (compound **2**) shows four signals associated with free isn in solution, at 8.73 ppm ( $\text{H}^{2,6}$ ,  $J = 4.5$  Hz), 7.77 ppm ( $\text{H}^{3,5}$ ,  $J = 5.1$  Hz), at 8.23 and 7.70 ppm. Possible coordinated isn signals are at 8.93 and 7.93 ppm ( $\text{H}^{2,6}$  and  $\text{H}^{3,5}$ , respectively,  $J = 5.4$  Hz) and at 8.42 ppm ( $\text{NH}_2$ ). Signal at 5.90 ( $\text{H}^3_{\text{dmab}}$ ,  $J = 7.5$  Hz) is due to the anisotropic effect of the pyridine ring *cis* to dmab. In the range 7.03 to 6.70 ppm is noticed a number of signals corresponding to the dmab ring. At 4.01 and 3.86 ppm are duplicate signals assigned to  $\text{CH}_2$  group ( $J = 7.8$  Hz). Single signals at 2.75, 2.69 and 2.58 ppm are observed for  $\text{CH}_3$ . These signals

indicate the presence of two cyclopalladated species and free isn in solution.

The  $^{13}\text{C}$  NMR spectrum in Figure S5 shows signals that indicate the presence of various species in solution. The NMR spectra of compound **3** showed two double signals at 8.72 and 7.78 ppm (*ortho*  $J = 6.0$  Hz, *meta*  $J = 3.0$  Hz, *para*  $J = 1.5$  Hz), associated respectively to  $\text{H}^{2,6}$  and  $\text{H}^{3,5}$  of free isn in solution. The  $-\text{NH}_2$  signals of free isn are at 8.26 and 7.70 ppm. Signals of isn coordinated are at 8.95 ppm ( $\text{H}^{2,6}$ ,  $J = 5.4$  Hz), 7.94 ppm ( $\text{H}^{3,5}$ ,  $J = 5.4$  Hz), 8.46 and 7.91 ppm ( $-\text{NH}_2$ ).

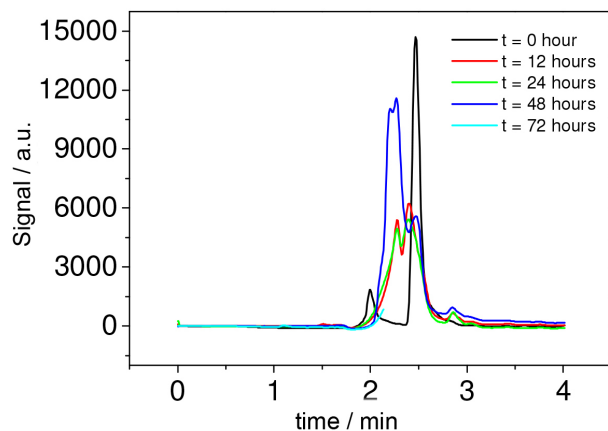
## Stability assay

Compound **1** (Figure S6) is possible observe the chromatogram profile which suggests that the sample remained stable as denoted by a single peak at 2.45 minutes.



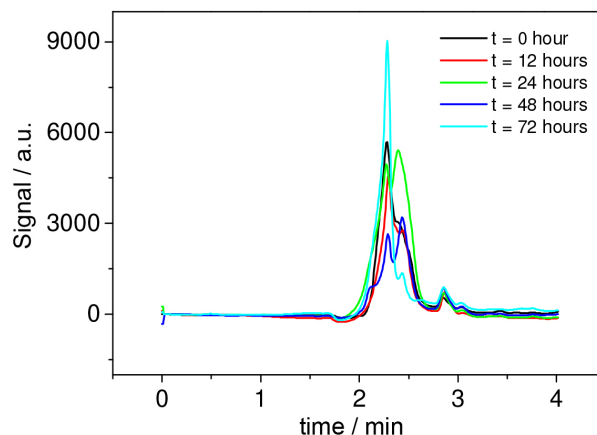
**Figure S6.** Chromatogram profile for compound  $[\text{Pd}(\text{dmmba})(\mu\text{-Cl})_2]$  (**1**). The measurements were performed using ODS (C-18) column, particle size  $5\ \mu\text{m}$ ,  $4.6 \times 250\ \text{mm}$ , mobile phase: methanol:water (70:30, v/v/v), flow  $0.8\ \text{mL min}^{-1}$  and  $\lambda = 254\ \text{nm}$ .

Figure S7 shows the chromatogram profile for compound **2** which suggesting that the sample was not stable in PBS at pH 7. It is possible to see a shift in the initial retention time from 2.29 to 2.47 minutes.



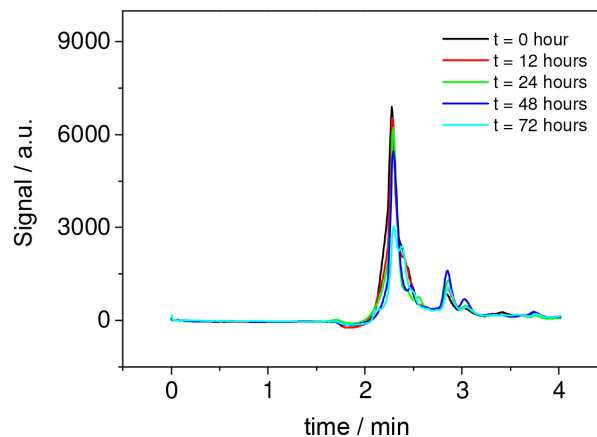
**Figure S7.** Chromatogram profile for compound  $[\text{Pd}(\text{dmmba})(\text{NCO})(\text{isn})]$  (**2**). The measurements were performed using ODS (C-18) column, particle size  $5\ \mu\text{m}$ ,  $4.6 \times 250\ \text{mm}$ , mobile phase: methanol:water (70:30, v/v/v), flow  $0.8\ \text{mL min}^{-1}$  and  $\lambda = 254\ \text{nm}$ .

For compound **3** (Figure S8), we could observe that the sample was stable at 72 hours when compared to the initial time (retention time at 2.4 min).



**Figure S8.** Chromatogram profile of compound  $[\text{Pd}(\text{dmmba})(\text{N}_3)(\text{isn})]$  (**3**). The measurements were performed using ODS (C-18) column, particle size  $5\ \mu\text{m}$ ,  $4.6 \times 250\ \text{mm}$ , mobile phase: methanol:water (70:30, v/v/v), flow  $0.8\ \text{mL min}^{-1}$  and  $\lambda = 254\ \text{nm}$ .

For compound **4** (Figure S9), according to the chromatogram profile, it is possible to note that the sample remained stable even after 72 hours with a unique retention peak of low intensity at 2.28 minutes.



**Figure S9.** Chromatogram profile of compound  $[\text{Pd}(\text{dmmba})(\mu\text{-NCO})_2]$  (**4**). The measurements were performed using ODS (C-18) column, particle size  $5\ \mu\text{m}$ ,  $4.6 \times 250\ \text{mm}$ , mobile phase: methanol:water (70:30, v/v/v), flow  $0.8\ \text{mL min}^{-1}$  and  $\lambda = 254\ \text{nm}$ .