Palladium(II)–purine nucleoside complexes: synthesis, characterization and X-ray determination

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(Received June 5, 1992; revised September 28, 1992)

Abstract

Twelve Pd(II) complexes containing the purine nucleosides adenosine (Ado), guanosine (Guo), inosine (Ino) and xanthosine (Xao) and chloride, bromide or thiocyanate as auxiliary ligands have been isolated and characterized by spectroscopic techniques. Moreover, crystal structures of *trans*-$[Pd(Ino)_2Cl_2]\cdot 5H_2O$ and *trans*-$[Pd(Ino)_2Br_2]\cdot 3H_2O$ have been solved. Both compounds are almost symmetry-centred, which introduces important problems into the solving process. The structure is *trans* square planar with N(7) coordinated inosine.

Introduction

The interaction of metal ions with nucleosides has gained interest in recent years after the discovery that some of these complexes show anticancer activity [1]. Among this type of complex, those corresponding to Pt(II) and Pd(II) have been the most studied ones. Most of the platinum–nucleoside complexes are binary or ternary complexes where halide ions [2], ammonia and amine derivatives [3] or amino acids [4] act as auxiliary ligands. Palladium–nucleoside complexes have also been studied, although to a smaller extent [5]. Crystallographic studies on metal–purine nucleoside complexes are scanty, probably due to their tendency to form polymeric and colloidal species; however, a few crystal structures have been solved by X-ray diffraction methods [6], including only one palladium compound, $[Pd(diethylentriamine)(guanosine)](ClO_4)_2$ [7].

In the present paper, we report the isolation and characterization by IR spectroscopy of several palladium(II) complexes of adenosine (Ado), guanosine (Guo), inosine (Ino) and xanthosine (Xao) with the auxiliary ligands chloride, bromide and thiocyanate. Likewise, the crystal and molecular structure of the complexes *trans*-$[Pd(Ino)_2Cl_2]\cdot 5H_2O$ and *trans*-$[Pd(Ino)_2Br_2]\cdot 3H_2O$ is described.

Experimental

Material

Adenosine, guanosine and inosine were obtained from Sigma Chemical Co.; xanthosine and $PdCl_2$ from Aldrich Chemie.

Instruments

IR spectra were obtained with a Perkin-Elmer 983G spectrophotometer, using KBr (4000–300 cm^{-1} range) and polyethylene (600–180 cm^{-1} range) as dispersant agents. Elemental analyses of C, H and N were performed in a Perkin-Elmer 240C microanalyzer. TG and DSC curves were carried out on a Mettler TA-3000 system in an atmosphere of pure air (flow rate 100 ml min^{-1}).

^1H NMR and ^{13}C NMR spectra were obtained in DMSO-d_6 solution and solid phase, respectively, with a Bruker AM300 NMR spectrometer. Doping with 100 ppm $CuCl_2$ was necessary to obtain ^{13}C NMR solid-phase spectra of free nucleosides. The spinning speed ranged from 3.0 to 3.2 kHz, cross-polarization times were about 1.5 ms, each spectrum resulting from av-

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0020-1693/93/$6.00

eraging as little as 200 and as many as 1000 scans, depending upon sample sensitivity.

Preparation of the complexes

(a) Dichloro bis(guanosine) palladium(II)

Guanosine (0.34 g) was dissolved in 50 ml of hot water and then 0.1 g of $PdCl_2$, previously dissolved in 10 ml of 1 M KCl, was added. After a few minutes, the solution became yellow, then it was left to stand at room temperature. After cooling, a yellow precipitate appeared, which was filtered off, washed with water, ethanol and ether and then dried at 110 °C for 24 h. *Anal.* Calc. for $C_{20}H_{26}PdCl_2N_{10}O_{10}$: C, 32.3; H, 3.5; N, 18.8. Found: C, 31.8; H, 3.0; N, 18.1%.

(b) Dibromo bis(guanosine) palladium(II)

The synthesis was analogous to the previous one, the only difference was the use of 1 M KBr instead of 1 M KCl to dissolve palladium chloride. *Anal.* Calc. for $C_{20}H_{26}PdBr_2N_{10}O_{10}$: C, 28.8; H, 3.1; N, 16.3. Found: C, 28.8; H, 3.1; N, 16.8%.

(c) Dichloro bis(xanthosine) palladium(II)

Procedure (a) was followed starting with 0.36 g of xanthosine. *Anal.* Calc. for $C_{20}H_{24}PdCl_2N_8O_{12}$: C, 32.2; H, 3.2; N, 15.0. Found: C, 31.8; H, 3.1; N, 14.8%.

(d) Dibromo bis(xanthosine) palladium(II)

Procedure (b) was followed starting with 0.36 g of xanthosine. *Anal.* Calc. for $C_{20}H_{24}PdBr_2N_8O_{12}$: C, 28.8; H, 2.9; N, 13.4. Found: C, 28.7; H, 2.2; N, 12.7%.

(e) Dichloro bis(inosine) palladium(II) pentahydrate

Inosine (0.30 g) was dissolved in 20 ml of 0.1 N HCl and heated to approximately 50 °C. $PdCl_2$ (0.10 g) was also dissolved in 20 ml of 0.1 N HCl at the same temperature. Both solutions were mixed and stirred, becoming yellow after a few minutes. The resulting solution was left at room temperature, yellow crystals appearing 24 h later. The crystals were filtered off, washed with cold water and left to dry in the air. *Anal.* Calc. for $C_{20}H_{34}PdCl_2N_8O_{15}$: C, 29.9; H, 4.3; N, 13.9. Found: C, 29.9; H, 3.9; N, 14.1%.

In previous reports, Pneumatikakis *et al.* [5a, b] have described two different paths to obtain the complexes $Pd(Ino)_2Cl_2$ and $Pd(Guo)_2Cl_2$ as non-crystalline solids, reaching the *cis* and *trans* isomer in each path. However, our attempts to obtain the *cis* isomer have been unsuccessful.

(f) Dibromo bis(inosine) palladium(II) trihydrate

Procedure (e) was followed, but employing 0.1 N HBr instead of hydrochloric acid. *Anal.* Calc. for $C_{20}H_{30}PdBr_2N_8O_{13}$: C, 28.0; H, 3.5; N, 13.1. Found: C, 27.7; H, 3.1; N, 13.1%.

(g) Dichloro adenosine palladium(II)

Adenosine (0.30 g) was dissolved in 30 ml of water. To this solution, another one, containing 0.20 g of $PdCl_2$ dissolved in 10 ml of KCl was added. A yellow precipitate immediately appeared, which was filtered off, washed with water, ethanol and ether and dried at 110 °C for 24 h. *Anal.* Calc. for $C_{10}H_{13}PdCl_2N_5O_4$: C, 27.0; H, 2.9; N, 15.8. Found: C, 27.6; H, 2.9; N, 16.3%.

(h) Dibromo adenosine palladium(II)

Procedure (g) was followed, employing KBr instead of KCl. *Anal.* Calc. for $C_{10}H_{13}PdBr_2N_5O_4$: C, 22.5; H, 2.5; N, 13.1. Found: C, 22.5; H, 2.4; N, 12.7%.

(i) Dithiocyanate guanosine palladium(II)

The synthesis was carried out in a manner similar to the one for $Pd(Guo)_2Cl_2$. When the solution became yellow, prior to the cooling step, 0.11 g of KSCN, dissolved in a minimum volume of water, was added. An orange precipitate appeared immediately, which was filtered off, washed with small portions of warm water and ethanol and then dried at 110 °C for 24 h. *Anal.* Calc. for $C_{12}H_{13}PdS_2N_7O_5$: C, 28.5; H, 2.6; N, 19.4. Found: C, 27.6; H, 2.0; N, 18.6%.

(j) Dithiocyanate xanthosine palladium(II)

Procedure (i) was followed but using 0.36 g of xanthosine. *Anal.* Calc. for $C_{12}H_{12}PdS_2N_6O_6$: C, 28.4; H, 2.4; N, 16.7. Found: C, 29.0; H, 1.6; N, 16.7%.

(k) Dithiocyanate inosine palladium(II)

Procedure (i) was followed but using 0.30 g of inosine. *Anal.* Calc. for $C_{12}H_{12}PdS_2N_6O_5$: C, 29.4; H, 2.5; N, 17.1. Found: C, 28.7; H, 2.4; N, 16.7%.

(l) Dithiocyanate hemi(adenosine) palladium(II)

0.2 g of $PdCl_2$, dissolved in 10 ml of 1 M KCl, was added to an aqueous solution containing 0.3 g of adenosine and 0.22 g of KSCN. A red colloidal precipitate immediately appeared, but stirring was continued for 10 min. The red solid was filtered off and stirred several times with 50 ml of warm water in order to wash it. After that it was dried at 110 °C for 24 h. *Anal.* Calc. for $C_7H_{6.5}PdS_2N_{4.5}O_2$: C, 23.6; H, 1.38; N, 17.7. Found: C, 23.7; H, 2.2; N, 17.4%.

Crystallographic work

trans-$[Pd(Ino)_2Cl_2]\cdot 5H_2O$, $FW = 803.7$, triclinic, space group $P\bar{1}$, $a = 15.681(4)$, $b = 7.406(3)$, $c = 6.846(3)$ Å, $\alpha = 92.99(2)$, $\beta = 105.25(3)$, $\gamma = 85.48(2)°$, $V = 764.3(8)$ Å^3, $D_c = 1.746$ g cm^{-3}, $Z = 1$, $F(000) = 410$, λ(Mo Kα) = 0.71069 Å, μ(Mo Kα) = 8.70 cm^{-1}, $T = 290$ K, crystal dimensions (faces): 0.1 mm (100–$\bar{1}$00) × 0.1 mm (001–00$\bar{1}$) × 0.2 mm (010–0$\bar{1}$0).

trans-$[Pd(Ino)_2Br_2]\cdot 3H_2O$, $FW = 803.7$, triclinic, space group $P1$, $a = 6.962(3)$, $b = 10.242(7)$, $c = 10.547(4)$ Å, $\alpha = 85.10(4)$, $\beta = 73.24(3)$, $\gamma = 89.17(4)°$, $V = 717(1)$ Å^3, $D_c = 1.983$ g cm^{-3}, $Z = 1$, $F(000) = 426$, λ(Mo Kα) = 0.71069 Å, μ(Mo Kα) = 34.72 cm^{-1}, $T = 200$ K, crystal dimensions (faces): 0.53 mm (010–0$\bar{1}$0) × 0.34 mm (101–$\bar{1}$0$\bar{1}$) × 0.14 mm (001–00$\bar{1}$).

A prismatic crystal of $[Pd(Ino)_2Cl_2]\cdot 5H_2O$ was chosen for the X-ray measurements. Crystal data were taken at 298 K on a Philips PW-1100 four-circle diffractometer. Low temperature data collection was not possible due to the existence of a crystal phase change. The unit-cell parameters were determined from automatic centring of 25 reflections ($4 \leqslant \theta \leqslant 12°$) and refined by least-squares. Intensities were collected using the ω-scan technique, scan width 1°, scan speed 0.03° s^{-1}. A total of 3234 reflections was measured in the range $2 \leqslant \theta \leqslant 25°$ ($-18 \leqslant h \leqslant 17$, $-8 \leqslant k \leqslant 8$, $0 \leqslant l \leqslant 8$), 2516 of which were assumed to be observed via the criterion $I \geqslant 2.5\sigma(I)$. Three reflections were measured every two hours as orientation and intensity control, significant intensity decay was not observed. Lorentz, polarization, but no absorption corrections were made.

For $[Pd(Ino)_2Br_2]\cdot 3H_2O$, a prismatic crystal was chosen. Data were taken on an Enraf-Nonius CAD-4 diffractometer at 200 K (no alteration was observed for this compound when lowering the temperature). Unit-cell parameters were determined as for the previous compound. A total of 5040 reflections was measured across the eight octants ($\theta \leqslant 25°$, $-8 \leqslant h \leqslant 8$, $-12 \leqslant k \leqslant 12$, $-12 \leqslant l \leqslant 12$). Equivalent hkl and $\bar{h}\bar{k}\bar{l}$ reflections were averaged to obtain 2520 independent data and 2326 with $I > 3\sigma(I)$ were retained for solving the structure. Seven standard reflections were checked every fifty measurements and showed no significative changes. An absorption correction was applied (gaussian integration, grid $10 \times 10 \times 10$, transmission range 0.3224–0.6307, $\mu = 34.72$ cm^{-1}). The data were finally corrected for Lorentz and polarization effects.

The coordinates for the palladium atom were selected, in both cases, to fix the arbitrary origin at (0, 0, 0) in space group $P1$. Peaks due to halogen atoms were identified and introduced from the Patterson maps, although both peaks overlap in the chlorine compound. The remaining atoms were introduced from successive ΔF maps with the aid of the SHELX76 computer program [8], which was also used for refining the structures by block-diagonal least-squares.

Both structures presented a serious problem as the palladium atom acts as a quasi-inversion centre for the purine atoms. This made the least-squares refinement impossible if no additional restrictions were imposed: temperature factors, distances and angles of pseudo-symmetry related atoms becoming clearly unacceptable. In order to avoid this problem, equal temperature factors were imposed to pseudo-symmetric atoms while their coordinates were independently refined in the $P1$ space group; such restriction was applied to all the atoms of the purine rings as well as the chlorines and the ribose atoms C1′, C4′, C5′ of the chloro complex and C3′ of the bromo complex, which incidentally are also related by the quasi-inversion centre. These restrictions could not be released even in the final stages of the refinement.

Most hydrogen atoms are seen in the last ΔF maps, so they were introduced and refined with fixed distances C–H (0.95 Å), N–H (0.87 Å), O–H (0.80 Å) and variable angles. Unobserved hydrogen atoms (H1′A, HO2A, HO3A, HW41, HW42, HW52 for the chloro complex and HW31, HW32 for the bromo complex) were not included.

The weight of the reflections in the refinement cycles was $(\sigma^2(F) + 0.0056F^2)^{-1}$ for the chloro complex whereas unit weights were applied for the bromo complex. f, f' and f'' were taken from International Tables for X-ray Crystallography [9]. In the last cycle, max. shift/e.s.d. values were about 0.2 for both compounds. The final R values were 0.040 and 0.026, respectively ($R_w = 0.044$ and 0.026, goodness-of-fit = 1.48 and 1.01).

Refined atomic coordinates of the non-hydrogen atoms are listed in Tables 1 and 2. Tables 3 and 4 give the bond distances and angles, respectively. Hydrogen coordinates and anisotropic temperature factors are included in the 'Supplementary material'.

Results and discussion

Infrared data

The most important IR bands for the $Pd(Nuc)_2X_2$ complexes (Nuc = Guo, Ino, Xao; X = Cl, Br) have been collected in Table 5. The analysis of these data shows that C=N and C=C bonds have a more pronounced double bond character than in the respective free ligands (a π-electron localization takes place), since their bands are shifted to higher frequencies in relation to their positions in the IR spectra of the free nucleosides [10]. Such a shift suggests that coordination of the nucleobases to Pd(II) takes place through a ring nitrogen atom [11].

In the 1200–1000 cm^{-1} region, the ν(C–O) bands due to the sugar moiety appear. These bands do not change their position on complexation, so we can think that ribose atoms do not participate in the complex formation. On the other hand, $Pd(Nuc)_2X_2$ complexes show a new band in the 342–338 (X = Cl) and 218–210 (X = Br) cm^{-1} wavenumber ranges. The presence of one single band suggests a *trans* geometry around the palladium atom, which we expect to be the thermodynamically more stable.

The main structural difference between adenosine and the other ligands is the absence of a hydrogen

TABLE 1. Atomic coordinates ($\times 10^4$) and equivalent temperature factors of non-hydrogen atoms of $[Pd(Ino)_2Cl_2]\cdot 5H_2O$

Atom	x/a	y/b	z/c	U_{eq}
Pd	0	0	0	1.52
Cl1	−843(1)	−322(3)	2308(3)	2.46
Cl2	780(1)	409(3)	−2332(3)	2.46
N1A	−536(4)	−5987(8)	−3541(11)	2.50
N1B	344(4)	5976(9)	3426(10)	2.50
C2A	−1341(6)	−6105(9)	−4906(14)	2.83
C2B	1139(6)	6226(9)	4813(14)	2.83
N3A	−1955(5)	−4739(9)	−5354(11)	2.33
N3B	1782(5)	5014(9)	5330(11)	2.33
C4A	−1715(5)	−3207(10)	−4344(12)	1.87
C4B	1583(5)	3408(10)	4230(12)	1.87
C5A	−906(5)	−2959(11)	−2898(12)	2.02
C5B	832(5)	3004(10)	2898(12)	2.02
C6A	−235(6)	−4433(11)	−2405(13)	2.10
C6B	121(6)	4312(11)	2391(13)	2.10
O6A	501(4)	−4389(8)	−1288(10)	2.80
O6B	−634(4)	4253(8)	1217(10)	2.80
N7A	−920(5)	−1207(9)	−2129(11)	2.01
N7B	925(5)	1220(9)	2179(11)	2.01
C8A	−1714(5)	−399(9)	−3054(13)	2.01
C8B	1730(5)	605(8)	3101(13)	2.01
N9A	−2198(4)	−1586(8)	−4394(10)	1.99
N9B	2168(4)	1892(8)	4428(10)	1.99
C1'A	−3120(5)	−1192(10)	−5566(12)	1.91
C1'B	3091(5)	1788(9)	5751(12)	1.91
O1'A	−3141(4)	286(8)	−6809(9)	2.97
O1'B	3525(4)	139(7)	5201(8)	2.32
C2'A	−3749(5)	−575(10)	−4289(12)	2.55
C2'B	3093(4)	1661(9)	7966(10)	1.84
O2'A	−4002(4)	−1980(10)	−3273(10)	4.18
O2'B	3908(3)	2279(7)	9176(8)	2.79
C3'A	−4532(4)	289(9)	−5894(11)	2.44
C3'B	3099(4)	−437(9)	8141(11)	2.07
O3'A	−5021(4)	−1110(8)	−7117(8)	2.93
O3'B	3313(3)	−1018(9)	10151(9)	3.13
C4'A	−4031(5)	1206(10)	−7286(10)	2.62
C4'B	3825(5)	−995(10)	6975(12)	2.62
C5'A	−3975(4)	3208(9)	−6761(12)	2.86
C5'B	3644(4)	−2991(10)	6145(11)	2.86
O5'A	−3497(4)	3925(8)	−8061(9)	3.62
O5'B	4317(3)	−3614(7)	5106(8)	2.78
OW1	2101(4)	−3216(8)	1040(9)	3.31
OW2	−2316(4)	3173(12)	−760(11)	5.24
OW3	3396(4)	4086(7)	2124(10)	3.96
OW4	−2578(6)	−2872(12)	−115(12)	5.56
OW5	5296(5)	3933(11)	−2093(11)	5.46

TABLE 2. Atomic coordinates ($\times 10^4$) and equivalent temperature factors of non-hydrogen atoms of $[Pd(Ino)_2Br_2]\cdot 3H_2O$

Atom	x/a	y/b	z/c	U_{eq}
Pd	0	0	0	1.40
Br1	−2817(2)	1260(1)	−335(1)	3.39
Br2	2855(2)	−1330(1)	171(1)	3.28
N1A	−1406(10)	−4516(7)	−701(7)	1.73
N1B	1804(10)	4354(7)	955(7)	1.73
C2A	−2534(12)	−5256(8)	360(8)	1.92
C2B	3124(12)	5055(8)	−42(8)	1.92
N3A	−3408(10)	−4836(6)	1547(6)	1.66
N3B	4003(9)	4664(6)	−1214(6)	1.66
C4A	−3008(12)	−3537(8)	1561(7)	1.40
C4B	3443(12)	3442(8)	−1317(7)	1.40
C5A	−1852(13)	−2724(8)	545(8)	1.44
C5B	2076(13)	2640(8)	−361(8)	1.44
C6A	−970(13)	−3173(9)	−725(8)	1.71
C6B	1194(13)	3077(9)	923(8)	1.71
O6A	−1(11)	−2556(7)	−1752(6)	2.78
O6B	46(11)	2495(7)	1904(6)	2.78
N7A	−1817(11)	−1498(7)	984(7)	1.70
N7B	1853(11)	1484(7)	−905(7)	1.70
C8A	−2900(13)	−1578(9)	2247(9)	1.71
C8B	3032(14)	1582(9)	−2121(8)	1.71
N9A	−3659(10)	−2812(6)	2647(6)	1.37
N9B	4062(10)	2760(6)	−2433(6)	1.37
C1'A	−4978(12)	−3332(8)	3934(8)	1.59
C1'B	5546(12)	3216(8)	−3682(7)	1.43
O1'A	−7006(7)	−3194(5)	3928(5)	1.85
O1'B	4530(7)	3502(5)	−4669(5)	1.79
C2'A	−4759(11)	−2649(7)	5102(7)	1.89
C2'B	7147(11)	2226(7)	−4187(8)	1.65
O2'A	−5336(10)	−3608(6)	6217(5)	3.47
O2'B	8941(7)	2967(5)	−4818(5)	2.03
C3'A	−6373(14)	−1582(9)	5250(9)	1.54
C3'B	6335(14)	1607(9)	−5203(9)	1.54
O3'A	−7010(9)	−1062(5)	6480(5)	2.47
O3'B	7712(8)	856(5)	−6123(5)	1.89
C4'A	−8013(11)	−2235(7)	4827(8)	1.61
C4'B	5448(11)	2780(6)	−5801(7)	1.33
C5'A	−9178(12)	−1330(8)	4149(9)	3.04
C5'B	3930(11)	2524(7)	−6525(7)	2.20
O5'A	−7886(10)	−451(6)	3161(6)	3.45
O5'B	2356(7)	1701(5)	−5699(5)	2.40
OW1	−39(10)	−4702(6)	3423(6)	2.36
OW2	500(13)	4618(9)	−3175(8)	4.67
OW3	−3241(14)	−1576(12)	7265(9)	6.15

atom bonded to N(1), so this atom can act as a new binding site. IR data for these complexes (Table 5) show, as more characteristic, the displacement to higher frequencies of the ν(C=N) and ν(C=C) bands in relation to the IR spectrum of free adenosine [12], which could be explained as in the above compounds. These complexes also display a single band for the vibrations ν(Pd–Cl) and ν(Pd–Br) at 346 and 253 cm^{-1}, respectively. We propose for these compounds a polymeric structure in which the palladium ion has a *trans* square planar geometry with either adenosine (through N(1) and N(7)) or halogen atoms acting as bridging ligands.

The IR spectra of the four isolated thiocyanate complexes are very similar to those corresponding to the $Pd(Nuc)_2X_2$ and $Pd(Ado)X_2$ complexes, with the additional feature of two new strong bands at about 2114 and 2163 cm^{-1} due to the vibration mode ν(C≡N). The first of these bands is characteristic of a sulfur-coordinated to the Pd(II) thiocyanate group, whereas the second one can be assigned to bridging thiocyanate groups [13], giving a polymeric structure.

TABLE 3. Bond distances (Å)

	$[Pd(Ino)_2Cl_2]\cdot 5H_2O$		$[Pd(Ino)_2Br_2]\cdot 3H_2O$	
Pd–X1	2.343(2)		2.425(1)	
Pd–X2	2.296(2)		2.434(1)	
	Inosine A	Inosine B	Inosine A	Inosine B
Pd–N7	1.991(6)	2.018(6)	2.014(7)	1.996(7)
N1–C2	1.365(10)	1.373(10)	1.345(10)	1.341(11)
C2–N3	1.330(10)	1.284(10)	1.329(10)	1.306(10)
N3–C4	1.325(10)	1.386(10)	1.366(10)	1.339(10)
C4–C5	1.408(10)	1.331(10)	1.363(11)	1.388(11)
C5–C6	1.443(11)	1.401(11)	1.416(11)	1.424(11)
C6–O6	1.208(9)	1.247(10)	1.225(10)	1.223(10)
C6–N1	1.397(10)	1.411(10)	1.409(11)	1.386(11)
C5–N7	1.375(10)	1.396(10)	1.378(11)	1.389(11)
N7–C8	1.348(10)	1.312(10)	1.325(11)	1.304(11)
C8–N9	1.359(9)	1.374(9)	1.362(11)	1.379(11)
N9–C4	1.365(10)	1.382(10)	1.380(10)	1.378(10)
N9–C1′	1.471(9)	1.490(9)	1.463(10)	1.464(10)
C1′–O1′	1.414(10)	1.432(9)	1.418(10)	1.427(9)
C1′–C2′	1.513(12)	1.523(11)	1.513(11)	1.507(11)
C2′–O2′	1.418(12)	1.423(7)	1.432(9)	1.428(9)
C2′–C3′	1.538(9)	1.563(10)	1.540(12)	1.531(12)
C3′–O3′	1.435(8)	1.410(9)	1.393(10)	1.422(10)
C3′–C4′	1.592(12)	1.573(11)	1.522(12)	1.515(11)
C4′–O1′	1.467(9)	1.465(9)	1.453(9)	1.442(8)
C4′–C5′	1.511(10)	1.575(10)	1.493(12)	1.508(11)
C5′–O5′	1.449(11)	1.454(10)	1.424(11)	1.422(9)

TABLE 4. Bond angles (°)

	$[Pd(Ino)_2Cl_2]\cdot 5H_2O$		$[Pd(Ino)_2Br_2]\cdot 3H_2O$	
X1–Pd–X2	177.5(1)		175.59(4)	
X1–Pd–N7A	89.0(2)		91.7(2)	
X1–Pd–N7B	90.4(2)		89.9(2)	
X2–Pd–N7A	90.2(2)		88.5(2)	
X2–Pd–N7B	90.4(2)		90.1(2)	
N7A–Pd–N7B	179.4(3)		177.4(3)	
	Inosine A	Inosine B	Inosine A	Inosine B
C2–N1–C6	125.5(6)	123.7(6)	125.1(7)	125.5(7)
N1–C2–N3	124.6(7)	125.6(7)	125.3(7)	125.7(7)
C2–N3–C4	113.5(7)	110.8(6)	111.1(6)	111.6(7)
N3–C4–C5	125.9(7)	128.6(7)	127.4(7)	127.4(7)
N3–C4–N9	128.3(7)	123.2(6)	125.5(7)	125.8(7)
C5–C4–N9	105.7(6)	108.2(7)	107.0(7)	106.7(7)
C4–C5–C6	120.8(7)	120.3(7)	121.0(8)	119.6(8)
C4–C5–N7	108.6(6)	109.0(7)	108.7(7)	108.5(7)
C6–C5–N7	130.5(7)	130.6(7)	130.3(8)	131.9(8)
N1–C6–C5	109.6(6)	110.8(7)	110.0(7)	110.0(7)
N1–C6–O6	122.4(7)	117.3(7)	121.0(8)	120.9(8)
C5–C6–O6	127.8(8)	131.9(8)	129.0(8)	129.1(8)
Pd–N7–C5	129.1(5)	124.6(5)	125.5(6)	125.9(6)
Pd–N7–C8	124.0(5)	129.1(5)	126.5(6)	127.3(6)
C5–N7–C8	106.9(6)	106.1(6)	106.8(7)	106.7(7)
N7–C8–N9	109.9(6)	111.2(6)	110.7(8)	111.8(8)
C4–N9–C8	108.9(6)	105.5(6)	106.7(7)	106.3(7)
C4–N9–C1′	126.5(6)	125.2(6)	123.8(7)	125.8(7)
C8–N9–C1′	124.3(6)	129.3(6)	129.5(7)	128.0(7)
N9–C1′–O1′	108.3(6)	107.2(5)	109.3(6)	108.4(6)
N9–C1′–C2′	114.2(6)	110.8(6)	114.2(7)	113.6(6)
O1′–C1′–C2′	104.6(6)	106.9(5)	106.9(6)	108.0(6)
C1′–O1′–C4′	109.2(6)	109.2(6)	110.7(5)	109.1(5)
C1′–C2′–O2′	114.6(6)	107.9(6)	105.3(6)	105.9(6)
C1′–C2′–C3′	101.0(6)	100.8(5)	102.6(6)	101.1(6)
O2′–C2′–C3′	112.6(6)	109.3(5)	109.4(6)	111.5(6)
C2′–C3′–O3′	109.5(6)	114.0(6)	116.4(7)	116.4(7)
C2′–C3′–C4′	101.3(6)	97.5(6)	102.8(7)	101.9(7)
O3′–C3′–C4′	106.7(6)	114.5(5)	115.0(7)	115.8(7)
O1′–C4′–C3′	104.7(5)	101.3(5)	105.8(6)	103.2(6)
O1′–C4′–C5′	110.2(6)	105.4(6)	109.3(6)	109.8(6)
C3′–C4′–C5′	110.4(6)	105.3(6)	115.1(7)	117.9(6)
C4′–C5′–O5′	106.8(6)	108.1(6)	111.3(7)	110.3(6)

Nuclear magnetic resonance studies

All isolated complexes decompose in DMSO-d_6 solutions. A similar pattern is observed in D_2O where, moreover, these complexes are poorly soluble at room temperature. Our attempts to find an adequate solvent have been unsuccessful. This behaviour has been observed by Hadjiliadis and Theophanides [2c] in their studies on Pt(II)–nucleoside complexes.

A detailed study of the ^1H NMR spectrum of $[Pd(Ino)_2Cl_2]\cdot 5H_2O$ in DMSO-d_6 indicates the presence of, at least, four different species, one of which is clearly free inosine while the others must be different Pd(II) complexes. From peak areas, we can infer that the proportion of free inosine is about 60%. The signals due to N(1)–H, C(2)–H and C(8)–H resonances of coordinated inosine are displaced downfield, with respect to free inosine. This displacement is higher for C(8)–H (0.5–0.8 ppm.) than C(2)–H (0.2–0.3 ppm.), which suggests that coordination takes place through the N(7) atom in all these species, which probably differ in the number and relative position of inosine, chlorine and solvent ligands in the coordination sphere of palladium atom or in the rotation position around the Pd–N bond (head-to-head or head-to-tail isomers).

The remaining xanthosine, guanosine and inosine complexes ^1H NMR spectra show a similar behaviour with a variable number of signals placed 0.4–0.9 ppm below the signals due to C(8)–H and N(1)–H of the free nucleoside. The ^1H NMR spectra of the adenosine complexes show a slightly different behaviour, since signals due to free adenosine do not appear, while their remaining features are similar to the other complexes.

Because of the unstable character of the DMSO solutions of these complexes, we have registered the ^{13}C NMR spectra in solid state. In Table 6 the chemical shifts of free nucleosides and their complexes have been collected. Assignments for the free ligands were made by comparison with their solution spectra and bibliographic data for Ado and Guo [14].

As can be seen in the Table, the chemical shift differences between the nucleosides and their complexes are small and very similar for all purine carbons which

TABLE 5. Selected bands (cm^{-1}) of the IR spectral data of the isolated compounds

Compound	ν(C≡N)	ν(C=O)	$\delta(NH_2)$	ν(C=C), ν(C=N)	ν(C–O)	ν(Pd–X)
$Pd(Guo)_2Cl_2$		1705, 1694	1630	1588, 1536, 1496	1176, 1099, 1052	338
$Pd(Guo)_2Br_2$		1705, 1695	1623	1585, 1536, 1495	1177, 1121, 1062	214
$Pd(Xao)_2Cl_2$		1703		1618, 1582, 1511, 1453	1174, 1117, 1086	342
$Pd(Xao)_2Br_2$		1702		1618, 1581, 1512, 1452	1173, 1118, 1086	210
$[Pd(Ino)_2Cl_2]\cdot 5H_2O$		1718		1592, 1555, 1515, 1492	1107, 1059, 1019	338
$[Pd(Ino)_2Br_2]\cdot 3H_2O$		1711		1592, 1559, 1513, 1492	1091, 1039, 1009	218
$Pd(Ado)Cl_2$			1647	1580, 1491	1087, 1056	346
$Pd(Ado)Br_2$			1646	1579, 1494	1088, 1054	253
$Pd(Guo)(SCN)_2$	2163, 2113	1693	1630	1589, 1536, 1496	1177, 1100, 1055	
$Pd(Xao)(SCN)_2$	2164, 2111	1694		1623, 1578	1176, 1123, 1087	
$Pd(Ino)(SCN)_2$	2163, 2114	1698		1593, 1558, 1492	1101, 1058	
$Pd(Ado)_{1/2}(SCN)_2$	2158, 2114		1645	1560, 1491	1084, 1052	

TABLE 6. ^{13}C NMR solid-phase chemical shifts (ppm) for the nucleosides and some of their Pd complexes

Compound	C(2)	C(4)	C(5)	C(6)	C(8)	C(1′)	C(2′)	C(3′)	C(4′)	C(5′)	SCN
Adenosine	155.8	149.3	120.3	155.8	138.8	89.9, 93.5	75.6	71.8	85.6	63.4	
$Pd(Ado)Cl_2$	155.6	147.5	118.3	155.6		89.2	75.8	73.0	88.0	63.7	
$Pd(Ado)Br_2$	155.6	148.8	119.8	155.6		89.9	74.4	72.6	88.8	63.4	
Guanosine	151.6	151.0	116.0	158.1	138.4	86.6	76.4, 79.1	72.9	86.6	63.1	
$Pd(Guo)_2Br_2$	153.3	153.3	116.5	156.2	135.0, 140.1	88.4	76.2	68.5, 72.2	85.6	63.4	
$Pd(Guo)(SCN)_2$	156.4	152.8	115.8	156.4	141.3	91.6	72.7	72.7	89.7	65.4	115.8
Inosine	143.0	147.3	125.3	158.7	140.5	90.2	75.4	69.7	85.2	63.3	
$[Pd(Ino)_2Cl_2]\cdot 5H_2O$	141.4	148.7	123.4	156.7	141.4	86.5	77.8	73.6, 71.7	82.0	64.1	
$[Pd(Ino)_2Br_2]\cdot 3H_2O$	142.0	149.2	122.2	155.3	142.0	85.8, 86.9	78.1, 76.3	71.9	80.9	59.5	
$Pd(Ino)(SCN)_2$	142.0	147.5	123.0	155.7	142.0	89.0	74.9	73.0	85.1	63.0	114.7
Xanthosine	152.0	139.6	119.0	160.8	138.1	89.3	72.9	71.0	85.5	64.0	
$Pd(Xao)_2Br_2$	152.8	141.2	115.9	156.9	141.2	91.8	72.9	72.9	89.7	64.6	
$Pd(Xao)(SCN)_2$	152.8	140.5	115.5	156.6	140.5	89.4	75.1	73.1	89.4	64.0	111.2

TABLE 7. Selected torsion angles

	$[Pd(Ino)_2Cl_2]\cdot 5H_2O$		$[Pd(Ino)_2Br_2]\cdot 3H_2O$	
	Inosine A	Inosine B	Inosine A	Inosine B
C8–N9–C1′–O1′ (ϕ_{CN})[a]	61.3(8)	8.4(9)	90.7(10)	71.5(10)
C8–N9–C1′–C2′	−54.8(9)	−108.0(9)	−29.0(12)	−48.6(11)
C2′–C1′–O1′–C4′ (ν_0)	−33.2(8)	−1.8(9)	12.4(8)	−2.0(8)
O1′–C1′–C2′–C3′ (ν_1)	44.2(8)	−28.3(7)	−28.5(8)	−22.7(8)
C1′–C2′–C3′–C4′ (ν_2)	−37.0(7)	44.6(7)	33.0(8)	37.5(7)
O1′–C4′–C3′–C2′ (ν_3)	18.8(7)	−46.2(8)	−26.5(8)	−39.6(8)
C1′–O1′–C4′–C3′ (ν_4)	8.4(8)	31.0(8)	9.4(8)	26.3(7)
O5′–C5′–C4′–O1′ (ϕ_{OO})	63.7(9)	75.4(9)	−72.8(8)	−64.3(7)
O5′–C5′–C4′–C3′ (ϕ_{CO})	178.9(9)	−178.0(8)	46.0(9)	53.4(9)

[a]Notation of Saenger [21] for the conformational torsion angles.

does not allow us propose a definitive binding site. C(8) of the adenosine complexes is not seen, its signal is probably hidden in the background (this signal is very weak in free adenosine). Only one signal is detected for the carbon of the thiocyanate groups, which seems to disagree with IR data.

Thermal behaviour

Thermogravimetric and DSC studies carried out on these complexes have revealed a similar thermal behaviour. Anhydrous complexes show in their thermogravimetric curves two principal weight loss steps. The first one takes place in the 200–250 °C temperature

range and was assigned to the partial dehalogenation and carbonization of the ribose moiety. The second one takes place in a variable temperature range (200–475 °C for $Pd(Xao)_2Cl_2$ and 300–675 °C for $[Pd(Ino)_2Br_2]\cdot 3H_2O$) and corresponds to the total combustion of the organic matter giving PdO as final residue in all cases. Between these two principal processes, a continuous weight loss occurs.

$[Pd(Ino)_2Cl_2]\cdot 5H_2O$ and $[Pd(Ino)_2Br_2]\cdot 3H_2O$ show, in the 50–120 °C temperature range, an initial weight loss process due to their dehydration. This process takes place in a single step and from DSC curves, dehydration enthalpy values have been calculated (29.3 and 44.7 kJ mol^{-1}, respectively).

Description of the structures

Pd(II) is coordinated, in both complexes, by the two halogen atoms and the two nitrogen atoms of position seven of the inosine molecules in a *trans* square planar arrangement, with a 'head-to-tail' relative situation of the two nucleoside moieties. Figure 1 shows a perspective view of the bromine compound. In such a disposition, the metal atom acts as a pseudo-inversion centre, which introduces severe difficulties in the structure solving process. In fact, if we attempt to solve the structure in the $P\bar{1}$ space group, we would be able to find and refine all purine atoms, though obviously not those corresponding to the chiral sugar ring. The problem is solved by introducing restrictions to the temperature factors, as indicated in 'Experimental'.

Pd–N(7) bond lengths (1.991–2.018 Å) are normal and agree well with the published data [7, 15]; Pd–Cl and Pd–Br distances are likewise normal and very similar

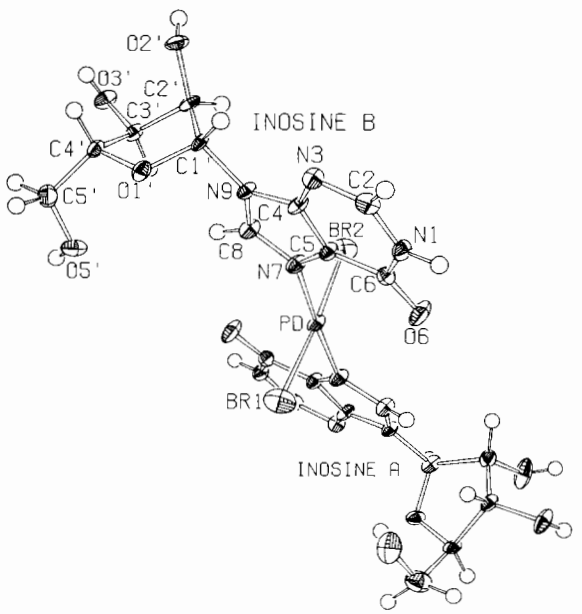

Fig. 1. ORTEP view of the molecule of the complex $[Pd(Ino)_2Br_2]$.

TABLE 8. Distances (Å) and angles (°) in hydrogen bonds

Donor	Acceptor[a]	Distance (D–A)	Distance (H–A)	Angle (D–H–A)
$[Pd(Ino)_2Cl_2]\cdot 5H_2O$				
N1A	Cl2 ($0\bar{1}0$)	3.245(7)	2.6(1)	125(13)
N1B	Cl1 (010)	3.199(7)	2.3(1)	166(11)
O2'A	O5'B ($\bar{1}0\bar{1}$)	2.910(9)		
O2'B	OW3 (001)	2.628(9)	1.9(1)	163(11)
O3'B	O3'A (102)	2.783(8)	2.1(1)	142(11)
O5'A	N3A (010)	2.844(9)	2.0(1)	168(9)
O5'B	OW5 ($0\bar{1}1$)	2.78(1)	2.1(1)	139(11)
OW1	O6A (000)	2.772(9)	2.0(1)	154(12)
OW1	O3'B ($00\bar{1}$)	2.798(9)	2.1(1)	154(12)
OW2	O6B (000)	2.788(8)	2.1(1)	151(11)
OW3	O5'B (010)	2.762(8)	2.0(1)	138(12)
OW3	OW1 (010)	2.719(9)	2.0(1)	146(13)
OW4	O2'A (000)	2.73(1)		
OW5	O5'A (101)	2.91(1)	2.2(1)	151(12)
$[Pd(Ino)_2Br_2]\cdot 3H_2O$				
N1A	OW2 ($0\bar{1}0$)	2.78(1)	1.93(5)	167(6)
N1B	OW1 (010)	2.797(9)	1.94(4)	170(6)
O2'B	O5'B (100)	2.653(7)	1.87(7)	168(8)
O3'A	O6A ($\bar{1}01$)	2.743(9)	2.09(8)	138(7)
O3'B	O6B ($10\bar{1}$)	2.705(9)	1.91(7)	171(8)
O5'A	Br2 ($\bar{1}00$)	3.248(6)	2.70(7)	127(7)
O5'B	O5'A ($10\bar{1}$)	2.629(8)	1.84(7)	169(8)
OW1	O1'A (100)	2.831(8)	2.1(1)	148(11)
OW1	O2'B ($\bar{1}\bar{1}1$)	2.860(8)	2.09(9)	162(10)
OW2	O2'B ($\bar{1}00$)	2.95(1)	2.2(1)	166(12)
OW3	O3'A (000)	3.00(1)		
OW3	O6A (001)	2.88(1)		

[a]Numbers in parentheses indicate the translation that has been applied to the corresponding atom. Thus, for example, OW5 ($0\bar{1}1$) refers to the atom placed at x, $y-1$, $z+1$, x, y, z being the coordinates of OW5 in Table 1.

to those found in tetrachloro and tetrabromopalladate anions [16]. Angles around the metal atom vary from the idealized 90° by ±1° and ±2° for the chloro and bromo complexes, respectively. The geometry is tetrahedrally distorted, with the halogen atoms placed on one side and the N(7) atoms placed on the other side of the average coordination plane.

Each structure includes two independent inosine molecules, so we have four values for each bond length or bond angle; we have also found in the literature five different free inosine molecules for comparison (two crystallographic independent ones for dihydrated inosine [17], two for orthorhombic anhydrous inosine [18] and one for monoclinic anhydrous inosine [19]). For each bond or angle, the fluctuation intervals of the corresponding data of the complexes and the ones of free inosine overlap, showing that no significant changes occur due to complexation. The only exceptions are the angles around N(7), which are slightly distorted (C(5)–N(7)–C(8) is increased and N(7)–C(8)–N(9) is decreased). The values are also similar to the only molecular inosine complex previously reported [20].

The purine rings labelled 'A' are planar within 2σ whereas the ones labelled 'B' are somewhat less planar (within 4σ). The exocyclic O(6) and C(1′) atoms are appreciably deviated from the planes, as well as the palladium atoms, especially in regard to purine A of the chloro complex (deviation = 0.326 Å). The angles between purine and coordination planes range from 72.0 to 76.0°.

The bond angles in the four ribose moieties are noticeably dissimilar, mainly due to conformational differences imposed by crystal packing and hydrogen bonding. Sugar Br–A is 'twist' puckered (C(3′)–endo–C(2′)–exo), Cl–B and Br–B are C(3′)–endo and Cl–A is C(2′)–endo. Table 7 clearly illustrates that ribose Cl–A puckering is quite different to those of the other sugar rings reported in this manuscript. Torsional angles in this Table also indicate the glycosidic conformation (*anti* in all cases) and the conformations around the C(4′)–C(5′) bond (*gauche–trans* for both riboses in the chloro complex and *gauche–gauche* in the bromo complex).

As expected, the structures are stabilized by very extensive hydrogen bonding, which determines the crystal packing. The positions of the hydrogen atoms, although not very accurate, are very helpful in assigning which atom is the donor and which one is the acceptor. Table 8 summarizes all intramolecular contacts assigned as hydrogen bonds.

The molecules are packed with all purine rings almost parallel (approximate directions $\bar{2}\bar{2}5$ and $\bar{3}1\bar{1}$ for the chloro and bromo complex, respectively), although no stacking interaction takes place, this being different to free inosine.

Supplementary material

Hydrogen coordinates, anisotropic temperature factors, angles between non-hydrogen atoms involved in hydrogen bonding, plane calculations and structure factors are available from the authors upon request.

Acknowledgements

The authors are grateful to Michel Simard (Université de Montréal) for collecting the diffraction data of $[Pd(Ino)_2Br_2]\cdot 3H_2O$. We also thank CICYT for financial support (project no. 0.402-86).

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