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Michael addition-driven synthesis of cytotoxic palladium(II) complexes from chromone thiosemicarbazones: Investigation of anticancer activity through *in vitro* and *in vivo* studies

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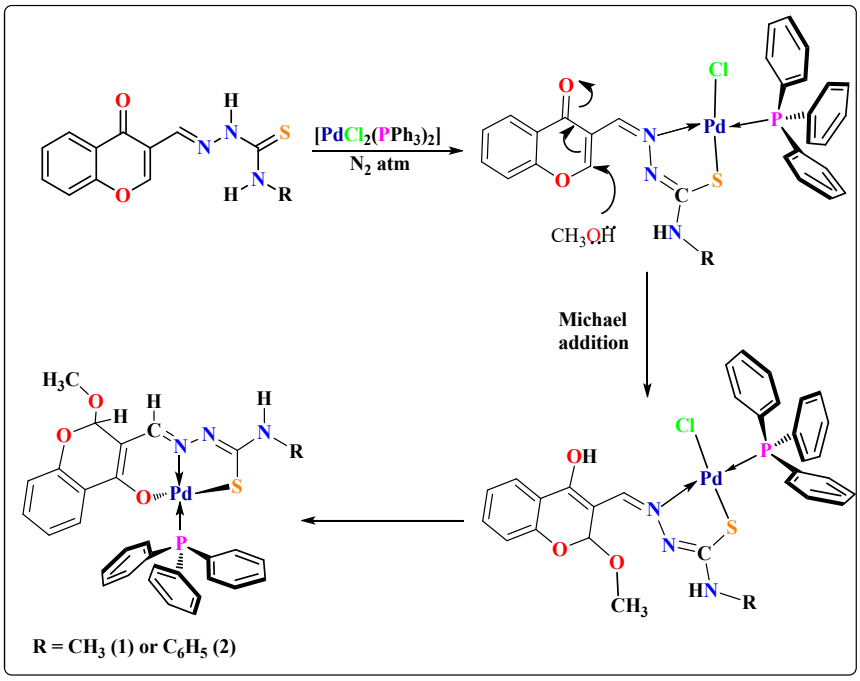
Table of contents

Materials and methods

Chemicals obtained from commercial suppliers were used as received and were of analytical grade. The melting points were measured on a Lab India instrument and are uncorrected. Elemental analyses were carried out using a PerkinElmer instrument. FT-IR spectra were obtained as KBr pellets using a Ncolet-iS5 spectrophotometer. UV-Visible spectra were recorded using a Shimadzu-2600 spectrophotometer. NMR spectra were recorded in deuterated chloroform by using TMS as an internal standard on a Bruker 500 MHz spectrometer. X-ray diffraction data collection and corrections for complex **3** were done at 113(2) K with an APEX K_α diffractometer using graphite monochromated MoK_α (k = 0.71073 Å) radiation. The structural solution was obtained readily using XT/XS in APEX2[1,2] and refined by full matrix least squares on F^2 using Olex2. The used (2*E*)-2-[(4-oxo-4*H*-chromen-3-yl)methylidene]hydrazinecarbothioamide-based chromone TSCs, bearing the terminal methyl (**SVSHL1**), phenyl (**SVSHL2**) or cyclohexyl (**SVSHL3**) substituent, were prepared according the formerly reported method.[3]



Scheme S1. Proposed mechanism for the formation of new Pd(II) complexes **1** and **2** based on previously reported mechanism for complex **3**.[3]

Results and discussion

Preliminary characterization using UV-Visible and FT-IR spectroscopy

UV-Visible spectra of the complexes were recorded in the wavelength range of 200-800 nm in DMSO. The absorption bands at 257 and 272 nm for complex **1** and 259 and 273 nm for complex **2** were specified to $\pi \rightarrow \pi^*$ and $n \rightarrow \pi^*$ transitions, respectively.[4-6] Complex **1** exhibited ligand to metal charge transfer transitions (LMCT) in the regions 368 and 381 nm. Similarly, the bands at 365 and 386 nm for complex **2** were related to LMCT.[4] FT-IR spectra of complexes **1** and **2** showed terminal N–H stretching frequency at 3365 or 3368 cm^{-1}, respectively. The complexes showed an absorption band at 1480 cm^{-1} due to the azomethine group. The bands at 1330 and 1332 cm^{-1} in the spectra of complexes **1** and **2**, respectively, were assigned to υ(C–O). A band due to υ(C–S) was observed at 1171 (**1**) or 1174 (**2**) cm^{-1}. In addition, a band appeared at 1574 (**1**) or 1573 (**2**) cm^{-1} was assigned to υ(C=C–O). The presence of PPh_3 in the complexes was confirmed by the appearance of bands at 1434, 1095 and 760 cm^{-1}.[4,6]

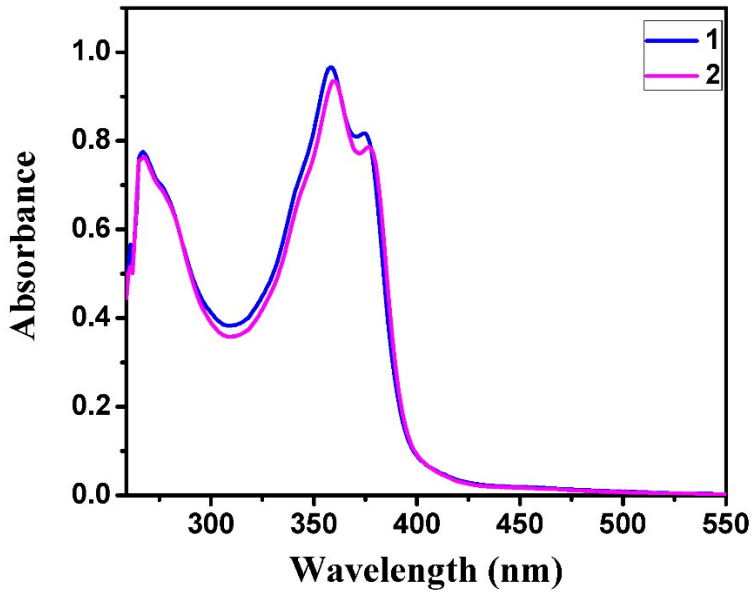


Fig. S1 UV-Visible spectra of the complexes.

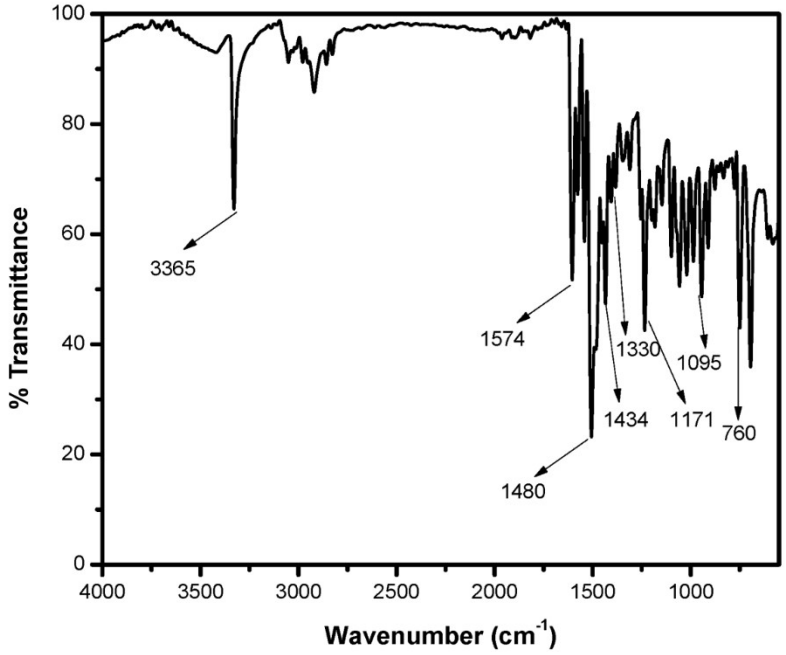


Fig. S2 FT-IR spectrum of complex **1**.

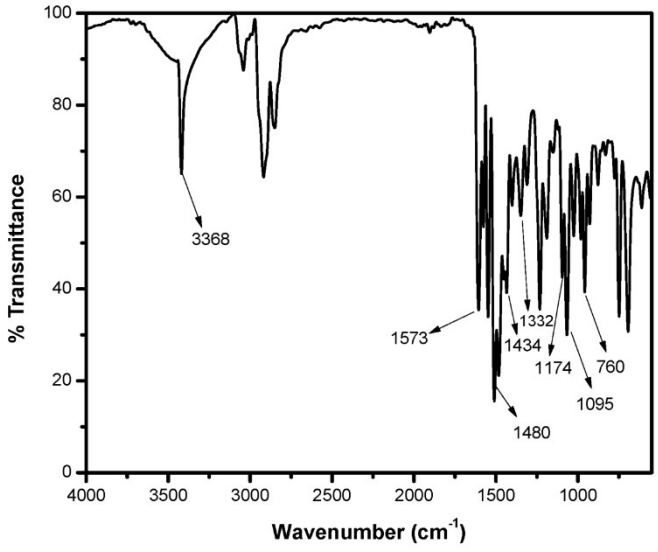


Fig. S3 FT-IR spectrum of complex **2**.

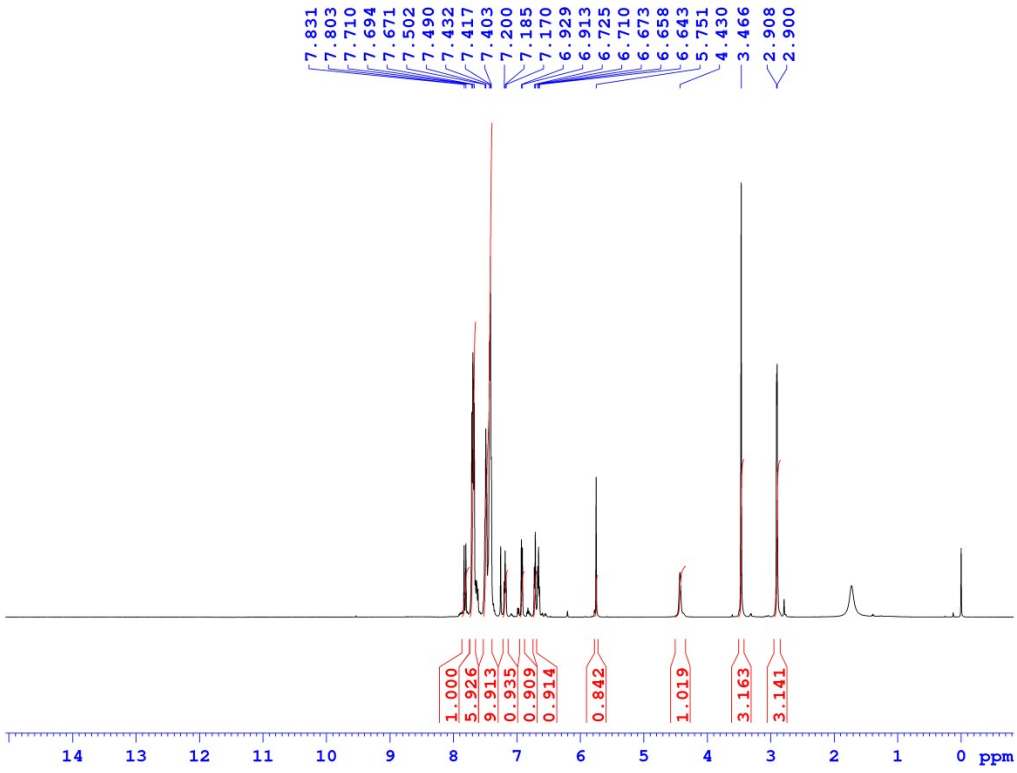


Fig. S4 ^{1}H NMR spectrum (500 MHz) of complex **1** in $CDCl_3$.

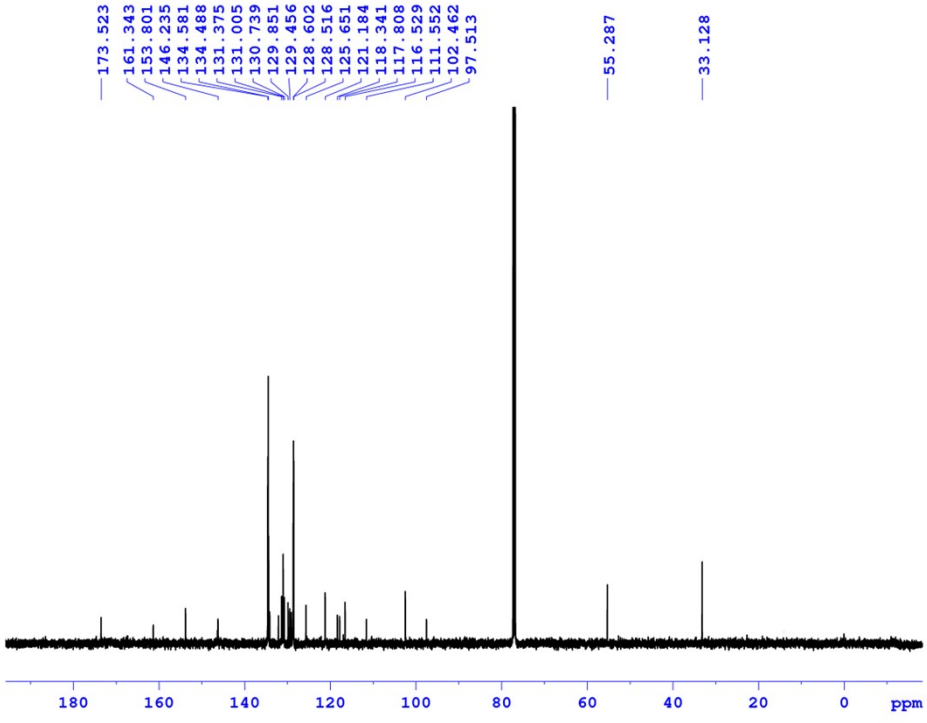


Fig. S5 $^{13}C\{^{1}H\}$ NMR spectrum (125 MHz) of complex **1** in $CDCl_3$.

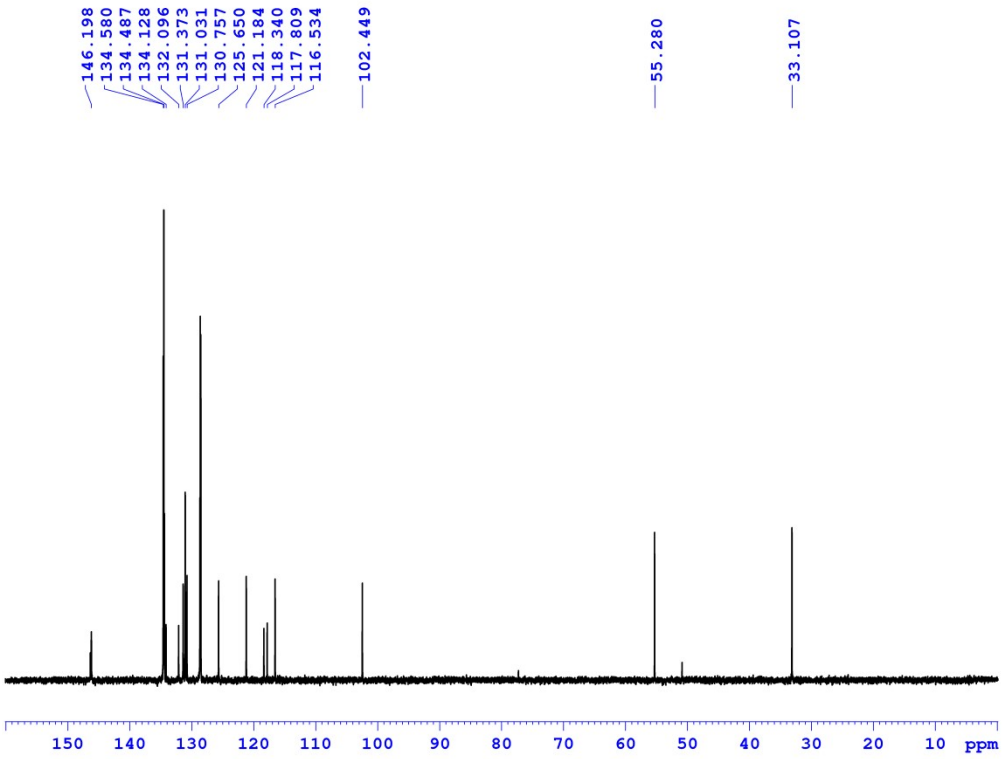


Fig. S6 DEPT-135 NMR spectrum (125 MHz) of complex **1** in $CDCl_3$.

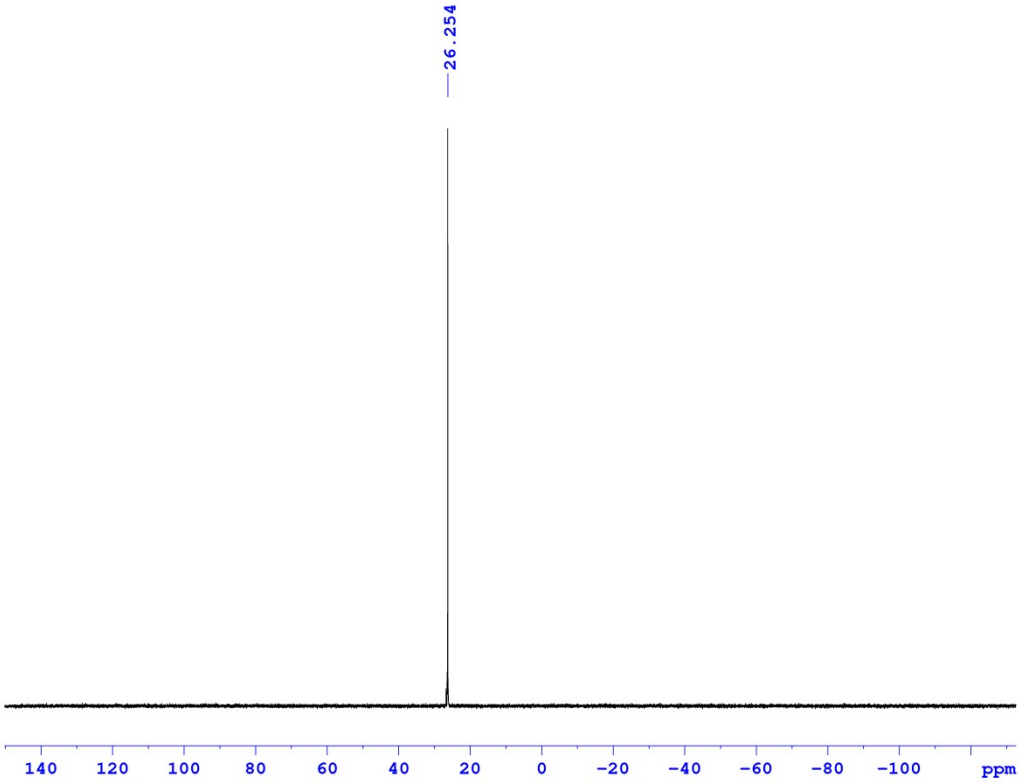


Fig. S7 $^{31}P\{^{1}H\}$ NMR spectrum (202 MHz) of complex **1** in $CDCl_3$.

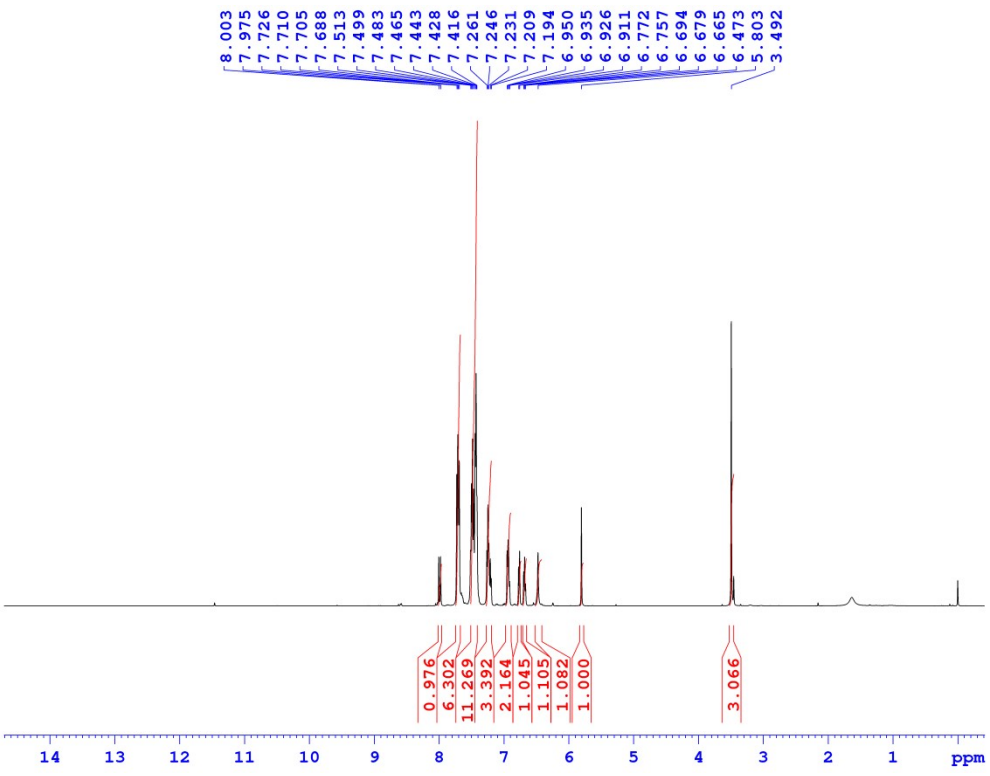


Fig. S8 ^{1}H NMR spectrum (500 MHz) of complex **2** in $CDCl_3$.

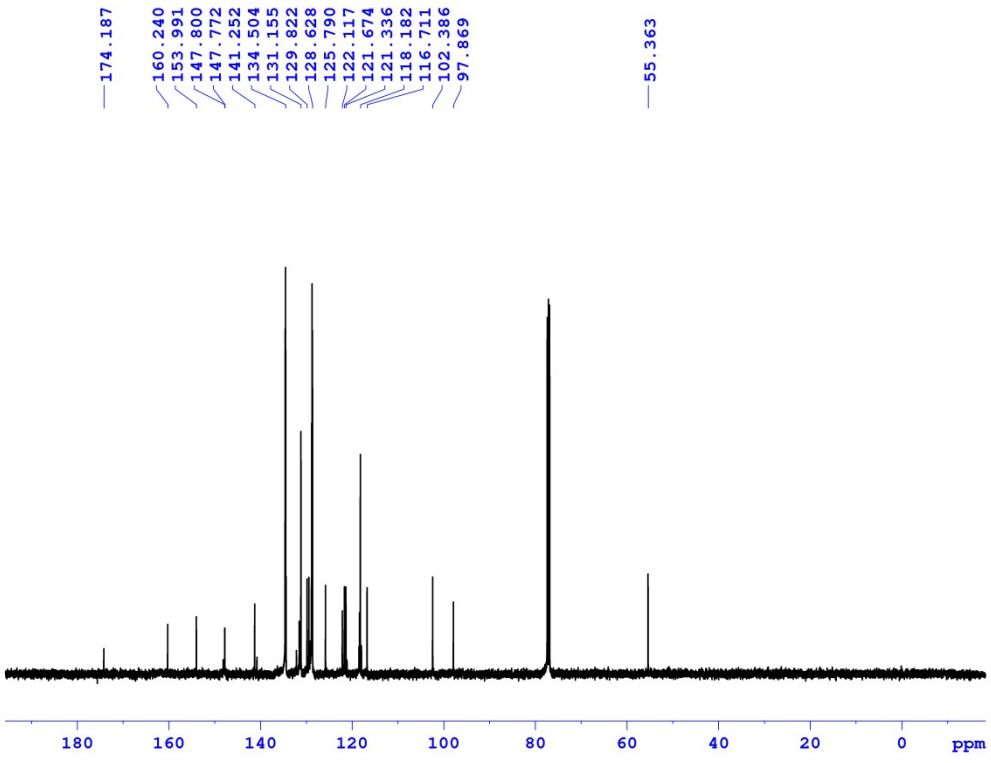


Fig. S9 $^{13}C\{^{1}H\}$ NMR spectrum (125 MHz) of complex **2** in $CDCl_3$.

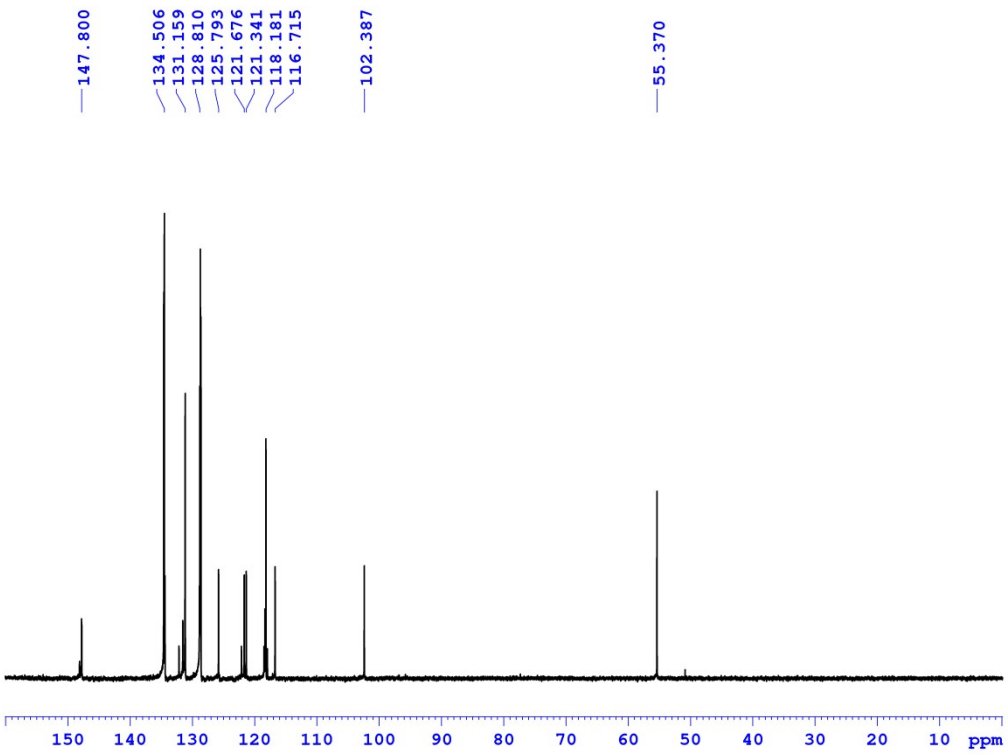


Fig. S10 DEPT-135 NMR spectrum (125 MHz) of complex **2** in $CDCl_3$.

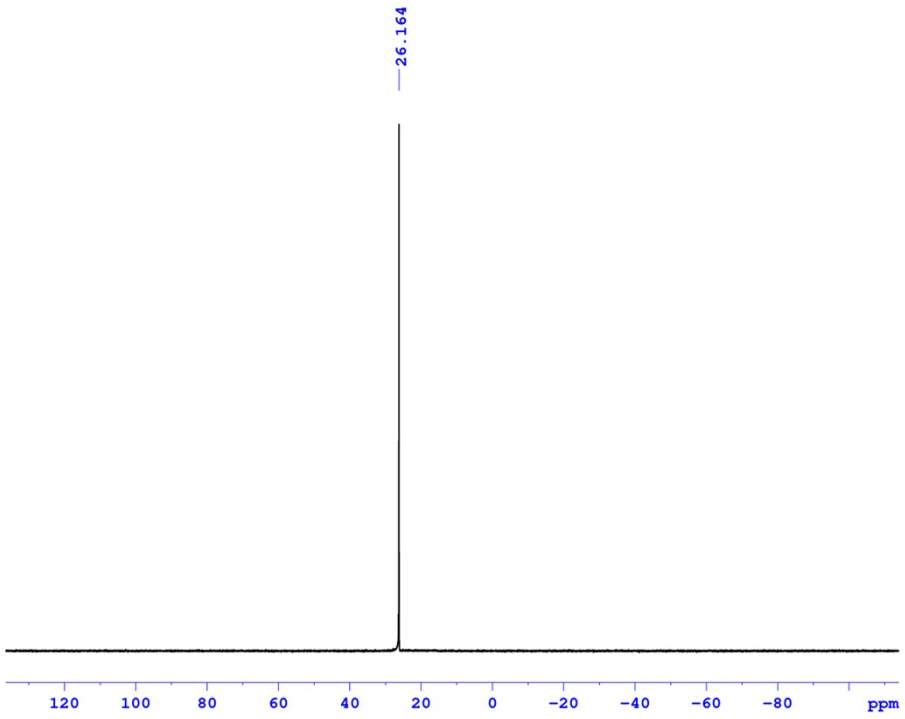


Fig. S11 $^{31}P\{^{1}H\}$ NMR spectrum (202 MHz) of complex **2** in $CDCl_3$.

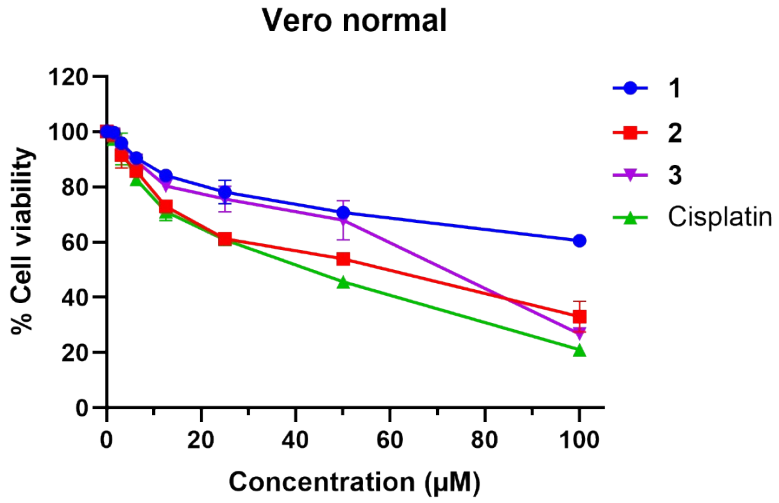


Fig. S12 Effect of Pd(II) complexes **1-3** and cisplatin against normal (Vero) cells. Data were calculated by mean ± S.D. with three replications.

References

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