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Formation of L-Threonic Acid from L-Ascorbic Acid Oxidative Ring Opening and its Coordination to Pt^{II}: X-ray Crystal Structures of [Pt(threonato-*O*,*O*′)-$(PPh_3)_2$] and [Pt(oxalato)$(PPh_3)_2$]

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The oxidative ring opening of L-ascorbic acid was obtained in three steps giving oxalic and L-threonic acid. The reactions of these acids with the carbonate complex [$Pt(CO)_3(PPh_3)_2$] yielded two Pt^{II} chelates, [Pt(oxalato)$(PPh_3)_2$] and the new complex [Pt(threonato-*O*,*O*′)$(PPh_3)_2$], respectively. The X-ray crystal structures of both complexes were determined.

Introduction

The discovery and development of platinum-based drugs has been one of the greatest achievements of cancer chemotherapy in the past century. Cisplatin and carboplatin are still first-choice drugs for the treatment of testis solid malignancies, and the mechanism of their pharmacological action on the primary target, cellular DNA, as well as their distribution and elimination pathways have been well documented.

However, the therapeutic efficacy of cisplatin is limited by the development of drug resistance and by major side effects like nephrotoxicity. Several attempts to overcome these negative aspects have led to the production of many cisplatin analogues. Less explored has been another problem related to cisplatin distribution in the human body; in fact, cisplatin is unable to reach specific body parts such as the lungs, colorectal region and central nervous system, and so it is ineffective on tumoral pathologies developing there. The design of new platinum complexes with suitable ligands able to overcome this drawback will allow an extension of the well-known platinum drugs' efficacy to other types of cancer, and therefore it is a very attractive goal for research.[1]

A few years ago it was reported that L-ascorbic acid, a vitamin provided with specific transporters across the blood-brain barrier, can be exploited as a carrier for drugs for CNS pathologies.[2] We considered the possibility of extending this strategy to platinum drugs, and therefore we are currently investigating the coordination modes to platinum of L-ascorbic acid itself, of its oxidated form (dehydroascorbic acid, DHA) and of some derivatives, like *O*-protected forms.[3]

In order to prepare a L-ascorbic acid derivative bearing the 2-OH hydroxy group as the only available oxygen donor, we attempted to obtain the 3-*O*-methylated form of 5,6-*O*-isopropylidene L-ascorbic acid through a modified version of the route reported by Wimalasena, which provided for the use of MeI in basic dmso.[4] In order to avoid the use of toxic high-boiling dmso, we tried to replace it with methanol. This change of solvent drove the reaction to a different, unexpected result. Because of the continuous interest in the chemistry and application of L-ascorbic acid, we decided to explore this process and estimate the value of the obtained products.

Results and Discussion

While trying to prepare the 3-OMe derivative of L-ascorbic acid, we observed that the reaction of **1**, a protected form of L-ascorbic acid, with K_2CO_3 and MeI in MeOH (see Experimental Section) gave a product the ^{1}H NMR spectrum of which shows the presence of a signal in the range of OMe groups. The spectrum, however, does not correlate with those reported[4] for 2- and/or 3-OCH_3 derivatives.

After addition of HCl, the ^{1}H NMR spectroscopic analysis shows the disappearance of both the *O*-isopropylidene and the OMe groups. At this stage, the addition of [$Pt(CO)_3$-$(PPh_3)_2$] gives a single product which was characterised by NMR spectroscopy and X-ray crystal structure analysis as [Pt(L-threonato-*O*,*O*′)$(PPh_3)_2$].

It is known that L-ascorbic acid is rapidly attacked by gaseous oxygen in aqueous alkaline solution, but its reducing properties are less pronounced in alcohol solution.[5] It

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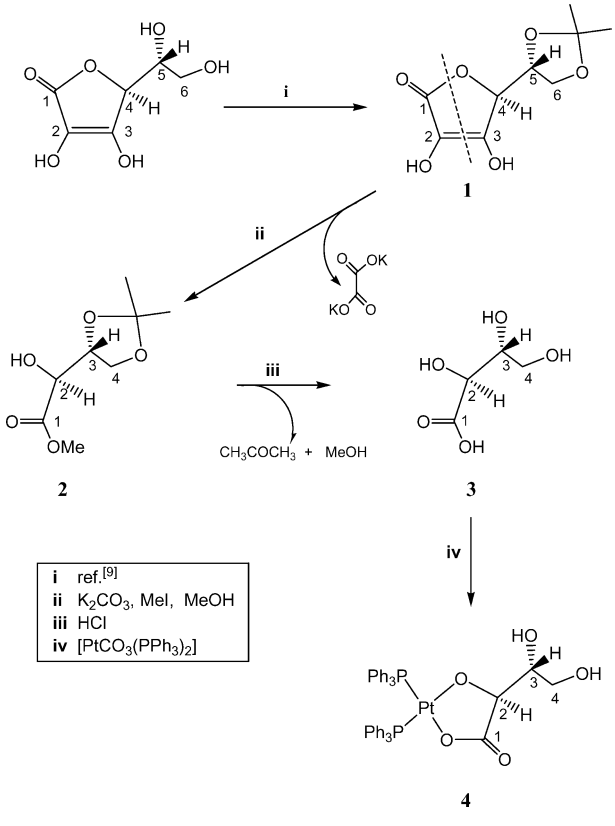
has also been observed that the subsequent hydrolytic opening of the lactone ring produces 2,3-diketogulonic acid, whose further oxidative degradation to oxalic and L-threonic acids seems to require a stronger oxidant than atmospheric molecular oxygen such as aqueous H_2O_2,[6] NaIO,[5] or $KMnO_4$.[7] Other authors attributed a similar ring-opening process to a catalytic involvement of a metal ion.[8]

Anderson reported that threonate complexes were never isolated in the reactions of platinum–phosphane precursors with ascorbate, and even the direct reaction of $[Pt(NO_3)_2(dppm)]$ with calcium threonate gave $[Pt(C_2O_4)(dppm)]$ as the only platinum-containing product.[8a] Under our conditions, the threonate complex is invariably formed and, once isolated, it is very stable in dichloromethane.

We investigated the mechanism of the formation of **4** in order to understand if the ring opening is induced by platinum or if it takes place before the addition of the metal. First, we identified the products of every step of the reaction characterising them by spectroscopic techniques. Thus we found that the treatment of **1** with K_2CO_3 and MeI in MeOH yielded a product that, after extraction with H_2O and AcOEt, was recovered from the organic phase and identified as methyl 3,4-*O*-isopropylidenethreonate (**2**) (Scheme 1).



Scheme 1.

The complete characterisation of **2** (see Experimental Section) has never been reported before. In the ^1H NMR spectrum, the positions of OMe (a singlet at δ = 3.86 ppm) and of 3-H (a triplet of doublets at 4.42 ppm) allow **2** to be easily distinguished from 3-*O*-methyl-5,6-*O*-isopropylidene-L-ascorbic acid (3-OMe singlet at 4.18 ppm, 4-H doublet at 4.5 ppm) and 2-*O*-methyl-5,6-*O*-isopropylidene-L-ascorbic acid (2-OMe singlet at 3.87 ppm, 4-H doublet at 4.71 ppm).[4] The ^{13}C NMR spectrum shows signals of only eight C atoms instead of the expected ten, showing that two carbons have been lost.

The identification of **2** demonstrates that the oxidative ring opening is independent of the presence of platinum and precedes its addition. The process must therefore be ascribed merely to the basicity of K_2CO_3 in MeOH.

The synthesis of 3,4-*O*-isopropylidene-L-threonate from 5,6-*O*-isopropylidene-L-ascorbic acid has been described,[10] as has been the preparation of ethyl (2*R*,3*R*)-3,4-*O*-isopropylidene-2,3,4-trihydroxybutanoate from D-isoascorbic acid,[11] but both reported processes require more drastic conditions (30% H_2O_2).

In step iii, the treatment of **2** with aqueous HCl in methanol first hydrolysed the 3,4-*O*-isopropylidene group and then the Me ester group to give **3**, in two distinct steps, as shown by monitoring the reaction by ^1H NMR spectroscopy. Finally, the addition of $[Pt(CO)_3(PPh_3)_2]$ allowed us to isolate complex **4**.

The ^{31}P NMR spectrum of **4** shows two doublets with satellites at 11.91 ppm (3891 Hz) and 8.73 ppm (3376 Hz) due to two phosphorus atoms with different O-donors in the *trans* positions. Comparing the $^1J_{Pt,P}$ value with the value for phosphorus *trans* to a carboxylate group, for example, 3770 Hz for $[Pt(oxalato)(PPh_3)_2]$[12] and 3300–3500 Hz for $PPh_3(diolato)Pt$,[3] we assign the signal at 11.91 ppm to the phosphorus *trans* to the carboxylate group.

The ^{195}Pt NMR spectrum of **4** in CD_2Cl_2 shows one signal: a doublet of doublets with satellites at –2449.7 ppm due to the couplings with two nonequivalent phosphorus atoms ($^1J_{Pt,P}$ = 3871 and 3354 Hz).

An ORTEP[13] view of compound **4** is shown in Figure 1. Selected bond lengths and angles are given in Table 1. The

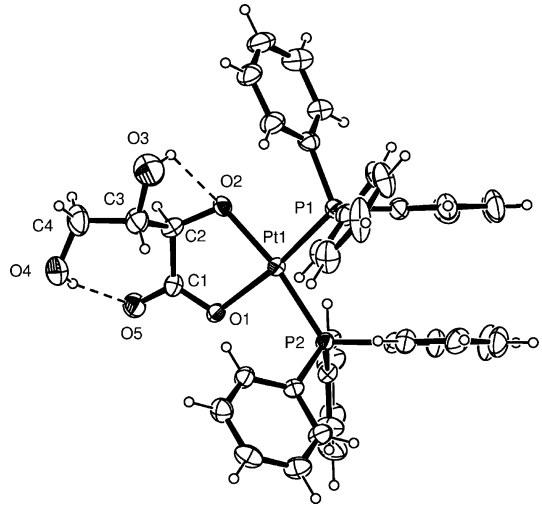


Figure 1. ORTEP[13] view of the complex **4** showing the thermal ellipsoids at 30% probability level.

coordination around Pt1 is nearly square planar with the Pt1 atom displaced from the mean plane passing through the basal atoms P1, P2, O1 and O2 by 0.0155(2) Å. The conformation of the coordination ring Pt1–O1–C1–C2–O2 is envelope E_5. The coordinated threonate ligand adopts a closed conformation owing to the formation of two intramolecular O4–H···O5 and O3–H···O2 hydrogen bonds (Table 1).

Table 1. Selected bond lengths [Å] and angles [°] for compound **4**.

Lengths			
Pt1–P1	2.231(2)	Pt1–P2	2.256(2)
Pt1–O1	2.105(4)	Pt1–O2	2.064(5)
C1–O1	1.285(8)	C1–O5	1.228(8)
C1–C2	1.519(10)	C2–C3	1.538(11)
C2–O2	1.399(8)	C3–O3	1.424(13)
C3–C4	1.522(12)	C4–O5	1.410(13)
Angles			
P1–Pt1–P2	99.41(7)	P1–Pt1–O2	90.4(1)
P1–Pt1–O1	172.6(1)	P2–Pt1–O2	170.2(1)
P2–Pt1–O1	87.8(1)	O1–Pt1–O2	82.3(2)
Pt1–O2–C2	110.0(4)	Pt1–O1–C1	111.2(4)
O1–C1–C2	119.2(6)	O2–C2–C1	114.4(6)
Hydrogen bonds			
O3–H3	0.82	O4–H4	0.82
O3···O2	2.556(9)	O4···O5	2.669(9)
H3···O2	2.11	H4···O5	1.90
O3–H3···O2	114	O4–H4···O5	154

To the best of our knowledge, complex **4** is the first isolated Pt complex of L-threonic acid. It presents a PtOCCOO five-membered ring analogous to that found in the clinically applied anticancer drug nedaplatin[14] (Figure 2) and, because of some formal analogy with L-ascorbic acid (Figure 2), could bind to specific ascorbate transporters.

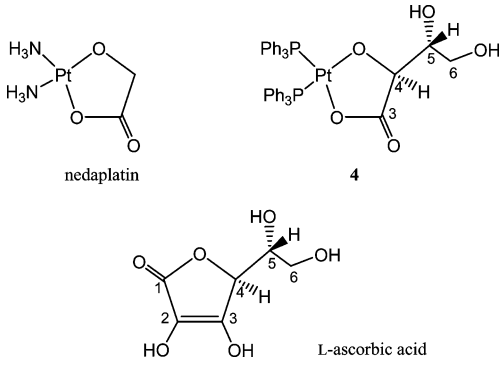


Figure 2. Comparison of complex **4** with nedaplatin and L-ascorbic acid structures.

The binding of ascorbic acid to its transporter, known as SVCT2,[15] seems to occur on the OH(2)C=COH(3) side of the ascorbic acid molecule,[16] but to the best of our knowledge it is not known if both functional groups are essential for bond formation. If π electrons and oxygen atoms involved in hydrogen bonding are needed, complex **4** should reasonably manage to bind to the transporter.

Moreover, it is worthwhile mentioning that the oxidised form of ascorbic acid, dehydroascorbic acid, can cross the blood-brain barrier using other less specific transporters.[17] The reduced (aa) and oxidised (DHA) forms of ascorbic acid are in equilibrium in the body.

Considering the overall pathway in Scheme 1 (from L-ascorbic acid to complex **4**), step i (O5–O6 protection), the addition of MeI and the successive treatment with HCl appear redundant for the process. We then performed some experiments in order to check if L-threonic acid **3** can be produced directly from L-ascorbic acid.

First we tried to treat L-ascorbic acid itself with K_2CO_3 in MeOH, without addition of MeI. We found that starting from unprotected L-ascorbic acid, any further reaction is prevented by the immediate precipitation of potassium ascorbate.

The treatment of 5,6-*O*-isopropylidene-L-ascorbic acid (**1**) with K_2CO_3 in MeOH, without addition of MeI, after the same reaction time (six hours) gave a mixture where unreacted **1** was the most abundant component, and the same result was obtained over a prolonged time period (20 hours). The reaction was completed after three days (72 hours) giving **2** plus minor quantities of unidentified products. Under these conditions, the esterification agent of threonic acid is methanol.

Finally we treated **1** with $[Pt(CO)_3(PPh_3)_2]$ in MeOH to see if complex **4** could be produced in a single step with the carbonate acting as a base, but the ^{31}P NMR spectroscopic observation found that the Pt precursor was unchanged after two days.

In order to confirm the reaction path depicted in Scheme 1, it was necessary to provide experimental evidence that step ii occurred with loss of oxalic acid. For this reason, the overall process was repeated with exclusion of water (no aqueous extraction of **2** for purification).

In this case, the final addition of $[Pt(CO)_3(PPh_3)_2]$ to a CH_2Cl_2 solution of unpurified ligand gave a mixture of complex **4** and of the known[12] complex [Pt(oxalato)-$(PPh_3)_2$], **5** that was obtained in crystalline form after slow evaporation of the solution. The crystal structure of this known complex is reported here for the first time.

An ORTEP[13] view of compound **5** is shown in Figure 3. Selected bond lengths and angles are reported in Table 2. The coordination around Pt1 is distorted square planar with the Pt1 atom displaced from the mean plane passing through the basal atoms P1, P2, O1 and O2 by 0.0265(1) Å. The coordination ring Pt1–O1–C1–C2–O2 is slightly puckered and assumes a mixed twisted/envelope $^2T_1/^2E$ conformation. The water molecule forms two asymmetric hydrogen bonds with the noncoordinated O3 and O4 oxalate oxygen atoms. The shorter contact, O4···O1w 2.768(13) Å, seems to induce a polarisation of the C1–O4 bond causing an extended π-conjugation on the O1–C1–O4 moiety as shown by the almost equivalent C1–O1 and C1–O4 bond lengths of 1.267(8) and 1.241(9) Å, respectively. Accordingly, the longer contact, O3···O1w 3.001(13) Å, does not produce a significant delocalisation on the related carboxylate O2–C2–O3 group where the C2–O2 and C2–O3 bonds exhibit distances of 1.294(7) and 1.227(7) Å, respectively. The asymmetry found in this oxalate anion was not ob-

served in other similar structures of square-planar platinum–oxalato complexes where the oxalate group is not involved in strong intermolecular interactions.[8,18]

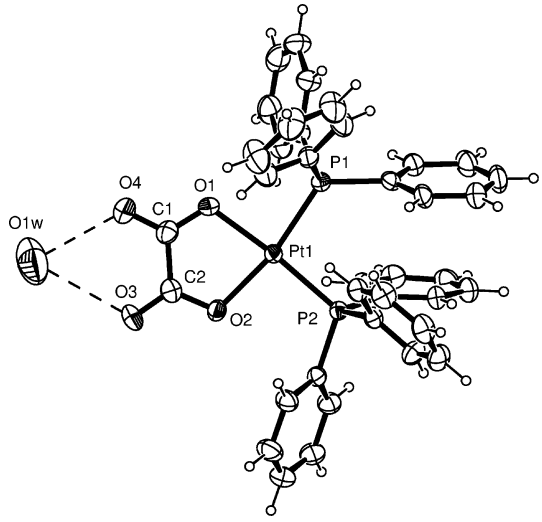


Figure 3. ORTEP[13] view of the hydrated complex **5** showing the thermal ellipsoids at 30% probability level.

Table 2. Selected bond lengths [Å] and angles [°] for compound **5**.

Lengths			
Pt1–P1	2.251(2)	Pt1–P2	2.243(1)
Pt1–O1	2.076(4)	Pt1–O2	2.080(4)
C1–O1	1.267(8)	C2–O2	1.294(7)
C1–O4	1.241(9)	C2–O3	1.227(7)
C1–C2	1.516(9)		
Angles			
P1–Pt1–P2	97.72(5)	P1–Pt1–O1	87.6(1)
P1–Pt1–O2	167.8(1)	P2–Pt1–O1	174.2(1)
P2–Pt1–O2	93.8(1)	O1–Pt1–O2	81.1(2)
Pt1–O1–C1	112.0(4)	Pt1–O2–C2	111.2(4)
Hydrogen bonds			
O3···O1w	3.001(13)	O4···O1w	2.768(13)

Conclusion

The process described in Scheme 1, starting from **1**, is different to the known oxidative degradation of L-ascorbic acid; in fact, it was reported that this latter process required either a stronger oxidant than air for the oxidation of L-ascorbic acid to DHA[5–7] or a metallic catalyst for further degradation.[8] The process we observed from **1** to **2** was simply caused by atmospheric molecular oxygen in a basic solution and did not involve metallic catalysis. It occurred both in the presence and without added MeI, although the methylation step seemed to favour the reaction and to drive it faster towards the formation of **2**.

This reaction, which we studied after its serendipitous finding, could be exploited to obtain L-threonic acid, its 3,4-*O*-isopropylidene derivative and its methyl ester derivative from ascorbate.

The potential of platinum complexes of threonic acid and its derivatives as anticancer drugs, as well as their ability to bind to ascorbate or dihydroascorbate transporters will be explored.

Experimental Section

General: 5,6-*O*-Isopropylidene-L-ascorbic acid (**1**)[9] and $[Pt(CO)_3(PPh_3)_2]$[19] were prepared as reported. All other chemicals and solvents were used as purchased (reagent grade). Elemental analyses (C,H,N) were performed using a Carlo–Erba instrument model EA1110. FTIR spectra were recorded with a Bruker Vertex 70 FTIR instrument (4000–300 cm^{-1}). NMR spectra were recorded with a Bruker 200 AM (^1H at 200 MHz, ^{13}C at 50.29 MHz, ^{31}P at 81.15 MHz) or a Varian 300 NMR spectrometer (^1H at 300 MHz, ^{13}C at 75.43 MHz, ^{31}P at 121.44 MHz) or a Varian 400 NMR spectrometer (^1H at 400 MHz, ^{195}Pt NMR at 85.67 MHz). Peak positions are relative to tetramethylsilane and were calibrated against the residual solvent resonance (^1H, ^{13}C), measured relative to external 85% H_3PO_4 with downfield values taken as positive (^{31}P) or measured relative to external $PtCl_4^{2-}$ (^{195}Pt). The ESI spectrum of **2** was acquired using a Micromass ZMD 2000 instrument.

Methyl 3,4-*O*-Isopropylidenethreonate (2): A solution of **1** (500 mg, 2.315 mmol) and 1.2 equiv. of K_2CO_3 (385 mg, 2.77 mmol) in MeOH (15 mL) was stirred for 20 min at room temp. Methyl iodide (395 mg, 173 μL, 2.78 mmol) was then added dropwise, and the solution was vigorously stirred for 6 h at room temp. The solvent was removed under reduced pressure, and the solid residue was extracted with ethyl acetate and water. The organic layer was dried with anhydrous Na_2SO_4, and the solvent removed under reduced pressure giving pure **2** (150 mg, 0.79 mmol, 34% yield). $C_8H_{14}O_5$ (190): calcd. C 50.52, H 7.37; found C 50.50, H 7.36. ^1H NMR (300 MHz, $CDCl_3$, 25 °C): δ = 4.42 (td, $^3J_{H,H}$ = 7 Hz, $^3J_{H,H}$ = 2.5 Hz, 1 H, 3-H), 4.16 (d, $^3J_{H,H}$ = 2.5 Hz, 1 H, 2-H), 4.12 (dd, $^2J_{H,H}$ = 8.5 Hz, $^3J_{H,H}$ = 7 Hz, 1 H, 4-H), 4.04 (dd, $^2J_{H,H}$ = 8.5 Hz, $^3J_{H,H}$ = 7 Hz, 1 H, 4′-H), 3.86 (s, 3 H, 5-H), 1.47 (s, 3 H, 7-H), 1.38 (s, 3 H, 7′-H) ppm. ^{13}C NMR (75.43 MHz, CD_3OD, 25 °C): δ = 173.8 (C-1), 110.8 (C-6), 78.0 (C-3), 71.7 (C-4), 66.4 (C-2), 52.6 (C-5), 26.4 and 25.5 (C-7 and C-7′) ppm. ESI-MS+: *m/z* (%) = 403.4 (2MW + Na^+), 254.3, 231.3, 213.3 (MW + Na^+).

L-Threonic Acid (3): HCl (2 N, 4 mL, 8 mmol) was added to a solution of **2** (210 mg, 1.1 mmol) in MeOH/thf (1:1, 10 mL), and the mixture was stirred for 1 h at 50 °C. The solvents were removed under vacuum, and the solid residue was then extracted with ethyl acetate and water. The water layer was taken to dryness under reduced pressure giving **3** (120 mg, 0.88 mmol, 80% yield). $C_4H_8O_5$ (136): calcd. C 35.29, H 5.92; found C 35.30, H 5.97. ^1H NMR (400 MHz, CD_3OD, 25 °C): δ = 4.29 (d, $^3J_{H,H}$ = 2.4 Hz, 1 H, 2-H), 3.93 (td, $^2J_{H,H}$ = 7 Hz, $^3J_{H,H}$ = 2.4 Hz, 1 H, 3-H), 3.64 (dd, $^2J_{H,H}$ = 11 Hz, $^3J_{H,H}$ = 7 Hz, 1 H, 4-H), 3.57 (dd, $^2J_{H,H}$ = 11 Hz, $^3J_{H,H}$ = 7 Hz, 1 H, 4′-H) ppm. ^{13}C NMR (50.29 MHz, CD_3OD, 25 °C): δ = 175.2 (C-1), 74.0 (C-3), 72.2 (C-4), 63.4 (C-2) ppm.

Platinum(II) Complex 4: The carbonate complex $[Pt(CO)_3(PPh_3)_2]$ (380 mg, 0.48 mmol) was dissolved in dichloromethane saturated with water (20 mL), and **3** (66 mg, 0.48 mmol) was added. The mixture was stirred overnight. ^{31}P NMR spectroscopic analysis of a solution aliquot showed the complete formation of **4**. The solution was dried with anhydrous Na_2SO_4, and the solvent removed under reduced pressure leaving **4** as a white solid (360 mg, 0.42 mmol, yield 87.5%). Recrystallisation from dichloromethane/acetone (1:2) gave crystals suitable for X-ray diffraction analysis. $C_{40}H_{38}O_5P_2Pt$

(855): calcd. C 56.14, H 4.48; found C 55.91, H 4.05. ^{1}H NMR COSY (400 MHz, $CDCl_3$, 25 °C): δ = 7.6–7.1 (m, 30 H, Ph), 4.46 (ddd with satellites, $^3J_{H2,H3}$ = 4.5 Hz, $^4J_{H2,Pcis}$ = 5 Hz, $^4J_{H2,Ptrans}$ = 1 Hz, $^3J_{H2,Pt}$ = 33 Hz, 1 H, 2-H), 3.71 (pseudo-quint, $^3J_{H3,H4}$ = 5 Hz, $^3J_{H3,OH}$ = 5.3 Hz, $^3J_{H3,H2}$ = 4.5 Hz, 1 H, 3-H), 3.62 (dd, $^2J_{H4,H3}$ = 5 Hz, $^3J_{H4,OH}$ = 6 Hz, 1 H, 4-H), 3.61 (dd, $^2J_{H4',H3}$ = 5 Hz, $^3J_{H4',OH}$ = 6 Hz, 1 H, 4′-H), 3.49 (t, $^3J_{OH,H4}$ = 6 Hz, 1 H, OH), 3.20 (d, $^3J_{OH,H3}$ = 5.3 Hz, 1 H, OH) ppm. ^{13}C NMR (50.29 MHz, CD_3OD, 25 °C): δ = 192.2 (C-1),[20] 135–128 (Ph), 81.7 (C-3), 73.9 (C-4), 66.6 (C-2) ppm. ^{31}P NMR (81.15 MHz, CD_2Cl_2, 25 °C): δ = 11.91 ($^1J_{Pt,P}$ = 3891 Hz, $^2J_{P,P}$ = 24.8 Hz), 8.73 ($^1J_{Pt,P}$ = 3376 Hz, $^2J_{P,P}$ = 24.8 Hz) ppm. ^{195}Pt NMR (85.67 MHz, CD_2Cl_2, 25 °C): δ = –2449.7 ($^1J_{Pt,P}$ = 3871, 3354 Hz) ppm.

Platinum(II) Complex 5: This complex was identified by comparing the ^{31}P NMR spectroscopic data with the reported data:[12] ^{31}P NMR (81.15 MHz, $CDCl_3$, 25 °C): δ = 8.2 ($^1J_{Pt,P}$ = 3780 Hz). Crystals suitable for X-ray crystal structure determination spontaneously separated by slow evaporation of a CH_2Cl_2 solution containing a mixture of **4** and **5** as shown by ^{31}P NMR spectroscopic analysis.

Crystal Structure Determinations: The crystal data of compounds **4** and **5** were collected using a Nonius Kappa CCD diffractometer with graphite-monochromated Mo-K_α radiation. The data sets were integrated with the Denzo-SMN package[21] and corrected for Lorentz, polarisation and absorption effects[22] (SORTAV). The structures were solved by direct methods[23] (SIR97) and refined using full-matrix least-squares with all non-hydrogen atoms anisotropically and hydrogen atoms included on calculated positions, riding on their carrier atoms. In compound **5** the hydrogen atoms of the water molecule, which displays some disorder, could not be determined. All calculations were performed using SHELXL-97[24] and PARST[25] implemented in WINGX[26] system of programs. The crystal data are given in Table 3.

Table 3. Crystallographic data.

Compound	**4**	**5**
Formula	$C_{40}H_{36}O_5P_2Pt$	$C_{38}H_{30}O_4P_2Pt{\cdot}H_2O$
Formula mass	853.72	825.67
Space group	$P2_12_12_1$	Pc
Crystal system	orthorhombic	monoclinic
a [Å]	10.2250(2)	9.0170(2)
b [Å]	14.4198(3)	10.7581(2)
c [Å]	24.1770(5)	17.9240(3)
β [°]	90	105.184(1)
V [Å^3]	3564.7(1)	1678.03(6)
Z	4	2
T [K]	295	295
D_c [g cm^{-3}]	1.591	1.634
F(000)	1696	816
μ(Mo-K_α) [cm^{-1}]	40.69	43.19
Measured reflections	16713	16826
Unique reflections	8487	6712
R_{int}	0.0512	0.0385
Obsd. refl. [$I \geq 2\sigma(I)$]	7277	6231
$\theta_{min.} - \theta_{max.}$ [°]	3.52–28.00	3.02–27.87
hkl ranges	–10,13; –15,19; –31,31	–11,11; –14,13; –23,20
$R(F^2)$ (obsd. refl.)	0.0437	0.0264
$wR(F^2)$ (all refl.)	0.0942	0.0649
Number of variables	433	415
Goodness-of-fit	1.054	1.050
Flack parameter	–0.018(8)	0.005(6)
$\Delta\rho_{max}$; $\Delta\rho_{min}$ [e Å^{-3}]	0.79; –1.79	1.17; –1.42

CCDC-665591 and -665592 contain the supplementary crystallographic data (excluding structure factors) for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.

Acknowledgments

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