Some preliminary stopped-flow measurements under pressure[15] clearly demonstrated the rapid formation of Ir(cod)(phen)I in 0.5 mol dm^{-3} NaI. The subsequent decreases in absorbance at ca. 300 nm, ascribed to the dioxygen-uptake reaction, results in good first-order plots at low pressures. However, at higher pressures a further reaction interferes at longer reaction times so that no usable infinity absorbances measurements are obtained. The Guggenheim method was applied in such cases to determine k_{obsd}. The interference increases markedly with pressure so that reaction 1 could not be studied at pressures higher than 750 bar in the presence of excess I^-. It is clear, therefore, that the mechanism of dioxygen uptake by the five-coordinate species Ir(cod)(phen)X is indeed a multistep process. No such effects were observed in the absence of excess I^-. The plots of ln k vs. pressure obtained by using the data in Table III are linear, and the volumes of activation were calculated from their slopes.

The large negative values of $\Delta V^{\ddagger}$ for k_1 (at $[I^-] = 0$) and k_2 (at $[I^-] = 0.5$ mol dm^{-3}) emphasize the associative nature of the dioxygen-uptake reactions, which is in agreement with the negative $\Delta S^{\ddagger}$ values reported in Table II. However, the trend in $\Delta V^{\ddagger}$ is opposite to that seen in $\Delta S^{\ddagger}$ for k_1 and k_2. Such tendencies have been reported for various systems in recent years.[16] In order to interpret the magnitude of $\Delta V^{\ddagger}$ it is important to keep in mind that $\Delta V^{\ddagger}$ in general consists of two major contributions: $\Delta V^{\ddagger}_{intr}$, which arises from the changes in bond lengths and bond angles, and $\Delta V^{\ddagger}_{solv}$, which is ascribed to the changes in solvation on going from the ground state to the transition state. For the dioxygen uptake by $Ir(cod)(phen)^+$ no significant contribution from $\Delta V^{\ddagger}_{solv}$ is expected since no changes in charge, i.e., in electrostriction, occur during this process. The measured $\Delta V^{\ddagger}$, therefore, mainly represents $\Delta V^{\ddagger}_{intr}$ and reflects the significant decrease in volume during the associative bond-formation step. However, for the dioxygen uptake by Ir(cod)(phen)I, the process must include release of I^- to produce the final product, viz., $IrO_2(cod)(phen)^+$. This is expected to cause significant changes in solvation due to the creation of charges and results in a negative contribution from $\Delta V^{\ddagger}_{solv}$ toward the overall $\Delta V^{\ddagger}$ values. The more negative value of $\Delta V^{\ddagger}$ for k_2 illustrates that at least some charge separation has occurred during this dioxygen uptake process. This is in line with the suggested reaction paths ii and iii in Scheme III. The complete release of I^-, which is probably a fast step at normal pressure, may slow down at higher pressures due to its dissociative nature and so interfere with the dioxygen-uptake reaction. In addition, electron transfer is expected to result in a negative contribution[17,18] toward $\Delta V^{\ddagger}$. It follows that although the magnitude of $\Delta V^{\ddagger}$ unequivocally depicts the nature of the dioxygen-uptake process, the various contributing effects do not allow a differentiation between routes i, ii, and iii in Scheme III at this stage.

Registry No. $[IrO_2(cod)(phen)]Cl$, 80584-38-9; $[IrO_2(cod)(phen)]I$, 80584-39-0; $[IrO_2(cod)phen)]SCN$, 80584-41-4; $[Ir(cod)(phen)]Cl$, 53522-11-5; Ir(cod)(phen)I, 41392-85-2; Ir(cod)(phen)SCN, 66779-01-9; O_2, 7782-44-7.

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Complexes of Platinum(II) with Chiral Diamines and Guanosine. Stereochemical Investigation Related to the Mechanism of the Antitumor Activity of *cis*-Bis(amine)platinum(II) Type Complexes

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Platinum(II) complexes of 2 mol of guanosine and a series of chiral and *meso*-1,2-diamines have been synthesized. Comparison of the circular dichroism spectra of these complexes with those of guanosine and of the complexes with only one guanosine show that in bis complexes the two guanosine molecules are arranged to form, stereospecifically, a guanosine–Pt–guanosine chirrole irrespective of the absolute configuration of the diamine. The geometry of the chirrole has been established by an analysis of the chiroptical properties of the derivatives of chiral cyclohexanediamines and 9-methylguanine to be that of a right-hand propeller with the two guanosine molecules arranged "head-to-tail". It is proposed that this arrangement arises from the formation of hydrogen bonds between O(6) of guanosine and the NH_2 groups of the diamines. In the case of chiral diamines the spatial orientation of the hydrogen bonds controls the thread of the propeller, the resulting structure being rather rigid. Variable-temperature ^1H NMR spectra help to support this picture.

Introduction

The antitumor activity of bis(amine)platinum(II) complexes with two cis anionic leaving groups is by far one of the most outstanding results in the field of the bioactivity of metal complexes.[1,2] Although the clinical application of *cis*-$[(NH_3)_2PtCl_2]$ is already widespread corresponding to the commercial production of the drug,[3] its mechanism of action is still a subject of intense research. Up to now a satisfactory and definitive answer has not been reached; the only well-established evidence is the direct interaction of platinum with DNA[4] and in particular with the guanine base.[5,6]

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(2) (a) Rosenberg, B. *Platinum Met. Rev.* **1971**, *15*, 42. (b) Cleare, M. J. *Coord. Chem. Rev.* **1974**, *12*, 349. (c) Rosenberg, B. "Metal Ions in Biological Systems"; Siegel, H., Ed.; Marcel Dekker: New York, 1980; Vol. 11, p 127. (d) Cleare, M. J.; Hydes, P. C. *Ibid.*, p 1.
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(4) (a) Howle, J. A.; Gale, G. R. *Biochem. Pharmacol.* **1970**, *19*, 2757. (b) Thomson, A. J. *Platinum Met. Rev.* **1977**, *21*, 2.
(5) Rosenberg, B. *Biochemie* **1978**, *60*, 859.

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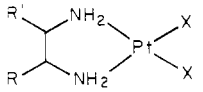
Table I. Analytical Data

compd	% C		% H		% N	
	calcd	found	calcd	found	calcd	found
$[(en)Pt(Guo)_2]Cl_2 \cdot 2Me_2CO$	33.33	33.10	4.56	4.28	16.67	16.50
$[((R)\text{-pn})Pt(Guo)_2]Cl_2 \cdot Me_2CO$	32.36	32.30	4.36	4.30	17.42	17.22
$[((S)\text{-pn})Pt(Guo)_2]Cl_2 \cdot Me_2CO$	32.36	31.99	4.36	4.31	17.42	17.35
$[((R,R)\text{-bn})Pt(Guo)_2]Cl_2 \cdot 0.5Me_2CO$	32.24	32.43	4.32	4.45	17.70	17.48
$[((S,S)\text{-bn})Pt(Guo)_2]Cl_2 \cdot Me_2CO$	33.12	32.90	4.50	4.40	17.16	17.00
$[(meso\text{-bn})Pt(Guo)_2]Cl_2 \cdot 1.5Me_2CO$	33.96	34.14	4.67	4.70	16.68	16.78
$[((R,R)\text{-chxn})Pt(Guo)_2]Cl_2$	32.98	33.28	4.23	4.36	17.75	17.53
$[((S,S)\text{-chxn})Pt(Guo)_2]Cl_2 \cdot 2H_2O$	31.77	31.85	4.48	4.38	17.10	16.92
$[(meso\text{-chxn})Pt(Guo)_2]Cl_2$	32.98	33.07	4.23	4.36	17.75	17.65
$[((R)\text{-pen})Pt(Guo)_2]Cl_2$	34.69	34.57	3.95	4.00	17.36	17.25
$[((R,R)\text{-dpen})Pt(Guo)_2]Cl_2$	39.06	38.88	4.02	4.15	16.08	15.95
$[((S,S)\text{-dpen})Pt(Guo)_2]Cl_2 \cdot 2H_2O$	37.70	37.60	4.25	4.18	15.55	15.25
$[(meso\text{-dpen})Pt(Guo)_2]Cl_2 \cdot 3H_2O$	37.15	37.30	4.37	4.27	15.30	15.20
$[((R,R)\text{-chxn})Pt(9\text{-MeG})_2]Cl_2 \cdot Me_2CO$	32.81	32.55	4.43	4.55	21.87	21.45
$[((S,S)\text{-chxn})Pt(9\text{-MeG})_2]Cl_2 \cdot 0.5Me_2CO$	31.66	31.85	4.19	4.25	22.73	22.34
$[(en)Pt(Guo)](NO_3)_2 \cdot 2H_2O$	20.63	20.42	3.58	3.61	18.05	17.93
$[((R,R)\text{-chxn})Pt(Guo)](NO_3)_2 \cdot H_2O$	26.15	25.97	3.95	4.03	17.16	17.00
$[((S,S)\text{-chxn})Pt(Guo)](NO_3)_2 \cdot 2H_2O$	25.53	25.37	4.12	4.09	16.75	16.58

The DNA double helix is per se a chiral structure;[7] therefore, platinum complexes carrying enantiomeric amines are expected to produce different diastereoisomeric interactions with this helical arrangement.

We have therefore synthesized a series of platinum(II) complexes with chiral chelating diamines of formula



$R = R' = CH_3, C_6H_5, {}^1/_2(C_4H_8)$
$R = H; R' = CH_3, C_6H_5$
$X = Cl, {}^1/_2SO_4$

The diamines investigated have *R*, *S*, *R,R*, *S,S*, or meso absolute configuration.[8,9]

The platinum complexes of the series reported above are currently being tested on tumors in mice, and this work is still in progress.[10] Up to now we did not find any striking difference in the antitumor activity of enantiomeric complexes; however, the complexes with diamines of *R* or *R,R* absolute configuration are slightly more active than the complexes with the corresponding diamines with *S*, *S,S*, or *R,S* configuration, but these differences are much less relevant than those previously reported for cyclohexanediamine derivatives.[11] These results suggest some small, but definitive differences in the interaction of enantiomeric platinum complexes with DNA.

We have therefore undertaken a physicochemical investigation on the interaction of the $[(diamine)PtX_2]$ complexes reported above with a series of model substrates of increasing complexity, namely, guanosine, other simple nucleotides, and finally DNA.

This paper describes the study of the interaction of the (chiral diamine)platinum moiety with one or two molecules of guanosine.

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(9) Gullotti, M.; Pasini, A.; Fantucci, P.; Ugo, R.; Gillard, R. D. *Gazz. Chim. Ital.* **1972**, *102*, 855.
(10) Ugo, R.; Spreafico, F.; Pasini, A.; Filippeschi, A., work in progress.
(11) Some scattered, independent, reports on the antitumor activity of platinum(II) complexes of (*R,R*)-, (*S,S*)-, or *meso*-cyclohexanediamines have already appeared. These enantiomeric complexes showed some significant differences in the antitumor activity against leukemia 1210 in mice. See: Kidani, Y.; Inagaki, K.; Saito, R.; Tsugagoshi, S. *J. Clin. Hematol. Oncol.* **1977**, *7*, 197. Noji, M.; Okamoto, K.; Kidani, Y. *J. Med. Chem.* **1981**, *24*, 508.

Experimental Section

Microanalyses were from the microanalytical laboratory of the University of Milan and are reported in Table I. In this work the following instruments were used: Beckman DK 2A for electronic spectra, Jobin-Yvonne Mark III for circular dichroism measurements (CD). The ^1H NMR spectra were recorded on a Bruker WP80 instrument and a Varian XL200, both operating in the FT mode; the spectra were obtained in D_2O, with DSS as internal standard. Conductivity measurements have been carried out on a Philips PR 9500 conductimeter. The preparation of the optically active diamines is described elsewhere.[9] Due to some hazard in the preparation of *trans*-1,2-diaminocyclohexane (see footnote to ref 9), this compound was purchased from Du Pont (technical grade) as a mixture of trans and cis isomers, which were separated through their nickel complexes.[12] The trans isomer was then separated into its optical isomers as already described.[9]

(Diamine)dichloroplatinum(II). The various complexes were prepared following a standard procedure.[13] No relevant differences were found in the preparation of the various isomers.

Bis(guanosine)(diamine)platinum(II) Chloride.[14] These compounds were prepared by mixing, in 100 mL of water, 1 mmol of the appropriate $[(diamine)PtCl_2]$ complex with 2.1 mmol of guanosine (Fluka). The resulting slurry was stirred overnight at 60 °C, obtaining a clear solution. The bn derivatives required a longer time (3 days). With dpen, a DMF/water (3/1) mixture was used as solvent. The solution was evaporated under reduced pressure to about 30 mL, filtered, and evaporated again to obtain an oily residue that was treated with a large excess of acetone. A white material crystallized in a few hours. The compounds crystallized with 0.5–2 mol of acetone, the presence of which is confirmed by elemental analyses (Table I) and ^1H NMR spectra. The pure compounds could be obtained only by dissolving the crystalline materials in 1–2 mL of water and evaporating the solution to dryness in vacuo.

Bis(9-methylguanine)(diamine)platinum(II) Chloride. These compounds were obtained as above, starting from 9-methylguanine (9-MeG) (Fluka).

(Guanosine)(diamine)platinum(II) Nitrate.[15] A 1-mmol sample of $[(diamine)PtX_2]$ (X = Cl, I) was treated, in water, with 2 mmol of $Ag(NO_3)$ and heated at 50 °C for 1 h. AgX was removed by filtration, and 1 mmol of guanosine was added to the solution; the slurry was stirred overnight at room temperature. The resulting clear solution was concentrated under reduced pressure. A white material separated by addition of a large excess of methanol. Analyses are reported in Table I.

Results and Discussion

Preparation of the Complexes. The complexes $[(chiral\ diamine)Pt(Guo)_2]Cl_2$ have been synthesized by a well-docu-

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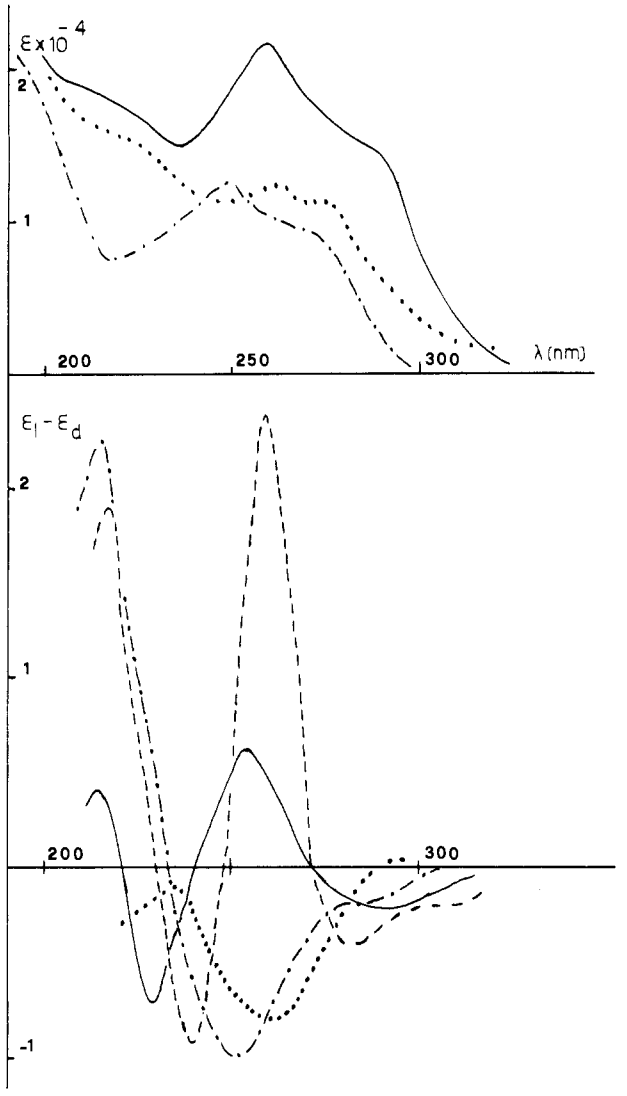

Figure 1. Electronic and circular dichroism spectra, water solutions, of Guo (-·-), GpG (---), $[(en)Pt(Guo)_2]Cl_2$ (—), and $[(en)Pt(Guo)](NO_3)_2$ (···). Units of ϵ and $\Delta\epsilon$ are mol^{-1} dm^3 cm^{-1}.

mented method.[14] They are very soluble in water from which they can be crystallized by the addition of a large excess of acetone, which is usually retained in the crystal structure (see Table I); the presence of acetone was confirmed by ^1H NMR spectroscopy in D_2O. The compounds behave as 2:1 electrolytes in water.[16] By analogy with $[(NH_3)_2Pt(Guo)_2]Cl_2$ and $[(en)Pt(Guo)_2]Cl_2$, for which the X-ray structures have been reported,[17,18] we can describe these compounds as having a cationic unity containing two guanosine molecules bound via N(7) to the (diamine)platinum moiety.

We have also synthesized some monoguanosine complexes of formula $[(chiral\ diamine)Pt(Guo)](NO_3)_2 \cdot xH_2O$ in which Guo is likely to be chelated through O(6)–N(7) (see ref 15 for a discussion on this point). They behave as 2:1 electrolytes in water in which they are very soluble.[15]

Trends of the Electronic and Circular Dichroism Spectra. In Figure 1 the electronic and CD spectra (water solutions) of Guo, $[(en)Pt(Guo)_2]Cl_2$, and $[(en)Pt(Guo)](NO_3)_2$ are reported. The electronic spectra of the platinum compounds

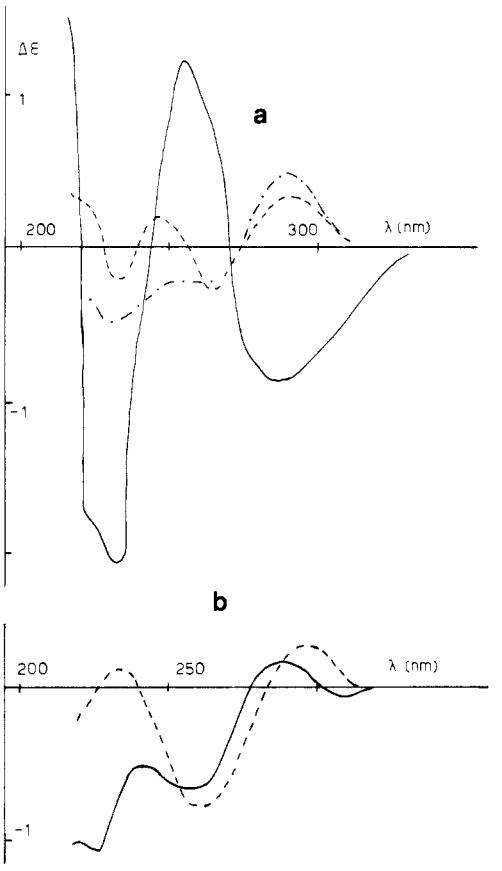

Figure 2. Circular dichroism spectra, water solutions, of (a) $[(chxn)Pt(Guo)_2]Cl_2$ and (b) $[(chxn)Pt(Guo)](NO_3)_2$. The configurations of the diamines are *S,S* (—), *R,R* (---), and *meso* (-·-). Units of $\Delta\epsilon$ are as in Figure 1.

are rather similar to that of free guanosine, with a slight bathochromic shift (Figure 1). The CD spectrum of $[(en)Pt(Guo)]^{2+}$ is rather similar to that of Guo, but with a relevant bathochromic shift, whereas that of $[(en)Pt(Guo)_2]^{2+}$ is completely different (Figure 1). In particular the broad negative band, centered at about 245 nm in free guanosine and at 255 nm in the monoguanosine complexes (Figures 1 and 2), is split into a positive–negative doublet with the positive component lying at lower energy. This feature of the spectrum resembles somewhat that of the dinucleotide GpG[18] (also reported in Figure 1) except for the intensity ratio of the two components. This latter spectrum has been rationalized in terms of an exciton coupling of electronic transitions localized on the two guanine rings.[19] Such a couplet seems therefore typical of an arrangement of two guanosine units linked together as, for instance, by a ribose–phosphate–ribose bridge (as in GpG) or via N(7)–Pt–N(7) bonds (as in $[(diamine)Pt(Guo)_2]^{2+}$) (see Figures 2 and 3).[20] The following discussion will be based on this assumption.

Analysis of the Conformational Aspects. Before examining in detail the spectroscopic properties of the diastereoisomeric complexes $[(chiral\ diamine)Pt(Guo)_2]^{2+}$, we shall briefly discuss the various conformations theoretically possible, in solution, for these complexes (Figure 4). Let us consider first the ribose residues. In the absence of any direct information on the structure in solution, we can assume that the preferred

(16) The plot of $A - A_0$ vs. $C^{1/2}$, in the concentration range 10^{-2}–5×10^{-4} mol dm^{-3} gave straight lines with slopes characteristic of 2:1 electrolytes. See: Feltham, R. D.; Hayter, R. G. *J. Chem. Soc.* **1964**, 4587.

(17) (a) Cramer, R. E.; Dahlstrom, P. L. *J. Clin. Hematol. Oncol.* **1977**, *7*, 330. (b) Cramer, R. E.; Dahlstrom, P. L.; Seu, M. J. T.; Norton, T.; Kashiwagi, M. *Inorg. Chem.* **1980**, *19*, 148.

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(19) (a) "Handbook of Biochemistry", 2nd ed.; Sober, H. A., Ed.; CRC Press: Cleveland, OH, 1973. (b) Brahms, J. In "Fundamental Aspects and Recent Developments in Optical Rotatory Dispersion and Circular Dichroism"; Ciardelli, F., Salvadori, P., Eds.; Heyden and Sons: London, 1973; p 307.

(20) This fact has already been observed; see, for instance: Marzilli, L. G.; Chalilpoyil, P. *J. Am. Chem. Soc.* **1980**, *102*, 873.

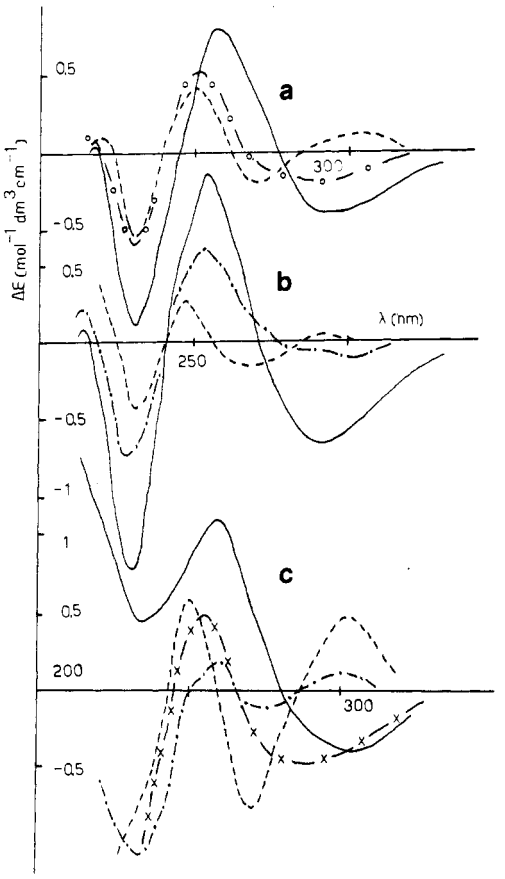

Figure 3. Circular dichroism spectra, water solutions, of (a) *cis*-$[(NH_3)_2Pt(Guo)_2]Cl_2$ (-○-) and $[(pn)Pt(Guo)_2]Cl_2$, (b) $[(bn)Pt(Guo)_2]Cl_2$, and (c) $[((R)\text{-pen})Pt(Guo)_2]Cl_2$ (-×-) and $[(dpen)Pt(Guo)_2]Cl_2$. Symbols for the configurations of the diamines are as in Figure 2.

orientation of the sugar moieties in these bis(guanosine) complexes is analogous to that found in the solid state in the ethylenediamine or bis(ammonia) complexes, i.e., anti,[17,18] as this is the less crowded structure. We must then take into account the rotation of the guanosine molecules around the coordinative Pt–N(7) bonds, which has been shown to occur in solution through NMR spectroscopy.[21] Such a rotation can give rise to two extreme situations with respect to the two guanosine molecules, i.e., head-to-tail (case a of Figure 4) and head-to-head (case b of Figure 4). Obviously other intermediate arrangements are possible where the guanine molecules are not perpendicular to the coordination plane.

Finally we must consider the flipping of the nonplanar, five-membered chelate ring of the diamine.[22] For C-substituted diamines the most stable conformation of the chelate ring in square-planar complexes of Pt is "gauche", with the substituents at the carbon atom equatorial[23] (see Figure 4). This conformation is the only one possible for chiral chxn because of the presence of the two fused rings (Figure 4, i and j); of course with the meso forms of the diamines, the most stable conformation of the chelate ring will be with one substituent in the equatorial and the other in the axial position.[23]

In conclusion the above analysis would suggest that the most stable arrangements for $[(\text{chiral diamine})Pt(Guo)_2]^{2+}$ complexes are a–d in Figure 4 with diamines of absolute configuration *S* or *S,S* (δ[24] conformation of the chelate ring corresponding to equatorial substituents) and e–h with *R* or *R,R* diamines (λ conformation of the chelate ring, again corresponding to equatorial substituents). Of course these are only extreme situations since unsymmetrical "gauche" and even envelope conformations of the chelate ring are also possible,[25] especially for monosubstituted diamines (viz., pn and pen). Finally with meso diamines, the λ and δ conformations are of equal stability,[23] and their interconversion probably involves a rather stable envelope transition state[26] (Figure 4k).

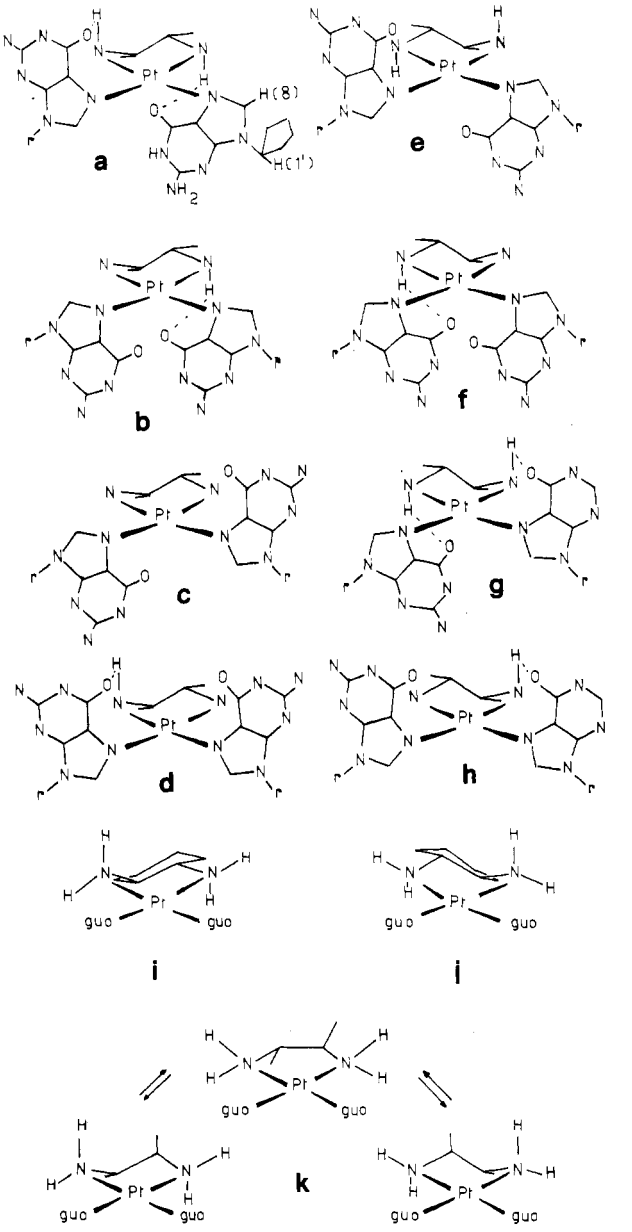

Figure 4. (a–h) The possible isomers obtainable through the rotation of the guanosine moieties around the Pt–N(7) bonds in the case of (*S*)-diamines (a–d) and of (*R*)-diamines (e–h) in the "gauche" equatorial conformation of the diamine chelate ring. r = ribose for guanosine and CH_3 for 9-methylguanine. The possible hydrogen bonds between O(6) and the diamine N–H(axial) atoms are depicted. In a the positions of H(8) and H(1′) are shown. (i, j) The conformation of the chelate ring of (*S,S*)-chxn (i) and (*R,R*)-chxn (j) derivatives. (k) The conformational equilibrium $\delta \rightleftharpoons$ "envelope" $\rightleftharpoons \lambda$ (left to right) of the chelate ring of a *meso*-diamine.

(21) Cramer, R. E.; Dahlstrom, P. L. *J. Am. Chem. Soc.* **1979**, *101*, 3679.
(22) Hawkins, C. J. "Absolute Configuration of Metal Complexes"; Wiley-Interscience: New York, 1971.
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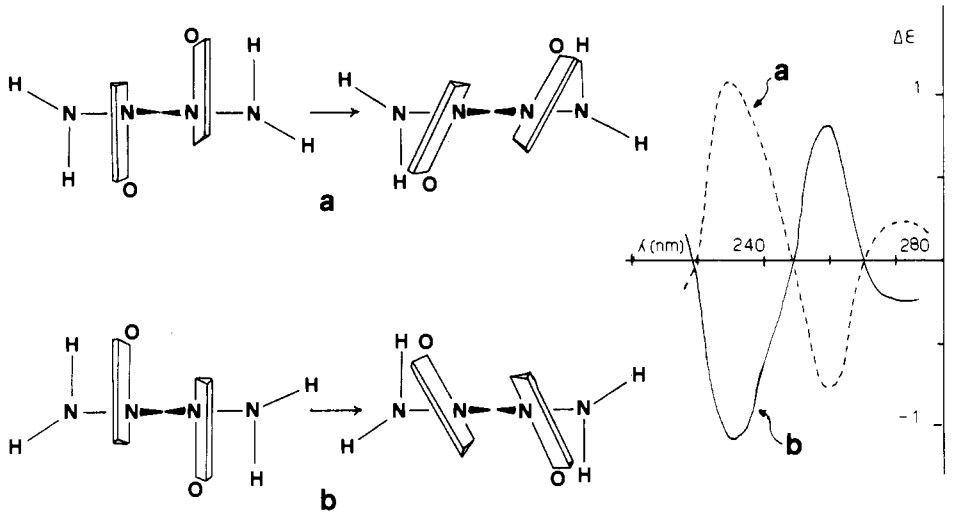

Figure 5. Schematic representation of (a) $[((R,R)\text{-chxn})Pt(9\text{-MeG})_2]^{2+}$ and (b) $[((S,S)\text{-chxn})Pt(9\text{-MeG})_2]^{2+}$ viewed down an axis lying on the coordination plane and bisecting the N(7)–Pt–N(7) angle. For explanation, see text.

Circular Dichroism Spectra of the Diastereoisomeric Complexes [(chiral diamine)Pt(Guo)$_2$]$^{2+}$. The CD spectra of the complexes [(chiral diamine)Pt(Guo)$_2$]$^{2+}$ are reported in Figures 2 and 3.

The general trends are similar to those of [(en)Pt(Guo)$_2$]$^{2+}$ with the exception of the derivatives of (*R,R*)- or (*S,S*)-1,2-diphenylethylenediamine, where the presence of Cotton effects associated with transitions of the phenyl group makes the spectra rather complicated below 270 nm (Figure 3). All the spectra show a small Cotton effect around 300 nm, the sign of which is related to the absolute configuration of the diamine, i.e., positive for *R* or *R,R* and negative for *S* or *S,S* diamines, in agreement with the related complexes [(chiral diamine)-Pt(NH$_3$)$_2$]$^{2+}$.[27] With achiral diamines (meso forms and ethylenediamine), we could not observe any general trend in this region. The negative Cotton effect of free guanosine, centered at about 290 nm, is present in all the complexes and overlaps with the band described above.

As already pointed out, a characteristic feature of the spectra of all the bis(guanosine) derivatives is the presence of a doublet centered at about 245 nm, with the positive component lying at lower energy, which is likely to arise from an exciton interaction between some electronic transitions localized on the guanine planes. From literature data it is likely that the absorption in the 240-nm region of guanosine is due to a $\pi \rightarrow \pi^*$ electronic transition of symmetry B_{1u}.[28] The direction of polarization of this transition has been established by means of polarized reflection spectra for 9-ethylguanine[29] to lie approximately in the C(4)–C(8) direction.[29] Exciton coupling calculations performed on GpG with this direction of polarization reproduced almost exactly the CD spectrum of this dinucleotide.[30] Moreover, since the absorption spectra of guanine and guanine hydrochloride are rather similar,[29] it can be safely assumed that the direction of polarization of the B_{1u} transition does not change too much either upon substitution in position 9 or by formation of a coordinate bond in position 7 (protonation and coordination are similar acid–base processes).

Discussion, Based on CD Spectra, of the Possible Conformations Dependent on the Nature of the Diamine. Before examining the problem of the conformation of these complexes, we must recall that the X-ray structures of [(NH$_3$)$_2$Pt-(Guo)$_2$]$^{2+}$ and [(en)Pt(Guo)$_2$]$^{2+}$ show remarkable intermolecular interactions originated by the stacking in the crystals of purine bases of adjacent molecules.[17,18] However, at the concentrations used for electronic and CD spectroscopy (about 10^{-4} mol dm^{-3}), these forces are less important. Therefore, only intramolecular interactions are relevant to the stabilization of the molecular conformation, especially for what concerns the relative orientation of the two purine rings.

The features of the CD spectra in the 230–260-nm region will therefore be discussed on this assumption. In the exciton approach, the intensity of the doublet depends on the relative orientation of the two guanine rings and/or the relative abundance of the various possible conformers.[31] Inspection of Figures 1–3 shows that while in the different monoguanosine complexes the intensity of the negative band at about 250 nm is roughly the same, in the case of the bis(guanosine) derivatives the intensity of the doublet at 245 nm depends on the nature and the configuration of the diamine. It is therefore likely that each diamine dictates a particular orientation of the two purine rings.

Chiral Cyclohexanediamines. These complexes are more easy to discuss since they possess a diamine chelate ring of a fixed conformation, because of the presence of a trans fused cyclohexane ring. In the complexes the major intramolecular interactions are either Guo–Guo or Guo–diamine. As for the latter, molecular models show that a likely interaction is the formation of hydrogen bonds between the carbonyl oxygen atoms of Guo, O(6), and those amine hydrogen atoms of the diamine, which are axial with respect to the five-membered chelate ring.[32]

In the absence of Guo–Guo interactions, these hydrogen bonds will dictate a head-to-tail arrangement of the two purine units, and two opposite arrangements will result for the complexes with the two enantiomeric cyclohexanediamines, in which the axial N–H bonds are fixed owing to the rigidity of the chelate ring. These structures are i of Figure 4 for $[((S,S)\text{-chxn})Pt(Guo)_2]Cl_2$ and j for $[((R,R)\text{-chxn})Pt(Guo)_2]Cl_2$. They should give rise, in the CD spectrum, to two enantiomeric doublets in the 230–260-nm region. This fact, however, is not observed with the above compounds but only with the nondiastereoisomeric complexes of an achiral

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(29) Clark, L. B. *J. Am. Chem. Soc.* **1977**, *99*, 3934.
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(31) (a) Schellman, A. *Acc. Chem. Res.* **1968**, *1*, 144. (b) Harada, N.; Nakanishi, K. *Ibid.* **1972**, *5*, 257.
(32) The interaction between O(6) and the equatorial NH group of the diamine would give rise to a severe crowding of the two purine rings. In fact they would be almost coplanar with the coordination plane and cannot be fitted in the cis position.

derivative of guanine, 9-methylguanine: [((*S*,*S*)-chxn)Pt(9-MeG)$_2$]Cl$_2$ and [((*R*,*R*)-chxn)Pt(9-MeG)$_2$]Cl$_2$ (Figure 5).

The doublet observed for [((*R*,*R*)-chxn)Pt(9-MeG)$_2$]Cl$_2$ can be referred to structure g (Figure 4, r = CH_3), in which the two guanine planes are twisted clockwise around the Pt–N(7) bonds (see Figure 5) as compared to the orientation shown in the figure. This movement approaches the two O(6) atoms of guanine to the axial hydrogen atoms of the diamine, giving rise to a better orientation for hydrogen bonding. A consequence of this movement is that the two guanine planes are no longer perpendicular to the coordination plane but form a left-handed propeller (see Figure 5a). With this geometry, the two purinic bases are in such a position that the moments of the B_{1u} transitions couple as a left-handed helix with a negative potential. This gives rise, in the CD spectrum, to a doublet with the negative component at lower energy,[31] as observed. The derivative of (*S*,*S*)-chxn must be arranged as in structure a of Figure 4 with a slight movement counterclockwise around the Pt–N(7) bonds (right-handed propeller); this originates an enantiomeric couplet in the CD spectrum (Figure 5b).

Such a straightforward relationship is not observed in the spectra of the related complexes with guanosine: when 9-MeG is substituted by Guo, the sign of the exciton doublet remains the same for the derivative of (*S*,*S*)-chxn, but it is inverted for the compound containing (*R*,*R*)-chxn. In other words the sign of the doublet is the same for the two diastereoisomeric derivatives (and indeed for all the bis(guanosine) compounds described here).

These observations suggest that the Guo–Guo interactions are relevant since they contribute to stabilize a particular propeller arrangement of the two guanosine groups, probably via interaction of the ribose groups. It is quite impossible, however, from simple molecular models, to find which particular groups of the sugar moiety are responsible for such a stereoselective interaction. In any case comparison of the CD spectra suggests the stabilization of an arrangement of the two guanosines similar to that of [((*S*,*S*)-chxn)Pt(9-MeG)$_2$]$^{2+}$ corresponding to the right hand propeller of Figure 5.

It is attractive to note that the couplet centered at 245 nm reproduces in sign and shape that of a series of polynucleotides, including DNA,[7,20] in which the purinic bases are placed in a helical structure. We can therefore assume that the linking of two guanosines via a N(7)–Pt–N(7) bridge is stereoselective, resulting in a spatial arrangement similar to that of Figure 5b, dictated purely by interguanosine forces, that we call Guo–Pt–Guo chirrole.[33] When this particular Guo–Pt–Guo chirrole is placed in a chiral environment, with spatially oriented hydrogen-bonding groups, as the N–H groups of the five-membered chelate ring of a chiral diamine, additional diastereoisomeric interactions such as N–H–O(6) hydrogen bonds will occur. These interactions will either favor or disfavor the original chirality of the Guo–Pt–Guo chirrole; any destabilization will result in a lowering of the intensity of the doublet centered at 245 nm.

Inspection of Figures 1–3 clearly shows that the order of stability is (*S*,*S*)-chxn > (*S*,*S*)-bn > (*S*)-pn > en ≥ *cis*-$(NH_3)_2$ > (*R*,*S*)-bn > (*R*)-pn > (*R*,*R*)-bn > (*R*,*R*)-chxn > (*R*,*S*)-chxn.[38] This series, which is symmetrical with respect to en, shows that chelating diamines with *S* or *S*,*S* absolute configuration stabilize the original chirality of the Guo–Pt–Guo chirrole. The largest effects of stabilization and destabilization are observed with the derivatives of cyclohexanediamine, in agreement with the great rigidity of the chxn chelate ring. In fact for [((*S*,*S*)-chxn)Pt(Guo)$_2$]$^{2+}$ the structure in solution is likely to be as in Figure 4a with a slight counterclockwise twist around the Pt–N(7) bond of the two Guo residues to form a right hand propeller as in the corresponding complex [((*S*,*S*)-chxn)Pt(9-MeG)$_2$]$^{2+}$ (see above, Figure 5). The stability of this particular structure arises from the original stability of the Guo–Pt–Guo chirrole, increased by hydrogen bonds between O(6) and the axial N–H, as already discussed for the 9-MeG derivative. On the contrary for [((*R*,*R*)-chxn)Pt(Guo)$_2$]$^{2+}$ a structure as in Figure 4e with the correct handedness of the Guo–Pt–Guo chirrole does not possess favorable geometry for O(6)–(axial)N–H bond to occur. These hydrogen bonds could be formed in a structure such as 4g, in which, however, the two purine bases are arranged in a chirrole with opposite handness. This structure is very unlikely because it should give rise to an exciton doublet of opposite sign rather than to the observed decrease in intensity. We must therefore assume that the original chirrole is still present, and the lower intensity can be interpreted as the result of a distortion of the Guo–Pt–Guo chirrole which occurs in order to reach a geometry compatible with the formation of hydrogen bonds with some amine hydrogen atoms. An alternative explanation would be the contemporaneous presence, in solution, of rotamers e and g (Figure 4) with a slight predominance of the former. NMR experiments, however, seem to rule out this explanation (see below).

Propylenediamines and Chiral Butanediamine Derivatives. The same trends of the CD spectra are observed. The complex with (*S*,*S*)-bn shows the higher intensity of the doublet at 245 nm, although not as high as that of (*S*,*S*)-chxn. This can be attributed to a minor rigidity since the δ conformation of the chelate ring of (*S*,*S*)-bn is less stable than that of (*S*,*S*)-chxn owing to the flexibility of chelated butanediamine for which a λ ⇄ δ equilibrium can exist.

A specular argument applies to the derivative of (*R*,*R*)-bn. The λ conformation of the chelate ring of the diamine does not favor the right-hand propeller of the Guo–Pt–Guo chirrole, but such a destabilization is not as large as in the (*R*,*R*)-chxn case because of the increased conformational freedom of the bn chelate ring. Similar differences in the CD spectra of the two diastereoisomers [((*S*)-pn)Pt(Guo)$_2$]$^{2+}$ and [((*R*)-pn)Pt(Guo)$_2$]$^{2+}$ are observed (Figure 3). The intensity of the doublets are lower than those in the complexes with bn, in agreement with a higher flexibility of the propylenediamine chelate ring.[23,39]

Derivatives of Achiral Diamines. The derivatives of *cis*-$(NH_3)_2$, *meso*-butanediamine, and ethylenediamine show very similar CD spectra, suggesting almost identical situations in solution. For these compounds, the λ and δ conformations of the chelate ring are of equal stability and probably interchange rapidly,[23,40] consequently the intensity of the doublet must reflect only the stability of the original Guo–Pt–Guo chirrole

(33) Stereoselectivity in the coordination of the nucleosides, nucleotides, and dinucleotides to metal ions has often been observed.[20,34-37] Although in some X-ray structures a chirrole, opposite to that inferred by us in solution, has been found; in at least one case the same handedness has been observed.[20,35a] Moreover, solution studies often agree with our findings.[36] These facts stress the difficulty of transferring X-ray results to solution studies for compounds that, in addition to having several hydrogen bonding groups, possess a tendency to form stacked structures.

(34) Goodgame, D. M. L.; Jeeves, I.; Phillips, F. L.; Skapski, A. C. *Biochim. Biophys. Acta* **1975**, *387*, 153.

(35) (a) Marzilli, L. G.; Chalilpoyil, P.; Chiang, C. C.; Kistenmacher, T. J. *J. Am. Chem. Soc.* **1980**, *102*, 2480. (b) Marzilli, L. G.; Kistenmacher, T. J. *Acc. Chem. Res.* **1977**, *10*, 146.

(36) See, for instance: Roos, I. A. G.; Thomson, A. J.; Mansy, S. *J. Am. Chem. Soc.* **1974**, *96*, 6484.

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(38) As already pointed out, the spectra of the complexes of pen and dpen are not clear enough to allow any comparison (see Figure 3).

(39) (a) Pasini, A.; Gullotti, M.; Ugo, R. *J. Chem. Soc., Dalton Trans.* **1977**, 346. (b) Gullotti, M.; Pasini, A. *Inorg. Chim. Acta* **1975**, *15*, 129.

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as such, i.e., when no stabilizing or destabilizing forces are present or when these opposite forces are of identical intensity. The fact that the "stability series" above reported is symmetrical with respect to the en and the *meso*-bn derivatives is in agreement with this assumption.

The derivative of *meso*-cyclohexanediamine should behave in the same way, but, strangely enough, the CD spectra suggest a dramatic destabilization of the Guo–Pt–Guo chirrole. At the moment we do not have any explanation for this fact.

Phenyl- and Diphenylethylenediamine Derivatives. The presence of the phenyl groups introduces new transitions in the 240-nm region, making the CD spectra rather complex. Although the general patterns of the CD spectra are similar to those of the other compounds investigated here, the relative intensities of the doublet originated by the exciton coupling of the purinic transitions cannot be discussed.

^{1}H NMR Investigations. The CD spectra discussed above could be explained either with the presence of distorted, rigid structures or with the contemporaneous existence of various conformers in equilibrium obtained through the free rotation around the Pt–N(7) bonds (Figure 4), which has been proposed to occur through ^{1}H NMR spectroscopy investigations.[21] To try to settle this point we have carried out a ^{1}H NMR investigation on the bis(guanosine) complexes in D_2O and in the temperature range 25–97 °C.[41]

The spectra of complexes with (*S*,*S*)-chxn and (*R*,*R*)-chxn are not temperature dependent; in both cases only one signal attributable to H(8) ($\delta \sim 8.3$) and one doublet assigned to H(1′) ($\delta \sim 5.9$)[14] are observed. This could imply either a fast rotation of the two guanosine moieties, even at room temperature, or a complete rigidity of the chirrole system with two equivalent guanosines even at 90 °C.

The NMR spectra of the derivatives of (*S*)-pn and (*R*)-pn are temperature dependent. Both compounds show, at room temperature, two resonances attributable to two magnetically different H(8) protons (Figure 6). If the preferential arrangement of the two guanosines is head to tail, substitution at only one carbon atom of the diamine produces a chelate ring which does not possess a C_2 axis; consequently the N–H bonds, interacting with O(6), are no longer equivalent. This gives rise to slightly nonequivalent guanosine moieties since they are tilted around the Pt–N(7) bond to a different extent. As a consequence the two H(8) protons experience two slightly different environments. This is obviously a local effect since the asymmetry of the diamine alone should not produce a long range differentiation; in fact the H(1′) protons are equivalent. When the temperature is raised, the two signals of H(8) collapse into a single signal at 80 °C for the (*R*)-pn and at 97 °C for the (*S*)-pn derivatives. This phenomenon can be explained not only by a rapid rotation around the Pt–N(7) bonds of 360° of the two guanosines, which takes place at high temperature,[21] but also by a twisting around the same bond, fast enough to render the two guanosine units equivalent on the NMR time scale.

The related diamine with a chelating ring without a C_2 axis is pen for which, unfortunately, we were able to obtain only the *R* isomer in a sufficiently pure form. The NMR spectrum of $[((R)\text{-pen})Pt(Guo)_2]^{2+}$ shows, at room temperature, only one signal for H(8) but two doublets for H(1′) (Figure 6). Moreover, the phenyl group, which is usually a singlet in

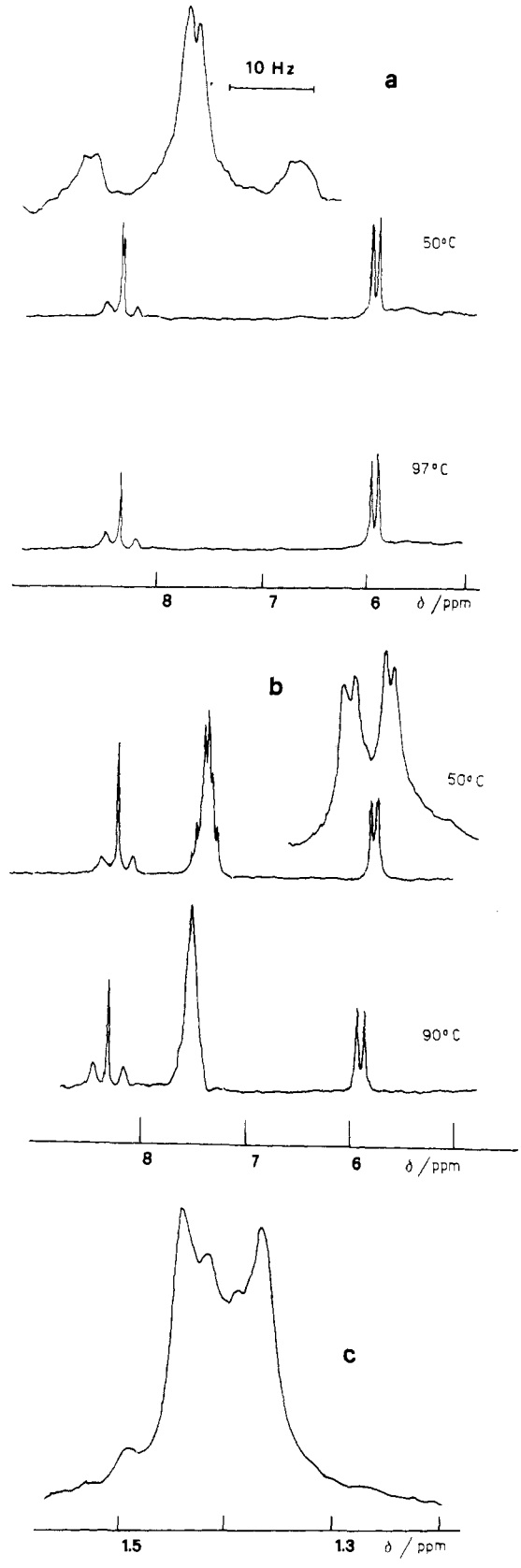

Figure 6. (a) NMR spectra at 80 MHz of $[((S)\text{-pn})Pt(Guo)_2]^{2+}$ at 50 and 97 °C. The spectrum of the derivative of (*R*)-pn is similar but coalescence is reached at 80 °C. (b) NMR spectra at 80 MHz of $[((R)\text{-pen})Pt(Guo)_2]^{2+}$ at 50 and 90 °C. (c) The methyl region of the NMR spectrum, at 200 MHz, of $[((S,S)\text{-bn})Pt(Guo)_2]^{2+}$ at 50 °C. The spectrum does not change with the temperature. The *R*,*R* derivative gives rise to a similar signal.

(41) The ^{1}H NMR spectra of complexes of the type reported here are concentration dependent presumably because of the stacking of the purine ligands at high concentration. This often gives rise to a substantial line broadening.[13] Our results refer to the concentration range 0.5–1 10^{-2} mol dm^{-3}. The main features of the spectra are as reported for similar compounds.[14] The coupling constant of H(8) with ^{195}Pt is the same for all the complexes (25–26 Hz) and will not be discussed any further. The variations of the spectra with the temperature were found completely reversible.

complexes of this diamine,[25,42] appears as a complex multiplet at $\delta \sim 7.4$. When the temperature is raised, the two doublets of H(1′) collapse into a single doublet with a simultaneous sharpening of the phenyl signal (Figure 6). These data would support a rather rigid structure of this complex, at room temperature, with a fixed arrangement of the two guanosines, the chelate ring, and even the phenyl group of the diamine, which is in a rather asymmetric environment.

Strangely enough in this compound the nonequivalence of the two guanosine moieties is not reflected in the H(8) but in H(1′) protons. This is indicative of some particular stereoselective interaction of the ribose ring or of some particular sugar pucker conformation originated by extensive hydrogen bonds. Although we are unable to rationalize these points, they can be related to the asymmetric field experienced by the phenyl ring of the diamine.

At high temperature the molecule becomes flexible. Here again, however, the rotation around the Pt–N(7) bond need not be complete (360°) since a rapid tilting around the equilibrium position would be enough to render the two guanosine molecules equivalent for the NMR time scale. It is to be stressed that the observed movement of the guanosines is concomitant to the calescence of the resonance of the phenyl ring, in agreement with the fact that strong hydrogen bonds (such as N–H···O(6)) are responsible for the rigid structures of these bis(guanosine) complexes observed at room temperature.

With complexes of symmetrically substituted diamines such as the chiral 2,3-butanediamines and 1,2-diphenylethylenediamines, we observed only one resonance for H(8) and one doublet for H(1′) protons at any temperature. In the case of butanediamine the resonance of the methyne group of the chelate ring is a complex multiplet at $\delta \sim 3$. Upon irradiation of the methyl signal (δ 1.3), the multiplet becomes a singlet with ill-defined shoulders, which are due to the coupling of the methyne protons with ^{195}Pt.[43] The value of this coupling (15 Hz) is in agreement with an axial orientation of these protons,[25] corresponding to the equatorial position of the methyl groups. This pattern is not temperature dependent.

The methyl resonance of both compounds is also rather complicated at any temperature and could not be resolved even at 200 Mz (Figure 6). On irradiation of the methyne signal, the methyl resonance becomes a broad singlet ($\Delta\nu_{1/2} \simeq 7$–8 Hz at 90 °C). These data suggest the presence of two nonequivalent CH_3 groups resonating at very close frequencies. In conclusion, in both complexes of bn the two equatorial methyl groups are firmly fixed, even at 90 °C, and are placed in an asymmetric environment, created by the Guo–Pt–Guo propeller, which renders them nonequivalent. NMR data suggest that in the bn derivatives this rigidity is maintained also at 97 °C. It is likely that this is due to the substantial preference of the equatorial orientation of the two methyl groups in the diamine chelate ring.[23]

The spectra of the derivatives of chiral dpen are rather difficult to analyze, owing to the overlap of the methyne resonances with some signal of the sugar moiety. In contrast to the pen derivative, the phenyl protons give rise to only one resonance at $\delta \sim 7.5$.

The ^1H NMR spectra of the compounds with achiral diamines (meso diamines and en) show only one signal for H(8) and one doublet for H(1′) at every temperature; in particular the spectrum of $[(meso\text{-bn})Pt(Guo)_2]^{2+}$ shows a single clear doublet for the methyl group of the diamine, which, by irradiation of the methyne resonance, becomes an expected sharp singlet ($\Delta\nu_{1/2}$ = 2 Hz at 90 °C). The coupling constant of the methyne hydrogen atoms, with ^{195}Pt, which can be observed by irradiating the CH_3 signal, is 36 Hz. This value and the sharpness of the methyl doublet suggest a rapid $\lambda \rightleftarrows \delta$ interconversion.[23,25,40] A similar value (J_{Pt-H} = 40 Hz) has been found for the singlet of the CH_2 protons of the ethylenediamine derivative.

In conclusion, NMR evidence stands for a high flexibility of the chelate ring of the derivatives of achiral diamines, whereas in the case of chiral diamines the evidence reported above support the presence, in solution, of only one conformer. The structure of the latter is firmly held by the formation of hydrogen bonds between the Guo–Pt–Guo chirrole and the diamine. The conformation of which is therefore frozen. The differences in the intensity of the doublets in the CD spectra at 245 nm must therefore be interpreted as arising from different values of the thread of the right-handed propeller of Figure 5. In summary, the overall conformation of the various derivatives will depend on the degree of the twisting of the purine rings around the Pt–N(7) bond and on the distortion of the chelate ring from a "pure" gauche to an unsymmetrical gauche conformation to meet the best geometry for the formation of the hydrogen bonds between O(6) and the amine hydrogen atoms. The conformation thus attained is very stable. Only with achiral diamines this can not occur because of the fast inversion of the chelate rings, and the CD spectra of these compounds must be considered as reflecting only the thread of the Guo–Pt–Guo chirrole.

Conclusions

Up to now the interaction between platinum and DNA has not been completely clarified, but it is almost certain that the first step is the nucleophilic attack[44] of N(7) of deoxyguanosine of DNA to $[(diamine)PtCl_2]$,[45] followed by either inter-[45] or intrastrand[46] cross-linking (with two bases bound to platinum) or by N(7)–O(6) chelation of guanine to platinum.[47,48] Evidence has been presented for all these possible modes of interaction, and many model compounds have been reported, including compounds of the type described in this paper.

The bis(guanosine) compounds are very naïve models of the Pt–two bases interaction; nevertheless, we have proved that this interaction is controlled by the formation of strong hydrogen bonds between the amine hydrogen atoms and O(6) of guanine,[49] resulting in a rather rigid Guo–Pt–Guo arrangement. This fact is relevant since O(6) of guanine is involved in the Watson–Crick base pairing with cytosine; therefore, it could be that the formation of these stereoselective hydrogen bonds (either inter- or intrastrand) is an important step in the damage of DNA induced by the cis platinum complex. It must be noted, here, that the highest antitumor activity is displayed by platinum complexes with primary amines or ammonia;[50] in fact only these ligands do not possess

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(43) The assignment of the ill-defined shoulder to the platinum satellites is corroborated by their disappearance when the same experiment is carried out at 200 MHz. It is in fact known that the platinum–hydrogen couplings broaden below recognition when the NMR spectra are recorded at high frequency. See: Lallemand, J. Y.; Soulié, J.; Chottard, J. C. *J. Chem. Soc., Chem. Commun.* **1980**, 436 and references therein.
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(47) (a) Millard, M. M.; Macquet, J. P.; Theophanides, T. *Biochim. Biophys. Acta* **1975**, *402*, 166. (b) Rosenberg, B. *J. Clin. Hematol. Oncol.* **1977**, *7*, 817. (c) Wing, R.; Drew, H.; Takano, T.; Broka, C.; Tonaka, S.; Itakura, K.; Dickerson, R. E. *Nature (London)* **1980**, *287*, 755.
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(49) Something similar has already been proposed;[35] of particular interest here is the finding that, in the addition compound of the cis platinum complex with poly(rG), the amino groups are strongly hydrogen bonded to the polynucleotide. See: Chu, G. Y. H.; Mansy, S.; Duncan, R. E.; Tobias, R. S. *J. Am. Chem. Soc.* **1978**, *100*, 593.
(50) Cleare, M. J.; Hoeschele, J. D. *Bioinorg. Chem.* **1973**, *2*, 187.

stereochemical restraints for the formation of hydrogen bonds.

The poorness of our model is shown by the fact that the absolute configuration of the diamine bound to platinum has very little effect on the antitumor activity of the complexes [(chiral diamine)PtX_2],[10,51] the *R* derivatives being only slightly more active. This difference is small when compared to what is expected on the grounds of the relevant differences of the chiroptical properties of the diastereoisomers [(chiral diamine)$Pt(Guo)_2]^{2+}$. Also, those diamines that do not produce rigid arrangements (en and meso diamines) possess comparable activity.

Although the bis(guanosine) complexes with (*R*)-diamines show exciton splittings lower than those of the corresponding (*S*)-diamines, it is difficult to establish a structure–activity relationship. It is therefore likely that the relevant conformational differences observed here could not have much biological significance presumably because of the small size of the chiral platinum compounds compared with DNA or because more subtle mechanisms are operative. Work is in progress on the interaction of DNA with platinum complexes with chiral ligands in order to elucidate this point.

Acknowledgment. We wish to thank Professor P. Fantucci for helpful discussion of the NMR spectra that were recorded under the skillful technical assistance of Mrs. M. Bonfà.

Registry No. [(en)$Pt(guo)_2]Cl_2$, 50790-42-6; [((*R*)-pn)$Pt(guo)_2]Cl_2$, 77943-59-0; [((*S*)-pn)$Pt(guo)_2]Cl_2$, 77863-65-1; [((*R*,*R*)-bn)$Pt(guo)_2]Cl_2$, 77902-46-6; [((*S*,*S*)-bn)$Pt(guo)_2]Cl_2$, 77981-96-5; [(*meso*-bn)$Pt(guo)_2]Cl_2$, 80629-84-1; [((*R*,*R*)-chxn)$Pt(guo)_2]Cl_2$, 77902-47-7; [((*S*,*S*)-chxn)$Pt(guo)_2]Cl_2$, 77981-97-6; [(*meso*-chxn)$Pt(guo)_2]Cl_2$, 80629-85-2; [((*R*)-pen)$Pt(guo)_2]Cl_2$, 80583-56-8; [((*R*,*R*)-dpen)$Pt(guo)_2]Cl_2$, 80655-69-2; [((*S*,*S*)-dpen)$Pt(guo)_2]Cl_2$, 80655-70-5; [(*meso*-dpen)$Pt(guo)_2]Cl_2$, 80583-57-9; [((*R*,*R*)-chxn)$Pt(9\text{-}MeG)_2]Cl_2$, 80583-58-0; [((*S*,*S*)-chxn)$Pt(9\text{-}MeG)_2]Cl_2$, 80629-86-3; [(en)Pt(guo)]$(NO_3)_2$, 79725-46-5; [((*R*,*R*)-chxn)Pt(guo)]$(NO_3)_2$, 80593-30-2; [((*S*,*S*)-chxn)Pt(guo)]$(NO_3)_2$, 80655-72-7; *cis*-$[(NH_3)_2Pt(guo)_2]Cl_2$, 50790-41-5; Guo, 118-00-3; GpG, 3353-33-1.

Supplementary Material Available: NMR spectra (Table II) of the complexes [(chiral diamine)$Pt(Guo)_2]Cl_2$ (2 pages). Ordering information is given on any current masthead page.

(51) We have confirmed that the nature of the nonleaving groups is very important in determining the antitumor activity.[52] Such effect is much larger than that of the absolute configuration of the diamine.[10] The particularly high activity of the chxn derivatives has also been confirmed.[52]

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Oxidative-Addition Reactions of Cyclometalated Platinum(II) Compounds with Mercury(II) Carboxylates. X-ray Crystal and Molecular Structure of *rac*-[*a*-(μ-$MeCO_2$)-*cf*,*de*-$(2\text{-}Me_2NCH_2C_6H_4)_2PtHg(O_2CMe)$]

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The reactions of *cis*-$[(2\text{-}Me_2NC_6H_4CH_2)_2Pt^{II}]$, obtained from $[PtCl_2(SEt_2)_2]$ and [(2-$Me_2NC_6H_4CH_2$)Li(TMEDA)] (TMEDA = tetramethylethylenediamine), and of *cis*-$[(2\text{-}Me_2NCH_2C_6H_4)_2Pt^{II}]$ with $Hg^{II}(O_2CR)_2$ (R = Me, *i*-Pr) yielded a novel type of cyclometalated Pt–Hg compound [(N–C)$_2$(RCO_2)PtHg(O_2CR)] (N–C = 2-$Me_2NC_6H_4CH_2$– and 2-$Me_2NCH_2C_6H_4$–). An X-ray crystallographic study defined the molecular structure of $[(2\text{-}Me_2NCH_2C_6H_4)_2(\mu\text{-}MeCO_2)PtHg(O_2CMe)]$. The pertinent crystal data are as follows: orthorhombic, space group *Pccn*, $Z = 8$, $a = 14.817$ (8) Å, $b = 17.339$ (9) Å, $c = 18.602$ (11) Å. The platinum center is six-coordinate with a Pt–Hg bond (2.513 (1) Å) bridged by one acetato group: Pt–O, 2.15 (1) Å; Hg–O′, 2.62 (1) Å. The other acetato ligand is monodentate bonded to Hg: Hg–O, 2.10 (1) Å. The mercury atom and the two carbon ligands are mutually cis. A cis oxidative addition, involving a platinum-to-mercury-bonded intermediate, is proposed for the reaction mechanism. The geometry of the other compounds $[(2\text{-}Me_2NCH_2C_6H_4)_2(i\text{-}PrCO_2)PtHg(O_2C\text{-}i\text{-}Pr)]$ and $[(2\text{-}Me_2NC_6H_4CH_2)_2(RCO_2)PtHg(O_2CR)]$ (R = Me, *i*-Pr), as deduced from ^1H and ^{13}C NMR spectra, is similar. Intramolecular exchange of the two carboxylato groups is not observed. Exchange of these carboxylato groups with free carboxylic acids occurs on different time scales. Reactions of *trans*-$[(2\text{-}Me_2NCH_2C_6H_4)_2Pt^{II}]$ with $Hg^{II}(O_2CR)_2$ proceeded via an unstable Pt–Hg intermediate, which then eliminated Hg^0 to form $[(2\text{-}Me_2NCH_2C_6H_4)_2Pt(O_2CR)_2]$ as a mixture of two isomers. Reaction of $\{[2,6\text{-}(Me_2NCH_2)_2C_6H_3]Pt^{II}X\}$ (X = Br, O_2CR), containing a terdentate ligand, with $Hg^{II}(O_2CR)_2$ resulted in formation of the stable Pt–Hg-bonded compounds $\{[2,6\text{-}(Me_2NCH_2)_2C_6H_3](RCO_2)PtHg(O_2CR)X\}$ (X = Br, O_2CR; R = Me, *i*-Pr). For these compounds a structure is proposed containing a five-coordinate Pt center and a carboxylato-bridged Pt-to-Hg donor bond. The structure of the compound with X = Br results from an exchange of the bromide atom and a carboxylato group between the platinum and mercury centers. Intramolecular carboxylato exchange is observed for which a mechanism, involving a six-coordinate Pt intermediate, is proposed. For the compound $\{[2,6\text{-}(Me_2NCH_2)_2C_6H_3](i\text{-}PrCO_2)PtHgCl_2\}$, prepared from $\{[2,6\text{-}(Me_2NCH_2)_2C_6H_3]Pt(O_2C\text{-}i\text{-}Pr)\}$ and $HgCl_2$, a structure with a carboxylato group bridging between Pt and $HgCl_2$ is proposed. The dynamic behavior of these compounds in solution is discussed.

Introduction

During the last decade interest has been growing in heterodinuclear group 8B metal complexes.[2a] The number of such compounds with CO or phosphine ligands is fairly large. Heterodinuclear complexes with organo groups have also been synthesized, involving either reaction of a metal complex anion with a metal complex cation[2b]

$$(CO)_xM^-Na^+ + RM'Cl \rightarrow NaCl + (CO)_xMM'R$$

or reaction of a neutral transition-metal complex with an electrophilic reagent[3]

$$M + XM'R \rightarrow X\text{-}M\text{-}M'\text{-}R \text{ or } R\text{-}M\text{-}M'\text{-}X$$

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