Binding of *cis*-Dichlorobis(1-methylimidazole-2-thiol)-palladium(II) and -platinum(II) to Nucleosides: Synthesis and Hydrogen-1 and Carbon-13 Nuclear Magnetic Resonance Studies †

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The reactions of *cis*-$[MCl_2(mit)_2]$ (M = Pd or Pt; mit = 1-methylimidazole-2-thiol) with guanosine (guo), cytidine (cyd), and adenosine (ado) have been studied in neutral solutions. Two types of complexes have been isolated, of general formula $[M(mit)_2L_2]X_2$ (L = guo or cyd) and $[ML_4]X_2$ (L = cyd or ado) with X = Cl^- and $[PF_6]^-$. By use of i.r. spectroscopy and of the chemical shifts occurring in ^1H and ^{13}C n.m.r. spectroscopy, it is possible to confirm co-ordination of Pd and Pt to N^7 in guo and ado, and to N^6 in cyd. The n.m.r. investigations reflect electronic modifications in the ring system of the co-ordinated nucleosides, which are discussed in terms of DNA denaturation by heavy transition-metal complexes.

RECENTLY the anti-tumour properties of *cis*-diaminedichloroplatinum(II) complexes have been actively investigated.[1-5] Evidence suggests that the nucleic acids are the most likely sites for functional interactions of the metal ion.[6,7] The specific binding of Pt to DNA rich in guanine–cytosine base pairs, reported by Stone *et al.*,[8] appears to cause a disruption of the hydrogen-bonded structure within the nucleic acid, as a result of its interaction with the metal ion.

We investigated previously[9] the *in vitro* activity against a hepatoma tissue culture of several new complexes[10] of Pd^{II} and Pt^{II} with *N*-donor ligands other than amines. We now report the reactions of *cis*-$[MCl_2(mit)_2]$ (M = Pt^{II} or Pd^{II}, mit = 1-methylimidazole-2-thiol) with the nucleosides adenosine, cytidine, and guanosine. The reaction products have been isolated and characterised. The ^1H and ^{13}C n.m.r.

† A preliminary report of this work was presented at the 17th Internat. Conf. Co-ordination Chem., Hamburg, 1976.

[1] A. J. Thomson, R. J. P. Williams, and S. Reslova, *Structure and Bonding*, 1972, **11**, 1.
[2] B. Rosenberg, *Naturwiss.*, 1973, **60**, 399 and refs. therein.
[3] 'Platinum Coordination Complexes in Cancer Chemotherapy,' eds. T. A. Connors and J. J. Roberts, Springer–Verlag, Heidelberg, 1974.
[4] M. J. Cleare, *Co-ordination Chem. Rev.*, 1974, **12**, 349 and refs. therein.
[5] P. D. Braddock, T. A. Connors, M. Jones, A. R. Khokhar, D. H. Melzack, and M. L. Tobe, *Chem.-Biol. Interactions*, 1975, **11**, 145.
[6] (*a*) J. J. Roberts and J. M. Pascoe, *Nature*, 1972, **235**, 282; (*b*) K. V. Shooter, R. Howse, R. K. Merrifield, and A. B. Robins, *Chem.-Biol. Interactions*, 1972, **5**, 289; (*c*) J. A. Howle, G. R. Gale, and A. B. Smith, *Biochem. Pharmacol.*, 1972, **21**, 1465; (*d*) J. Drobnik and P. Horacek, *Chem.-Biol. Interactions*, 1973, **7**, 223.
[7] H. C. Harder, *Chem.-Biol. Interactions*, 1975, **10**, 27.
[8] P. J. Stone, A. D. Kelman, and F. M. Sinex, *Nature*, 1974, **251**, 736.
[9] J. Dehand, J. Jordanov, and J. P. Beck, *Chem.-Biol. Interactions*, 1975, **11**, 605.
[10] J. Dehand and J. Jordanov, *Inorg. Chim. Acta*, 1976, **17**, 37.

studies are discussed with reference to a possible modification of the hydrogen bonds between the nucleic acids and their complementary bases.

RESULTS AND DISCUSSION

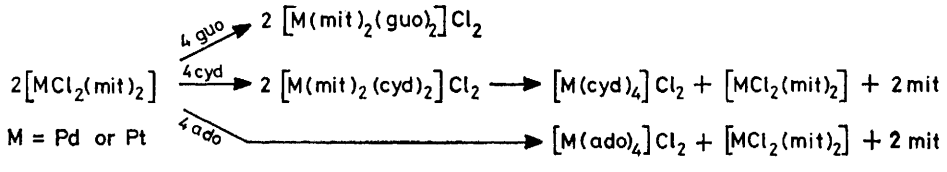
The displacement of both chlorine atoms from $[MCl_2(mit)_2]$ by the nucleosides was verified by following the disappearance of the ν(M–Cl) stretching vibrations in the range 300—350 cm^{-1}. The cationic character of the final products (see Table 1) was verified by metathesis of the two chlorides with $[NH_4][PF_6]$. However, the ligand substitutions by the various nucleosides were not limited just to the halides, since the following species were obtained:

TABLE 1

Analytical data (%) *

Complex	Colour	C	H	N
$[Pd(mit)_2(guo)_2]Cl_2$ (1)	Light brown	34.5 (34.55)	3.4 (3.7)	20.1 (20.2)
$[Pt(mit)_2(guo)_2]Cl_2$ (2)	Red-brown	31.3 (31.7)	3.5 (3.6)	18.3 (18.5)
$[Pt(mit)_2(guo)_2][PF_6]_2$ (3)	Brown	26.3 (26.3)	2.8 (2.95)	15.2 (15.3)
$[Pt(mit)_2(cyd)_2]Cl_2$ (4)	Orange	35.1 (35.0)	4.1 (4.25)	15.5 (15.7)
$[Pt(mit)_2(cyd)_2]Cl_2 \cdot 3H_2O$ (5)	Orange	30.2 (30.2)	4.2 (4.25)	13.6 (13.55)
$[Pt(mit)_2(cyd)_2][PF_6]_2$ (6)	Orange-brown	26.2 (26.05)	3.0 (3.2)	11.8 (11.7)
$[Pd(cyd)_4]Cl_2$ (7)	Light orange	37.9 (37.5)	4.8 (4.5)	14.5 (14.6)
$[Pt(cyd)_4]Cl_2$ (8)	Yellow	34.7 (34.9)	4.3 (4.2)	13.3 (13.56)
$[Pt(cyd)_4][PF_6]_2$ (9)	Light brown	29.5 (29.65)	3.45 (3.55)	11.7 (11.54)
$[Pd(ado)_4]Cl_2$ (10)	Light orange	38.1 (38.6)	4.2 (4.2)	22.8 (22.5)
$[Pt(ado)_4]Cl_2$ (11)	White	35.9 (36.0)	3.8 (3.9)	21.1 (21.0)
$[Pt(ado)_4][PF_6]_2$ (12)	Yellow	31.1 (30.8)	3.4 (3.35)	17.9 (18.1)

* Calculated values are given in parentheses.



In the case of guanosine (guo) * only the disubstituted species, (A), was formed, even when the reaction was carried out with an excess of nucleoside. The most important i.r. bands of the ligands guo and mit and of their complexes are in Table 2. The mit vibrations (at 1 565, 1 461, and 1 278 cm^{-1}) are unchanged in the final products, indicating that the imidazole moiety has not been displaced by guanosine. The ν(C=N) vibrations of free guanosine occur at 1 640, 1 544, and 1 494 cm^{-1}. The bands shift towards lower wavenumbers and become less intense on complex formation [complexes (1) and (2)].

With cytidine (cyd), the complexes $[M(mit)_2(cyd)_2]Cl_2$ isolated initially are also of type (A) [(4) and (5)]. On recrystallising them from ethanol–diethyl ether, redistribution of the ligands occurred and both the type (B) complexes $[M(cyd)_4]Cl_2$ [(7) and (8)] and the initial $[MCl_2(mit)_2]$ were formed. As expected, the mit ring-stretching vibrations present in the i.r. spectra of (4) and (5) disappeared on recrystallisation and formation of (7) and (8). As for the cytidine bands, the ν(C=N) vibrations move generally to lower frequencies on complexing to the Pd (from 1 650 and 1 534 to 1 640 and 1 520 cm^{-1}), to higher frequencies with Pt (1 670 and 1 546 cm^{-1}), while the ν(C=C) band appears in all cases at a lower frequency and is much less intense. Moreover, the ν(C=O) vibration, at 1 660 cm^{-1} in free cytidine, occurs at 1 716—1 730 cm^{-1} in complexes (4), (5), (7), and (8).

For the adenosine (ado) complexes, only the tetra-substituted species $[M(ado)_4]Cl_2$, type (B), were obtained, even in the presence of excess of metal. The intermediate disubstituted complex, with mit still bound to the metal, could not be isolated when operating under the same conditions as with guo and cyd. No mit vibrations were observed for (10) and (11), whereas the ν(C=N) and ν(C=C) bands of free adenosine shift to lower frequencies on complex formation (from 1 675 and 1 576 to 1 634 and 1 559 cm^{-1}). No shift of ν(N–H) was observed, and therefore the amine group does not appear to be involved in the bonding, in the solid state.[6a,11]

The i.r. results can hardly be used, because of their variability, to indicate any precise metal-binding sites on the nucleosides. It may only be assumed that the spectral changes in the 1 500—1 700 cm^{-1} region are indicative of co-ordination of the nucleoside ring to palladium and platinum.[12,13] Infrared studies are generally not a very reliable method of analysing nucleoside–metal interactions. The cobalt and zinc complexes of cytidine 5′-monophosphate are one of the few cases where *X*-ray analyses [14,15] are consistent with the i.r. investigations reported by Ogawa and Sakaguchi.[16]

Hydrogen-1 *N.M.R. Spectra.*—The proton n.m.r.

* The abbreviations for guanosine, cytidine, and adenosine recommended by the I.U.P.A.C.–I.U.B. Commission on Biochemical Nomenclature (1970) are Guo, Cyd, and Ado respectively.

[11] S. Mansy, B. Rosenberg, and A. J. Thomson, *J. Amer. Chem. Soc.*, 1973, **95**, 1633.

[12] N. Hadjiliadis and T. Theophanides, *Inorg. Chim. Acta*, (*a*) 1976, **16**, 67; (*b*) *ibid.*, p. 77.

[13] J. Dehand and J. Jordanov, *J.C.S. Chem. Comm.*, 1976, 598.

[14] G. R. Clark and J. D. Orbell, *J.C.S. Chem. Comm.*, 1975, 697.

[15] K. Aoki, *Biochim. Biophys. Acta*, 1976, **447**, 379.

[16] M. Ogawa and T. Sakaguchi, *Yakugaku Zasshi*, 1972, **92**, 1166.

studies were performed both in D_2O at pD 5.5—6.5, to ensure the nucleoside donor sites are not protonated,[17] and in [$^2H_6$]dimethyl sulphoxide ([$^2H_6$]dmso) to observe the amine-proton resonances. The chemical shifts thus observed (see Table 3) should result only from metal co-ordination to the donor site, and not from protonation.[18,19]

[$^2H_6$]dmso solutions) were only slightly shifted downfield. These results are indicative of guanosine co-ordinating to the metal only through N^7,[12b,20,21] and supporting evidence is provided by the *X*-ray analysis of two analogous complexes of Pt with inosine 5′-monophosphate [22] and guanosine.[23]

Analogous effects were found with the adenosine

TABLE 2

Infrared absorption bands (cm^{-1}) of the nucleosides and of the complexes

Compound	ν(N–H)	ν(C=O)	ν(C=N), ν(C=C)	mit bands *
guo	3 360m, 3 248m	1 740s	1 640s, 1 544s, 1 494s	
$[Pd(mit)_2(guo)_2]Cl_2$	3 342m	1 730s	1 628s, 1 530m, 1 470m	1 570m, 1 462m, 1 278m
$[Pt(mit)_2(guo)_2]Cl_2$	3 374m, 3 271m 3 358m	1 734s	1 640w, 1 518w, 1 475m	1 569m, 1 470m, 1 285m
cyd	3 375s	1 660s	1 650s, 1 534m, 1 507s	
$[Pd(mit)_2(cyd)_2]Cl_2$	3 330s	1 720s	1 640m, 1 525m, 1 485w	1 570m, 1 465m, 1 280s
$[Pt(mit)_2(cyd)_2]Cl_2·3H_2O$	3 382s	1 730s	1 670m, 1 546m	1 570m, 1 460m, 1 280s
$[Pd(cyd)_4]Cl_2$	3 340s	1 716s	1 645m, 1 520m, 1 480w	
$[Pt(cyd)_4]Cl_2$	3 370s	1 724s	1 670m, 1 542m, 1 482w	
ado	3 360s		1 675s, 1 576m	
$[Pd(ado)_4]Cl_2$	3 408m 3 348m		1 634m, 1 559m	
$[Pt(ado)_4]Cl_2$	3 398m 3 350m		1 632m, 1 559w	

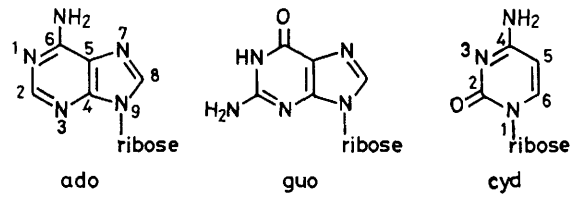
* $[MCl_2(mit)_2]$: 1 565m, 1 461m, and 1 278s cm^{-1}.

TABLE 3

Hydrogen-1 chemical shifts [a] for $[M(mit)_2L_2]Cl_2$ and $[ML_4]Cl_2$ (L = nucleoside) [b]

Compound	H^8	H^6	H^5	H^2	NH_2	N^1H	mit Protons [c] aromatic	mit Protons [c] CH_3
Guanosine [d]	7.93				6.46	10.68		
$[Pd(mit)_2(guo)_2]Cl_2$	8.81				6.51	10.78	7.48	3.58
$[Pt(mit)_2(guo)_2]Cl_2$	8.92				6.55	10.80	7.50	3.58
Cytidine		7.78—7.79	5.75—5.66		7.13			
$[Pd(mit)_2(cyd)_2]Cl_2$		8.20—8.11	6.10—6.01		8.40—7.91		7.45	3.50
$[Pt(mit)_2(cyd)_2]Cl_2·3H_2O$		8.35—8.26	6.26—6.17		9.78—8.69		7.50	3.62
$[Pd(cyd)_4]Cl_2$		8.11—8.03	6.02—5.91		8.32—7.93			
$[Pt(cyd)_4]Cl_2$		8.25—8.17	6.18—6.09		9.70—8.61			
Adenosine [d]	8.36			8.15	7.44			
$[Pd(ado)_4]Cl_2$	8.66			7.25	8.45			
$[Pt(ado)_4]Cl_2$	8.67			8.28	9.04			

[a] In p.p.m. downfield from Na[tps], at a concentration of 2×10^{-2} mol dm^{-3} in D_2O and [$^2H_6$]dmso. [b] Proton positions:



[c] $[MCl_2(mit)_2]$: aromatic, 7.50 (m); CH_3, 3.60 p.p.m. [d] The spectrum was run at 70 °C to increase solubility and resolution.

In guanosine complexes, the H^8 singlet disappeared through D_2O exchange at room temperature in *ca.* 2 h. This singlet was shifted downfield (0.88—0.99 p.p.m.) on complex formation compared with the spectrum of free guanosine. The N^1–H and N^2–H_2 singlets (in the complexes. A downfield shift of H^8 (0.31 p.p.m.) was observed after complex formation, whereas the H^2 resonance was deshielded by only 0.10 p.p.m. It has already been reported that adenosine tends to bind through both N^7 and N^1.[11,12,24,25] However, this does not appear to be the case when there is an excess of

[17] R. B. Simpson, *J. Amer. Chem. Soc.*, 1964, **86**, 2059.
[18] L. G. Purnell and D. J. Hodgson, *J. Amer. Chem. Soc.*, 1976, **98**, 4759.
[19] W. R. Walker, J. M. Guo, and N. C. Li, *Austral. J. Chem.*, 1973, **26**, 2391.
[20] P. C. Kong and F. D. Rochon, *J.C.S. Chem. Comm.*, 1975, 599.
[21] G. Y. H. Chu and R. S. Tobias, *J. Amer. Chem. Soc.*, 1976, **98**, 2641.
[22] D. M. L. Goodgame, I. Jeeves, F. L. Phillips, and A. C. Skapski, *Biochim. Biophys. Acta*, 1975, **378**, 153.
[23] R. W. Gellert and R. Bau, *J. Amer. Chem. Soc.*, 1975, **97**, 7379.
[24] N. Hadjiliadis, P. Kouzounakis, and T. Theophanides, *Inorg. Chim. Acta*, 1973, **7**, 226.
[25] C. J. L. Lock, R. A. Speranzini, G. Turner, and J. Powell, *J. Amer. Chem. Soc.*, 1976, **98**, 7865.

adenosine over metal (4 : 1). N^7 may therefore be considered as a preferential binding site for adenosine. The N^6–H_2 singlet is also deshielded, 1.0 p.p.m. for Pd and 1.6 p.p.m. for Pt. Although amine shifts should be interpreted with much caution, we suppose that this deshielding effect is due to an overall change in the electron density at the nitrogen, reflecting a decrease in the amine basicity on metallation at N^7. Furthermore, a calculation [26] of the M–H–N^6 distance when M is bound to N^7 gave 2.56—2.62 Å. It cannot thus be excluded that the amine shift may also be due to the proximity of the amino-group to the metal centre.

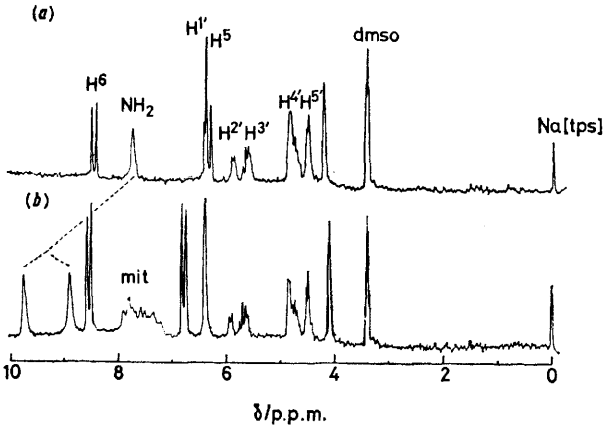
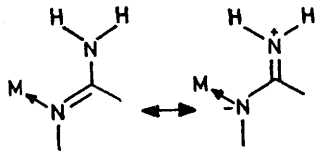


FIGURE 1 The 90-MHz ^1H n.m.r. spectra of: (*a*) ree seifydine (where the $H^{1'}$ and H^5 doublets are part superpoc);dt (*b*) cytidine + *cis*-$[PtCl_2(mit)_2]$ in $[^2H_6]$dmso (pD 5.6)

scopy appeared to be complete after 20 min (*cf.* Figure 1). Both the H^5 and H^6 doublets shifted downfield, with the larger shift for H^5. This indicates that H^5 is closer to the co-ordination site on the ligand, probably N^3,[27] and this has been confirmed by the crystallographic investigations of the interaction of Pt^{II} with the analogous base 1-methylcytosine.[28]

Following complex formation, two signals appeared for the amine protons, both deshielded, and with a difference in chemical shift of 0.9 p.p.m. in the platinum complexes and of 0.5 p.p.m. in the palladium species. The rate of rotation of the amino-group is slow; the two proton environments are different and therefore separate resonances are observed. Coalescence could not be observed on increasing the temperature of the sample to re-establish free rotation along the C^4–N bond, because the exchange rate of the amine protons was enhanced and both signals disappeared rapidly. Metal bonding *via* N^3 is consistent with these results, postulating the following resonance in solution:



The low concentration of the solutions (2×10^{-2} mol dm^{-3}) prevented us from seeing any ^1H–^{195}Pt spin–spin coupling, as observed in previous studies.[12,18,24,27,29,30]

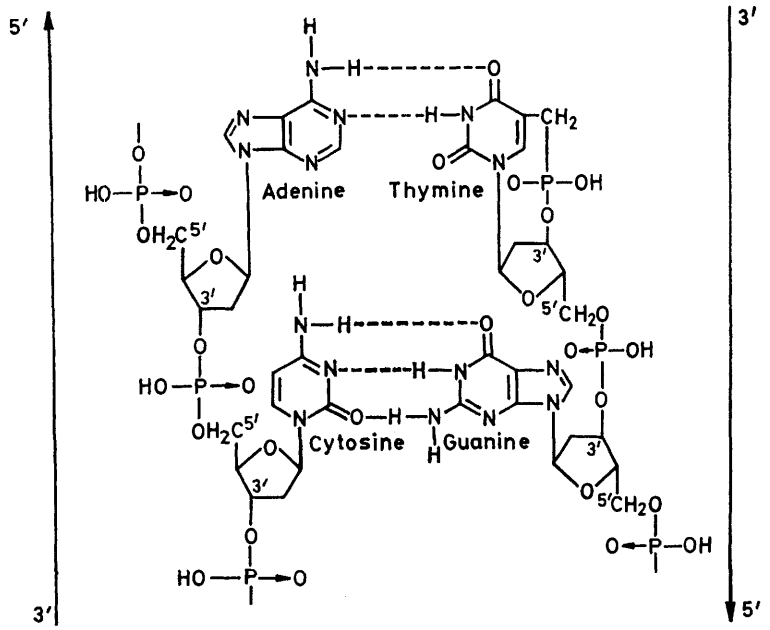


FIGURE 2

In the case of cytidine, its reaction with $[MCl_2(mit)_2]$ at room temperature followed by ^1H n.m.r. spectro-

[26] T. F. Lai and R. E. Marsh, *Acta Cryst.*, 1972, **B28**, 1982.
[27] P. C. Kong and T. Theophanides, *Inorg. Chem.*, 1974, **13**, 1981.
[28] C. J. L. Lock, R. A. Speranzini, and J. Powell, *Canad. J. Chem.*, 1976, **54**, 53.
[29] K. W. Jennette, J. T. Gill, J. A. Sadownik, and S. J. Lippard, *J. Amer. Chem. Soc.*, 1976, **98**, 6159.
[30] G. Kotowicz and O. Suzuki, *Biochemistry*, 1973, **13**, 3434; **12**, 5325.

This coupling appears to be concentration dependent since, on increasing the concentrations to 0.2 mol dm^{-3} a ^{195}Pt–H^8 coupling (30 Hz) was observed for $[Pt(mit)_2(guo)_2]Cl_2$ and $[Pt(ado)_4]Cl_2$ and is consistent with co-ordination at N^7.

It should be noted that the shifts brought about by complex formation of the nucleosides to Pd^{II} are always smaller (up to 50%) than those produced by Pt^{II}, and imply that the Pd atom will accept less electronic charge from the nucleosides than Pt on co-ordination.

While no change of the amino-groups was observed in the solid state by i.r. spectroscopy, the unusual deshielding of the amine-proton signals noted in the spectra of both adenosine and cytidine on complex formation in solution suggests that the electron density of the amines has been modified. This is interesting in view of the fact that these groups, as well as the cytidine N^3 metal-binding site, are normally involved in hydrogen bonding with the complementary bases, thymine and guanosine, in double-stranded DNA.

Carbon-13 N.M.R. Spectra.—The purine and pyrimidine rings of the nucleosides bear at most two non-exchangeable protons, so ^1H n.m.r. gives only limited information. In contrast, the ^{13}C n.m.r. gives more information since the bases contain either four or five carbon atoms. This method has been recently used to investigate the interactions between the paramagnetic ions Cu^{2+} and Mn^{2+} and various nucleosides.[30,31] There is only one report [32] on diamagnetic complexes of the type $[Pd(en)L_2]^{2+}$ (en = ethylenediamine, L = nucleoside), which indicates that ^{13}C n.m.r. may be a very precise method for delineating these species in solution.

The ^{13}C n.m.r. assignments are summarised in Table 4; they were identified by reference to nucleoside assignments made by Jones *et al.*[33] and by comparison with the undecoupled spectra (for C^2 and C^8 of the purine rings, C^5 and C^6 of cytidine). The chemical-shift changes in the proton-decoupled spectra of the complexes enabled us to confirm that the nucleoside binding sites were as suggested above. In the case of guanosine, the downfield shifts observed for the C^5 and C^8 resonances are consistent with the co-ordination at N^7, since these carbons are adjacent to this nitrogen. For the cytidine complexes, the downfield shifts observed for the C^2 and C^4 resonances, in contrast to the upfield shifts of the C^5 and C^6 signals, support co-ordination of the cytidine to the metal ions through N^3. The largest chemical-shift differences occurred between free and bound adenosine, at C^8 and C^5 (see Figure 3). Co-ordination through N^7 is thus confirmed. The C^6 shift is consistent with a decrease in electron density at the nearby amine nitrogen.

TABLE 4

Carbon-13 chemical shifts [a] for $[M(mit)_2L_2]Cl_2$ and $[ML_4]Cl_2$ (L = nucleoside)

Compound	C^2	C^4	C^5	C^6	C^8
Guanosine [b]	154.7	152.0	117.7	157.7	136.5
$[Pd(mit)_2(guo)_2]Cl_2$	155.8	153.3	119.7	159.0	139.8
$[Pt(mit)_2(guo)_2]Cl_2$	155.1	153.2	120.1	159.3	142.7
Cytidine	151.7	162.7	98.6	147.6	
$[Pd(mit)_2(cyd)_2]Cl_2$	155.5	165.3	96.9	146.3	
$[Pt(mit)_2(cyd)_2]Cl_2 \cdot 3H_2O$	154.5	165.3	97.7	146.9	
$[Pd(cyd)_4]Cl_2$	156.4	167.2	97.2	146.1	
$[Pt(cyd)_4]Cl_2$	156.1	167.8	97.9	146.6	
Adenosine [b]	146.5	144.9	111.5	149.7	132.8
$[Pd(ado)_4]Cl_2$	148.7	145.0	120.4	154.4	141.8
$[Pt(ado)_4]Cl_2$	150.0	145.2	121.9	154.6	142.6

[a] In p.p.m. downfield from Na[tp]. [b] Measured at 70 °C for solubility purposes.

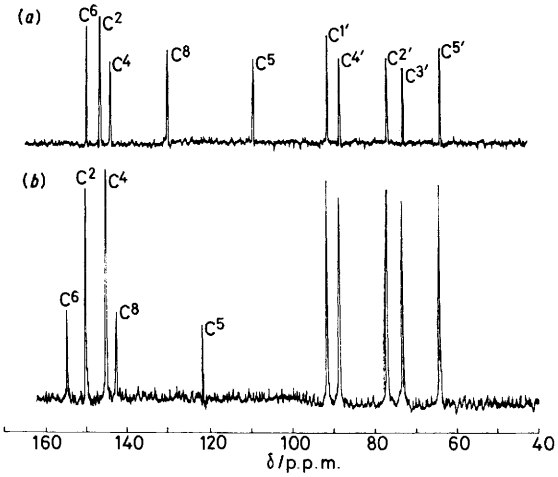


FIGURE 3 The 250-MHz ^{13}C n.m.r. spectra of: (*a*) free adenosine; (*b*) $[Pt(ado)_3]Cl_2$ in D_2O (pD 6.5)

EXPERIMENTAL

Physical Measurements.—Infrared spectra were recorded on a Polytec FIR 30 interferometer (50—400 cm^{-1}) and on a Beckman IR 12 spectrophotometer (400—4 000 cm^{-1}). The complexes were sampled as polyethylene and KBr pellets respectively. Hydrogen-1 n.m.r. spectra were obtained using a Brucker WH 90 spectrometer, over a frequency range of 1.2 kHz, by Fourier transform of the free-induction decays over 2 048 data points. The samples were lyophilised from ^2H_2O, and run as 2×10^{-2} mol dm^{-3} solutions in ^2H_2O and $[^2H_6]$dmso, with sodium 3-(trimethyl-

[31] G. Kotowicz, *Canad. J. Chem.*, 1974, **52**, 924.

[32] D. J. Nelson, P. L. Yeagle, T. L. Miller, and R. B. Martin, *Bioinorg. Chem.*, 1976, **5**, 353.

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silyl)propane-1-sulphonate Na[tps] as internal standard. The pD was adjusted (5.5—6.5) with concentrated Na[OD].

The proton-decoupled ^{13}C n.m.r. spectra were obtained using a Cameca 250 MHz spectrometer (22.63 MHz) operating in the Fourier-transform mode and equipped with a Nicolet 1080 computer. The free-induction decay signals were accumulated in 8 k data points, over a frequency range of 15 KHz, and 10 000 accumulations were carried out. The solutions were prepared in ^2H_2O, at a concentration of 0.1—0.2 mol dm^{-3}, with sodium 3-(trimethylsilyl)propionate Na[tp] as internal standard. The temperature for all the experiments was determined directly using the Brucker or Cameca temperature-control unit.

Preparation of the Complexes.—The complexes $[M(mit)_2L_2]Cl_2$ and $[M(ado)_4]Cl_2$ (M = Pd or Pt; L = cyd or guo) were prepared by mixing *cis*-$[MCl_2(mit)_2]$ (1 mmol) with the corresponding nucleosides (2 mmol) in ethanol–water (10 : 1, 75 cm^3) at room temperature. During the reaction, which occurs with a change of colour, the pH was maintained at 6—7 by addition of dilute K[OH]. Crystalline products appeared when the reaction mixtures were set aside overnight.

The complexes $[M(cyd)_4]Cl_2$ were isolated by vapour diffusion of an ethanol solution of $[M(mit)_2(cyd)_2]Cl_2$ against diethyl ether; $[M(cyd)_4]Cl_2$ were the first to crystallise out, followed by *cis*-$[MCl_2(mit)_2]$, and finally by free mit. Microanalyses for C, H, and N were performed by the Service Central de Microanalyses du C.N.R.S. in Strasbourg.

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