^{13}C NMR Spectra. The data for thiamine were in agreement with the coordination at the N-1′ nitrogen since significant downfield chemical shifts are exhibited by carbon atoms near to the pyrimidine N-1′ donor (C-6′, C-2′ and 2′-CH_3).

The present data strongly support the binding of dioxouranium(VI) to thiamine at the pyrimidine N-1′ site. The major bonding site of cocarboxylase to uranyl(VI) seems to be the pyrophosphate group even if a possible involvement of the N-1′ donor should be considered.

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T12

Chelation of the *cis*-$Pt^{II}(NH_3)_2$ Moiety by the Guanines of the Oligonucleotides d(T-G-G-C-C-A), d(A-T-G-G) and d(C-C-A-T-G-G)

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It is generally accepted that, within the cell, DNA is the primary target of the active aquated forms of the antitumor *cis*-$[Pt(NH_3)_2Cl_2]$ drug (*cis*-DDP) [1, 2]. The fact that only the *cis* isomer of the complex exhibits antineoplastic activity, suggests that the cytotoxic lesion could result from a particular bifunctional coordination of the *cis*-$Pt^{II}(NH_3)_2$ moiety [1]. Intrastrand cross-linking is one possibility [3] and platinum chelation by two adjacent guanines has received much support from studies with various DNAs [4–8] and oligonucleotide models [9–14]. We report here that the three d(T-G-G-C-C-A), d(A-T-G-G) and d(C-C-A-T-G-G) oligonucleotides give GG-platinum chelates.

We have studied the stoichiometric reactions between *cis*-$[Pt(NH_3)_2(H_2O)_2](NO_3)_2$ and the deoxyoligonucleotides d(T-G-G-C-C-A), d(A-T-G-G) and d(C-C-A-T-G-G) (1 Pt per oligonucleotide) in the 10^{-5}–10^{-4} *M* concentration range, in water at 37 °C. In the reaction conditions ^1H NMR shows that the self complementary hexanucleotides are essentially in the single strand form. For the three reactions, HPLC and ^1H NMR analyses show that the oligonucleotide is completely converted to a single complex. The same complex is obtained from the reaction with *cis*-DDP. High pressure gel permeation chromatography and atomic absorption spectroscopy coupled with the UV absorption of the complex, show that one platinum atom is bound per oligonucleotide.

^1H NMR (400 and 500 MHz) of the two hexanucleotide complexes ($1-5 \times 10^{-3}$ *M*) shows that they are single stranded in conditions where the free self-complementary oligonucleotides adopt a duplex structure [14, 15].

The metal binding sites in the d(T-G-G-C-C-A)[Pt], d(A-T-G-G)[Pt] and d(C-C-A-T-G-G)[Pt] complexes have been determined by the analysis of the pH dependence of the chemical shifts of the non exchangeable base protons. In the three cases, on going from basic to acidic pH, one observes the successive protonations of the thymine N3 (apparent pK_a *ca.* 10), of the N1 of the two guanines (app. $pK_a \approx 8.3$–8.5 instead of *ca.* 10 for the free oligonucleotides), of the N3 of the two cytosines (app. $pK_a \approx 4.1$–4.5) and of the adenine N1 (app. $pK_a \approx 3.4$–3.5). These data, together with the two different GH8 downfield shifts already encountered for the d(G-G)[Pt] and d(C-C-G-G)[Pt] chelates [10, 11], show that the *cis*-$Pt^{II}(NH_3)_2$ moiety is chelated by the N7 atoms of the adjacent guanines.

T_1 relaxation times of the base protons, nuclear Overhauser enhancements between the GH8 and deoxy-ribose H2′ and H3′, allowed the assignment of the external and internal guanines and together with two dimensional NMR (J-δ) allowed the identification of the C3′-*endo* deoxy-ribose that is characteristic of the diguanosine chelates [10, 16].

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T13

Palladium Compounds of Xanthine and Xanthine Derivatives

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The biological importance of purine bases is well known. The interaction of metal ions with nucleic acids, nucleosides and nucleotides has been an active area of inorganic and structural chemistry during the last few years, and a number of recent reviews exist on the subject [1, 2]. Recently much attention has been paid to palladium-containing complexes, due to their potent anti-tumor activities [3–7]. We report here the synthesis and characterisation of Pd(II) complexes with xanthine (XH), theophylline (TH), theobromine (TBH), 3,8-dimethylxanthine (DMH), caffeine (C) and 1,3,8-trimethylxanthine (TMH).

Experimental

The chemicals theophylline, theobromine, caffeine and $PdCl_2$ were purchased from Carlo Erba; and were used without further purification. 3,8-dimethylxanthine and 1,3,8-trimethylxanthine were synthesized in our laboratory [8, 9]. The Pd(II) complexes of these ligands were prepared in acid media (HCl 0.25 *N*), mixing solutions of the ligands and metal salt, $PdCl_2$ (2:1 mole ratio). Tetrachloro palladates were obtained from solutions with ligand: cation relation equal to 1:1 in acid media (HCl 2.5 *N*). The precipitates formed in each case were washed with distilled water, ethanol and ether and then air-dried.

The IR spectra were run on Beckman 4250. ^1H NMR studies were performed in DMSO-d_6 on Hitachi Perkin Elmer R-600 high resolution NMR spectrometer. TMS was used as internal reference.

Results and Discussion

Table I gives the colour, elemental analysis and the position of the stretching bands Pd–Cl and Pd–N of the isolated complexes.

TABLE I. Colour, Elemental Analysis and ν(Pd–Cl) and (Pd–N)[a] (cm^{-1}).

Compound	Colour	C	H	N	Cl	Pd	ν(Pd–Cl)	ν(Pd–N)
$[XH_2]_2[PdCl_4]\cdot 2H_2O$	brown	20.32	2.37	18.97	24.05	18.02	310	
		21.19	2.42	18.74	23.87	17.52		
$Pd(XH)_2Cl_2\cdot 2H_2O$	yellow	23.27	2.31	21.72	13.77	20.63	350	260
		22.90	2.03	21.41	13.85	19.72		
$[TH_2]_2[PdCl_4]$	brown	27.52	2.95	18.35	23.26	17.43	330	
		27.68	2.98	18.53	23.10	16.80		
$Pd(TH)_2Cl_2$	yellow	31.26	2.98	20.84	13.21	19.80	340	250
		31.40	2.84	20.88	13.52	19.20		
$[TBH_2]_2[PdCl_4]$	brown	27.52	2.95	18.35	23.26	17.43	305	
		27.39	3.01	18.64	23.35	17.26		
$Pd(TBH)_2Cl_2$	yellow	31.26	2.98	20.84	13.21	19.80	345	255
		30.78	3.01	20.69	13.52	19.40		
$Pd(DMH)_2Cl_2$	yellow	31.26	2.98	20.84	13.21	19.80	340	250
		30.28	2.89	20.27	12.80	19.80		
$Pd(C)_2Cl_2$	yellow	33.95	3.54	19.81	12.56	18.82	340	260
		33.92	3.42	19.60	13.05	18.71		
$Pt(TMH)_2Cl_2$	yellow	31.92	3.99	18.62	11.80	17.70	335	250
		32.34	3.96	18.17	11.70	18.20		

[a]Calculated values of elemental analysis in first row.