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Can an elusive Pt(III) oxidation state be exposed in an isolated complex?

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Abstract. Platinum(IV) complexes are extensively studied for their activity against cancer cells as potential substitutes for the widely used platinum(II) drugs. Pt(IV) complexes are kinetically inert and need to be reduced to Pt(II) species to play their pharmacological action, thus acting as prodrugs. The mechanism of the reduction step inside the cell is however still largely unknown. Gas-phase activation of platinum(IV) deprotonated prodrugs was found to generate fragments in which platinum has a formal +3 oxidation state. IR multiple photon dissociation spectroscopy is thus used to obtain structural information helping to define the nature of both the platinum atom and the ligands. In particular, comparison of calculations at DFT, MP2 and CCSD levels with experimental results demonstrates that the localization of the radical is about equally shared between the d_{xz} orbital of platinum and the p_z of nitrogen on the amino group, the latter acting as a noninnocent ligand.

Introduction

The redox chemistry of platinum complexes usually regards three oxidation states, namely 0, +2 or +4. Complexes of Pt(III) are seldom encountered due to the nature of the unpaired electron which is formally located on an exposed d_z^2 orbital.^[1,2] Mononuclear complexes are particularly elusive, while more common are binuclear Pt(III) complexes presenting a metal-metal σ bond involving the unpaired electrons on each metal center, thus abolishing radical character and improving stability.^[2,3-5] Pt(III) has been also described in the solid state as component of the polymeric material named "platinblau".^[6] A formal Pt(III) dimeric cation has been generated by electrospray ionization of a tetrameric Pt(II) precursor.^[7] Evidence is reported of short-lived Pt(III) species generated by photolysis or radiolysis.^[1] An example regards the photolysis of $[\text{PtX}_6]^{2-}$ (X = Cl, Br, SCN) in a system containing $[\text{Ru}(\text{bipy})_3]^{2+}$ which produces $[\text{PtX}_4]^-$.^[8,9] Formation of the $[\text{PtCl}_4(\text{OH})(\text{H}_2\text{O})]^{2-}$ complex was reported both from photolysis of $[\text{PtCl}_6]^{2-}$ and $[\text{PtCl}_4(\text{OH})_2]^{2-}$ in aqueous solution,^[10] and from reaction of $[\text{PtCl}_4]^{2-}$ with the hydroxyl radical.^[11] Despite their typical elusiveness, long lived Pt(III) mononuclear complexes have been prepared using bulky ligands such as 1,4,7-trithiacyclononane,^[12] or heterocyclic carbenes.^[13] In both cases electron paramagnetic resonance (EPR) spectroscopy and DFT calculations assessed the localization of the radical on the platinum atom. Formal platinum(III) compounds have also been assayed for clinical applications.^[14] Transient platinum(III) complexes are also hypothesized in the reduction mechanism of cisplatin-based platinum(IV) prodrugs, which is supposed to be stepwise, involving a

preliminary reduction to Pt(III) with loss of only one of the axial ligands and a subsequent one-electron reductive elimination which produces the square-planar platinum(II) drug.^[15,16] Indeed, a preliminary exploration of the gas-phase unimolecular reactivity of deprotonated Pt(IV) complexes allowed to highlight the formation of complexes containing platinum in the formal oxidation state of +3.^[17] In this process reduction proceeds by cleavage of equatorial ligands instead of the axial ones, in contrast with the evidence observed in solution^[18-20] and with the postulated mechanism for the electrochemical activation of Pt(IV) antitumor prodrugs.^[15,16] The nature of the so-formed formal Pt(III) species generated by collision-induced dissociation (CID) is however unclear. In many cases in fact, ligands were found to be the bearers of the radical site in the complex.^[1] Thus, a proper characterization of the oxidation state of platinum is required. Given that the ions are formed in the gas-phase, the use of standard spectroscopy methods for radical species, such as EPR spectroscopy, is unachievable. However, the use of IR multiple photon dissociation (IRMPD) spectroscopy in combination with theoretical methods, was proven to be informative in the analysis of metal complexes with non-innocent ligands,^[21-23] as well as in the differentiation between different spin-states of iron(IV) oxo complexes.^[24] Therefore, IRMPD spectroscopy is promising for the characterization of the effective oxidation state of platinum.

In this work, three odd-electron species, namely **m297**, **m369** and **m411**, which were generated from CID of the deprotonated Pt(IV) complexes **1**, **2** and **3** respectively, have been characterized using IRMPD spectroscopy and quantum chemical calculations. The dissociation paths leading to the formation of the three formal Pt(III) complexes is schematically reported in Figure 1, while the thorough description of the gas-phase fragmentation behavior of **[1-H]⁻**, **[2-H]⁻** and **[3-H]⁻** was reported previously.^[17]

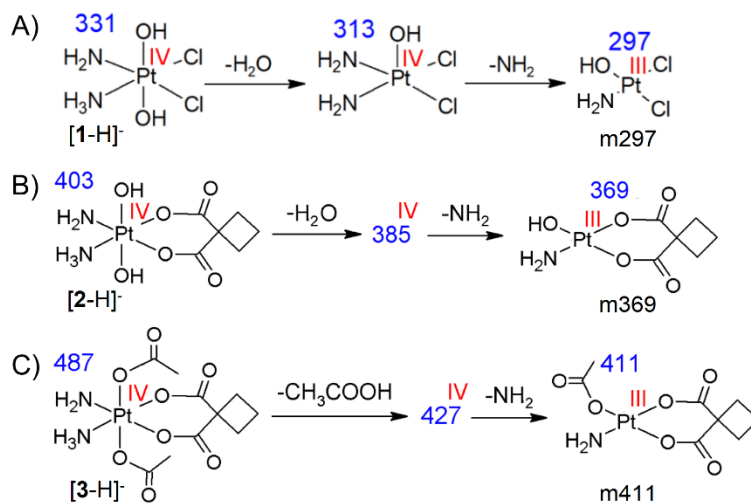


Figure 1. Schematic representation of the fragmentation path leading A) from **[1-H]⁻** to **m297**, B) from **[2-H]⁻** to **m369** and C) from **[3-H]⁻** to **m411**. The *m/z* ratio of each species is indicated in blue and the formal oxidation state of platinum in red. Each complex is negatively charged; charges are not made explicit.

Figure 1 shows clearly that there are similarities in the mechanism leading to **m297**, **m369** and **m411**. In particular, each dissociation path begins with the neutral loss of one of the axial ligands.

Only after this first step an amino radical is cleaved and the ion of interest is formed. Details on the experimental setup which allowed to obtain the ionic fragments **m297**, **m369** and **m411**, together with calculated thermodynamic data for reaction A of Figure 1 have been already reported.^[17] Platinum(III) complexes are indeed elusive species, which are seldom observed as mononuclear complexes and the radical is often found to be localized on the ligands rather than on the metal center,^[1-3,12,13,25,26] thus further investigations are required to assess the electronic structure of the three odd-electron ions **m297**, **m369** and **m411**. EPR is indeed the technique of choice to obtain information about the oxidation state of platinum, since Pt(III) is paramagnetic and shows a characteristic hyperfine coupling with the ¹⁹⁵Pt isotope which has a relatively high abundance of 33.7%.^[12,26] However, EPR is not amenable to gaseous complexes.

A computational study was then undertaken. Sampling the conformational space of **m297** and **m369** we were able to find two local minima for each species, namely **297_1**, **297_2** and **369_1**, **369_2**, respectively, both at the B3LYP and MP2 levels. They present structural features that may be attributed to a different localization of the radical site, thus suggesting the possibility to use IRMPD spectroscopy to discriminate about the oxidation state of platinum. Regarding the ion **m411**, it was possible to find just one minimum energy structure, namely **411_1**. The whole set of optimized geometries is reported in Figure 2, together with the SNO distribution.

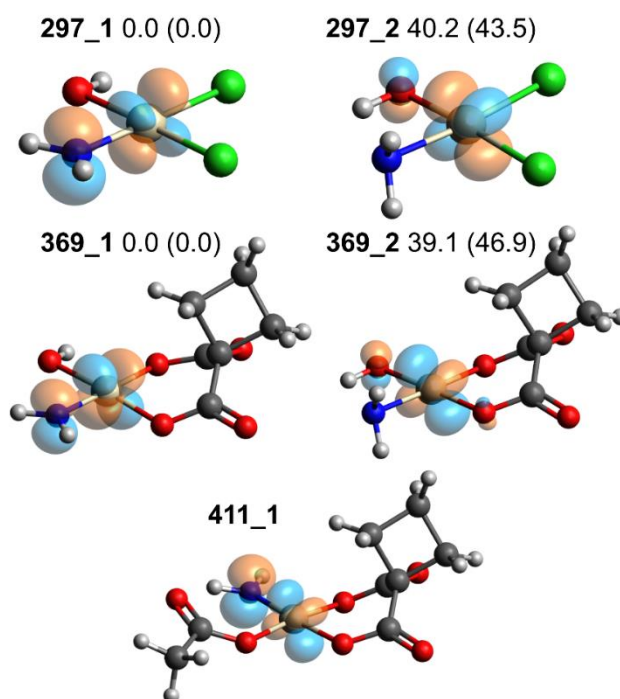


Figure 2. Optimized geometries of **297_1**, **297_2**, **369_1**, **369_2** and **411_1** at the MP2/6-311++G(d,p) (Pt = def2-TZVP) level. SNOs obtained at the MP2/6-311++G(d,p) (Pt = def2-TZVP) level are shown with an isovalue of 0.20. Relative free energies in kJ mol^{-1} are reported at the B3LYP and MP2 (in brackets) levels.

Focusing on the simpler species **m297**, as shown in Figure 2, the lowest lying structure **297_1** presents a planar amino ligand and the hydrogen of the hydroxido ligand oriented toward

chlorine. In contrast, in **297_2**, which lies at 43.5 kJ mol^{-1} , the OH interacts with the nitrogen atom of the amino ligand. The resulting H bond stabilizes NH_2 in a tetrahedral geometry. Intriguingly, the trigonal planar geometry is characteristic of amino radicals, while an even-electron amino group typically assumes a close to pyramidal geometry.^[27-29] We have therefore inspected the results obtained from the analysis of the SNOs of the two conformers looking for any structure-electronic state relationship.^[30] Indeed, in the most stable structure **297_1** the SNO is mostly localized on the amino group in agreement with its geometry, while there is no significant radical character on the amino group of **297_2**. In particular, in **297_1** the radical site is about equally distributed between the d_{xz} orbital of platinum and the p_z orbital of the amino nitrogen, while in **297_2** there is a major spin localization on platinum (d_{yz} orbital) and only some distributed on the p_z orbitals of the hydroxido oxygen.^[13] In order to obtain quantitative spin-density values, natural bond orbital (NBO) analyses were performed with the NBO3 version available in G09 on the CCSD densities of **297_1** and **297_2**, which were obtained from CCSD single-point calculations on the MP2 optimized structures. Figure S1 in the Supporting Information (SI) shows the plotted density of singly occupied orbitals of **297_1** and **297_2** obtained from SNO analysis of the CCSD density and the corresponding NBO atomic spin-density values. The CCSD SNOs appear very similar to the MP2 ones, thus suggesting that the MP2 density can be used to properly represent the electronic structure of the inspected complexes. NBO spin-density values confirm the discussion on the electron localization in the complexes **297_1** and **297_2**. In fact in **297_1** the spin-density distribution is 47% on the nitrogen atom and 50% on platinum while in **297_2** it is 63% on platinum with a 30% contribution on the OH oxygen and 7% on Cl. Based on the reported theoretical data, it appears that the unpaired electron is not fully localized on platinum in both **297_1** and **297_2**, as might have been expected if the d_z^2 orbital had been involved in the SNO. Eventually, the structural differences between **297_1** and **297_2** are indicative of the participation of either the amino ligand or the hydroxido one, respectively, on the stabilization of the unpaired electron in the complex. In both cases, there is no clear discrimination between a complete localization of the radical on platinum or on the ligands, even though **297_2** shows a higher spin-density on platinum compared to **297_1**. However, this difference may result from the relative electronegativity of oxygen versus nitrogen. Be this as it may, it is clear that both ligands are noninnocent ones, participating in the molecular spin distribution.

Based on the computational results, **m297** was assayed using IRMPD spectroscopy looking for vibrational fingerprints indicative of the geometry of the NH_2 ligand and therefore of the spin localization in the complex. The experimental spectrum of **m297** compared with the IR spectra calculated for structures **297_1** and **297_2** is reported in Figure 3.

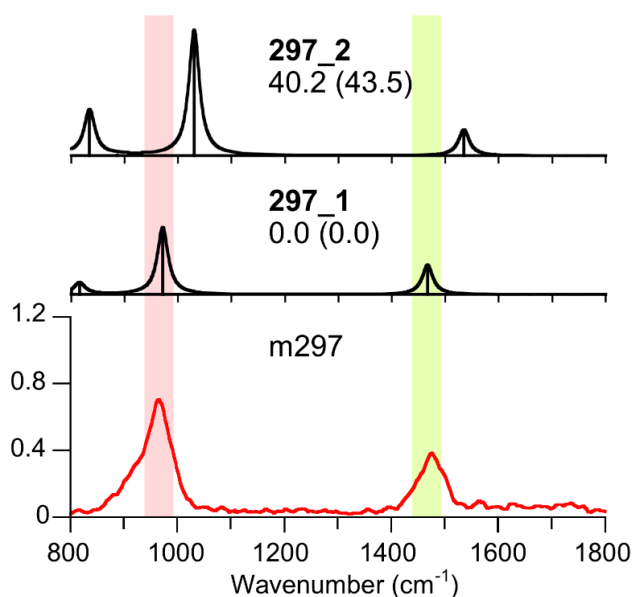


Figure 3. IRMPD spectrum of **m297** (red profile) compared with the calculated IR spectra of **297_1** and **297_2** (black profile, scaling factor = 0.974). Relative free energies in kJ mol^{-1} are reported at the B3LYP and MP2 (in brackets) levels.

The IRMPD spectrum presents two signals centered at 1470 and 965 cm^{-1} , which are accounted for by the NH_2 scissoring mode and OH bending calculated for **297_1** at 1467 and 971 cm^{-1} , respectively. The same vibrational modes are considerably blue-shifted in the theoretical IR spectrum of **297_2**, in ranges where the experimental spectrum does not display any IRMPD activity. Thus, in agreement with the thermodynamic data, one can assign the sampled gas-phase population to structure **297_1**.

The same reasoning can be applied to fragment **m369** from complex **2**. In this case the chlorido ligands are replaced by a chelating 1,1-cyclobutanedicarboxylate group. The two calculated conformers **369_1** and **369_2** (Figure 2) share the same electronic differences of the **m297** congeners. In fact, the SNO of **369_1** shows the unpaired electron localized on both the amino ligand and the platinum atom, while in **369_2** the electron is almost entirely placed on platinum, but it is still shared to some extent with the hydroxido ligand. Also the difference in free energy is similar, in fact **369_2** lies 46.9 kJ mol^{-1} higher than **369_1**. On the contrary, it was not possible to optimize a structure for **m411** with a tetrahedral amino group, probably due to the absence of a ligand able to establish a H-bond with the amino nitrogen. In fact, the hydroxido ligand in *cis* position to the amino one in both **m297** and **m369** is here substituted by an acetate. The calculated thermodynamic data confirm thus the preference for platinum(III) to share an electron with the amino nitrogen rather than with the oxygen of either the acetato or hydroxido ligands, when the platinum(III) fragment is generated by a homolytic bond fission from platinum, such as the neutral amino radical loss observed in the CID process.^[17] Calculations also confirm the ligand in *trans* position to the amino group to have a limited importance for the energetics of the complex compared with the effect of a hydrogen-bond donor group in *cis*. The resulting interaction, in fact, stabilizes the structure in which the spin-density is mainly localized on platinum with the participation of the hydroxido ligand.

The analysis of the IRMPD spectra of **m369** and **m411** confirms the presence of the cited species, as shown in Figure 4. All the reported experimental bands and their assignment are listed in Table S1 in the SI.

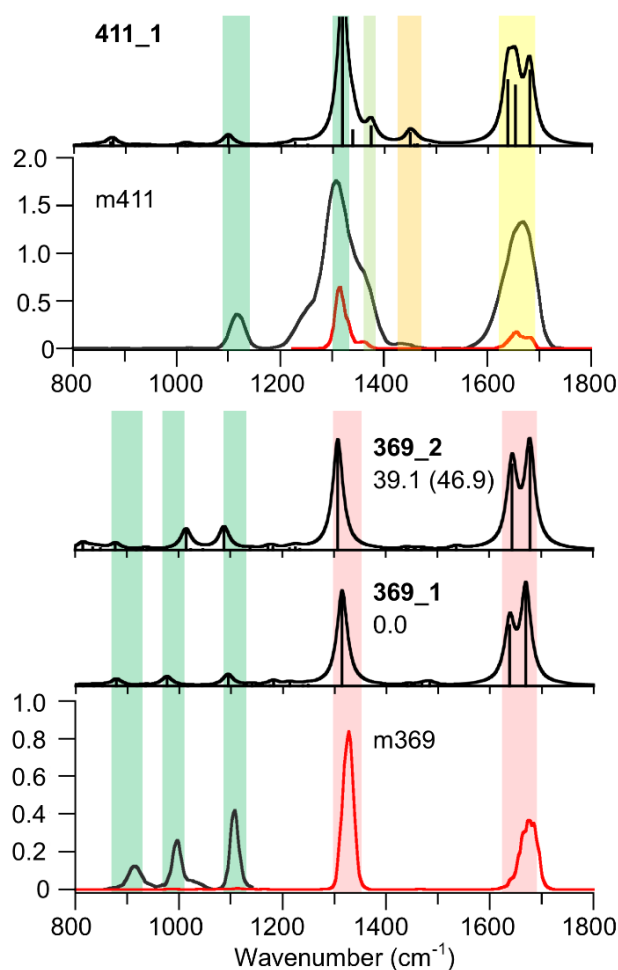


Figure 4. IRMPD spectra of **m369** and **m411** (red and grey profiles, on complete and partial frequency ranges, respectively) compared with the calculated IR spectra of **369_1**, **369_2** and **411_1**, respectively (black profiles, scaling factor = 0.974). The grey profiles of both species refer to 410 ms irradiation time, while the red profile to 180 ms with one attenuator. Relative free energies in kJ mol^{-1} are reported at the B3LYP and MP2 (in brackets) levels.

The experimental spectrum of **m369** is well matched by the one calculated for **369_1** and the same can be said about **m411** and **411_1**. Regarding **m369** in particular, the difference in wavenumber values between the bands at 991 and 1103 cm^{-1} is best justified by the 976 and 1094 cm^{-1} pair in the IR spectrum of **369_1** rather than by the 1014 and 1088 cm^{-1} couple in the spectrum of **369_2**. Unfortunately, the NH_2 scissoring mode that was found diagnostic in the spectrum of **m297** is now poorly active at the expected wavenumbers of 1483 for **369_1** and 1537 cm^{-1} for **369_2**, to be experimentally revealed.

To finally answer the question that motivated this work, whether elusive Pt(III) species can be identified in small isolated complexes, the answer is yes, with some qualification. In particular, the participation of platinum in the spin-density of the assayed ions is a sign of the presence of a

radical character on platinum. Nevertheless, the generation of these species is linked to the possibility of obtaining an important delocalization of spin density on the amino ligand, as it is proved by the comparison of the IRMPD spectra with the calculated ones. In fact, in the whole set of sampled ions (**m297**, **m369** and **m411**) there are clear indications of the planar configuration of the amino ligand, which is a characteristic sign of its radical character. Therefore, the noninnocence of the amino ligand, expressed in the high degree of delocalization of the unpaired electron onto the amino ligand can be identified as the main reason behind the unexpected finding of platinum(III)-containing ions along the dissociation path of the deprotonated complexes that are precursors of **m297**, **m369** and **m411**.

Experimental section

IRMPD experiments.

The Pt(IV) complexes under investigation were synthesized according to published procedures: (*SP-6-33*)-diamminedichloridodihydroxidoplatinum(IV) (oxoplatin, **1**, *cis,trans,cis*-[PtCl₂(OH)₂(NH₃)₂]) was prepared with a microwave-assisted synthesis,^[31] whereas (*SP-6-33*)-diammine(cyclobutane-1,1-dicarboxylato)dihydroxidoplatinum(IV) (**2**, *cis,trans,cis*-[Pt(C₆H₆O₄)(OH)₂(NH₃)₂]),^[32] and (*SP-6-33*)-diacetatodiammine(cyclobutane-1,1-dicarboxylato)platinum(IV) (**3**, *cis,trans,cis*-[Pt(C₆H₆O₄)(CH₃COO)₂(NH₃)₂]),^[33] were prepared with traditional synthetic methods.

IRMPD experiments in the 800-1800 cm⁻¹ frequency range, have been performed using the free-electron laser (FEL) beamline of the Centre Laser Infrarouge d'Orsay (CLIO). The FEL beamline (operated at 42.3 MeV for the present experiments) is coupled with a hybrid Fourier transform ion cyclotron resonance (FT-ICR) tandem mass spectrometer (APEX-Qe Bruker Daltonics),^[34] equipped with a 7.0 T actively shielded magnet and a quadrupole-hexapole interface. The ions of interest were produced by CID in the quadrupole and accumulated in the hexapole for 1 ms before being irradiated in the FT-ICR cell for 180 to 410 ms with the IR FEL light operating at a repetition rate of 25 Hz. The photofragmentation products are mass analyzed and IR spectra are obtained by plotting the photofragmentation yield $R = -\log(I_p / (I_p + \Sigma I_f))$, where I_p and ΣI_f are the integrated intensities of the parent and sum of the fragment ions, respectively, as a function of the photon energy.^[35]

Computational details.

In order to characterize the molecular structure and vibrational features of the ions assayed by IRMPD spectroscopy DFT calculations were performed using the hybrid B3LYP functional and the 6-311++G(d,p) basis set for the light atoms. The def2-TZVP quasi-relativistic *ab initio* pseudopotential,^[36] and associated valence basis set,^[37] were employed for the treatment of the platinum atom in order to obtain a better description of Pt core electrons and reduce computational time. A scaling factor of 0.974 was used to correct the calculated frequencies in agreement with previous works on platinum complexes.^[38,39] The whole set of structures has been reoptimized with the post Hartree-Fock method MP2 employing the same basis set described for the B3LYP calculations. All calculations were carried out with the Gaussian09 package.^[40] Spin natural orbital (SNO) analyses were performed at the MP2 level of theory.^[41] Thermal corrections

were obtained from frequency calculations at the MP2 level. Single-point calculations at the CCSD/6-311++G(d,p) (Pt=def2TZVP) level on the isomers of **m297** were also performed.

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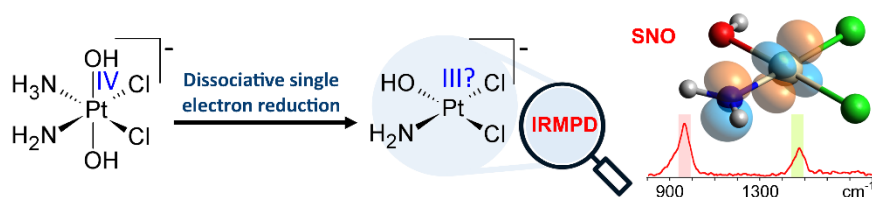
Keywords: IRMPD spectroscopy, Reactive intermediates, Radical ions, Noninnocent ligands, ab initio calculations

References

- [1] K. K. Pandey, *Coord. Chem. Rev.* **1992**, *121*, 1–42.
- [2] J. J. Wilson, S. J. Lippard, *Inorg. Chem.* **2012**, *51*, 9852–9864.
- [3] G. Bandoli, A. Dolmella, F. P. Intini, C. Pacifico, G. Natile, *Inorganica Chim. Acta* **2003**, *346*, 143–150.
- [4] G. Natile, C. Pacifico, F. P. Intini, F. Nushi, *Bioinorg. Chem. Appl.* **2010**, *2010*, DOI 10.1155/2010/102863.
- [5] H. R. Shahsavari, E. Lalinde, M. T. Moreno, M. Niazi, S. H. Kazemi, S. Abedanzadeh, M. Barazandeh, M. R. Halvagar, *New J. Chem.* **2019**, *43*, 7716–7724.
- [6] K. Matsumoto, K. Sakai, in *Adv. Inorg. Chem.*, **1999**, pp. 375–427.
- [7] B. Butschke, H. Schwarz, *Chem. - A Eur. J.* **2011**, *17*, 11761–11772.
- [8] A. Goursot, H. Chermette, E. Penigault, M. Chanon, W. L. Waltz, *Inorg. Chem.* **1984**, *23*, 3618–3625.
- [9] A. Goursot, H. Chermette, M. Chanon, W. L. Waltz, *Inorg. Chem.* **1985**, *24*, 1042–1047.
- [10] K.P. Balashev, L.L. Blinov and G.A. Shigisultanava, *Zh. Neorg. Khim.* **1987**, *32*, 2470-2477.
- [11] W. L. Waltz, J. Lilie, A. Goursot, H. Chermette, *Inorg. Chem.* **1989**, *28*, 2247–2256.
- [12] E. Stephen, A. J. Blake, E. S. Davies, J. McMaster, M. Schröder, *Chem. Commun.* **2008**, 5707.
- [13] O. Rivada-Wheelaghan, M. A. Ortuño, S. E. García-Garrido, J. Díez, P. J. Alonso, A. Lledós, S. Conejero, *Chem. Commun.* **2014**, *50*, 1299–1301.
- [14] G. Momekov, M. Karaivanova, I. Ugrinova, E. Pasheva, G. Gencheva, D. Tsekova, S. Arpadjan, P. R. Bontchev, *Invest. New Drugs* **2011**, *29*, 742–751.
- [15] M. C. McCormick, K. Keijzer, A. Polavarapu, F. A. Schultz, M. H. Baik, *J. Am. Chem. Soc.* **2014**, *136*, 8992–9000.
- [16] I. Tolbatov, C. Coletti, A. Marrone, N. Re, *Inorg. Chem.* **2018**, *57*, 3411–3419.
- [17] D. Corinti, M. E. Crestoni, S. Fornarini, F. Ponte, N. Russo, E. Sicilia, E. Gabano, D. Osella, *J. Am. Soc. Mass Spectrom.* **2019**, *30*, 1881–1894.
- [18] M. D. Hall, T. W. Hambley, *Coord. Chem. Rev.* **2002**, *232*, 49–67.
- [19] D. Gibson, *Dalt. Trans.* **2009**, 10681.
- [20] D. Gibson, *Dalt. Trans.* **2016**, *45*, 12983–12991.
- [21] P. Milko, J. Roithová, D. Schröder, J. Lemaire, H. Schwarz, M. C. Holthausen, *Chem. - A Eur. J.* **2008**, *14*, 4318–4327.

- [22] M. Katari, E. P. De La Garanderie, E. Nicol, V. Steinmetz, G. Van Der Rest, D. Carmichael, G. Frison, *Phys. Chem. Chem. Phys.* **2015**, *17*, 25689–25692.
- [23] G. Yassaghi, L. Jašíková, J. Roithová, *Int. J. Mass Spectrom.* **2016**, *407*, 92–100.
- [24] E. Andris, J. Jašík, L. Gómez, M. Costas, J. Roithová, *Angew. Chemie - Int. Ed.* **2016**, *55*, 3637–3641.
- [25] R. Usón, J. Forniés, M. Tomás, B. Menjón, K. Sünkel, R. Bau, *J. Chem. Soc., Chem. Commun.* **1984**, 751–752.
- [26] R. Ojha, J. F. Boas, G. B. Deacon, P. C. Junk, A. M. Bond, *J. Inorg. Biochem.* **2016**, *162*, 194–200.
- [27] M. N. R. Ashford, R. N. Dixon, R. J. Stickland, C. M. Western, *Chem. Phys. Lett.* **1987**, *138*, 201–208.
- [28] R. Weinkauff, F. Lehrer, E. W. Schlag, A. Metsala, *Faraday Discuss.* **2000**, 363–381; discussion 407-429.
- [29] D. Corinti, D. Catone, S. Turchini, F. Rondino, M. E. Crestoni, S. Fornarini, *J. Chem. Phys.* **2018**, *148*, 164307.
- [30] S. Ye, C. Y. Geng, S. Shaik, F. Neese, *Phys. Chem. Chem. Phys.* **2013**, *15*, 8017–8030.
- [31] E. Gabano, M. Ravera, F. Trivero, S. Tinello, A. Gallina, I. Zanellato, M. B. Gariboldi, E. Monti, D. Osella, *Dalt. Trans.* **2018**, *47*, 8268–8282.
- [32] H. P. Varbanov, S. M. Valiahdi, C. R. Kowol, M. A. Jakupec, M. Galanski, B. K. Keppler, *Dalt. Trans.* **2012**, *41*, 14404.
- [33] [1] C. M. Giandomenico, M. J. Abrams, B. A. Murrer, J. F. Vollano, C. F. J. Barnard, K. R. Harrap, P. M. Goddard, L. R. Kelland, S. E. Morgan, in *Platin. Other Met. Coord. Compd. Cancer Chemother.*, Springer US, Boston, MA, **1991**, pp. 93–100.
- [34] J. M. Bakker, T. Besson, J. Lemaire, D. Scuderi, P. Maître, *J. Phys. Chem. A* **2007**, *111*, 13415–13424.
- [35] J. Lemaire, P. Boissel, M. Heninger, G. Mauclaire, G. Bellec, H. Mestdagh, A. Simon, S. Le Caer, J. M. Ortega, F. Glotin, et al., *Phys. Rev. Lett.* **2002**, *89*, 273001–273002.
- [36] D. Andrae, U. Häußermann, M. Dolg, H. Stoll, H. Preuß, *Theor. Chim. Acta* **1990**, *77*, 123–141.
- [37] F. Weigend, R. Ahlrichs, *Phys. Chem. Chem. Phys.* **2005**, *7*, 3297.
- [38] D. Corinti, C. Coletti, N. Re, R. Paciotti, P. Maître, B. Chiavarino, M. E. Crestoni, S. Fornarini, *Int. J. Mass Spectrom.* **2019**, *435*, 7–17.
- [39] D. Corinti, M. E. Crestoni, S. Fornarini, E. Dabbish, E. Sicilia, E. Gabano, E. Perin, D. Osella, *JBIC J. Biol. Inorg. Chem.* **2020**, DOI 10.1007/s00775-020-01789-w.
- [40] M. J. Frisch, et al. Complete reference is given in the SI.
- [41] D. Danovich, S. Shaik, H. Chen, in *Compr. Inorg. Chem. II*, Elsevier, **2013**, pp. 1–57.

Entry for the Table of Contents



Formal platinum(III) complexes obtained after collisional activation of Pt(IV) prodrugs are assayed using IR ion spectroscopy to identify vibrational features characteristic of their electronic

structure. The role of the noninnocent NH_2 ligand for the formation of these elusive Pt(III) complexes is discussed on the basis of spin natural orbital analyses.