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Trans-Amidate Platinum Complexes Anchoring Water and N-donor Molecules. The Importance of Hydrogen Bonding

Antonio Gimeno-Prat,[a] Antonio Martín,[a] Miguel Baya,*[a] and José M. Casas*[a]

Dedicated to Professor Rinaldo Poli on the occasion of his 65th birthday.

The square planar bisnitrile platinum(II) derivatives $PtCl_2(NCR)_2$ (R = Ph (**1 a**); Et (**1 b**); *p*-C_6H_4F (**1 c**); *p*-$C_6H_4{}^tBu$ (**1 d**); *m*-$C_6H_3Me_2$ (**1 e**); *o,p*-$C_6H_2Me_3$ (**1 f**)) react with tetrabutylammonium hydroxide to render the monoaquo $[NBu_4]$[*trans*-$PtCl(HNCOR)_2(OH_2)$] (**2 a**–**2 f**). The water molecule is σ-coordinated to platinum and the binding is reinforced by two strong hydrogen bonds to the neighboring amidate ligands (OH···OC). Substitution of water in **2 a** by N-donor ligands can be efficiently achieved only in the presence of a dehydrating agent as magnesium sulphate or 4 Å molecular sieves. By following this strategy, compounds $[NBu_4]$[*trans*-$PtCl(HNCOPh)_2(NH_2R')$] (R' = H (**3**), NH_2 (**4**), ^tBu (**5 a**), *p*-C_6H_4Me (**5 b**) have been isolated. The incoming ligands are σ-coordinated to platinum and also establish strong hydrogen bonds to the amidates (NH···OC). Treatment of **2 a** with halogens causes oxidation at the metal center, rendering the platinum(IV) derivatives $[NBu_4][PtClX_2(HNCOPh)_2(OH_2)]$ (X = Cl (**6 a**), Br (**6 b**), I (**6 c**)).

Introduction

Platinum(II) compounds are at the heart of coordination chemistry. Seminal works by Peyrone, first synthesizing cisplatin,[1] Werner, who set decisive ideas for unveiling its structure,[2] and Chugaeff, who prepared the chloropentammineplatinum(IV) trichloride, so called "Chugaev's salt",[3] and described nucleophilic addition reactions onto methyl isocyanide platinum(II) complexes affording probably the first metal carbene complex ever reported,[4] paved the way for the extraordinary development of platinum chemistry along the following decades.

A crucial milestone in coordination chemistry was the discovery in the 60's of the antiproliferative property of cisplatin by Rosenberg, Van Camp, and Kigras in 1965,[5] which boosted the research on platinum compounds applied to cancer therapies. Since then, several thousand platinum compounds have been tested as potential anticancer drugs and prodrugs, and at least six of them have obtained marketing approval for medical use.[6] In this context, platinum complexes with aquo and ammine ligands have been widely developed,[7] as well as other more sophisticated compounds. The role of hydrogen bonding becomes critical when coordination compounds are released in biological media.

Nitriles are commonly used as co-ligands for metal halides, in order to facilitate their solubility in organic media. Coordination to a metal center typically enhances the electrophilicity of the carbon C≡N atom. Thus, nucleophilic addition reactions of alcoxides, hydroxide, amines, and phosphines have been described, giving rise to complexes containing iminoether, amidates, amidines, or phosphines.[8,9]

In the specific case of platinum complexes, the chemistry of the resulting compounds has attracted attention, particularly those bearing amidate and iminoether ligands. The former are able to act as terminal or bridging ligands. Indeed, tetranuclear platinum complexes bridged by amidates have been carefully studied starting from the 70's, because of their singular chain crystal structures and the intermediate oxidation states on the metal centers.[10] Later on, octanuclear chains were also prepared and studied.[11] Otherwise, iminoether and amidate platinum complexes have shown remarkable antitumoral activities.[12]

Amidate ligands also offer the possibility of hydrogen bond interactions. Such property is potentially interesting in the design of metal based drugs and also for other type of studies and applications. In this context, we have previously described the controlled monohydration of sulfur dioxide by reaction with a platinum-water compound.[13] The operation of hydrogen bonds at different steps of the process is decisive for the progress of the reaction. Following these results, we wish to report here the synthesis of a full series of Pt-OH_2 complexes and their behavior towards other molecules possessing N–H bonds, as ammonia, hydrazine and amines, as well as towards oxidants, such as chlorine, bromine, and iodine.

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Part of the "celebratory collection for Rinaldo Poli".

Results and Discussion

Access to our starting materials, the well-known square-planar bisnitrile platinum(II) derivatives $PtCl_2(NCR)_2$ (R = Ph (**1 a**); Et (**1 b**); p-C_6H_4F (**1 c**); p-$C_6H_4{}^tBu$ (**1 d**); m-$C_6H_3Me_2$ (**1 e**); o,p-$C_6H_2Me_3$ (**1 f**)), has been accomplished by refluxing $PtCl_2$ suspensions in the corresponding liquid nitrile or, in the case where the nitrile is solid, in toluene as solvent. The resulting compounds have been isolated in pure form with yields ranging from 52 % to 83 %. Three of these have been crystallized and their structures have been determined by X-ray diffraction methods (see SI). They all show the expected square-planar geometries, with minor differences. Due to crystallographic symmetry, N–Pt-N and Cl–Pt–Cl angles are 180°. The Pt–N distances lay in the 1.95 to 1.96 Å range, the Pt–Cl ones, in the 2.29 to 2.31 Å range, and the N≡C ones, in the 1.12 to 1.14 Å range. The IR spectra of this set of complexes present absorptions that can be assigned to the Pt–Cl (range: 325–343 cm^{-1}) and N≡C (range: 2279–2317 cm^{-1}) bond stretching vibrations.

Coordination of nitrile ligands to a metal center typically enhances the electrophillicity on the carbon –C≡N atom.[8] Indeed, hydration of nitriles is a common reaction that can be easily achieved with different metal systems.[14,8c,15] Profiting of this, we have performed the reactions of these derivatives with tetrabutylamonium hydroxide, in the presence of small amounts (a few drops) of distilled water and a non-coordinating solvent. Careful workouts of the respective reaction mixtures have allowed the isolation of a set of pure compounds of formula $[NBu_4][$*trans*-$PtCl(HNCOR)_2(OH_2)]$ (R = Ph (**2 a**); Et (**2 b**); p-C_6H_4F (**2 c**); p-$C_6H_4{}^tBu$ (**2 d**); m-$C_6H_3Me_2$ (**2 e**); o,p-$C_6H_2Me_3$ (**2 f**), Scheme 1). Such formulation is supported by diverse spectroscopical and structural data.

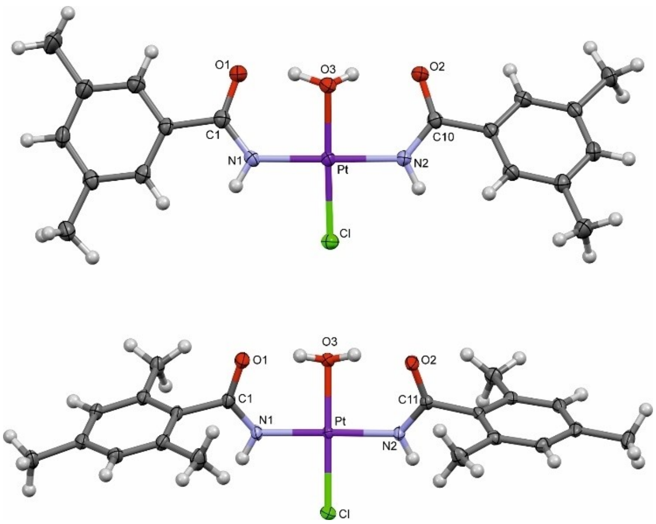
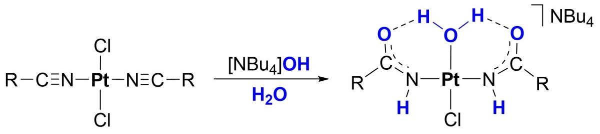


Figure 1. Thermal ellipsoids of the complex anion found in the crystal lattice of **2 e** (above) and **2 f** (below). Selected bond lengths (Å) and angles (°). **2 e**: Pt–N1 2.014(2), Pt–N2 2.005(2), Pt–O3 2.041(2), Pt–C 2.2935(7), N(1)-C(1) 1.314(4), C(1)-O(1) 1.272(3), N(2)-C(10) 1.312(3), C(10)-O(2) 1.271(3), O3-H3A 0.97(6), O3-H3B 0.80(4), O1···H3A 1.54(5), O2···H3B 1.86(5), N1-Pt–N2 178.69(9), Cl-Pt–O3 178.83(6). **2 f**: Pt–N1 2.0068(16), Pt–N2 2.0066(16), Pt–O3 2.0512(13), Pt–Cl 2.2818(4), N(1)-C(1) 1.314(3), C(1)-O(1) 1.263(2), N(2)-C(11) 1.312(2), C(11)-O(2) 1.268(2), O3-H3A 0.86(3), O3-H3B 0.87(3), O1···H3A 1.69(3), O2···H3B 1.72(3), N1-Pt–N2 176.59(6), Cl-Pt–O3 178.63(4).

Indeed, slow diffusion of diethyl ether into dichloromethane solutions of **2 e** and **2 f** has afforded crystalline materials suitable for X-Ray Diffraction (XRD) characterization. Views of the molecular structures of the complex anions of these compounds are shown in Figure 1. The found geometries are qualitatively similar, and present a water molecule σ-coordinated to platinum. The binding is strengthened by the formation of two hydrogen bonds to the *cis*-amidate ligands, with hydrogen bond distances (CO···HO) of 1.54(5) (H–O1), 1.86(5) (H–O2) Å for **2 e** and 1.70(3) Å (average) for **2 f**. As a result, the C–N and C–O interatomic distances are in-between the usual values for single and double bonds (respective average distances: 1.313(4) and 1.272(3) Å in **2 e**, 1.313(3) and 1.270(2) Å in **2 f**), proving the delocalization along the N–C–O peptidic bond. This bonding pattern is remarkable and results in the water molecule being tightly bound in the metal coordination sphere, as confirmed by DFT calculations. A distinctive feature between these structures is the different relative orientation of the aromatic rings. Whereas in **2 e** the rings are basically coplanar with regard to the coordination plane, in **2 f** the rings are disposed almost perpendicular. This fact must be due to the steric hindrance generated by the *ortho*-methyl groups present in the aromatic substituent in the latter compound.



1a-1f **2a-2f**

Scheme 1. Synthesis of $[NBu_4][$*trans*-$PtCl(HNCOR)_2(OH_2)]$ complexes (**2 a**–**2 f**).

The formation of complexes **2 a**–**2 f** is interesting and deserves additional comment. Nucleophillic addition of hydroxide onto a coordinated nitrile is a well-known reaction giving rise to the formation of an amidate ligand. In previous reports, Natile and coworkers have studied the hydrolysis of platinum-bound nitriles under basic conditions, using potassium hydroxide. The authors have observed the selective formation of the dianionic platinate complexes $K_2[$*trans*-$PtCl_2(HN{=}C(O)R)_2]$, which have been readily isolated.[16] Protonation of these derivatives affords the neutral [*trans*-$PtCl_2(HN{=}C(OH)R)_2]$, whereas subsequent treatment in water under basic conditions affords the diaquo [*trans*-$Pt(HN{=}C(O)R)_2(OH_2)_2]$.[17] This sequence contrasts with our reaction, that uniquely leads to a sole monoanionic, monoaquo platinum(II) derivative. The origin of this difference must be related to the base used. Arguably, the presence of the $[NBu_4]^+$ cation instead of K^+ shall avoid the formation of weak interactions to the amidate ligand in different phases of the process, thus favoring the entry and notable stabilization of a water molecule into the coordination sphere of platinum, by means of the Pt–O bond itself and two additional -and undisputed- hydrogen bonds. In sum, the current reaction implies a subtle balance of factors causing the substitution of only one of the chlorido ligands by a water molecule and the marked stabilization of the outcoming complex.

In this context, it also has to be noted that when the reaction is carried out strictly in the absence of water, decomposition processes occur, and formation of a bischlorine, bisamidate complexes in reasonable amounts is not observed. This fact strongly suggests that the intervention of hydrogen bonding processes is a crucial factor for the outcome of these reactions.

The IR spectra collected for **2a**–**2f** are fully consistent with the structures proposed. No stretching vibrations corresponding to Pt-coordinated N≡C bonds can be found, but instead sets of two absorptions are present (except for **2b** and **2e**, where only one is apparent, probably due to accidental superposition of bands), in the range 1550–1610 cm^{-1}, supporting the formation of the amidate units. Furthermore, N–H and O–H bond stretching vibrations are observed, in the range 3300–3400 cm^{-1}. Other absorptions assignable to the Pt–Cl moiety and to the presence of the tetrabutylammonium cation are also evident in the spectra.

Besides, the ^{1}H NMR spectra in dichloromethane-d^2 at RT are consistent with the discussed structures, and present as most significant signals one broad singlet at very low field (range: 12.15–12.44 ppm), which corresponds to the coordinated water molecule, and another broad singlet (range: 4.98–5.98 ppm), which can be assigned to the NH proton as suggested by the ^{1}H-^{15}N HMQC spectra. The latter, performed for **2a** at 232 K, shows a signal at (5.93, 88.0 ppm). ^{195}Pt NMR spectrum has been also run for **2a** as a representative of this set of complexes, which presents a broad singlet centered at −1688.3 ppm.

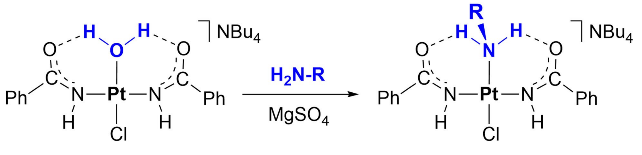
We have further studied complexes **2a**–**2f** by means of DFT calculations. Atoms In Molecules (AIM) analysis have allowed to locate Bond Critical Points (BCP) relating the H-water atoms and the O-benzamidate ones, confirming the hydrogen bond interactions between both ligands. The calculated parameters for these BCPs indicate strong interactions, estimated in the range −11.5 to −12.4 kcal/mol. Moreover, the results obtained from NCI analyses are fully consistent with the formation of strong hydrogen bond interactions (Table S5 and Figures S82–S93 in SI). Proton transfer to the amidate ligands leading to the formation of OH tautomers has also been examined. The behavior of the whole set of complexes is very similar. The processes are in all cases strongly disfavored; the first tautomerization presents ΔG° values in the +13.8 to +15.5 kcal/mol range, whereas the second requires more than +61 kcal/mol (Figure S108 in SI).

In view of the robust interactions established between the platinum bisamidate moiety and the water molecule, we wondered if it would be possible to exchange this ligand by other small N-donor molecules, as ammonia or hydrazine. We chose complex **2a** as benchmark material for the following reactions. We first tried a reaction in solid state, by exposing complex **2a** to an ammonia atmosphere. Unfortunately, we observed neither visual change nor spectroscopical evidence suggesting water substitution. We then tried the reaction in dichloromethane solution, and we spectroscopically observed the formation of a small amount of one new product, presumably the target compound. This result suggested that the substitution is a feasible but not a straightforward process. Consequently, we decided to use a dehydrating agent in order to capture the water molecules displaced from the metal complex and push the reaction ahead. Thus, repetition of the synthetic procedure in the presence of anhydrous magnesium sulphate and an ammonia atmosphere finally led to the quantitative formation of a novel compound, which was isolated after workup as a white solid of formula $[NBu_4][$*trans*-$PtCl(HNCOPh)_2(NH_3)]$ (**3**), as deduced from spectroscopical evidence, in a 64% yield (Scheme 2). Interestingly, exposition of **3** in the solid state to an open air atmosphere lead to slow ligand exchange and regeneration of the precursor **2a**, a process that shall be favored by the gaseous nature of ammonia.

Profiting of the successful procedure developed, we then tried to coordinate hydrazine to platinum. We performed the reaction of a dichloromethane solution of **2a** and hydrazine, in the presence of anhydrous magnesium sulphate. We succeeded in isolating a white solid, corresponding to the compound of $[NBu_4][$*trans*-$PtCl(HNCOPh)_2(NH_2NH_2)]$ formula (**4**), as deduced from spectroscopical evidence, in a 76% yield.

The IR spectra of **3** and **4** show bands fully consistent with the proposed formulations. These include N–H bond stretching vibrations at 3391, 3379 (**3**) and 3383 (**4**) cm^{-1}, CO and NC vibrations at 1614, 1590 (**3**) and 1604, 1556 (**4**) cm^{-1}, Pt–Cl vibrations at 322 (**3**) and 303 (**4**) cm^{-1}, and other absorptions assignable to the tetrabutylammonium cation.

Moreover, the NMR spectra are also in good agreement with the structures proposed. The ^{1}H spectrum of **3** in dichloromethane-d^2 at RT shows two broad singlets at 5.98 and 5.71 ppm, corresponding to the NH protons, together with the expected signals derived from the presence of phenyl substituents (range: 7.4–7.7 ppm) and the tetrabutylammonium cation (3.28, 1.58, 1.34, and 0.91 ppm). Lowering the temperature down to 232 K causes a sharpening in the NH signals, which emerge more clearly at 5.95 and 5.67 ppm showing a relative intensity ratio of 3:2. Consequently, the former can be attributed to the ammine ligand, which rotates around the Pt–N axis therefore exchanging the NH positions faster than the NMR timescale, whereas the latter is due to the amidate ligands. The bidimensional ^{1}H-^{15}N HMQC spectrum at 232 K shows two signals at (5.95, −63.0 ppm) and (5.67, 85.2 ppm), allowing to indirectly find out the ^{15}N NMR shifts for the ammine and



2a-2f

R = H (**3**), NH_2 (**4**),
^{t}Bu (**5a**), C_6H_4Me (**5b**)

Scheme 2. Synthesis of $[NBu_4][$*trans*-$PtCl(HNCOR)_2(NH_2R)]$ (R = H (**3**), NH_2 (**4**), ^{t}Bu (**5a**), C_6H_4Me (**5b**)).

amidate N atoms. The latter value agrees well with that found for the analogous N atom of the amidate ligands in **2a**.

The ^{1}H spectrum of **4** in dichloromethane-*d*^{2} at RT shows, beside the signals corresponding to the phenyl groups and the cation, three broad singlets at 9.72, 5.82 and 3.67 ppm. Interestingly, the former presents platinum satellites, with a Pt–H coupling constant of 78 Hz. The bidimensional ^{1}H-^{15}N HMQC spectra at 232 K shows three signals at (9.81, −18.2 ppm), (5.85, 87.4 ppm), and (3.63, 71.9 ppm). Consequently, the above-mentioned broad singlets in the ^{1}H spectrum can be assigned to the N^{α}-H_2 (hydrazine), the N^{α}-H (amidate), and N^{β}-H_2 (hydrazine) protons, respectively.

We have completed the characterization by means of MS spectrometry. The ESI-HRMS^{-} experiment performed on a sample of **3** has allowed to observe a peak with m/z (487.050) and a pattern consistent with a $[PtCl(HNCOPh)_2(NH_3)]^{-}$ formula, whereas the ESI^{-} experiment performed on a sample of **4** has allowed to observe a peak with m/z (503.1) and a pattern consistent with a $[PtCl(HNCOPh)_2(NH_2NH_2)]^{-}$ formula.

Once we have characterized the compounds, we have modelled and studied them by means of DFT calculations. AIM analyses on **3** and **4** have allowed to find BCPs confirming the existence in each complex of two hydrogen bonds between the ammonia/hydrazine $N^{\alpha}H$ units and the O atoms of the amidate ligands, confirming the relevance of these interactions in the stabilization of the small N-donor molecules (Table S5 and Figures S94–S97 in SI). The bonding situation in **4** is slightly asymmetric, generating two dissimilar interactions. The estimated strengths of these hydrogen bonds are −8.6 (**3**) and −9.2 and −6.3 (**4**) $kcal\,mol^{-1}$. NCI results agree with the existence of the referred hydrogen bonds. We have also revised the Pt-NH_3 rotation that would explain the observed proton equivalence in the N-coordinated ligand in **3**. The calculated $\Delta G^{\neq}$ for this process in solution is +3.0 kcal/mol, in good coherence with the experimental observations. Furthermore, we have analyzed the thermodynamic stability of two isomers derived from the two possible H-transfer processes. The corresponding tautomers are highly disfavored, by +25.5 and +76.1 kcal/mol (**3**), and by +21.8 and +61.7 kcal/mol (**4**) (Figure S109 in SI).

Unfortunately, we systematically failed in crystallizing **3** and **4**. Therefore, we intended to synthesize analogous complexes with a simple primary amine instead. For that purposes, we chose *tert*-butylamine and *para*-toluidine. We then followed the previously discussed strategy, and we succeeded to isolate two white solids, corresponding to the compounds of $[NBu_4]$[*trans*-$PtCl(HNCOPh)_2(NH_2R)$] (R = ^{t}Bu (**5a**), *p*-C_6H_4Me (**5b**)) formula, in 73 and 80 % yields respectively. Such formulations were inferred from spectroscopical and structural data.

We succeeded in growing crystalline materials of complex **5b** suitable for XRD analysis. The obtained structure, shown in Figure 2, presents the expected square planar arrangement around the platinum center. The primary amine is σ-coordinated to the metal, and two strong hydrogen bonds to the neighboring amidate ligands are formed, with hydrogen bond CO···HN distances of 1.82(3) and 1.96(3) Å. As observed in the previously described structures, the C–N and C–O distances are intermediate for single and double bonds (average: 1.319(3) and 1.260(3) Å, respectively), highlighting its peptidic character. Again, this bonding pattern results in the amine being tightly bound in the metal coordination sphere, as presumably happens in the related complexes **3**, **4**, and **5a**.

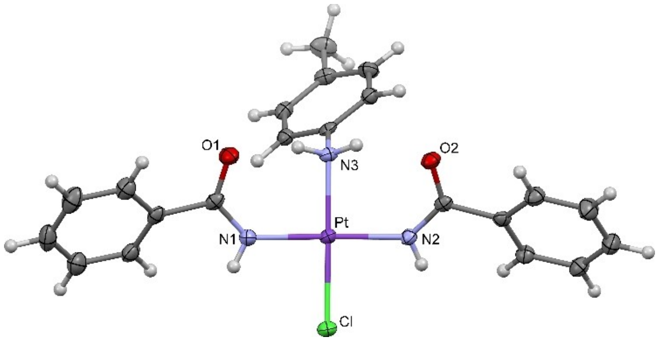


Figure 2. Thermal ellipsoids of the complex anion found in the crystal lattice of **5b**. Selected bond lengths (Å) and angles (°): Pt–N1 2.016(2), Pt–N2 2.019(2), Pt–N3 2.0452(18), Pt–Cl 2.3131(5), N(1)-C(1) 1.320(3), C(1)-O(1) 1.260(3), N(2)-C(8) 1.318(3), C(8)-O(2) 1.260(3), N3-H3A 0.91(3), N3-H3B 0.86(3), O1···H2N 1.82(3), O2···H1N 1.96(3), N1-Pt–N2 177.67(8), Cl-Pt–N3 178.97(6).

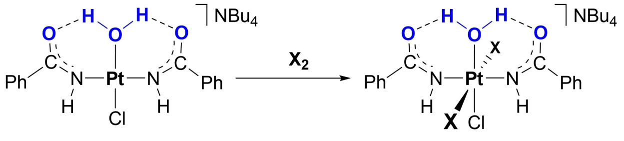
The IR spectra of **5a** and **5b** show bands in the ranges 3387–3401 cm^{-1} (N–H stretching), 1611–1615 and 1541–1557 cm^{-1} (CO and CN, respectively), and 322–320 cm^{-1} (Pt–Cl), as well as other absorptions consistent with the presence of the cation. The ^{1}H NMR spectra in dichloromethane-*d*^{2} at 232 K show broad singlets at 8.36 (**5a**) and 10.86 (**5b**) ppm, corresponding to the coordinated amine NH_2 protons, and 5.62 (**5a**) and 5.75 (**5b**) ppm, corresponding to the amidate NH protons. These assignations are backed by the bidimensional ^{1}H-^{15}N HMQC spectra. Besides, the spectrum of **5a** presents signals corresponding to the phenyl groups in the 7.35–7.71 ppm range, and a singlet at 1.34 ppm corresponding to the *tert*-butyl group; otherwise, the spectrum of **5b** shows signals in the 7.80–7.00 ppm range, corresponding to the aromatic CH protons, and a singlet at 2.26 ppm, which corresponds to the methyl substituent in the aromatic amine ring. The ^{195}Pt NMR spectrum of **5b** as a representative of these complexes presents a broad signal at 98.6 ppm.

Complexes **5a** and **5b** have also been studied by DFT methods. Combined AIM and NCI analyses have confirmed the presence of BCPs in-between the amidate O atoms and the amine NH protons, supporting the formation of hydrogen bonds between these ligands (Table S5 and Figures S98–S101 in SI). The estimated strengths of each of the hydrogen bonds, based on the BCP parameters, are −8.4 (**5a**) and −8.6 (**5b**) $kcal\,mol^{-1}$. The equilibria between the tautomers derived from the two possible proton transfer processes have also been modelled. They are clearly disfavored, especially for the latter, and present ΔG° values of +26.4 and +79.5 kcal/mol (**5a**), and +19.3 and +54.9 kcal/mol (**5b**) (Figure S109 in SI).

Finally, and with the target of obtaining bis-amidate platinum(IV) derivatives, we studied the behavior of **2a** towards halogens. Luckily, we observed that the oxidation reactions with chlorine, bromine and iodine proceeded smoothly in all cases. Indeed, treatment of dicholoromethane solutions of **2a** with each of the halogens led to the formation of the corresponding trihalogen derivatives, of [NBu$_4$][*trans,trans*-PtClX$_2$(NHCOPh)$_2$(OH$_2$)] (X=Cl (**6a**), Br (**6b**), I (**6c**)) formula (Scheme 3).

The structure of these compounds was established on the basis of spectroscopical and structural information. Crystals suitable for XRD were obtained for **6c**. A view of its complex anion is shown in Figure 3. The found structure reveals an octahedral geometry around the metal, as expected for a platinum(IV) center. Interestingly, the two iodide ligands are mutually *trans* disposed, therefore suggesting and S$_N$2 mechanism for the oxidation.[18] As is observed in the previous structures, the distances between the OH$_2$ protons and the benzamidate O atoms are remarkably small (1.84(2) and 1.68(2) Å). Also, the C–N and C–O interatomic distances are intermediate for single and double bonds (average distances: 1.312(8) and 1.263(8) Å, respectively), supporting the peptidic character of the amidate ligand.

The spectroscopical data collected for **6a**–**6c** are mutually consistent, and agree well with the XRD structure. The IR spectra present in all cases the characteristic absorptions corresponding to the NH (range: 3406–3417 cm^{-1}), the CO and CN (ranges: 1605–1612 and 1566–1567 cm^{-1} respectively), and the Pt-Cl$_{equatorial}$ (range: 317–318 cm^{-1}) bond stretching vibrations, as well as other bands confirming the presence of the tetrabutylammonium cation. In the case of **6a**, an additional absorption corresponding to the Pt-Cl$_{axial}$ bonds is observed (340 cm^{-1}). The ^{1}H NMR spectra present in each case one broad singlet corresponding to the NH proton of the amidate ligand, located in the 5.78–6.08 ppm range. The water ligands give rise to very broad signals that are distinguishable from the baseline only for **6c**, at 13.13 ppm. Besides, signals corresponding to the phenyl groups (range: 7.45–7.80 ppm) and the tetrabutylammonium cation are observed, all of them presenting the expected relative integration areas. Also, the ^{195}Pt NMR spectrum of **6b** shows a broad signal centered at −2238.9 ppm. Finally, the mass spectra obtained by ESI$^-$ display peaks with m/z ratios and patterns perfectly consistent with the formulations proposed for the complex anions.



2a-2f

X = Cl (**6a**), Br (**6b**), I (**6c**)

Scheme 3. Synthesis of [NBu$_4$][*trans*-PtClX$_2$(HNCOR)$_2$(OH$_2$)] (X=Cl (**6a**), Br (**6b**), I (**6c**).

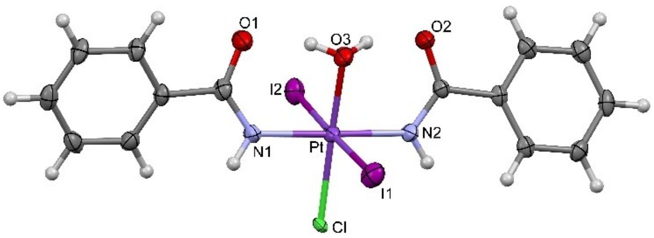


Figure 3. Thermal ellipsoids of the complex anion found in the crystal lattice of **6c**. Selected bond lengths (Å) and angles (°): Pt–N1 2.041(5), Pt–N2 2.018(5), Pt–O3 2.040(4), Pt–Cl 2.3728(13), Pt–I1 2.6646(5), Pt–I2 2.6568(5), N1-C1 1.305(8), C1-O1 1.266(8), N2-C8 1.318(7), C8-O2 1.259(7), O3-H3A 0.84(2), O3-H3B 0.85(2), O1···H3A 1.84(2), O2···H3B 1.68(2), N1-Pt–N2 178.3(2), Cl-Pt–O3 178.02(14), I1-Pt–I2 177.910(17).

We have also modelled complexes **6a**–**6c** by means of DFT calculations. AIM and NCI analyses confirm the formation of hydrogen bonds, as observed in the whole set of compounds described herein (Table S5 and Figures S102–S107 in SI). The estimated strengths of the hydrogen bonds are in the −13.6 and −14.0 kcal/mol range, making them the strongest in this whole series of compounds. Interestingly, the tautomerization processes are not as disfavored as in the platinum(II) compounds. The first tautomerization presents ΔG° values in the +8.9 to +11.2 kcal/mol range, whereas the second is disfavored by more than +49 kcal/mol (Figure S110 in SI).

Conclusion

In this article we have described the preparation of a set of novel platinum bis-amidate compounds which are able to coordinate water or other small N-donor molecules through σ-Pt–O or σ-Pt–N bonds. These entities containing either O–H or N–H bonds also establish remarkably strong hydrogen bonds with the amidate ligands, and thus become tightly anchored to the metal center. The strength of these interactions are in the −6.3 to −14.0 kcal/mol range, as estimated by DFT calculations.

Platinum(II) bisamidate derivatives can be obtained from well-known platinum bisnitrile starting materials, by reaction in a wet, basic media of tetrabutylammonium hydroxide. Monoanionic, monoaquo platinum(II) complexes are obtained therefrom, an outcome that is in sharp contrast with the products obtained in other related reactions previously described in the literature. Subsequent substitution of the water ligand by ammonia, hydrazine, or primary amines are not straightforward processes, but can be forced and completed in the presence of a dehydrating agent. On the other hand, oxidation of the monoaquo platinum(II) derivative proceeds readily when using halogens, and renders monoanionic, monoaquo platinum(IV) compounds.

Binding of "hard" oxygen/nitrogen donor atoms to "soft" platinum(II) centers is expected to be weak, and therefore the coordinating ligands are expected to be labile. Nevertheless, the combined ligand system H**N**CO···H-**E**-H···OC**N**H (E=O, N–R) allows to anchor water, ammonia, hydrazine or a primary amine to the metal coordination sphere firmly, therefore distorting the initially expected *trans* effect. We are intrigued about the implications of the hydrogen bonds on the reactivity of these series of complexes. Further studies dealing with substitution reactions on the platinum bisamidate precursors described herein by common ligands as phosphines or pyridines are currently underway in our laboratories, and will be reported in due course.

Experimental Section

Complete details on some synthetic procedures, full characterization and spectra, XRD diffraction studies, and DFT analyses are included in the Supporting Information (SI).

General methods. Solvents were purified by using a MBraun SPS-800 solvent purification system. All reagents were purchased from commercial sources and used as received. Elemental analyses were carried out using a Perkin-Elmer 2400 CHNS/O Series II microanalyzer. IR spectra were recorded on neat solid samples using a Perkin-Elmer Spectrum 100 FT-IR spectrometer (4000–250 cm^{-1}) equipped with an ATR Sampling Accessory. NMR spectra were recorded on a Bruker ARX-300, a Bruker AV-400, or a Bruker AV-500 spectrometer. ^{1}H chemical shifts (δ, ppm) are given relative to the standard references for each nucleus. Coupling constants (J) are given in Hertz (Hz). Standard mass spectra (MS) and high-resolution mass spectra (HRMS) were registered using electrospray ionization (ESI) techniques on Bruker Esquire 3000+, Bruker Autoflex III Maldi-TOF, and Bruker Microflex Maldi-TOF spectrometers. Complex [PtCl$_2$(NCPh)$_2$] (**1a**) was prepared as described elsewhere,[19] and complexes **1b**–**1f** were prepared similarly (see SI). Complex [NBu$_4$][*trans*-PtCl(NHC(O)Ph)$_2$(H$_2$O)] (**2a**) was prepared as previously described by us,[13] and complexes **2b**–**2f** were prepared similarly. Preparations and characterization data corresponding to **2b**–**2f**, **3**, **4**, **5a**, **5b**, **6a**, **6b**, and **6c** are included herein. IR, NMR and MS spectra are included in SI.

General synthetic procedure of [NBu$_4$][PtCl(NHCOR)$_2$(OH$_2$)] (R = Et (2b), C$_6$H$_4$F (2c), C$_6$H$_4$^{t}Bu (2d), C$_6$H$_3$Me$_2$ (2e), C$_6$H$_2$Me$_3$ (2f)). To a solution of *trans*-[PtCl$_2$(NCR)$_2$] (R = Et (**1b**), C$_6$H$_4$F (**1c**), C$_6$H$_4$^{t}Bu (**1d**), C$_6$H$_3$Me$_2$ (**1e**), C$_6$H$_2$Me$_3$ (**1f**)) in CH$_2$Cl$_2$ (20 mL), a volume of a 1 M NBu$_4$OH-MeOH solution corresponding to a 1:2 molar ratio of the reagents was added, together with a few drops of water (amounts of reagents are given in Table 1). After 1 h of stirring, the resulting orange solution was evaporated to dryness. The residue was treated with a mixture of ^{i}PrOH/OEt$_2$ (0.5 mL/4 mL) rendering a yellow solid which was filtered off, washed with ^{i}PrOH/OEt$_2$ (0.5 mL/4 mL), washed with OEt$_2$ (4 mL), and dried under vacuum. Yields included in Table 1.

Analytical and spectroscopic data for complexes 2b–2f:

[NBu$_4$][*trans*-PtCl(NHCOPh)$_2$(OH$_2$)] (2a). General data has been already provided in ref 13. ^{195}Pt-NMR (CD$_2$Cl$_2$, 64.5 MHz, 298 K): 1688.3.

[NBu$_4$][*trans*-PtCl(NHCOEt)$_2$(OH$_2$)] (2b). Anal. Found (Calcd. for C$_{22}$H$_{50}$ClN$_3$O$_3$Pt: C, 41.55 (41.60); H, 7.90 (7.93); N, 6.63 (6.62). IR (cm^{-1}): (N–H) 3537 w, (O–H) 3326 w, (C–H) 2958 m, 2874 w, (C=O, C–N) 1580 s, (C–C Ar) 1481 s, (NBu$_4$$^+$) 884 m, 737 m, $_v$(Pt–Cl) 326 m. ^{1}H RMN (CD$_2$Cl$_2$, 300 MHz, 298 K): 12.27 (br s, 2H, H$_2$O), 5.01 (br s, 2H, NHCO), 3.36, 1,71, 1.48, 1.05 (36H, (NBu$_4$$^+$)), 2.08 (q, 4H, COC*H*$_2CH_3$, $^{3}J_{\text{H-H}}$ = 7.7), 1.05 (overlaped with a signal of (NBu$_4$$^+$), C(O)CH$_2$C*H*$_3$). ^{13}C-NMR (APT, CD$_2Cl_2$, 75 MHz, 298 K): 184.0 (−), 59.3 (−), 33.4 (−), 24.5 (−), 20.2 (−), 14.0 (+), 11.1 (+). MS (ESI$^-$): [PtCl(NHCOEt)$_2$(OH$_2$)]$^-$ 393.0 *m/z.*

[NBu$_4$][*trans*-PtCl(NHCOC$_6$H$_4$F)$_2$(OH$_2$)] (2c). Anal. Found (Calcd. for C$_{30}$H$_{48}$ClF$_2$N$_3$O$_3$Pt: C, 46.99 (46.96); H, 6.41 (6.31); N, 5.57 (5.48). IR (cm^{-1}): (N–H, O–H) 3401 w, (C–H) 2960 m, 2873 w, (C=O) 1609 s, (C–N) 1563 s, (C–C Ar) 1487 s, 1451 s, (NBu$_4$$^+$) 881 w, (Pt–Cl) 337 m. ^{1}H RMN (CDCl$_3$, 300 MHz, 298 K): 12.15 (br s, 2H, H$_2$O), 7.69 (dd, 4H, *o*-C$_6$*H*$_4$F, $^{3}J_{\text{Ho-Hm}}$ = 8.7, $^{4}J_{\text{Ho-F}}$ = 5.4), 7.00 (dd, 4H, *m*-C$_6$*H*$_4$F, $^{3}J_{\text{Hm-Ho}}$ = 8.7, $^{3}J_{\text{Hm-F}}$ = 8.7), 5.88 (br s, 2H, NHCO), 3.42, 1,62, 1.37, 0.91 (36H, (NBu$_4$$^+$)). ^{19}F-NMR (CD$_2Cl_2$, 282 MHz, 298 K): −113.6 (tt, $^{3}J_{\text{F-Hm}}$ = 8.7, $^{4}J_{\text{F-Ho}}$ = 5.4). ^{13}C-NMR (APT, CD$_2$Cl$_2$, 75 MHz, 298 K): 176.3 (−), 166.1 (−), 162.7 (−), 129.2 (+), 115.3 (+), 59.6 (−), 24.7 (−), 20.3 (−), 14.0 (+). MS (ESI$^-$): [PtCl(NHCOC$_6$H$_4$F)$_2$(OH$_2$)]$^-$ 524.1 *m/z.*

[NBu$_4$][*trans*-PtCl(NHCOC$_6$H$_4$^{t}Bu)$_2$(OH$_2$)] (2d). Anal. Found (Calcd. for C$_{38}$H$_{66}$ClN$_3$O$_3$Pt): C, 55.15 (55.11); H, 7.81 (7.89); N, 4.93 (4.98). IR (cm^{-1}): (N–H, O–H) 3396 w, (C–H) 2957 m, 2870 m, (C=O) 1598 m, (C–N) 1551 m, (C–C Ar) 1451 s, (NBu$_4$$^+$) 883 w, 739 w, $_v$(Pt–Cl) 335 s. ^{1}H RMN (CDCl$_3$, 300 MHz, 233 K): 12.43 (br s, 2H, H$_2$O), 7.64 (d, 4H, *o*-C$_6$*H*$_4$C(CH$_3$)$_3$, $^{3}J_{\text{Ho-Hm}}$ = 8.5), 7.41 (d, 4H, *m*-C$_6$*H*$_4$C(CH$_3$)$_3$, $^{3}J_{\text{Hm-Ho/F}}$ = 8.5), 5.91 (br s, 2H, NHCO), 3.32, 1.63, 1.42, 0.97 (36H, (NBu$_4$$^+$)), 1.35 (s, 18H, ^{t}Bu). ^{13}C-NMR (APT, CD$_2$Cl$_2$, 75 MHz, 298 K): 177.1 (−), 153.5 (−), 135.8 (−), 126.5 (+), 125.3 (+), 59.1 (−), 35.0 (−), 31.3 (+), 24.4 (−), 20.1 (−), 13.8 (+). MS (MALDI$^+$): [PtCl(NHCOC$_6$H$_4$^{t}Bu)]$^-$ 406.1 *m/z.* Crystalline materials for XRD analysis were obtained by slow diffusion of diethylether into a dichloromethane solution of **2d** at 4 °C.

[NBu$_4$][*trans*-PtCl(NHCOC$_6$H$_3$Me$_2$)$_2$(OH$_2$)] (2e). Anal. Found (Calcd. for C$_{34}$H$_{58}$ClN$_3$O$_3$Pt): C, 51.99 (51.86); H, 7.41 (7.42); N, 5.29 (5.34). IR (cm^{-1}): (N–H) 3535 w, (O–H) 3312 w, (C–H) 2953 m, 2872 m, (C=O, C–N) 1569 s, (C–C Ar) 1483 s, 1455 s, (NBu$_4$$^+$) 882 w, $_v$(Pt–Cl) 342 s. ^{1}H RMN (CDCl$_3$, 300 MHz, 233 K): 12.29 (br s, 2H, H$_2$O), 7.29 (s, 4H, *o*-C$_6$*H*$_3$(CH$_3$)$_2$), 6.98 (s, 2H, *p*-C$_6$*H*$_3$(CH$_3$)$_2$), 5.93 (s, 2H, NHCO), 3.41, 1,60, 1.35, 0.88 (t, 36H, (NBu$_4$$^+$)), 2.28 (s, 12H, C$_6H_3$(C*H*$_3$)$_2$). ^{13}C-NMR (APT, CD$_2Cl_2$, 75 MHz, 298 K): 177.2 (−), 138.2 (−), 137.5 (−), 131.3 (+), 124.2 (+), 58.6 (−), 24.1 (−), 21.2 (+), 19.7 (−), 13.7 (+). MS (MALDI$^+$): [Pt(NHCOC$_6$H$_3$Me$_2$)$_2$]$^-$ 490.1 *m/z.* Crystalline materials for XRD analysis were obtained by slow diffusion of diethylether into a dichloromethane solution of **2e** at 4 °C.

[NBu$_4$][*trans*-PtCl(NHCOC$_6$H$_2$Me$_3$)$_2$(OH$_2$)] (2f). Anal. Found (Calcd. for C$_{37}$H$_{65}$ClN$_3$O$_3$Pt): C, 53.28 (53.51); H, 8.08 (7.89); N, 5.18 (5.06). IR (cm^{-1}): (N–H, O–H) 3368 w, (C–H) 2959 m, 2873 w, (C=O) 1610 m, (C–N) 1575 s, (C–C Ar) 1456 s, (NBu$_4$$^+$) 876 w, 738 w, $_v$(Pt–Cl) 343 m. ^{1}H RMN (CD$_2$Cl$_2$, 300 MHz, 298 K): 12.13 (br s, 2H, H$_2$O), 6.79 (s, 4H, -C$_6$*H*$_2$(CH$_3$)$_3$), 5.13 (br s, 2H, NHCO), 3.20, 1,62, 1.42, 1.01 (36H, (NBu$_4$$^+$)), 2.34 (s, 12H, *o*-C$_6H_2$*(CH$_3$)$_3$*), 2.25 (s, 6H, *p*-C$_6H_2$*(CH$_3$)$_3$*). ^{13}C-NMR (APT, CD$_2Cl_2$, 75 MHz, 298 K): 180.1 (−), 139.6 (−), 136.5 (−), 133.1 (−), 127.7 (+), 58.8 (−), 23.9 (−), 20.7 (+), 19.7 (−), 19.3 (+), 13.4 (+). MS (ESI$^-$): [PtCl(NHCOC$_6$H$_2$Me$_3$)$_2$(OH$_2$)]$^-$ 572.0 *m/z.*

Synthesis of [NBu$_4$][*trans*-PtCl(NH$_3$)(NHCOPh)$_2$] (3). A solution of **2a** (0.17 g, 0.23 mmol) in CH$_2$Cl$_2$ (2 mL) was prepared over MgSO$_4$ under argon atmosphere in a schlenk tube and cooled down to −30 °C. The argon was evacuated and replaced by an ammonia

Table 1. Amounts of reagents and yields obtained in the syntheses of **2b**–**2f**.

Complex	[PtCl2(NCR)2] [mg]	[PtCl2(NCR)2] [mmol]	NBu4OH-MeOH 1 M [mL]	NBu4OH-MeOH 1 M [mmol]	Yield [mg]	Yield [%]
2b	122	0.32	0.65	0.65	60	28
2c	404	0.79	1.60	1.60	157	26
2d	648	1.22	2.44	2.44	531	53
2e	462	0.87	1.75	1.75	200	29
2f	121	0.22	0.43	0.43	89	51

atmosphere. After 5 h. of stirring the temperature was slowly raised up to RT and the solution was filtered. OEt$_2$ was added causing the precipitation of a white solid that was filtered off, washed with OEt$_2$ (2 mL) and dried under vacuum. Yield: 64 %. Anal. Found (Calcd. for $C_{30}H_{51}ClN_4O_2Pt$): C, 49.47 (49.34); H, 7.02 (7.04); N, 7.70 (7.67). IR (cm^{-1}): (N–H) 3391 w, 3379 w, (C–H) 2955 m, 2872 m, (C=O) 1614 m, (C–N) 1554 m, (C–C Ar.) 1455 m, 1448 s, (NBu$_4$)$^+$ 882 m, 737 m, $_{v}$(Pt–Cl) 307 s. ^{1}H RMN (CD$_2$Cl$_2$, 400 MHz, 298 K): 7.65, 7.32 (10H, Ph), 5.94 (s, 3H, NH$_3$), 5.67 (br s, 2H, NHCO), 3.24, 1,54, 1.30, 0.87 (36H, (NBu$_4$)$^+$). ^{13}C-NMR (APT, CD$_2$Cl$_2$, 100 MHz, 298 K): 175.2 (−), 140.6 (−), 129.6 (+), 128.4 (+), 127.0 (+), 59.3 (−), 24.5 (−), 20.2 (−), 14.0 (+). MS (HRMS$^-$): [PtCl(NHCOPh)$_2$(NH$_3$)]$^-$ 487.1 *m/z.* ^{15}N,^{1}H-HMQC (CD$_2$Cl$_2$, 400 MHz, 233 K): (−63.14, 5.94) (Pt-NH$_3$); (85.15, 5.67) (Pt-NH-C).

Synthesis of [NBu$_4$][*trans*-PtCl(NHCOPh)$_2$(NH$_2$NH$_2$)] (4) To a cold (−30 °C) solution of **2a** (0.20 g, 0.27 mmol) in CH$_2$Cl$_2$ (10 mL), prepared over MgSO$_4$ under argon atmosphere, NH$_2$NH$_2$ (54 µL, 1.1 mmol) was added. After 3 h. of stirring the temperature was slowly raised up to RT, and NH$_2$NH$_2$ was again added (54 µL, 1.1 mmol). After 3 h. of stirring, the suspension was filtered. The resulting solution was concentrated until *ca.* 1 mL and OEt$_2$ (5 mL) was added, causing the precipitation of a white solid that was filtered off, washed with OEt$_2$ (2 mL) and dried under vacuum. Yield: 76 %. Anal. Found (Calcd. for $C_{30}H_{52}ClN_5O_2Pt$): C, 48.46 (48.35); H, 7.01 (7.03); N, 9.50 (9.40). IR (cm^{-1}): (N–H) 3383 w, 3352 w, (C–H) 2959 m, 2873 w, (C=O) 1604 s, (C–N) 1556 s, (C–C Ar.) 1485 m, 1450 s, (NBu$_4$)$^+$ 881 w, 738 w, $_{v}$(Pt–Cl) 308 m. ^{1}H RMN (CD$_2$Cl$_2$, 400 MHz, 298 K): 9.74 (s, 2H, Pt-NH_2NH$_2$, $^2J_{H\text{-}Pt}=80.0$), 7.74, 7.37 (10H, Ph), 5.82 (br s, 2H, NHCO), 3.62 (s, 2H, Pt-NH$_2$NH_2), 3.28, 1.60, 1.36, 0.94 (36H, (NBu$_4$)$^+$). ^{13}C-NMR (APT, CD$_2$Cl$_2$, 100 MHz, 298 K): 175.4 (−), 140.3 (−), 129.7 (+), 128.4 (+), 127.0 (+), 59.2 (−), 24.5 (−), 20.2 (−), 13.9 (+). ^{15}N,^{1}H-HMQC (CD$_2$Cl$_2$, 400 MHz, 233 K): (−18.08, 9.74) (Pt-NH_2-NH$_2$); (87.26, 5.82) (Pt-NH-C); (71.90, 3.62) (Pt-NH$_2$-NH_2) ppm. MS (HRMS$^-$): [PtCl(NHCOPh)$_2$(NH$_2$NH$_2$)]$^-$ 503.1 *m/z.*

Synthesis of [NBu$_4$][*trans*-PtCl(NHCOPh)$_2$(NH$_2$^{t}Bu)] (5a). To a solution of **2a** (0.12 g, 0.16 mmol) in CH$_2$Cl$_2$ (5 mL), prepared with 4 Å molecular sieves and under argon atmosphere, NH$_2$^{t}Bu (35 µL, 0.652 mmol) was added. After 6 h of stirring at RT the mixture was filtered and the resulting solution was concentrated until *ca.* 0.5 mL. Addition of *n*-hexane (4 mL) caused precipitation of a white solid that was filtered off, washed with *n*-hexane (2×3 mL) and dried under vacuum. Yield: 73 %. Anal. Found (Calcd. for $C_{34}H_{59}ClN_4O_2Pt$): C, 51.85 (51.93); H, 7.48 (7.56); N, 7.07 (7.12). IR (cm^{-1}): (N–H) 3401 w, (C–H) 2959 w, 2873 w, (C=O) 1615 m, (C–N) 1557 s, (C–C Ar.) 1451 s, 1433 s, (NBu$_4$$^+$) 887 m, 708 w, $_{v}$(Pt–Cl) 320 m. ^{1}H RMN (CD$_2$Cl$_2$, 400 MHz, 298 K): 8.36 (br s, 2H, Pt-NH$_2$–), 7.71, 7.36 (10H, Ph), 5.62 (br s, 2H, NHCO), 3.49, 1.67, 1.40, 0.93 (36H, (NBu$_4$$^+$)), 1.34 (s, 9H, ^{t}Bu). ^{13}C-NMR (APT, CD$_2$Cl$_2$, 100 MHz, 298 K): 174.9 (−), 141.0 (−), 129.5 (+), 128.3 (+), 127.0 (+), 59.1 (−), 54.2 (−), 29.8 (+), 24.6 (−), 20.2 (−), 14.0 (+). ^{15}N,^{1}H-HMQC (CD$_2$Cl$_2$, 400 MHz, 233 K): (−13.20, 8.36) (Pt-NH$_2$-C); (87.31, 5.62) (Pt-NH-C). MS (HRMS$^-$): [PtCl(NHCOPh)$_2$(NH$_2$^{t}Bu)]$^-$ 543.1 *m/z.*

Synthesis of [NBu$_4$][*trans*-PtCl(NHCOPh)$_2$(NH$_2$C$_6$H$_4$CH$_3$)] (5b). To a solution of **2a** (0.12 g, 0.16 mmol) in CH$_2$Cl$_2$ (5 mL) prepared with 4 A molecular sieves and under argon atmosphere, NH$_2$C$_6$H$_4$CH$_3$ (0.069 mg, 0.64 mmol) was added. After 17 h of stirring the mixture was filtered and the resulting solution was concentrated until *ca.* 0.5 mL. Addition of *n*-hexane (4 mL) caused precipitation of a white solid that was filtered off, washed with *n*-hexane (2×3 mL) and dried under vacuum. Yield: 80 %. Anal. Found (Calcd. for $C_{37}H_{57}ClN_4O_2Pt$): C, 54.07 (54.17); H, 6.95 (7.00); N, 6.80 (6.83). IR (cm^{-1}): (N–H) 3387 w, (C–H) 2956 w, 2871 w, (C=O) 1611 m, (C–N) 1541 m, (C–C Ar) 1514 m, 1436 s, (NBu$_4$$^+$) 887 m, 705 w, $_{v}$(Pt–Cl) 322 m. ^{1}H RMN (CD$_2$Cl$_2$, 400 MHz, 298 K): 10.89 (br s, 2H, Pt-NH$_2$–), 7.80, 7.41 (10H, Ph), 7.24, 7.02 (4H, –C$_6$H$_4$–), 5.75 (br s, 2H, NHCO), 3.40, 1.65, 1.41, 0.94 (36H, (NBu$_4$$^+$)), 2.26 (s, 3H, –CH$_3$). ^{13}C-NMR (APT, CD$_2Cl_2$, 100 MHz, 298 K): 175.5 (−), 143.4 (−), 140.3 (−), 133.7 (−), 130.0 (+), 129.8 (+), 128.4 (+), 127.1 (+), 121.7 (+), 59.20 (−), 24.56 (−), 21.1 (+), 20.2 (−), 14.0 (+). ^{15}N,^{1}H-HMQC (CD$_2$Cl$_2$, 400 MHz, 233 K): (−25.57, 10.89) (Pt-NH$_2$-C); (87.80, 5.75) (Pt-NH-C). ^{195}Pt-NMR (CD$_2$Cl$_2$, 64.5 MHz, 298 K): 98.6. MS (ESI$^-$): [PtCl(NHCOPh)$_2$(NH$_2$C$_6$H$_4$CH$_3$)]$^-$ 578.1 *m/z.* Crystalline materials for XRD analysis were obtained by slow diffusion of *n*-hexane into a dichloromethane solution of **5b** at 4°C.

Synthesis of [NBu$_4$][PtCl$_3$(NHCOPh)$_2$(OH$_2$)] (6a). To a solution of **2a** (0.13 g, 0.18 mmol) in CH$_2$Cl$_2$ (10 mL), 50 mg of Cl$_2$IPh (0.182 mmol) were added. After 30 minutes of stirring, the solution was evaporated to dryness and the residue was treated with a mixture of 1 mL of ^{i}PrOH and 5 mL of OEt$_2$, rendering complex **6a** as a brown solid that was filtered off, washed with 2 mL of OEt$_2$ (3 times) and dried under vacuum. Yield: 70 %. Anal. Found (Calcd. for $C_{30}H_{50}Cl_3N_3O_3Pt$): C, 44.56 (44.92); H, 6.00 (6.28); N, 5.15 (5.24). IR (cm^{-1}): (N–H) 3417 w, (C–H Ar) 2961 w, 2873 w, (C=O) 1612 m, (N=C) 1567 m, (C–C Ar) 1455 s, 1380 w, (NBu$_4$$^+$) 879 w, 738 w, $_{v}$(Pt–Cl) 341 m, 318 m. ^{1}H-RMN (CDCl$_3$, 300 MHz, 298 K): 7.81, 7.41 (10H, Ph), 6.10 (br s, 2H, NHCO), 3.18, 1.55, 1.36, 0.92 (36H, (NBu$_4$$^+$)). MS (ESI$^-$): [PtCl$_3$(NHCOPh)$_2$(OH$_2$)$_2$]$^-$ 577.4 *m/z.*

Synthesis of [NBu$_4$][PtClBr$_2$(NHCOPh)$_2$(OH$_2$)] (6b). To a solution of **2a** (0.21 g, 0.28 mmol) in CH$_2$Cl$_2$ (5 mL), a solution of Br$_2$ in CCl$_4$ (0.25 M, 1.15 mL, 0.174 mmol) was added. After 2 h of stirring, the solution was evaporated to dryness and ^{i}PrOH (3 mL) was added, causing the precipitation of a brown solid that was filtered off, washed with OEt$_2$ (3×2 mL), and dried under vacuum. Yield: 59 %. Anal. Found (Calcd. for $C_{30}H_{50}ClBr_2N_3O_3Pt$): C, 40.52 (40.44); H, 5.68 (5.66); N, 4.61 (4.72). IR (cm^{-1}): (N–H) 3406 w, (C–H Ar.) 2958 w, 2873 w, (C=O) 1606 m, (N=C) 1567 m, (C–C Ar.) 1454 s, 1440 s, 1379 w, (NBu$_4$$^+$) 881 w, 738 w, $_{v}$(Pt–Cl) 318 m. ^{1}H-RMN (CD$_2$Cl$_2$, 300 MHz, 298 K): 7.81, 7.46 (10 H, Ph), 5.88 (br s, 2H, NHCO), 3.13, 1.58, 1.40, 0.98 ((36H, (NBu$_4$$^+$)). ^{13}C-NMR (APT, CD$_2Cl_2$, 75 MHz, 298 K): 177.1 (−), 137.5 (−), 131.4 (+), 128.7 (+), 127.5 (+), 59.4 (−), 24.4 (−), 20.2 (−), 13.9 (+). ^{195}Pt-NMR (CD$_2$Cl$_2$, 64.5 MHz, 298 K): −2238.9. MS (ESI$^-$): [PtClBr$_2$(NHCOPh)$_2$(OH$_2$)]$^-$ 648.6 *m/z.*

Synthesis of [NBu$_4$][PtClI$_2$(NHCOPh)$_2$(H$_2$O)] (6c). To a solution of **2a** (0.12 g, 0.16 mmol) in CH$_2$Cl$_2$ (5 mL), a solution of I$_2$ (0.044 g, 0.174 mmol) in CH$_2$Cl$_2$ (10 mL) was added. After 30 min of stirring the solution was evaporated to dryness and *n*-hexane was added (3 mL), causing the precipitation of a brown solid that was filtered off, washed with *n*-hexane (2×3 mL), and dried under vacuum. Yield: 97 %. Anal. Found (Calcd. for $C_{30}H_{50}ClI_2N_3O_3Pt$): C, 36.78 (36.58); H, 5.20 (5.12); N, 4.31 (4.27). IR (cm^{-1}): (N–H, O–H) 3409 w, (C–H Ar) 2959 m, 2872 w, (C=O) 1606 m, (N–C) 1566 m, (C–C Ar) 1454 s, 1440 s, 1379 d, (NBu$_4$$^+$) 878 w, 736 w, $_{v}$(Pt–Cl) 317 m. ^{1}H-RMN (CD$_2$Cl$_2$, 300 MHz, 298 K): 13.13 (br s, 2H, Pt-OH$_2$), 7.80, 7.47 (10H, Ph), 5.79 (br s, 2H, NHCO), 3.14, 1.61, 1.44, 1.01 (36H, (NBu$_4$$^+$)). MS (ESI$^-$): [PtClI$_2$(NHCOPh)$_2$(OH$_2$)]$^-$ 741.5 *m/z.*

Computational details. Quantum mechanical calculations were performed with the Gaussian 09 package at the DFT/M06 level of theory. The SDD basis set and its ECPs together were used for Pt and I atoms, also including f-type (Pt) or d-type (I) polarization functions. Light atoms (H, C, N, O, F, Cl, and Br) were described with a 6-31G** basis set. See SI for full details and references.

X-ray structure determinations. Crystal growing, data, and full details of the data collection and structure analyses are included in the SI.

Deposition Numbers 2158366 (for **1c**), 2158367 (for **1d**), 2158368 (for **1e**), 2158369 (for **2e**), 2158370 (for **2f**), 2158371 (for **5b**), and 2158372 (for **6c**) contain the supplementary crystallographic data for this paper. These data are provided free of charge by the joint

Cambridge Crystallographic Data Centre and Fachinformationszentrum Karlsruhe Access Structures service www.ccdc.cam.ac.uk/structures.

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Conflict of Interest

The authors declare no conflict of interest.

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[1] a) M. Peyrone, *Ann. Chem. Pharm.* **1844**, *51*, 1–29; b) G. B. Kauffman, *Platinum Met. Rev.* **2010**, *54*, 250–256.
[2] a) A. Werner, *Z. Anorg. Chem.* **1893**, *3*, 267–330; b) A. Werner, *"Neuere Anschauungen auf dem Gebiete der anorganischen Chemie"*, 4th ed.; Vieweg & Sohn: Braunschweig, **1920**; c) G. B. Kauffman, *Platinum Met. Rev.* **1997**, *41*, 34–40.
[3] a) G. B. Kauffman, *Platinum Met. Rev.* **1973**, *17*, 144–148; b) K. V. Yusenko, A. V. Zadesenets, I. A. Baidina, Yu. V. Shubin, D. B. Vasil'chenko, S. V. Korenev, *Zh. Strukt. Khim.* **2006**, *47*, 749–753.
[4] a) L. Chugaev, M. Skanavy-Grigorizeva, *J. Russ. Chem. Soc.* **1915**, *47*, 776; b) L. Chugaev, M. Skanavy-Grigorizeva, A. Posnjak, *Z. Anorg. Allg. Chem.* **1925**, *148*, 37–42; c) G. Rouschias, B. L. Shaw, *J. Chem. Soc. D* **1970**, 183–183; d) G. Rouschias, B. L. Shaw, *J. Chem. Soc. A* **1971**, 2097–2104.
[5] B. Rosenberg, L. Van Camp, T. Krigas, *Nature* **1965**, *205*, 698–699.
[6] a) R. Oun, N. J. Wheate, *Platinum Anticancer Drugs. In Encyclopedia of Metalloproteins* (Eds. R. H. Kretsinger, V. N. Uversky, E. A. Permyakov); Springer, New York, NY; **2013**; b) T. C. Johnstone, K. Suntharalingam, S. J. Lippard, *Chem. Rev.* **2016**, *116*, 3436–3486; c) S. Dilruba, G. V. Kalayda, *Cancer Chemother. Pharmacol.* **2016**, *77*, 1103–1124; d) A. M. F. Phillips, A. J. L. Pombeiro, *Curr. Med. Chem.* **2019**, *26*, 7476–7519; e) M. Ravera, E. Gabano, M. J. McGlinchey, D. Osella, *Dalton Trans.* **2022**, *51*, 2121–2134.
[7] a) J. J. Wilson, S. J. Lippard, *Chem. Rev.* **2014**, *114*, 4470–4495; b) B. Lippert, P. J. Sanz-Miguel, *Coord. Chem. Rev.* **2016**, *327–328*, 333–348.
[8] a) R. A. Michelin, M. Mozzon, R. Bertani, *Coord. Chem. Rev.* **1996**, *147*, 299–338; b) V. Yu. Kukushkin, A. J. L. Pombeiro, *Chem. Rev.* **2002**, *102*, 1771–1802; c) V. Yu. Kukushkin, A. J. L. Pombeiro, *Inorg. Chim. Acta* **2005**, *358*, 1–21.
[9] a) G. Rouschias, G. Wilkinson, *J. Chem. Soc. A* **1968**, 489–496; b) N. Storhoff, H. C. Lewis Jr, *Coord. Chem. Rev.* **1977**, *23*, 1–29; c) N. G. Granik, *Russ. Chem. Rev.* **1983**, *52*, 377–394; d) J. M. Casas, M. H. Chisholm, M. V. Sicilia, W. E. Streib, *Polyhedron* **1991**, *10*, 1573–1578; e) R. Cini, P. A. Caputo, F. P. Intini, G. Natile, *Inorg. Chem.* **1995**, *34*, 1130–1137.
[10] a) J. K. Barton, H. N. Rabinowitz, D. J. Szalda, S. J. Lippard, *J. Am. Chem. Soc.* **1977**, *99*, 2827–2829; b) L. S. Hollis, S. J. Lippard, *J. Am. Chem. Soc.* **1981**, *103*, 1230–1232; c) K. Matsumoto, K. Fuwa, *J. Am. Chem. Soc.* **1982**, *104*, 897–898; d) K. Matsumoto, H. Takahashi, K. Fuwa, *Inorg. Chem.* **1983**, *22*, 4086–4090; e) L. S. Hollis, S. J. Lippard, *J. Am. Chem. Soc.* **1983**, *105*, 3494–3503; f) P. K. Mascharak, I. D. Williams, S. J. Lippard, *J. Am. Chem. Soc.* **1984**, *106*, 6428–6430.
[11] a) K. Sakai, K. Matsumoto, *J. Am. Chem. Soc.* **1989**, *111*, 3074–3075; b) K. Uemura, K. Fakui, K. Yamasaki, K. Matsumoto, *Inorg. Chem.* **2010**, *49*, 7323–7330.
[12] a) M. Coluccia, A. Nassi, F. Loseto, A. Boccarelli, M. A. Mariggiò, D. Giordano, F. P. Intini, P. Caputo, G. Natile, *J. Med. Chem.* **1993**, *36*, 510–512; b) N. Farrell, in *Metal Ions in Biological Systems* Vol. 32 (Eds. A. Siegel, H. Siegel), Marcel Dekker, New York, **1996**, pp. 603–639; c) L. R. Kelland, C. F. J. Barnard, I. G. Evans, B. A. Murrer, B. R. C. Theobald, S. B. Wyer, P. M. Goddard, M. Jones, M. Valenti, A. Bryant, P. M. Rogers, K. R. Harrap, *J. Med. Chem.* **1995**, *38*, 3016–3024; d) M. Coluccia, A. Boccarelli, M. A. Mariggiò, P. A. Caputo, F. Intini, G. Natile, *Chem.-Biol. Interact.* **1995**, *98*, 251–266; e) A. Boccarelli, M. Coluccia, F. P. Intini, G. Natile, D. Locker, M. Leng, *Anti-Cancer Drug Des.* **1999**, *14*, 253–64.
[13] A. Gimeno-Prat, A. Cortés-Sanchón, A. Martín, M. Baya, J. M. Casas, *Dalton Trans.* **2018**, *47*, 16846.
[14] a) T. J. Ahmed, S. M. M. Knapp, D. R. Tyler *Coord. Chem. Rev.* **2011**, *255*, 949–974; b) R. García-Álvarez, J. Francos, E. Tomás-Mendivil, P. Crochet, V. Cadierno, *J. Organomet. Chem.* **2014**, *771*, 93–104; c) Yujie Xia, Huanfeng Jiang, Wanqing Wu, *Eur. J. Org. Chem.* **2021**, 6658–6669; d) D. S. Glueck, *Dalton Trans.* **2021**, *50*, 15953–15960; e) P. Crochet, V. Cadierno, *Eur. J. Inorg. Chem.* **2021**, 3225–3238.
[15] For platinum catalysts, see: a) M. A. Bennett, T. Yoshida, *J. Am. Chem. Soc.* **1973**, *95*, 3030–3031; b) M. A. Bennett, T. Yoshida, *J. Am. Chem. Soc.* **1978**, *100*, 1750–1759; c) C. M. Jensen, W. C. Trogler, *J. Am. Chem. Soc.* **1986**, *108*, 723–729; d) T. Ghaffar, A. W. Parkins, *Tetrahedron Lett.* **1995**, *36*, 8657–8660; e) A. W. Parkins, *Platinum Met. Rev.* **1996**, *40*, 169–174; f) T. Ghaffar, A. W. Parkins, *J. Mol. Catal. A* **2000**, *160*, 249–261; g) C. J. Cobley, M. van den Heuvel, A. Abbadi, J. G. de Vries, *Tetrahedron Lett.* **2000**, *41*, 2467–2470; h) V. Cadierno, *Appl. Sci.* **2015**, *5*, 380–401; i) X. Xing, C. Xu, B. Chen, C. Li, S. C. Virgil, R. H. Grubbs, *J. Am. Chem. Soc.* **2018**, *140*, 17782–17789.
[16] R. Cini, F. P. Fanizzi, F. P. Intini, L. Maresca, G. Natile, *J. Am. Chem. Soc.* **1993**, *115*, 5123–5131.
[17] F. P. Intini, M. Lanfranchi, G. Natile, C. Pacifico, A. Tiripicchio, *Inorg. Chem.* **1996**, *35*, 1715–1717.
[18] a) C. E. Skinner, M. M. Jones, *J. Am. Chem. Soc.* **1969**, *91*, 4405–4408; b) J. A. M. van Beek, G. van Koten, I. C. M. Wehman-Ooyevaar, W. J. J. Smeets, P. van der Sluis, A. L. Spek, *J. Chem. Soc. Dalton Trans.* **1991**, 883–893; c) M. Safa, R. J. Puddephatt, *J. Organomet. Chem.* **2013**, *724*, 7–16; d) S. M. Nabavizadeh, H. Amini, M. Rashidi, K. R. Pellarin, M. S. McCready, B. F. T. Cooper, R. J. Puddephatt, *J. Organomet. Chem.* **2012**, *713*, 60–67.
[19] T. Uchiyama, Y. Toshiyasu, Y. Nakamura, T. Miwa, S. Kawaguchi, *Bull. Chem. Soc. Jpn.* **1981**, *54*, 181–185.