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Synthesis of platinum(II) complexes of thymidine and 1-methylthymine (1-MeThy); crystal structure of *cis*-[PtCl(1-MeThy)(PPh_3)$_2$]

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Received 22nd February 1999, Accepted 20th April 1999

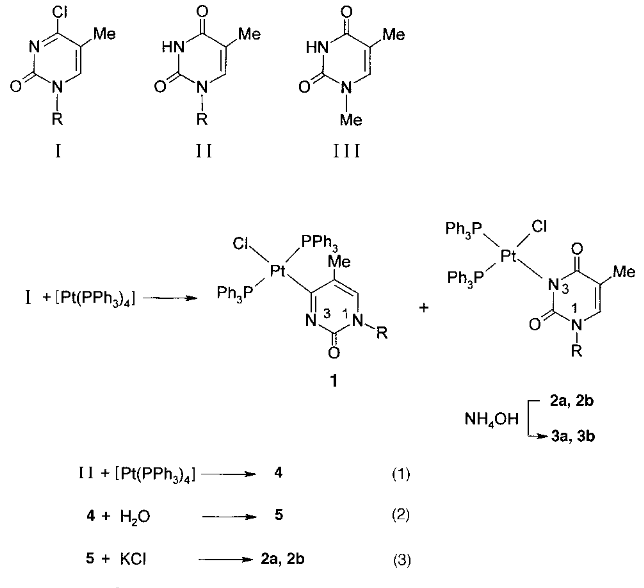
The reaction of 3′,5′-di-*O*-acetylthymidine with [Pt(PPh_3)$_4$] and KCl yielded a platinum(II) complex where the platinum is co-ordinated to the nucleobase through the N3 atom. In a similar reaction 1-methylthymine (1-MeThy) furnished the complex *cis*-[PtCl(1-MeThy)(PPh_3)$_2$], whose structure was determined by spectroscopic data and single crystal X-ray diffraction. When 1-MeThy was treated with [Pt(PPh_3)$_4$] in the absence of chloride ions the complex *trans*-[Pt(OH)(1-MeThy)(PPh_3)$_2$] was obtained.

Introduction

Platinum compounds, particularly *cis*-diamminedichloroplatinum(II) (cisplatin or *cis*-DDP) and several related derivatives, show important cytostatic effects and are clinically used in the treatment of tumour diseases.[1] Their biological activity is related to the ability to form covalent adducts with adjacent guanine bases in DNA.[2] The synthesis of a plethora of different platinum nucleobase or nucleoside complexes has largely contributed to clarifying the mechanism of these drugs. Some toxicological side-effects of cisplatin and the drug resistance developed by some tumours further stimulated research towards the synthesis of new platinum derivatives.

To the best of our knowledge, reported studies on the platination of nucleobases have been carried out using exclusively complexes of Pt^{II} or Pt^{IV}[3] as the starting material. In this framework we have investigated the reactivity of tetrakis(triphenylphosphine)platinum(0) [Pt(PPh_3)$_4$] towards thymine or related nucleosides. This complex was chosen as a substrate by considering that some phosphines and a certain number of arylphosphine complexes have been found to be potent cytotoxic agents against tumour cells in culture or *in vivo*.[4]

In a previous paper[5] we have described the synthesis of complex **1**, which is characterized by the rare σ bond between Pt^{II} and C4 of the thymine base. This complex was obtained by reaction of [Pt(PPh_3)$_4$] with 3′,5′-di-*O*-acetyl-4-chlorothymidine **I** (Scheme 1) which proceeds by an oxidative addition mechanism. A careful analysis of this reaction showed that, together with **1** (85% yield), a minor product **2** (5–7% yield) was formed when equimolecular quantities of [Pt(PPh_3)$_4$] and **I** were refluxed under a nitrogen atmosphere in toluene for 2 h. Product **2** presented the well documented, for pyrimidine nucleobases, Pt^{II}–N3 co-ordination bond,[6] the formation of which was not immediately explainable in our reaction system. In fact, as reported,[6c,7] the N3 platination of thymine or uracil residues can easily be achieved only starting from their N3 deprotonated forms by reaction with appropriate platinum(II) complexes.



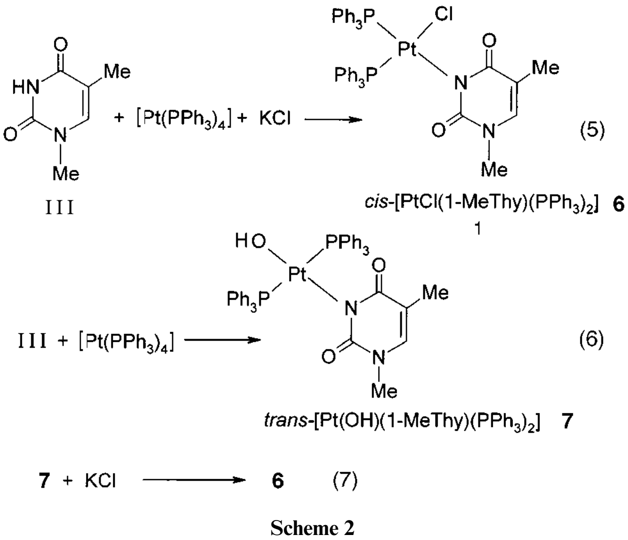
Scheme 1 R = 3,5-Di-*O*-acetyl-2-deoxy-β-D-ribofuranosyl except in **3a**,**3b** where it is 2-deoxy-β-D-ribofuranosyl.

Aiming at explaining the unexpected formation of complex **2** the reaction was reinvestigated. Herein we describe the results of our study which disclosed an alternative, straightforward route for the preparation of **2** in high yield. The structure of this complex has been assigned on the basis of its ^1H, ^{31}P and ^{13}C NMR, IR and FAB MS data, as well as on single crystal X-ray diffraction studies carried out on the related complex *cis*-[PtCl(1-MeThy)(PPh_3)$_2$] (1-MeThy = 1-methylthyminate).

Results and discussion

By monitoring the reaction between **I** and [Pt(PPh_3)$_4$] by TLC analysis, small amounts of 3′,5′-di-*O*-acetylthymidine **II** were detected, which disappeared in the final mixture. This suggested a possible intervention of **II**, obtained by an undesired hydrolysis of the very reactive 4-chloro derivative **I**, in the formation of complex **2**. So we hypothesized an oxidative addition of the imidic N3 atom of **II** on [Pt(PPh$_3$)$_4$] generating a transient platinum hydride complex **4** [Scheme 1, eqn. (1)]. This reaction mechanism was suggested by the reported reactivity of some zerovalent platinum complexes which reacting with imides generated platinum(II) hydrides.[8] Further reaction of **4** with water (probably due to trace amounts of water), followed by elimination of H$_2$, furnished complex **5** which, by exchange with chloride ions, finally gave **2** [eqns. (2) and (3)]. To confirm this hypothesis we tested the reactivity of [Pt(PPh$_3$)$_4$] towards **II** in the presence of chloride ions. The reaction (4), performed under a nitrogen atmosphere in boiling benzene, gave complex **2** in high yield (80% after purification).

The ^{1}H and ^{13}C NMR spectra of complex **2** showed two signals for each type of observed nucleus, thus indicating the presence of a mixture of two isomeric species (**2a** and **2b** in 45:55 ratio). These isomers separated by HPLC on a silica gel column, are stable as solids but, when dissolved in CHCl$_3$, they interconverted, re-establishing the original mixture in *ca.* 24 h. These results can be explained by assuming restricted rotation around the Pt–N3 bond in complex **2**, inducing a further chirality in the molecule, which, associated with the presence of fixed configurations at the sugar carbons, gives rise to two diastereoisomeric forms.[6a,d,9] For a better comprehension of the structure of **2** we then synthesized a similar complex using 1-methylthymine **III** as pyrimidine ligand, where the hindered rotation around the Pt–N3 bond was expected to generate two enantiomeric complexes. The reaction [Scheme 2, eqn. (5)], performed as described for **2**, led smoothly to complex **6**, recovered after silica gel chromatography in 82% yield. As expected, **6** exhibited only one signal for each observed nucleus in the ^{1}H, ^{31}P and ^{13}C NMR spectra, closely related to the NMR data of **2**. The ^{1}H NMR spectrum of **6** in the presence of a chiral shift reagent confirmed its existence as two enantiomeric forms (see discussion on spectral data). The single-crystal structure of **6** is shown in Fig. 1 (see later). When the reaction of **III** with [Pt(PPh$_3$)$_4$] was carried out in the absence of chloride ions, eqn. (6), complex **7** was obtained in 85% yield. The structure and the *trans* geometry of **7** were ascertained by spectroscopic data and FAB MS analysis. Complex **6** could be alternatively prepared by treating **7** with potassium chloride in boiling benzene (2 h, 80% yield).



Scheme 2

Removal of the acetyl groups at the 5′ and 3′ positions of the sugar residues of the **2a**,**2b** mixture was achieved by treatment with concentrated aqueous ammonia for 2 h at 50 °C, giving **3a**,**3b** (not separated, 90%), whose structure was confirmed by spectral data. This reaction, demonstrating the stability of the platinum–nucleobase linkage to basic conditions and furnishing a further derivatizable sugar compound, showed this new platinated nucleoside to be suitable for insertion into oligonucleotide chains by automated procedures.

Spectroscopic data

The IR spectrum of complex **2a** shows strong bands at 1749, 1664 and 1588 cm^{-1} attributed respectively to carbonyl functions of the acetyl groups and to carbonyls of the thymine base. The band at 1588 cm^{-1} has been considered diagnostic for the N3 platinum co-ordinated thyminate ion.[6a,c] A weak band due to ν(Pt–Cl) was observed at 305 cm^{-1}. An almost identical IR pattern was observed for isomer **2b**. Analogously for complex **3**, strong ν(CO) bands were detected at 1653 and 1577 cm^{-1}. For complex **6** carbonyl resonances were found at 1655 and 1578 cm^{-1}, whereas only a weak signal, for ν(Pt–Cl), was detected at 300 cm^{-1}. Similarly for **7** ν(CO) gave strong bands at 1655 and 1579 cm^{-1}.

The ^{31}P NMR spectrum of complex **2a** shows two non-equivalent phosphorus atoms due to two magnetically different *trans* influences on each phosphine; ^1J(Pt–P) values are 3265 and 3960 Hz, attributed respectively to phosphorus *trans* to N and *trans* to chloride.[8] The ^{31}P NMR spectrum of **2b** is identical. For complex **6** the ^{31}P NMR spectrum displayed the same pattern due to two *cis* phosphines having ^1J(Pt–P) values of 3235 (*trans* to N) and 3984 Hz (*trans* to chloride). The spectrum of **7** showed a single phosphorus signal [^1J(Pt–P) = 3091 Hz] which was attributed to two *trans* magnetically equivalent phosphines.

In the ^{1}H NMR spectrum of complex **2a** protons H-6 and CH$_3$-5 showed upfield shifts ($\Delta\delta$ 0.92 and 0.33) compared to their resonances for free nucleoside **II**, suggesting N3 platination of the base.[6d,10] Analogous upfield shifts were observed for complexes **2b**, **6** and **7** for all the protons of the nucleobase. For **3a**,**3b** the H-6 signals are submerged by the phosphine protons, whereas for CH$_3$-5 signals upfield shifts of $\Delta\delta$ 0.3 were observed. When the ^{1}H NMR spectrum of **6** was recorded in the presence of the chiral shift reagent europium tris[3-(heptafluoropropylhydroxymethylene)(+)-camphorate] [Eu(hfc)$_3$],-{camphor = (1*R*)-1,7,7-trimethylbicyclo[2.2.1]heptan-2-one} a doubling and a downfield shift of the signals CH$_3$-N1 (δ 3.43 and 3.32) and CH$_3$-5 (δ 2.10 and 1.92) were observed. In ^{1}H NMR experiments, performed on the diastereomeric mixture **2** dissolved in DMSO, increasing the temperature to 125 °C, no fluxionality was observed suggesting a high barrier to rotation around the Pt–N3 bond.

In the ^{13}C NMR spectra all the isolated complexes showed for the nucleobase carbons a downfield shift in comparison with the resonances of the "free" ligands. This effect is particularly evident for C2, C4 and CH$_3$-5 ($\Delta\delta$ from 1 to 5), in agreement with literature data of similar platinum(II) nucleobase complexes.[11]

Molecular structure of *cis*-[PtCl(1-MeThy)(PPh$_3$)$_2$]·MeOH 6

The crystal structure of *cis*-[PtCl(1-MeThy)(PPh$_3$)$_2$]·MeOH **6** is illustrated in Fig. 1, which also gives the atom numbering scheme. Selected bond distances and angles are in Table 1. The platinum atom displays square planar co-ordination: two *cis* corners of the square plane are occupied by the P atoms of two triphenylphosphines and the chlorine atom and the amide nitrogen of the MeThy ligand are in *cis* position to each other. The four atoms co-ordinated to the metal lie in a plane with very small (less than 0.08 Å) deviation from it.

The plane of the MeThy ligand is approximately perpendicular to the platinum co-ordination plane, as seen by the torsion angles Cl(1)–Pt–N(1)–C(1) and Cl(1)–Pt–N(1)–C(6) of 87.3(4)

Table 1 Selected intramolecular bond distances (Å) and angles (°) for *cis*-[PtCl(1-MeThy)(PPh_3)$_2$] with estimated standard deviations in parentheses

MeThy moiety			
Pt–N(1)	2.072(5)	N(2)–C(6)	1.406(9)
Pt–P(1)	2.241(2)	N(2)–C(5)	1.498(10)
Pt–P(2)	2.268(2)	O(1)–C(1)	1.220(8)
Pt–Cl(1)	2.354(2)	O(2)–C(6)	1.246(8)
N(1)–C(6)	1.356(8)	C(1)–C(2)	1.406(9)
N(1)–C(1)	1.373(8)	C(2)–C(4)	1.337(11)
N(2)–C(4)	1.336(10)	C(2)–C(3)	1.490(11)
C(6)–N(1)–C(1)	123.4(5)	N(1)–C(1)–C(2)	117.0(6)
C(6)–N(1)–Pt	121.7(4)	C(4)–C(2)–C(1)	119.7(6)
C(1)–N(1)–Pt	114.8(4)	C(4)–C(2)–C(3)	122.2(7)
C(4)–N(2)–C(6)	119.9(6)	C(1)–C(2)–C(3)	118.0(7)
C(4)–N(2)–C(5)	120.9(7)	N(2)–C(4)–C(2)	122.7(6)
C(6)–N(2)–C(5)	119.1(7)	O(2)–C(6)–N(1)	120.3(6)
O(1)–C(1)–N(1)	120.6(5)	O(2)–C(6)–N(2)	122.5(6)
O(1)–C(1)–C(2)	122.4(6)	N(1)–C(6)–N(2)	117.2(6)
Triphenylphosphine ligands			
N(1)–Pt–P(1)	88.94(15)	C(21)–P(1)–Pt	113.4(2)
N(1)–Pt–P(2)	171.22(14)	C(11)–P(1)–Pt	111.5(2)
P(1)–Pt–P(2)	97.64(8)	C(31)–P(1)–Pt	114.4(2)
P(1)–Pt–Cl(1)	175.10(5)	C(51)–P(2)–C(41)	101.6(3)
P(2)–Pt–Cl(1)	87.05(8)	C(51)–P(2)–C(61)	107.3(3)
N(1)–Pt–Cl(1)	86.54(15)	C(41)–P(2)–C(61)	102.5(3)
C(21)–P(1)–C(11)	111.4(3)	C(51)–P(2)–Pt	114.9(2)
C(21)–P(1)–C(31)	102.5(3)	C(41)–P(2)–Pt	120.6(2)
C(11)–P(1)–C(31)	102.8(3)	C(61)–P(2)–Pt	108.7(2)

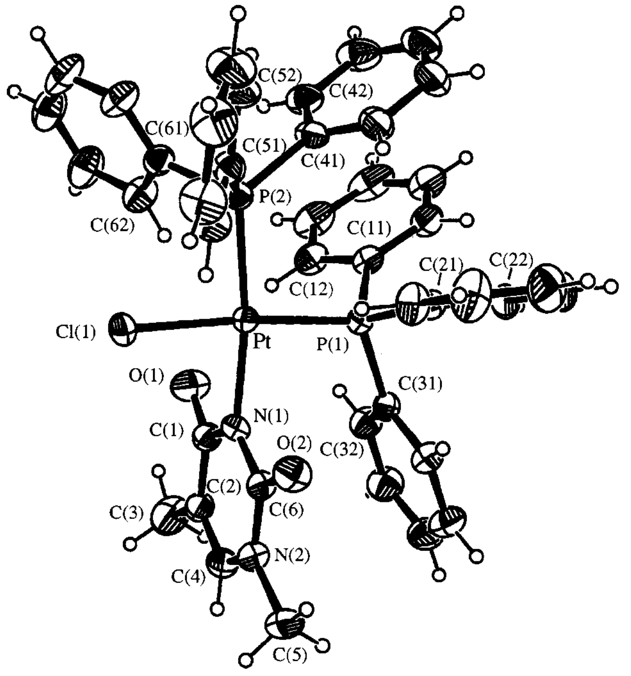


Fig. 1 An ORTEP[12] projection of two molecules of *cis*-[PtCl(1-MeThy)(PPh_3)$_2$] **6**. The thermal ellipsoids are drawn at 30% probability level.

and −96.4(5)°, respectively. The P–Pt distances [P(1)–Pt 2.241(2), P(2)–Pt 2.268(2) Å] are different, which is consistent with the amide [*trans* to P(2)] having a slightly larger *trans* influence than chloride.[9,13,14] The analysis of the Pt–N co-ordination distances shows the *trans* effect of the P atom. In fact, this distance [N(1)–Pt 2.072(5) Å] is longer (≈0.08 Å) than that observed in platinum(II) complexes with amide nitrogen ligands without co-ordinated P atoms.[13] The remaining bond lengths and bond angles are normal.[15,16]

The analysis of the triphenylphosphine moiety in *cis* position with respect to the Cl(1) atom shows the Cl(1) atom in a staggered conformation with respect to the C(41), C(51), C(61) atoms of the phenyl rings: the dihedral angles Cl(1)–Pt–P(2)–C(41), Cl(1)–Pt–P(2)–C(51) and Cl(1)–Pt–P(2)–C(61) are −172.9(3), 65.0(2), and −55.2(2)° respectively.

In the crystal packing the molecules are characterized by one intermolecular hydrogen-bond between the oxygen of the methanol molecule and O(2) atom of the MeThy ligand [distance O–H···O(2) 2.89(1) Å; angle O–H···O(2)=C(6) 153.2(5)°]. The crystal structure is further stabilized by van der Waals interactions involving the phenyl and the methyl groups.

Experimental

Material and methods

The ^{1}H and ^{13}C-{^{1}H} NMR spectra were recorded on a Bruker WM-400 spectrometer at 400 and 100.13 MHz respectively. All chemical shifts are expressed in ppm with respect to the signal of the protonated solvent ($CDCl_3$: δ 7.26 and 77.0. DMSO-d$_6$: δ 2.55 and 39.5. CD_3OD: δ 3.31 and 49.5). The ^{31}P NMR spectra were run on a Bruker WM-400 spectrometer at 161.98 MHz, with external reference to 85% H_3PO_4 (δ 0.0). The complex [Eu(hfc)$_3$] was purchased from Aldrich. The IR spectra were recorded on a Perkin-Elmer 457 spectrophotometer, FAB mass spectra (positive) on a ZAB 2SE spectrometer. The HPLC analyses and purifications were carried out on a Beckman System Gold instrument equipped with a UV detector module 166 and a Shimadzu Chromatopac C-R6A integrator. Compound **II** was used as supplied by Sigma.

Syntheses

Complexes 2a,2b. A mixture of compound **II** (205 mg, 0.63 mmol), [Pt(PPh_3)$_4$] (783 mg, 0.63 mmol) and finely powdered KCl (68 mg, 1.26 mmol) was suspended in benzene (8 cm^3) and refluxed with stirring under a nitrogen atmosphere for 2 h. After cooling, the mixture was filtered and the solid washed with benzene. The filtrates and washings, evaporated to dryness under reduced pressure, were chromatographed on a silica gel column (3 × 50 cm) eluted with increasing amounts of MeOH in $CHCl_3$ (from 0 to 2%, v/v) to give 544 mg of the isomeric mixture **2a**,**2b** (80%). TLC: R_f 0.4 (eluent $CHCl_3$–MeOH 97:3, v/v). The isomeric mixture was separated by HPLC on a silica gel column (Lichrosphere Si-60, 250 × 4 mm, 5 μm) eluted in $CHCl_3$ (1 cm^3 min^{-1}) to give pure **2a** and **2b** (ratio 45:55, retention times 5.1 and 5.7 min, respectively). FAB MS on mixture (^{195}Pt, ^{35}Cl): *m*/*z* 1044, [M − Cl]$^+$ and 754 [M-nucleoside]$^+$.

Complex **5a**: IR ($CHCl_3$) 1749, 1664, 1588 [strong, ν(CO)], 305 cm^{-1} [weak, ν(Pt–Cl)]; ^{31}P NMR (DMSO-d$_6$) δ 15.3 [d, PPh_3 *trans* to Cl, ^1J(Pt–P) = 3960] and 8.6 [d, PPh_3 *cis* to Cl, ^1J(Pt–P) = 3265 Hz]; ^{1}H NMR (DMSO-d$_6$) δ 8.32–7.00 (30 H, m, phenyl protons), 6.67 (1H, s, H-6), 6.17 [1H, dd, J(H$^{1'}$H$^{2'}$) = 5.8 and 6.0, H-1′], 5.14 (1H, m, H-3′), 4.23 (2H, m, H-5′), 4.10 (1H, m, H-4′), 2.14 and 2.07 (3H each, s, CH_3CO), 2.1–1.9 (2H, m, H-2′) and 1.47 (3H, s, CH$_3$-5); ^{13}C-{^{1}H} NMR (DMSO-d$_6$): δ 170.0 (CH$_3$*C*O), 167.9 (C-4), 153.6 (C-2), 134.7–127.5 (phenyl carbons and C-6), 110.1 (C-5), 83.6 (C-4′), 80.4 (C-1′), 73.2 (C-3′), 63.6 (C-5′), 35.4 (C-2′), 20.7 and 20.5 (2 *C*H$_3$CO) and 13.3 (CH$_3$-5).

Complex **5b**: IR ($CHCl_3$) 1750, 1663, 1590 [strong, ν(CO)], 308 cm^{-1} [weak, ν(Pt–Cl)]; ^{31}P NMR (DMSO-d$_6$) δ 15.3 [d, PPh_3 *trans* to Cl, ^1J(Pt–P) = 3960] and 8.6 [d, PPh_3 *cis* to Cl, ^1J(Pt–P) = 3265 Hz]; ^{1}H NMR (DMSO-d$_6$) δ 8.30–7.00 (30 H, m, phenyl protons), 6.64 (1H, s, H-6), 6.26 [1H, dd, J(H$^{1'}$H$^{2'}$) = 6.0 and 5.9, H-1′], 5.19 (1H, m, H-3′), 4.26 (2H, m, H-5′), 4.13 (1H, m, H-4′), 2.25 (2H, m, H-2′), 2.14 and 2.11 (3H each, s, CH_3CO) and 1.48 (3H, s, CH$_3$-5); ^{13}C-{^{1}H} NMR (DMSO-d$_6$) δ 170.0 (CH$_3$*C*O), 167.8 (C-4), 154.1 (C-2), 134.7–127.5 (phenyl carbons and C-6), 109.2 (C-5), 83.6 (C-4′), 80.3 (C-1′), 74.2 (C-3′), 63.6 (C-5′), 35.3 (C-2′), 20.7 and 20.5 (2 *C*H$_3$CO) and 13.3 (CH$_3$-5).

Complexes 3a,3b. Complex **2a**,**2b** (150 mg, 0.14 mmol) was treated with aqueous concentrated NH_3 (5 cm^3, 35%) and MeOH (5 cm^3) for 2 h at 50 °C. The resulting solution, dried under reduced pressure, was purified on a silica gel column (2 × 50 cm) eluted with increasing amounts of MeOH in $CHCl_3$ (from 5 to 20%, v/v) to give **3a**,**3b** (126 mg, 90%). Diastereomeric mixture: IR ($CHCl_3$) 3667 [broad, ν(OH)], 1653, 1577 cm^{-1} [strong, ν(CO)]; ^{31}P NMR (CD_3OD) δ 13.5 [d, PPh_3 *trans* to Cl, ^1J(Pt–P) = 3971] and 6.8 [d, PPh_3 *cis* to Cl, ^1J(Pt–P) = 3305 Hz]; ^{1}H NMR (CD_3OD) δ 7.80–7.10 (62H, m, phenyl protons and H-6), 6.19 and 6.01 (1H each, dd, H-1′), 4.33 (2H, m, H-3′), 3.87 (2H, m, H-4′), 3.72 (4H, m, H-5′) 2.30–2.00 (4H, m, H-2′), 1.69 and 1.62 (3H each, s, CH_3-5); ^{13}C-{^{1}H} NMR (CD_3OD) δ 172.7 (C-4), 156.9 (C-2), 137–128.0 (phenyl carbons and C-6), 111.9 and 108.7 (C-5), 88.8 (C-4′), 87.5 and 86.9 (C-1′), 72.5 and 72.4 (C-3′), 63.2 (C-5′), 41.8 and 41.4 (C-2′) and 13.8 (CH_3-5).

***cis*-[PtCl(1-MeThy)(PPh_3)$_2$ 6.** *From III.* A mixture of compound **III** (200 mg, 1.44 mmol), [Pt(PPh_3)$_4$] (1.79 g, 1.44 mmol) and finely powdered KCl (155 mg, 2.88 mmol) was suspended in benzene (10 cm^3) and refluxed with stirring under a nitrogen atmosphere for 2 h. After cooling, the mixture was filtered and the solid washed with benzene. The filtrate and washings, evaporated to dryness under reduced pressure, were chromatographed on a silica gel column (2.5 × 50 cm) eluted with increasing amounts of MeOH in $CHCl_3$ (from 0 to 3%, v/v) to give pure complex **6** (1.05 g, 82%). TLC: R_f 0.44 (eluent $CHCl_3$–MeOH 97 : 3, v/v).

From **7**. A mixture of complex **7** (200 mg, 0.23 mmol), and finely powdered KCl (25 mg, 0.46 mmol) was suspended in benzene (5 cm^3) and refluxed with stirring under a nitrogen atmosphere. After 2 h TLC analysis showed the disappearance of **7** and the formation of **6** (164 mg, 80%) which was purified as described above and identified by spectroscopic analyses. FAB MS (^{195}Pt, ^{35}Cl): *m*/*z* 893, $[M + H]^+$ and 957 $[M - Cl]^+$. IR ($CHCl_3$) 1655, 1578 [strong, ν(CO)], 300 cm^{-1} [weak, ν(Pt–Cl)]. ^{31}P NMR (DMSO-d_6): δ 15.4 [d, PPh_3 *trans* to Cl, ^1J(Pt–P) = 3984] and 8.6 [d, PPh_3 *cis* to Cl, ^1J(Pt–P) = 3235 Hz]. ^{1}H NMR (DMSO-d_6): δ 8.20–7.00 (30 H, m, phenyl protons); 6.31 (1H, s, H-6); 3.0 (3H, s, CH_3-1); and 1.62 (3H, s, CH_3-5). ^{13}C-{^{1}H} NMR (DMSO-d_6): δ 169.9 (C-4); 155.1 (C-2); 138.6 (C-6); 109.3 (C-5); 36.1 (CH_3-1); and 12.1 (CH_3-5).

***trans*-[Pt(OH)(1-MeThy)(PPh_3)$_2$] 7.** A solution of compound **III** (200 mg, 1.44 mmol) and [Pt(PPh_3)$_4$] (1.79 g, 1.44 mmol) was refluxed in benzene (8 cm^3) under a nitrogen atmosphere for 2 h. After cooling, the mixture, evaporated to dryness under reduced pressure, was chromatographed on a silica gel column (2.5 × 50 cm) eluted with increasing amounts of MeOH in benzene (from 0 to 5%, v/v) to give pure complex **7** (107 mg, 85%). TLC: R_f 0.4 (eluent $CHCl_3$–MeOH 95 : 5, v/v). FAB MS (^{195}Pt): *m*/*z* 875 $[M + H]^+$; and 859, $[M - OH]^+$. IR ($CHCl_3$) 3334 [broad, ν(OH)], 1655, 1579 cm^{-1} [strong, ν(CO)]. ^{31}P NMR ($CDCl_3$): δ 18.6 [d, PPh_3, ^1J(Pt–P) = 3091]. ^{1}H NMR ($CDCl_3$): δ 7.90–7.20 (30 H, m, phenyl protons); 5.93 (1H, s, H-6); 2.67 (3H, s, CH_3-1); and 1.31 (3H, s, CH_3-5). ^{13}C-{^{1}H} NMR ($CDCl_3$): δ 170.3 (C-4); 155.2 (C-2); 137.6 (C-6); 107.8 (C-5); 36.2 (CH_3-1); and 13.2 (CH_3-5).

Crystallography

Suitable crystals of *cis*-[PtCl(1-MeThy)(PPh_3)$_2$] **6** for X-ray analysis were obtained by slow evaporation of $CHCl_3$–MeOH (9 : 1, v/v) at room temperature. Intensity data collection was performed using graphite-monochromated Cu-Kα radiation (λ = 1.54178 Å) and a pulse-high discrimination on a CAD4 Enraf-Nonius automated diffractometer equipped with a MicroVax 3100 Digital computer of the "Centro di Studio di Biocristallografia del CNR" at Università di Napoli "Federico II". The independent reflections were measured in the θ range 1–70°. Unit cell parameters were determined by least-squares refinement of the setting angles of 25 high angle reflections ($18 < \theta < 22°$). Three standard reflections were monitored periodically and showed no significant change during data collection. A total of 7789 independent reflections were measured with a ω–2θ scan mode. Using a prescan speed of 4.12° min^{-1}, reflections with a net intensity $I < 0.5\sigma(I)$ were flagged as "weak"; those with $I \geq 0.5\sigma(I)$ were measured at lower speed depending on the value of $\sigma(I)/I$. The structure was solved by direct methods using the SIR 97 program.[17] The best E maps revealed all the non-H atoms and the methanol solvent molecule. Refinement by the full-matrix least-squares procedure on F^2 (all data) used the SHELXL 93 program[18] with anisotropic thermal factors for all non-hydrogen atoms. Hydrogen atom positions were calculated and allowed to ride on their attached atoms, with U_{iso} s = 1.2 U_{eq} of the attached atom.

The scattering factors for all atomic species were calculated from Cromer and Waber.[19]

Crystal data. $C_{42}H_{34}ClN_2O_2P_2Pt{\cdot}CH_3OH$, $M = 923.23$, triclinic, space group $P\bar{1}$ (no. 2), $a = 11.176(8)$, $b = 13.892(9)$, $c = 13{,}36(1)$ Å, $\alpha = 97.31(6)$, $\beta = 91.32(6)$, $\gamma = 88.00(6)°$, $U = 2056(3)$ A^3, $T = 293$ K, $Z = 2$, μ(Cu-Kα) = 8.029 mm^{-1}, 7789 unique reflections ($R_{int} = 0.0$) used in all calculations. The final $wR(F^2)$ was 0.1334; $R1 = 0.0515$.

CCDC reference number 186/1433.

See http://www.rsc.org/suppdata/dt/1999/1945 for crystallographic files in .cif format.

Acknowledgements

We are grateful to Ministero dell'Università e della Ricerca Scientifica e Tecnologica, Consiglio Nazionale delle Ricerche for grants in support of this investigation and to Centro di Metodologie Chimico-Fisiche dell'Università degli Studi di Napoli "Federico II" for the NMR facilities. We also thank Rita Carolla for technical assistance.

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Paper 9/01459D