1:1 Complexes of Palladium(II) and Platinum(II) with Caffeine and Their Interaction with Nucleosides

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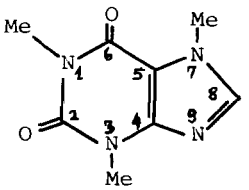
Abstract

The reaction of palladium(II) and platinum(II) with caffeine was studied in dmf and acid aqueous solutions. From dmf solution the 1:1 complexes $K[McfCl_3]$ have been isolated and characterized by various physicochemical methods. The complexes are unstable in water, where they decompose to metallic palladium or platinum. The complexes are stabilized in the presence of nucleosides, with which they react, and the following mixed ligand complexes were isolated: $[McfNuclCl_2]$ (Nucl = Ado, Guo, or Ino) and $[Mcf(Nucl–H^+)Cl]$ (Nucl = Guo or Ino). These mixed ligand complexes were characterized using various physicochemical methods. Potassium tetrachloroplatinate(II) in acid aqueous solution reacts with caffeine to give the complex $[Pt(cf–H^+)Cl]_2$, in which caffeine is bound to platinum through its C(8) atom, forming a Pt–C(8) bond after the removal of the proton bound to that carbon.

Introduction

Caffeine (1,3,7-trimethylxanthine, cf), is a purine type alkaloid:



The influence of caffeine on both animal and vegetable cells' behaviour in normal and abnormal situations is under continuous investigation. It has been shown that caffeine potentiates the lethal and chromosone-damaging effects of the antitumour agent *cis*-$Pt(NH_3)_2Cl_2$ in Chinese hamster cells, which when treated with *cis*-$Pt(NH_3)_2Cl_2$ in the presence of caffeine, synthesize low molecular weight DNA [1].

It is also known that the solubility of caffeine in water is increased on the addition of metal salts. The preparation of some complexes in the solid state [2] or in aqueous solution [3] has been reported. The copper complexes of caffeine have been studied extensively and it has been found by X-ray structural determinations that caffeine coordinates to the metal through its N(9) atom [4, 5]. Caffeine may also coordinate to metals through its C(8) atom, after deprotonation, and form M–C(8) bonds as has been found in some amino ruthenium(III) complexes [6, 7].

In this paper I wish to report on some monocaffeine complexes of Pd(II) and Pt(II), on their properties in water solution and on some of their reactions with nucleosides.

Results and Discussion

Potassium tetrachloropalladate(II) and potassium tetrachloroplatinate(II) react with caffeine (cf) in dmf solution, at room temperature and at ~55 °C respectively and give 1:1 complexes according to the general equation:

$$K_2MCl_4 + cf \longrightarrow K[McfCl_3] + KCl$$

The complexes behave as 1:1 electrolytes in dmf solutions and the analytical results (Table I) fit well the proposed formulation.

The binding site of caffeine to the metals was deduced mainly from the ^1H and ^{13}C nmr spectra of the complexes, which were taken in dmso-d_6: D_2O (9:1) solutions (Table II).

The assignment of the ^1H nmr spectra of free caffeine has already been made by Lichtenberg *et al.* [8] who also studied the effect of its protonation on the chemical shifts of H_8 and the methyl protons. The protonation of caffeine has very little effect on the chemical shifts of H_8 and the methyl protons, and this has been explained by assuming that the carbonyl oxygen of the 6th position is the protonation site and not the nitrogen of the 9th position, with the predominant form:

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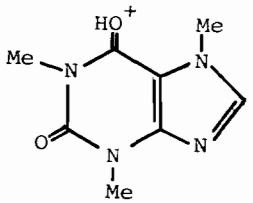
TABLE I. Analytical and Conductivity Data of the Complexes.[a]

Compound	%C	%H	%N	%Cl	%M	Λ_M Ohm^{-1} cm^2 mol^{-1}
$K[PdcfCl_3]$	24.40 (23.93)	2.63 (2.49)	14.40 (13.96)	26.10 (26.55)	26.80 (26.52)	82 (dmf)
$PdcfInoCl_2$	34.12 (33.76)	3.78 (3.47)	17.81 (17.51)	11.61 (11.10)	16.90 (16.63)	7(dmf)
$Pdcf(Ino - H^+)Cl$	35.42 (35.80)	3.81 (3.51)	18.12 (18.56)	5.29 (5.88)	17.32 (17.64)	5(dmso)
$PdcfGuoCl_2$	33.40 (32.98)	3.35 (3.54)	18.85 (19.24)	10.38 (10.84)	16.50 (16.25)	6(dmf)
$Pdcf(Guo - H^+)Cl$	35.45 (34.93)	3.84 (3.59)	20.80 (20.38)	5.19 (5.74)	17.50 (17.21)	4(dmso)
$PdcfAdoCl_2$	33.41 (33.81)	3.41 (3.63)	20.31 (19.72)	11.50 (11.11)	16.32 (16.65)	5(dmf)
$K[PtcfCl_3]$	19.21 (19.60)	2.37 (2.06)	11.12 (11.43)	21.32 (21.74)	39.50 (39.82)	75(dmf)
$PtcfInoCl_2$	30.02 (29.65)	2.84 (3.04)	15.80 (15.37)	9.50 (9.75)	26.42 (26.78)	5(dmf)
$Ptcf(Ino - H^+)Cl$	31.70 (31.21)	3.25 (3.06)	16.50 (16.18)	5.45 (5.13)	28.50 (28.19)	4(dmso)
$PtcfGuoCl_2$	29.51 (29.05)	3.41 (3.12)	16.45 (16.94)	9.90 (9.55)	26.51 (26.24)	6(dmf)
$Ptcf(Guo - H^+)Cl$	30.95 (30.55)	2.92 (3.14)	17.50 (17.82)	5.41 (5.02)	27.20 (27.59)	5(dmso)
$PtcfAdoCl_2$	29.96 (29.69)	2.95 (3.19)	16.98 (17.32)	9.40 (9.76)	26.50 (26.82)	6(dmf)
$[Pt(cf - H^+)Cl]_2$	25.80 (25.34)	2.51 (2.39)	15.10 (14.78)	9.21 (8.84)	51.30 (51.50)	5(dmf)

[a]The numbers in parentheses represent calculated figures. cf = caffeine, Ino = Inosine, Guo = guanosine, Ado = adenosine, M = Pd or Pt.



The metallation of caffeine, on the other hand, causes a very pronounced downfield shift of the H_8 chemical shift (0.5 ppm and 0.7 ppm for the palladium and the platinum complex respectively) and this suggests that the nitrogen at the 9th position is the metallation site in both cases. Furthermore in the platinum complex the resonance of the H_8 appears as a triplet due to the coupling with ^{195}Pt, with a coupling constant of 20 Hz.

The ^{13}C nmr spectra of the complexes were also recorded (see Table III) and compared with that of free caffeine. It is evident from these spectra that the C_4 and C_8 are affected the most upon metallation. The resonances of both these carbons are shifted downfield (3.5 and 3.8 ppm for the palladium and 4.2 and 4.5 ppm for the platinum complex respectively) and this also suggests that the nitrogen at the 9th position is the metallation site.

TABLE II. ^1H Nmr Chemical Shifts of the Monocaffeine Complexes (ppm).

Compound	H(8)	1-CH_3	3-CH_3	7-CH_3
Caffeine, cf	7.87	3.32	3.50	3.95
Protonated cf	7.92	3.31	3.52	3.99
$K[PdcfCl_3]$	8.37	3.32	3.55	3.98
$K[PtcfCl_3]$	8.57	3.32	3.54	3.99

The carbonyl oxygen at the 2nd and 6th positions may be excluded from coordination as is indicated by the ir spectra of the complexes. In both complexes the carbonyl stretchings remain essentially unchanged and appear at the same frequencies as in the free caffeine. Finally the M–Cl stretchings appear as strong bands at 330 and 325 cm^{-1} for the palladium and platinum complexes respectively.

Recently Cramer *et al.* [10] prepared the complex trichloro(caffeine)platinum(II), which they isolated as triphenylmethylphosphonium salt and showed by X-ray crystallography that the N_9 of caffeine is the metallation site. For the prepara-

TABLE III. ^{13}C Chemical Shifts of Caffeine and Complexes (ppm).

Compound	C_2	C_4	C_5	C_6	C_8	N_1-CH_3	N_3-CH_3	N_7-CH_3
Caffeine[a]	152.9	148.7	108.1	156.4	144.2	30.6	28.7	34.2
$K[PdcfCl_3]$	153.4	152.2	108.5	156.7	148.0	30.8	28.9	34.4
$K[PtcfCl_3]$	153.6	152.9	108.6	156.8	148.7	30.7	29.0	34.5

[a]Taken from reference [9].

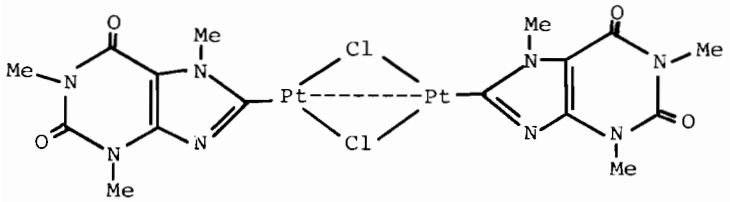
tion of the complex, they used an entirely different method.

The monocaffeine complexes are soluble in water but they both decompose very rapidly giving the free metals and oxygen. The mixtures attain very high conductivities and the acidity increases by two equivalents. The overall redox reaction may be:

$$K[McfCl_3] + H_2O \longrightarrow M^\circ + cf + HClO + HCl + KCl \quad (1)$$

This reaction proceeds more rapidly in alkaline solution but is completely hindered in acid solution (0.5 *N* HCl).

Taube and his co-workers [6, 7] showed that caffeine may form $M-C_8$ σ-bonds with Ru(III). Using similar experimental conditions the complex $[Pt(cf - H)Cl]_2$ has been isolated. The analytical results fit well the above formulation (see Table I). The participation in coordination of both carbonyl oxygens was excluded as was shown by the study of the ir spectrum of the complex. The resonance of the H_8 is completely absent from the ^1H nmr spectrum of the complex, which suggests that deprotonation has taken place with the simultaneous formation of a $Pt-C_8$ σ-bond. The medium band at 305 cm^{-1} may be assigned to the Pt–Cl–Pt stretching, and the dimeric character of the complex was confirmed by its molecular weight determination (calculated for $[Pt(cf-H)Cl]_2$: 849.4, found: 838.2). In view of the above experimental data, the structure of this complex may be as follows:



A similar procedure for the preparation of the analogous palladium complex was not successful.

The interaction of the monocaffeine complexes of palladium and platinum with nucleosides was further examined in order to prepare mixed ligand complexes of these metals, with the aim of further elucidating the mechanism of the antitumour action of Pd(II) and Pt(II) complexes.

It was mentioned above that the monocaffeine complexes of both palladium and platinum, $K[McfCl_3]$ are very unstable in water where they undergo the redox reaction (1). These complexes, however, are stabilized in the presence of the nucleosides adenosine (Ado), guanosine (Guo), and inosine (Ino). The monocaffeine complexes react with these nucleosides in water solution to give the mixed ligand complexes:

$PdcfAdoCl_2$, $Pdcf(Guo - H^+)Cl$, $Pdcf(Ino - H^+)Cl$

$PtcfAdoCl_2$, $PtcfGuoCl_2$, $PtcfInoCl_2$.

The analytical results (see Table I) fit well with the above formulation.

The reaction with adenosine, in both cases, is a straightforward replacement of one chloride with adenosine:

$$KMcfCl_3 + Ado \longrightarrow McfAdoCl_2 + KCl$$

The metallation sites of caffeine and adenosine in these complexes were deduced from their ^1H nmr spectra (see Table IV).

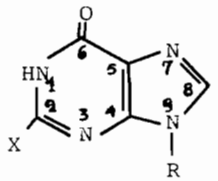
The H(8) signal of the caffeine remains essentially at the same position as in the respective monocaffeine complexes, and this suggests that caffeine remains coordinated through its N(9) atom in all mixed ligand complexes. Adenosine, on the other hand, exhibits two bands in the aromatic proton region, at 8.08 and 8.70 ppm for the palladium complex, and at 8.10 and 8.95 ppm for the platinum complex assigned to H(2) and H(8), respectively. The assignment was confirmed using 8-deuterated adenosine for the preparation of the complexes. The above results

TABLE IV. ^{1}H Nmr Chemical Shifts of the Mixed Ligand Complexes (ppm).

Compound	H(2)	H(8), cf	H(8), nucl.	H(1')
Caffeine	–	7.87	–	–
Adenosine	7.95	–	8.17	5.90, 5.80
Guanosine	–	–	7.80	5.74, 5.68
Inosine	8.11	–	8.22	6.03, 5.93
PdcfAdoCl$_2$	8.08	8.35	8.70	6.31, 6.23
PdcfGuoCl$_2$	–	8.35	8.41	5.85, 5.78
PdcfInoCl$_2$	8.23	8.33	8.70	5.85, 5.76
Pdcf(Guo – H$^+$)Cl	–	8.36	8.36	5.85, 5.74
Pdcf(Ino – H$^+$)Cl	8.20	8.35	8.65	5.83, 5.73
PtcfAdoCl$_2$	8.10	8.53	8.95	6.32, 6.24
PtcfGuoCl$_2$	–	8.55	8.65	5.86, 5.76
PtcfInoCl$_2$	8.25	8.54	8.91	5.87, 5.75
Ptcf(Guo – H$^+$)Cl	–	8.52	8.57	5.85, 5.78
Ptcf(Ino – H$^+$)Cl	8.22	8.54	8.86	5.84, 5.74

indicate that adenosine is coordinated only through its N(7) atom, acting as monodentate, as was found in other mixed ligand complexes [11].

The reaction with guanosine and inosine is more complicated. Both these nucleosides contain an ionizable N(1)H imino proton with a pK_a around 9.5:



X = H (Ino)

X = NH$_2$ (Guo)

The first metallation site of both these nucleosides was found to be the N(7) of the purine ring in most cases.

The coordination at the N(7) atom affects the pK_a of the N(2)H imino proton, lowering it by about 3.5 units when the metal is Pd and by about 2 units when the metal is platinum [12–14]. So in neutral aqueous solutions, the first step of the reaction of the trichloromonocaffeinepalladium(II) complex with inosine or guanosine is the replacement of one chloride in the coordination sphere of palladium by Ino or Guo, which coordinate through their N(7) atom to palladium. The first attack is followed by ionization of the N(1)H imino proton, accumulation of negative charge on the O(6), due to resonance, and finally nucleophilic substitution of one more chloride by this negatively charged exocyclic oxygen, in a chelate (I) or dimeric (II) form.

The ^{1}H nmr chemical shifts of these complexes are consistent with N(7) coordination of both guanosine and inosine. Thus the downfield shift of the H(8) resonance by 0.56 and 0.43 ppm for the guanosine and inosine complex respectively is a good indication for the N(7) being the ligation site in both cases. On the other hand, the downfield shift of the H(2) resonance of inosine by 0.09 ppm is too small to account for any N(1)–Pd interaction.

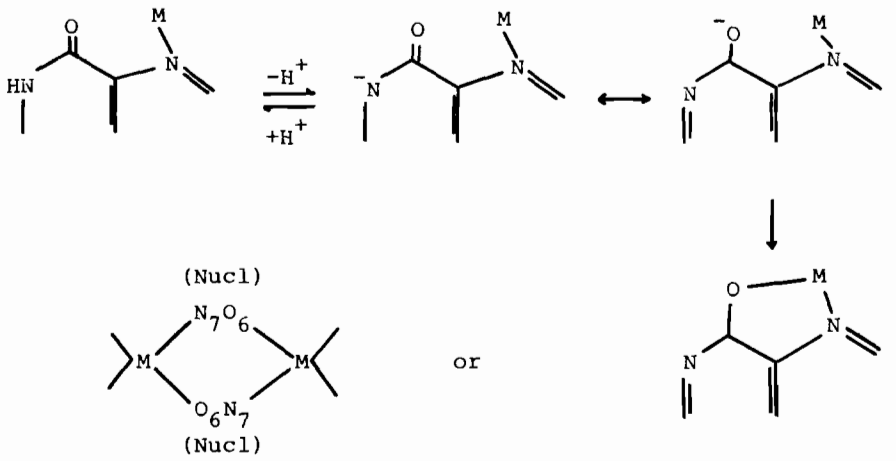
The evidence for the exocyclic O(6) participating in coordination comes from the study of the ir spectra of the complexes (see Table V). The ν(C=O) drops by *ca.* 75 cm^{-1} and appears at about 1620 cm^{-1} in both complexes. This lowering of the ν(C=O) frequency may be taken as a good indication of the O(6) keto oxygen involvement in bonding to the metals [15–18].

The shift to lower frequencies of the ν(C=O) band upon ionization of the N(1)H iminoproton in guanosine and inosine indicates the loss of the double bond character of the C=O group [19, 20]. This is possibly more pronounced in the ionic sodium salt of guanosine (shift to 1595 cm^{-1}) [18] and less whenever the metal–oxygen bonding is more covalent, as in the case of Pt(II) and Pd(II), for example (shift to 1625' cm^{-1}) [11, 12, 21]. Certainly, the double bond character of the C=O is also lowered when the oxygen interacts covalently with a metal, without ionization of the N(1)H imino proton [15a]. Oxygen involvement in bonding with metals, following deprotonation of the imino proton, has also been found in the crystal structure of *cis*-diamminoplatinum a-pyridone blue [22] where both O$^-$ and N atoms bridge two platinum atoms. Kistenmacher *et al.* [23] have also found an O–Ag(I) interaction in the crystal structure of nitrato(1-methylcytosine)silver(I). Bau *et al.* showed the participation of the exocyclic O(6) in coordination, in the crystal structure of a

TABLE V. Characteristic ir Bands of the Complexes (in the C=O and M–Cl regions, cm^{-1}).[a]

Compound	$\nu_{C=O}$ (cf, Nucl)	$\nu_{C=O}$(Nucl – H^+)	ν_{M-Cl}
Caffeine	1706 vs	–	–
Adenosine	–	–	–
Guanosine	1700 vs,br	–	–
Inosine	1700 vs,br	–	–
$K[PdcfCl_3]$	1703 vs	–	330 s
$PdcfAdoCl_2$	1705 vs	–	335, 327[b]
$PdcfGuoCl_2$	1700 vs,br	–	335, 327[b]
$PdcfInoCl_2$	1700 vs,br	–	335, 326[b]
Pdcf(Guo – H^+)Cl	1705 vs	1622 vs	325 m
Pdcf(Ino – H^+)Cl	1703 vs	1620 vs	323 m
$K[PtcfCl_3]$	1705 vs	–	325 m
$PtcfAdoCl_2$	1703 vs	–	328, 320[b]
$PtcfGuoCl_2$	1700 vs,br	–	327, 320[b]
$PtcfInoCl_2$	1700 vs,br	–	328, 321[b]
Ptcf(Guo – H^+)Cl	1703 vs	1620 vs	320 m
Ptcf(Ino – H^+)Cl	1702 vs	1618 vs	321 m
$[Pt(cf - H^+)Cl]_2$	1700 vs	–	305 m

[a]Measured in KBr discs. [b]Doublet. s = Strong, vs = very strong, m = medium, br = broad.



Scheme I (II) (I)

tetranuclear Cu(II)–inosine monophosphate *o*-phenanthroline complex with Cu–O(6) distance 1.956 Å. Also, recently, Marzilli *et al.* have presented evidence for O(6) binding with metals, mainly from ^{13}C nmr spectra [25].

In acid solution, the equilibriae shown in Scheme I are shifted to the left and complexes of the formula $Pd(cf)(Nucl)Cl_2$ (Nucl = Guo, Ino) have been isolated. In these complexes the ν(C=O) of the nucleosides is restored to about 1700 cm^{-1} and this excludes the participation of the exocyclic O(6) in coordination. The only ligation site of guanosine and inosine in these complexes is the N(7) atom of the purine ring. The evidence for this comes from the ^1H nmr spectra of the complexes (see Table IV). The downfield shift of the H(8) resonance by 0.61 and 0.48 ppm for the guanosine and inosine complex, respectively, indicates that these nucleosides participate through their N(7) atom in coordination. Again, the downfield shift of the H(2) resonance of the inosine complex by only 0.12 ppm excludes the participation of the N(2) atom in coordination.

The behavior of the trichloro(caffeine)platinum(II) complex towards guanosine and inosine differs

from that of the respective palladium(II) complex. Thus, direct interaction of the monocaffeine platinum(II) complex with guanosine or inosine in neutral aqueous solutions leads to the complexes $PtcfNuclCl_2$.

In these complexes, guanosine and inosine act as monodentate ligands, with their N(7) atoms as ligation sites. The evidence for the N(7) of guanosine and inosine acting as ligation site in these complexes comes from the study of their ^1H nmr spectra. The downfield shift of the H(8) resonance by 0.85 and 0.69 ppm of the guanosine and inosine respectively, indicates that they participate in coordination through their N(7) atoms. The ν(C=O) frequency remains unchanged and this excludes the participation of the exocyclic O(6) in coordination.

The coordination of guanosine and inosine to platinum(II) through their N(7) atoms causes a lowering of the pK_a of their N(1)H imino protons by only 2 units. This lowering is not enough for any appreciable ionization of the N(1)H imino protons, which remain unionized in the platinum(II) complexes obtained from neutral or slightly acidic solutions, in contrast with the respective palladium(II) complexes. In slightly alkaline solutions however, the ionization of the N(1)H imino protons is facilitated, and the complexes Ptcf(Nucl – H^+)Cl (Nucl = Guo, Ino) are formed. Again, the nucleosides in these complexes act as bidentate ligands through their N(7) and O(6) atoms either in a chelate (I) or dimeric (II), N(7) O(6) form. The downfield shift of the H(8) resonances by 0.77 and 0.64 ppm of guanosine and inosine, respectively, suggests coordination to platinum through their N(7) atoms. On the other hand the ν(C=O) frequency of the exocyclic carbonyl oxygen of the nucleosides is lowered by about 75 cm^{-1} (see Table V), and this again may be taken as a good indication for the O(6) participating in coordination.

The medium band at 320–325 cm^{-1} was assigned to the M–Cl stretching of the monochloro, deprotonated nucleoside complexes, Mcf(Nucl – H^+)Cl. The same band appears as a doublet at 335 and 327 cm^{-1} for the palladium non-deprotonated nucleoside complexes $PdcfNuclCl_2$, and at 328 and 320 cm^{-1} for the respective platinum complexes, $PtcfNuclCl_2$. The doublet character of this band may be taken as an indication for these complexes having *cis* geometry [26]. The *cis*-geometry of these complexes was also deduced using Kurnakoff's test [27]. This test, originally applied to platinum(II) complexes, was also found to apply to the palladium(II) complexes [12b, 28].

Experimental

Materials

Caffeine and nucleosides were from Fluka A.G. and used without further purification. Potassium tetrachloropalladate(II) and potassium tetrachloroplatinate(II) were from Johnson Matthey.

Methods

IR spectra were recorded on a JASCO-DS 701 G spectrophotometer. ^1H nmr spectra were recorded on a Varian T60 spectrometer, using TMS as internal standard. ^{13}C nmr spectra were obtained on a Varian XL 100 nmr spectrometer, operating in Fourier transform mode, with proton noise decoupling at frequency 25.2 MHz. Chemical shifts were measured relative to internal dmso-d_6 and converted to TMS scale using δdmso-d_6 = +39.6 ppm. Conductivity measurements were performed using an E365B conductoscope, Methohm, Herisau, Switzerland. The molecular weight was determined by a Hewlett-Packard 300 Vapor Pressure Osmometer.

Microanalyses

These were performed in the Laboratories of the National Research Foundation of Greece in Athens by Dr. Mantzos.

Preparation of the Complexes

Potassium trichloro(caffeine)palladate(II), KPdcf-Cl_3

Potassium tetrachloropalladate(II), K_2PdCl_4, 2 mmol, and caffeine, 2 mmol, were suspended in 10 ml dmf and stirred at room temperature for 3 hr. The mixture was refrigerated and filtered. The compound was then precipitated from the filtrate with excess acetone: ether (1:5). Yield *ca.* 85%.

Potassium trichloro(caffeine)platinate(II), KPt-$cfCl_3$

Potassium tetrachloroplatinate(II), K_2PtCl_4, 2 mmol, and caffeine, 2 mmol, were suspended in 10 ml dmf and heated at 55 °C for 6 hr. The mixture was refrigerated and filtered. The compound was then precipitated from the filtrate with excess isopropanol:ether (1:5). Yield *ca.* 80%.

Bis[μ-chloro(caffeinato)platinum(II)], [Pt(cf – H^+)$Cl]_2$

Potassium tetrachloroplatinate(II), 1 mmol and caffeine, 1 mmol, were dissolved in 25 ml 0.5 *N* HCl and heated at 50 °C overnight. The mixture was refrigerated and filtered. The compound was then precipitated from the filtrate with excess isopropanol: ether (1:5). Yield *ca.* 70%.

Dichloro(adenosine)(caffeine)palladium(II), Pdcf-$AdoCl_2$, or -platinum(II), $PtcfAdoCl_2$

Adenosine, 1 mmol, was dissolved in 25 ml water and to that was added 1 mmol of the respective solid monocaffeine complex, in small portions with

vigorous stirring. The mixture was then left at room temperature for several days, and the precipitate formed was filtered, washed with cold water, ethanol:ether (1:2), ether and dried at 60 °C under vacuum. Yield *ca.* 65%.

Chloro(guanosinato)(caffeine)palladium(II), Pdcf(Guo–H⁺)Cl, or Chloro(inosinato)palladium-(II), Pdcf(Ino – H⁺)Cl

Guanosine (or inosine), 1 mmol, was dissolved in 3 ml dmso and diluted with 10 ml water. Potassium trichloro(caffeine)palladate, 1 mmol, was then added and the mixture neutralized to pH = 6.5 with 1 *N* NaOH. The yellow precipitate formed was filtered, washed with water, ethanol ether and dried at 60 °C under vacuum. Yield *ca.* 70%.

Dichloro(caffeine)(guanosine)palladium(II), PdcfGuoCl₂, or Dichloro(caffeine)(inosine)palladium(II), PdcfInoCl₂

Chloro(guanosinato)(caffeine)palladium(II), 1 mmol, or chloro(inosinato)(caffeine)palladium(II), 1 mmol, was dissolved in 3 ml dmso and diluted with 5 ml H_2O. The solution was acidified to pH = 2 with 1 *N* HCl, and the compound was precipitated from the solution with excess isopropanol: ether (1:2). The yellow precipitate formed was filtered, washed with ethanol and ether and dried at 60 °C under vacuum. Yield *ca.* 65%.

Dichloro(caffeine)(guanosine)platinum(II), PtcfGuoCl₂

Guanosine, 1 mmol, was dissolved in 25 ml water at 55 °C and to this was added solid potassium trichloro(caffeine)platinate(II) in small portions, with vigorous stirring. This temperature (55 °C) was maintained overnight and then reduced. The yellow precipitate formed was washed with cold water, ethanol:ether (1:2) and ether and dried at 60 °C under vacuum. Yield *ca.* 70%.

Dichloro(caffeine)(inosine)platinum(II), PtcfInoCl₂

The procedure for the adenosine complex was followed except that inosine was dissolved in 10 ml water.

Chloro(guanosinato)(caffeine)platinum(II), Ptcf(Guo – H⁺)Cl, or Chloro(inosinato)-(caffeine)platinum(II), Ptcf(Ino – H⁺)Cl

Dichloro(caffeine)(guanosine)platinum(II), 1 mmol, or dichloro(caffeine)(inosine)platinum(II), 1 mmol, was dissolved in 15 ml water and neutralized to pH = 7.5 to 8.0, with 1 *N* NaOH. This pH was maintained for several days and the precipitate formed was filtered, washed with water, ethanol, ether, and dried at 60 °C under vacuum. Yield *ca.* 60%.

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