TABLE II. ^{1}H NMR Chemical Shifts in ppm.

Proton	XH	$Pd(XH)_2Cl_2$	TH	$Pd(TH)_2Cl_2$	TBH	$Pd(TBH)_2Cl_2$
C-8-H	7.90	8.30	7.95	8.05	7.97	7.97
C-8-CH_3						
Proton	DMH	$Pd(DMH)_2Cl_2$	C	$Pd(C)_2Cl_2$	TMH	$Pd(TMH)_2Cl_2$
C-8-H			7.95	7.95	2.40	2.40
C-8-CH_3	2.35	2.70				

From magnetic data, (all the compounds are diamagnetic) square planar structures for PdL_2Cl_2 complexes (where L = XH, TH, TBH, DMH, C and TMH) and tetrachloro palladate anion have been proposed.

In PdL_2Cl_2 complexes complexation of the purine base to Pd(II) causes downfield shifts of protons adjacent to the coordination site. Table II shows the proton chemical shifts in parts per million of the ligand and its Pd(II) complexes. The shift to downfields experienced by C-8-H and C-8-CH_3 protons is indicative of complexation at the N_9 position of the ligand (except for the xanthine).

The infrared spectra of PdL_2Cl_2 complexes showed single Pd–Cl and Pd–N stretching bands. This is consistent with a *trans*-configuration. In the tetrachloro palladate compound only the ν(Pd–Cl) is present.

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T14

Crystal Structure of the $[Pt(9\text{-Methylguanine})_4]^{2+}$ Cation

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The $[Pt(9\text{-methyl-guanine})_4]^{2+}$ cation is the first example of a Pt^{2+} compound to have four purine bases as ligands. This compound is especially interesting as it was suggested earlier that the anti-tumor drug *cis*-dichlorodiammineplatinum(II) could lose all four ligands in order to interact with the purine bases of the DNA double helix [1].

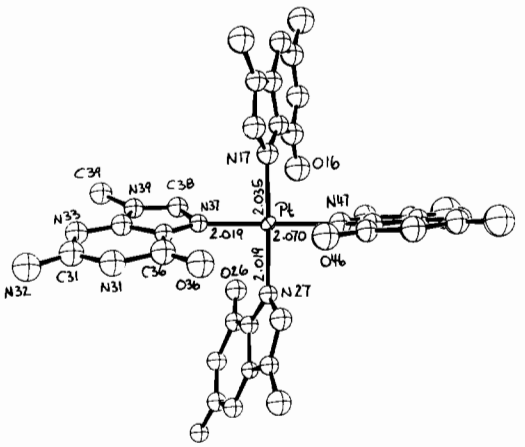

Fig. 1. Structure of the complex.

The title compound was prepared by heating K_2PtCl_4 with excess 9-methylguanine (ratio 1:6) under reflux for several hours. The reaction mixture was separated by preparative reverse-phase high-performance liquid chromatography to remove excess ligand and some minor impurities possibly due to the formation of other Pt–guanine complexes. $[Pt(9\text{-Methylguanine})_4]^{2+}Cl^-(CF_3COOH)^-$ crystallizes as colorless bricks in the triclinic space group $P\bar{1}$, with $a = 16.234(8)$ Å, $b = 13.475(7)$ Å, $c = 10.856(5)$ Å, $\alpha = 103.80(4)°$, $\beta = 91.40(4)°$, $\gamma = 115.50(3)°$, $Z = 2$. The structure consists of a $Pt(9\text{-MeG})_4^{2+}$ cation in which each purine ligand is coordinated through its N(7) nitrogen atom (Fig. 1) to result in a PtN_4-square plane. The purine ligands are in the usual alternating head to tail arrangement with the adjacent C(6)–O(6) pointing in opposite directions. The average Pt–N distance is 2.036 Å. The current R-value is 7.8% with 4475 independent reflections.

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T15

Formation of Chelates between *cis*-Diamminedichloroplatinum(II) and either GG or GCG Units in Oligonucleotides and DNA

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After the discovery of the cytostatic properties [1] of *cis*-diamminedichloroplatinum(II) and its subsequent successful use as an anti-tumor drug [2], a large number of investigations on structure–activity relations and on the mechanism of action have evolved [3]. The main target of the drug is now generally accepted to be the chromosomal DNA in the cell, and a specific binding to this DNA is supposed to be a crucial step in cell death [4].

Early investigations have shown that the kinetically most favoured binding site is the N7 atom of the guanine bases, although other sites (such as N7 of adenine, N1 of adenine and of guanine after deprotonation, N3 of cytidine) also bind to metal ions and in particular to platinum [5, 6].

Since *cis*-$PtCl_2(NH_3)_2$ possesses two binding sites after complete hydrolysis [7], there has to be a second binding in addition to guanine N7. The following possibilities have been put forward in the literature:

(a) The formation of a specific chelate with one guanine base [8] through N7 and O6.

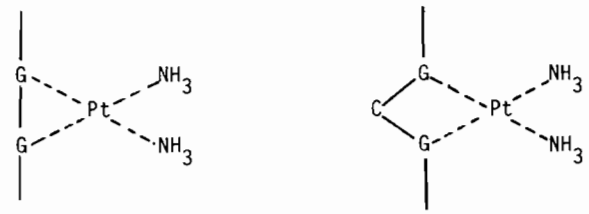
(b) The formation of an interstrand crosslink between two bases in opposite strands of DNA [9].

(c) The formation of an intrastrand crosslink between two bases in the same strand of DNA [10].

(d) The formation of a crosslink between DNA and a protein residue [11].

As has been summarized elsewhere [12], most results point towards intrastrand crosslinks as the most likely target responsible for the antineoplastic activity, although a key rôle for the other possibilities cannot be completely ruled out. Because several single-stranded oligonucleotides are commercially available or can be synthesized rather easily, we are working on the synthesis and characterization of adducts formed between *cis*-$Pt(NH_3)_2^{2+}$ and oligonucleotides. The results of this work are compared with those obtained from mutation studies in bacterial cells (specific hotspots for *cis*Pt-induced base-pair substitutions) [13], and with those from enzymatically hydrolysed *cis*-Pt treated salmon sperm DNA [14].

From a series of GG- and GCG-containing di-, tri-, tetra-, hexa- and octanucleotides the following two specific intrastrand crosslinks have been unequivocally found so far:



Mutation studies have indicated that apart from GCG sequences, GAG sequences may also occur [13]. This has not yet been investigated in oligonucleotides. The occurrence of GG-Pt chelates has also been recently found by other groups [15, 16].

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