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A ^{1}H and ^{13}C NMR Study of some *Cis*-$[Pt(NH_3)_2X_2]Y_2$ Complexes (X = Imidazoles, Pyrimidines, 3-Substituted Pyridines, Inosine and Guanosine; Y = Cl^-, ClO_4^-) in Aqueous Solutions

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^{195}Pt–^{1}H and ^{195}Pt–^{13}C coupling constants are reported for species of the type cis-$[Pt(NH_3)_2X_2]Y_2$ *When X is an imidazole or substituted imidazole two and three bond coupling to ring carbon nuclei are observed and the two ^{2}J couplings are significantly different in size When Pt is coordinated to an imidazole ring fused to a second ring as in benzimidazole or the purine nucleosides a similar pattern of coupling is observed In general the trend is $^{2}J_{C2} > {}^{3}J > {}^{2}J_{C4}$*

In none of the substituted pyridine complexes was a ^{2}J observed ^{3}J was very sensitive to the nature of the substituent on the observed nucleus In most cases a ^{4}J of ca. *11 Hz was observed Coupling in pyrimidine complexes to C nuclei was more extensive and ^{2}J, ^{3}J and ^{4}J coupling is observed*

It has been shown that water is a far superior solvent to DMSO and yields narrower resonances and thus the possibility of observing smaller coupling constants. In DMSO most of the complexes studied also displayed some solvolysis

Introduction

Following the discovery of the marked interference of *cis*-diamminodichloroplatinum(II) with bacterial growth patterns [1] and subsequently the potent antineoplastic activity of the above and of structurally similar platinum(II) compounds [2, 3], there has been considerable interest in the interaction of platinum(II) with molecules of biological significance There can be little doubt that the primary mode of action of these antitumour agents involves co-ordination to nucleic acids *in vivo* specifically to DNA [3–8]

Numerous studies involving the reaction of *cis*-$[Pt(NH_3)_2Cl_2]$ with nucleosides and nucleotides have appeared, and have been reviewed by Marzilli [9] Initial binding studies employed UV spectrophotometry [10], and more recently ^{1}H nmr [11–15] to determine specific binding sites of the platinum(II) nucleophile to common nucleosides and nucleotides Shifts induced on complexation, as well as ^{195}Pt–^{1}H coupling constants in favourable cases were observed

Ettorre [16] used ^{1}H and ^{13}C nmr to investigate binding of Pd(II) and Pt(II) to cytidine, assignments were made only on the basis of diamagnetic shifts induced and comparison with the corresponding protonation shifts No coupling constants were reported, dimethylsulphoxide being used as solvent. Martin has reported ^{13}C magnetic resonance data using Pd(II) as a model for platinum to investigate complexation to a number of pyrimidine and purine nucleosides [17]

Previous reports of ^{13}C nmr with simple nitrogen heterocycle interactions with platinum are limited, Martin [18] having investigated spin–spin coupling constants between ^{195}Pt and ^{13}C for pyridine and 2,2′-bipyridyl systems ^{13}C parameters for pyridine have also been established in nonaqueous solvents in which some substituted pyridine organo-platinum adducts were studied [19–21]

As part of a study of heavy metal–nucleoside interactions, Tobias *et al* [22–26] have employed ^{1}H nmr, Raman and ^{13}C nmr spectroscopy, the latter only in interactions involving cytidine and uridine with *cis*-diammineplatinum(II) No ^{195}Pt–^{13}C coupling constants were reported

In an attempt to gain some insight into the nature of spin–spin coupling between ^{195}Pt and ^{13}C as transmitted through a nitrogen atom we investigated some model compounds of the general structure *cis*-$[Pt(NH_3)_2(X)_2]Y_2$ where X = imidazole derivatives, 3-substituted pyridines, pyrimidines, cytidine, guanosine and inosine, while Y = Cl^- or ClO_4^- The danger of using a co-ordinating solvent such as DMSO is underlined

Experimental

^{13}C spectra were obtained on a Bruker WH-90DS spectrometer operating in the Fourier transform mode at 22 63 M Hz The probe temperature was 40 ± 1 °C with broad-band ^{1}H decoupling Typically,

in the presence of Gd (triethylenetetramine hexaacetate) as shiftless relaxation agent [33], a 45° pulse with no delay gave good results with an acquisition time of 682 milliseconds. In the absence of Gd-(TTHA), a 0.5 sec. delay between each pulse was employed. Suitable spectra of platinum complexes were obtained from solutions of concentration 0.25–1.0 *M* requiring from 3–80 K transients.

All ^{13}C chemical shifts are accurate to an estimated 0.1 ppm while coupling constants are accurate to ±1.2 Hz. In the majority of spectra, shifts are taken relative to internal dioxane in dilute aqueous solution, resonating at 67.73 ppm relative to TMS [34].

Proton magnetic resonance was carried out at 100 MHz on a Varian XL-100 CW instrument, using 3-(trimethylsilyl)-propane sulphonic acid as internal standard in all cases.

Cis-[*Pt(NH$_3$)$_2$Cl$_2$*]

It was prepared from K_2PtCl_4 according to the literature method [29].

Cis-[*Pt(NH$_3$)$_2$(Imidazole)$_2$*]*Cl$_2$*

Imidazoles that were commercially available were used without further purification. These compounds reacted with a hot aqueous solution of *cis*-[Pt(NH$_3$)$_2$Cl$_2$] according to the general reaction:

$$Cis\text{-}[Pt(NH_3)_2Cl_2] + 2IMD \xrightarrow[H_2O,\ 80\ ^\circ C]{2\ hr} cis\text{-}[Pt(NH_3)_2(IMD)_2]\,Cl_2 \quad (>80\%)$$

IMD = imidazoles.

Typically, a 2 mmol (600 mg) quantity of *cis*-[Pt(NH$_3$)$_2$Cl$_2$] dissolved in 100 ml deionised water at 80 °C. To the magnetically stirred, clear, yellow solution was added 4.01 mmol imidazole in 10 ml H_2O. The mixture was stirred at 80 °C for a further 2 hours after which the yellow colour had generally been discharged. This, along with conductivity measurements, indicated that reaction had gone to completion. After cooling the excess water was evaporated under reduced pressure, upon which the residue was twice extracted with 50 ml portions of diethylether (to remove any uncoordinated imidazole). The *cis*-[Pt(NH$_3$)$_2$(IMD)$_2$]Cl$_2$ complex was dissolved in a minimum of H_2O, filtered if necessary, and precipitated by a 1:1 mixture of acetone/diethylether.

The white crystalline precipitate was collected by filtration under dry nitrogen, and dried under vacuum at *ca.* 60 °C. Yields were generally better than 80%.

In the case of benzimidazole the above isolation procedure was unnecessary due to direct crystallisation of a much less water soluble *cis*-diamminobis-(benzimidazole)platinum(II) chloride.

Finally, where the imidazole was 4(5)-bromoimidazole, the platinum complex was prepared as the perchlorate salt.

The preparation of bromoimidazole followed the literature method [30].

cis-[*Pt(NH$_3$)$_2$(pyridine)$_2$*]*(ClO$_4$)$_2$*

These compounds are conveniently prepared using *cis*-[Pt(NH$_3$)$_2$(H$_2$O)$_2$](ClO$_4$)$_2$ instead of the *cis*-diamminodichloro platinum(II).

TABLE I. Microanalysis of Isolated Platinum Complexes *cis*-[Pt(NH$_3$)$_2$(X)$_2$]Y$_2$.

Y	X	Found			Calculated		
		%H	%C	%N	%H	%C	%N
Cl	imidazole	3.1	16.6	18.7	3.2	16.5	19.3
Cl	1-methylimidazole	4.3	18.8	17.0	4.4	19.2	16.8
Cl	2-methylimidazole	4.0	18.7	17.2	4.4	19.2	16.8
Cl	benzimidazole	3.7	30.3	14.6	3.6	30.3	15.2
ClO_4	pyrimidine	2.5	16.0	14.2	2.4	16.4	14.3
ClO_4	4-methylpyrimidine	2.9	18.2	13.1	2.9	19.5	13.7
ClO_4	5-methylpyrimidine	2.9	19.0	13.4	2.9	19.5	13.7
ClO_4	pyridine	2.8	20.0	9.6	2.7	20.5	9.6
ClO_4	3-methylpyridine	3.4	24.1	9.4	3.3	23.5	9.1
ClO_4	3-acetylpyridine·H_2O	3.1	24.4	8.1	3.2	24.5	8.2
ClO_4	3-cyanopyridine·H_2O	2.7	22.4	12.2	2.5	22.1	12.8
ClO_4	3-methylcarboxylato-pyridine	2.9	23.9	7.9	2.85	24.0	8.0
ClO_4	3-iodopyridine	1.7	14.2	6.7	1.7	14.3	6.7
ClO_4	3-bromopyridine	2.1	15.8	7.4	1.9	16.1	7.5
ClO_4	3-chloropyridine	2.5	19.0	8.2	2.1	18.3	8.6
ClO_4	3-hydroxypyridine	2.6	18.9	9.1	2.6	19.5	9.1
ClO_4	3-carbinolpyridine	3.2	22.4	8.8	3.1	22.3	8.7
ClO_4	guanosine·1½H_2O	3.5	23.5	15.6	3.2	24.1	16.9
ClO_4	inosine·1½H_2O	3.4	25.0	14.0	3.1	24.9	14.5

6 g *cis*-$[Pt(NH_3)_2Cl_2]$ in 500 ml water were treated with a twice equimolar portion of $AgClO_4$ in 30 ml water. The mixture, protected from light, was stirred at 50 °C for some 5 hours. Centrifugation removed the precipitated AgCl, while filtration through a small quantity of active charcoal yielded a clear pale yellow solution of *cis*-$[Pt(NH_3)_2(H_2O)_2]$-$(ClO_4)_2$. Evaporation of excess water quantitatively yielded a yellow hygroscopic complex which was stored under nitrogen below 0 °C.

The 3-substituted pyridines were used without further purification. A 2 mmol quantity in 20 ml water was mixed with 1 mmol *cis*-$[Pt(NH_3)_2(H_2O)_2]$-$(ClO_4)_2$ in 20 ml water. Warming to 60 °C completed reaction rapidly and subsequent evaporation of excess water gave colourless crystalline material. Any free pyridine was extracted into ether. Yields in excess of 80% were recorded in all cases. Microanalysis data are collected in Table I.

cis-$[Pt(NH_3)_2(pyrimidine)_2](ClO_4)_2$

In the case of the pyrimidines, an exactly analogous procedure was followed as described for the 3-substituted pyridine adducts mentioned above.

These compounds were readily isolated in yields of 85%, by crystallisation from cold water.

Microanalysis data are given in Table I.

cis-$[Pt(NH_3)_2(nucleoside)_2](ClO_4)_2$

Again, similar methods as given above are applicable in the synthesis of these compounds, which are all readily soluble in water. In the case of cytidine a white crystalline complex was initially isolated which on subsequent dissolution gave an intensely purple coloured solution.

The numbering system used for the complexes is shown in Fig. 1.

Results

5-Membered Heterocycles

Imidazole and its substituted methyl derivatives readily displace chloride anions from the partly hydrolysed *cis*-$[Pt(NH_3)_2Cl_2]$ complex [31] to form *cis*-diamminobis(imidazole)platinum(II) chloride. The readily water soluble complex cations give clean ^{13}C and ^1H nmr spectra as summarised in Tables II and III. It is evident from Table II that only small shifts are induced on complexation with platinum, C2 is deshielded in the range 0.8–6.9 ppm while C4 is deshielded from 1.8–5.5 ppm with C4 of the thiazole ring being shielded by 0.2 ppm. For C5 of the imidazole ring the situation is more complex with induced shifts being either upfield or downfield depending on the substituents present. Unfortunately no correlations are easily discernable (see discussion).

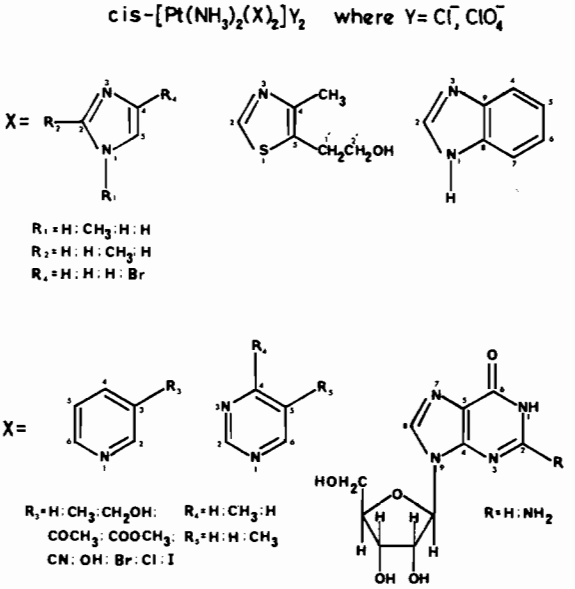

Fig. 1. Structures and numbering system used for the complexes studied.

The $^{195}Pt-^{13}C$ coupling constants are more interesting with the general observation that $^2J_{Pt-C2} > {}^3J_{Pt-C5} > {}^2J_{Pt-C4} \simeq {}^3J_{Pt-CH_3}$ for the diazole systems. In the thiazole complex $^2J_{Pt-C2}$ is slightly smaller than $^3J_{Pt-C5}$. In the case of 4-bromoimidazole the coupling constant at the bromo-substituted carbon atom is very small *ca.* 6Hz, while other couplings are only slightly smaller than for imidazole itself probably reflecting the lower basicity of 4-bromoimidazoles. An unexpectedly large four bond coupling constant $^4J_{Pt-C5}$ *ca.* 28 Hz in benzimidazole is observed although the multiplet is poorly resolved.

The purine nucleosides, Table IV, show reduced coupling of Pt to the 5-membered ring in comparison with imidazole itself. No coupling is observed to C6 in the guanosine or inosine complexes although this might be expected by comparison with the spectra of the thiazole and benzimidazole complexes. We are unable to report 3 bond coupling in the inosine complex. This is because the C4 and C2 resonances are very close obscuring one of the expected satellites. In general we have not reported coupling unless both satellites were observed as minor resonances and could not be confused with unbound ligand or impurity resonances that were present in some cases.

Although the ^{13}C spectra of the cytidine complex were sharp no coupling to Pt was observed. Presumably this arises through the presence of rapid exchange on an nmr time scale.

^{13}C spectra of the 1-methyl imidazole and guanosine complexes are shown in Figure 2.

The ^1H nmr spectra for the above compounds have been observed and details are given in Table III. Only three bond $^{195}Pt-^1H$ couplings are observed. In

TABLE II. ^{13}C Nmr Data for *cis*-$[Pt(NH_3)_2X_2]Y_2$ in ^2H_2O Containing Gd(TTHA) (≃0.05 *M*). (X = 5-Membered Heterocycle).

Compound		Chemical Shifts, ppm from TMS[a]							$^n\lvert J_{^{195}Pt-^{13}C}\rvert$ Coupling Constants/(Hz)			
X	Y	C2	C4	C5	CH_3				^2J	^2J	^3J	^3J
imidazole	Cl^-	137.9 (+1.5)[b]	128.3 (+5.8)	119.1 (−3.4)	– –				50.5(C2)	23.5(C4)	39.5(C5)	–
1-methylimidazole	Cl^-	139.8 (+6.9)	128.7 (+5.5)	123.4 (+6.3)	35.5 (−1.8)				50.5(C2)	21.8(C4)	37.5(C5)	–
2-methylimidazole	Cl^-	147.4 (+0.8)	128.3 (+5.9)	118.5 (−3.9)	14.4 (+0.3)				45.2(C2)	22.5(C4)	44.1(C5)	23.0(CH_3)
4-bromoimidazole	ClO_4^-	140.0 (+2.0)	120.1 (+2.3)	114.9 (+1.3)	–				41.9(C2)	≃6(C4)[c]	23.4(C5)	
5-(2-hydroxyethyl)-4-methylthiazole	ClO_4^-	157.0 (+4.9)	149.6 (−0.2)	133.1 (+1.5)	16.4 (+1.1)	30.4(C2') (−0.2)		62.1(C1') (−0.8)	35.5(C2)	25.5(C4)	35.7(C5)	20.5(CH_3)
		C2	C9	C8	C4	C5	C6	C7				
benzimidazole	ClO_4^-	144.3 (+2.8)[d]	139.7 (+1.8)	132.3 (−5.6)	117.8 (+2.4)	125.1[e] (+2.2)	126.1[e] (+3.2)	114.2 (−1.2)	50.5(C2)	19.0(C9)	28.6(C8)	20.9(C4)
									^4J			
									28.0(C5)			

Parentheses denote shift on complexation relative to free ligand parameters in water. (+) downfield, (−) upfield shift. [a]Relative to internal dioxane at 67.73 ppm from TMS. [b]Using data for free imidazole in ^2H_2O from ref. [34, 60]. [c]Not clearly resolved, but estimable. [d]Relative to unbound benzimidazole in ethanol [49]. [e]Not unambiguous, based on apparent coupling constant $^4\lvert J_{Pt-C}\rvert \simeq 28.0$ Hz.

TABLE III. ^{1}H Nmr Data for *cis*-[$Pt(NH_3)_2(X)_2$] Y_2 in ^2H_2O. (X = 5-Membered Heterocycle, Nucleoside).

Compound		Chemical Shift, ppm from DSS[a]								$^n\lvert J_{^{195}Pt-H}\rvert$ Coupling Constant/(Hz)		
X	Y	H2	H4	H5	Other					^3J	^3J	Other
imidazole	Cl^-	7.95 (+0.19)	7.06 (−0.08)	7.20 (+0.06)						20.2(H2)	≃24(H4)	[e]
1-methylimidazole	Cl^-	7.84 (+0.23)	7.01 (+0.01)	7.14 (+0.06)	3.70(CH_3) (+0.01)					19.8(H2)	≃22.3(H4)	[e]
2-methylimidazole	Cl^-	–	7.20 (+0.22)	7.10 (+0.12)	2.65(CH_3) (+0.29)					–	≃20.7(H4)	[e]
4-bromoimidazole	Cl^-	8.20[b] (+0.57)	–	7.36[b] (+0.17)	–					20.5(H2)	–	^4J ≃7.5(H5)[b]
5-(2-hydroxyethyl)-4-methylthiazole	ClO_4^-	9.17 (+0.66)	–	–	2.76(CH_3) (+0.46)	3.00(H1′) (+0.08)	3.46(H2′) (+0.05)			28.6(H2)	–	–
benzimidazole	ClO_4^-	8.7 (+0.43)	–	–	8.22(H4, 7) (+0.48)	7.54(H5, 6) (+0.14)				20.6(H2)	–	–
		H8	H2		H1′	H2′	H3′	H4′	H5′			
inosine	ClO_4^-	8.80[c] (+0.64)	8.24 (+0.18)		6.07 (+0.07)	4.60[d]	4.40[d]	4.27[d]	3.87[d]	24.0(H8)	–	–
guanosine	ClO_4^-	8.43[c] (+0.58)	–		5.91[d] (+0.05)					≃23.5(H8)	–	–

Complexation shifts induced by platinum are given in parentheses. (+) deshielded, (−) shielded. [a]Reference, 3-(trimethylsilyl)-propanesulphonic acid (as sodium salt). [b]Assignment based on long range $^4\lvert J_{Pt-H}\rvert$ coupling constant. Additional $^4\lvert J_{H2-H5}\rvert$ = 1.6 Hz observed. [c]^{1}H nmr data from refs [13], [15]. [d]Small complexation shifts, and resonances broad. [e]Not resolved.

TABLE IV. ^{13}C Nmr Data for *cis*-$[Pt(NH_3)_2(nucleoside)_2](ClO_4)_2$ in ^2H_2O Containing Gd(TTHA) (≃0.05 *M*). (X = Nucleoside).

Nucleoside	Chemical shift, ppm relative to TMS										$^nJ_{^{195}Pt-^{13}C}$ Coupling Constants/(Hz)		
	C8	C5	C4	C2	C6	C1′	C2′	C3′	C4′	C5′	^2J	^2J	^3J
guanosine	140.9[a] (+4.0)	115.6 (−2.0)	151.5 (−0.9)	155.5 (+0.9)	157.8 (0.0)	80.2 (+2.9)	71.0 (−0.6)	75.1 (+2.0)	86.5 (+0.1)	62.4 (+0.2)	40.0(C8)	16(C5)	27.0(C4)
inosine	143.7[a] (+3.8)	124.5 (−0.9)	149.1[b] (−0.1)	149.4[b] (+2.4)	158.0 (+0.3)	91.7 (+2.9)	71.3 (0.0)	76.3 (+1.1)	86.9 (+0.2)	61.2 (−0.2)	38.0(C8)	≃12(C5)	[c]
	C2	C6	C4	C5									
cytidine[d]	155.8	142.4[e] 142.9 143.5	166.6[e] 165.3	96.7 97.1		92.6[e] 91.5	75.8[e] 75.5	69.7[e] 70.2 70.5	85.1[e] 84.7	73.8 73.5	[f]	[f]	[f]

[a] Shifts on complexation are based on free nucleoside chemical shifts from ref. [34, page 472] (solvent DMSO). [b] Assignment, due to resonance overlap, not unambiguous. [c] Not resolved (see b). [d] An intense blue colour developed on dissolving dry isolated *cis*-$[Pt(NH_3)_2(cytidine)_2](ClO_4)_2$ in water (see text). [e] Major resonance. [f] No coupling observed.

general the spin–spin coupling constants to H2 for the imidazoles and H8 for inosine and guanosine range from 19.8–23 Hz (the values obtained for inosine and guanosine are in accord with the data previously published [13]). The ^3J couplings to H4 are slightly larger than those to H2. A four bond coupling $^4J_{Pt-H5}$ is observed for the compound *cis*-$[Pt(NH_3)_2(4\text{-bromoimidazole})_2](ClO_4)_2$ and is of the order of 7.5 Hz. It is on this basis that the bromoimidazole is assigned 4-bromoimidazole in which platinum co-ordinates to N3 rather unexpectedly (see below).

Very recently a study of compounds of the structure *cis*-$[Pt(1\text{-methylimidazole})_2X_2]$ and $[Pt(imidazole)_4]X_2$ has described the ^1H nmr data for these compounds [54]. In agreement with our results, $^3J_{Pt-H2}$ = 20–22 Hz, $^3J_{Pt-H4}$ = 23–24 Hz while $^4J_{Pt-H5}$ = 7–9 Hz were obtained. This lends direct support to our proposal of N3 co-ordination in the case of 4-bromoimidazole.

6-Membered Heterocycles

The 3-substituted pyridine and methyl pyrimidine derivatives of *cis*-diamminodiaquoplatinum(II) perchlorate are readily prepared yielding ^{13}C nmr data shown in Table V, and ^1H nmr results shown in Table VII.

The proton magnetic resonance data for 3-substituted pyridine complexes shows that generally H2, H6 and H4 are deshielded relative to the uncomplexed pyridine, while H5 is shielded for most substituents except for 3-methylpyridine. The diamagnetic shifts as given in Table V are obtained from chemical shift data for free pyridines either neat or in DMSO solution previously published [32], and solvent effects cannot be ignored. The 3-hydroxopyridine complex is the obvious anomaly since it is thought that hydroxypyridines are in fact pyridones [32].

The pyrimidine analogues show very similar behaviour, all proton resonances being deshielded on complexation. In this case no solvent effects are operative since complex and free ligand spectra were obtained under identical conditions.

Only $^3J_{Pt-H}$ coupling constants could be detected for the substituted pyridine and pyrimidine complexes. In the former case, the platinum to H2 coupling constants tend to be slightly larger (by 1–4 Hz) than the corresponding values for H6. These couplings also tend to show low sensitivity to the nature of the substituent.

$^3J_{Pt-H2}$ for the pyrimidine analogues is approximately 50% smaller than the corresponding coupling constant for pyridine. It is observed that H2 in the pyrimidines is substantially deshielded by the presence of the second ring nitrogen atom relative to the pyridines. Coupling to H6 of the pyrimidines is of the same order as in the pyridine systems. As is

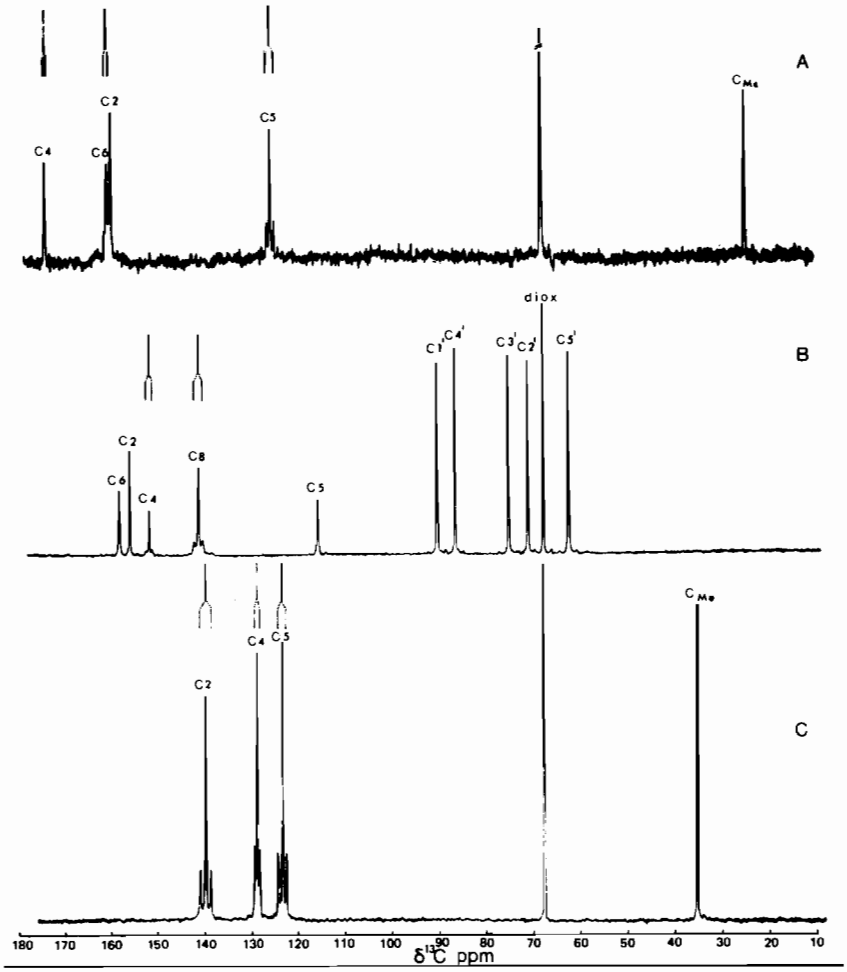

Fig. 2. Typical ^{13}C nmr spectra obtained in $^{2}H_2O$ in the presence of Gd(TTHA), with dioxane as internal reference. A: *cis*-$[Pt(NH_3)_2(4\text{-methylpyrimidine})_2](ClO_4)_2$; B: *cis*-$[Pt(NH_3)_2(guanosine)_2](ClO_4)_2$; C: *cis*-$[Pt(NH_3)_2(1\text{-methylimidazole})_2]Cl_2$.

evident from the proton nmr data, platinum coordinates to N1 of 4-methylpyrimidine, since N3 is the sterically unfavourable binding site.

Reference to Table V shows that all aromatic carbon atoms for the pyridine and pyrimidine platinum complexes are deshielded on complexation excepting C3 of the hydroxo and iodopyridine complexes, while some substituent carbon atoms show small upfield shifts. A plot of δC3 (bound pyridine) against δC3 (unbound pyridine) is linear, only hydroxo and iodopyridine showing some deviation. Most unbound chemical shifts of substituted pyridines were taken from previously published data [33–35], and some solvent effects may be operative. However, 3-pyridylcarbinol, 3-hydroxopyridine and 3-methylnicotinate ^{13}C shifts were obtained under the same conditions as their platinum complexes. Evidently no major solvent effects contribute to our observed complexation shifts.

Very similar results were obtained for the pyrimidine analogues, the complexation induced shifts having been obtained from free ligand spectra under similar conditions.

The J_{Pt-C} coupling constants are of interest. For substituted pyridine complexes the trend is $^{3}J_{Pt-C3,5} > {}^{4}J_{Pt-C4} > {}^{2}J_{Pt-C2,6}$. In fact, $^{2}J_{Pt-C2,6}$ is consistently not observed in any pyridine compounds we have studied, even under conditions of the highest resolution, in which coupling constants of the order of 9–10 Hz are observable. Furthermore, the $^{3}J_{Pt-C3}$ value shows substantial variation with the nature of the substituent group, R. In particular, $^{3}J_{Pt-C}$ increases in the order $-CH_2OH < -CH_3 < -H < -COOCH_3 \simeq -COCH_3 < -CN < -OH < -I < -Br \simeq -Cl$ from 41.5 Hz to 58.0 Hz (see Table V). Coupling to C5 defines a much narrower interval.

$^{3}J_{Pt-C5}$ varies from 41–44.5 Hz with the exception of 3-hydroxopyridine. $^{4}J_{Pt-C4}$ is clearly resolved under favourable conditions and remains almost constant at a value between 10.5–11.8 Hz.

Although attempts were made to delineate the substituent effect on the coupling constants in terms

TABLE V. ^{13}C Nmr Data for *cis*-$[Pt(NH_3)_2(X)_2](ClO_4)_2$ in ^2H_2O containing Gd(TTHA) (≃0.05 *M*) (X = 6-Membered Heterocycle).

Compound		Chemical Shifts, ppm from TMS[a]							$^n\lvert J_{^{195}Pt-^{13}C}\rvert$ Coupling Constants/(Hz)			
X	R	C2	C3	C4	C5	C6	Other		^2J	^3J	^3J	^4J
3R-pyridine	$-CH_2OH$	152.1[d] (+2.8)	141.5 (+3.9)	140.1 (+2.8)	128.1 (+2.9)	151.6[d] (+3.1)	61.5(CH_2OH) (−1.0)		n.o.[e] (C2, 6)	41.5 (C3)	43.5 (C5)	10.5 (C4)
	$-CH_3$	152.2 (+2.0)[b]	138.9 (+5.1)	141.6 (+4.3)	127.0 (+2.9)	149.6 (+1.8)	18.3(CH_3) (−0.7)		n.o.	41.9	43.2	11.1
	-H	153.1 (+2.5)[b]	128.5 (+4.0)	141.7 (+5.3)	128.5 (+4.0)	153.1 (+2.5)			n.o.	42.5	42.5	≃11[f]
	$-COOCH_3$	154.1 (+3.8)	130.8 (+4.2)	142.2 (+3.8)	128.6 (+3.7)	156.3 (+2.7)	54.7(CH_3) (+1.0)	165.8 (−1.2)	n.o.	44.0	41.5	≃11[f]
	$-COCH_3$	153.5 (+3.4)	136.4 (+3.9)	141.0 (+5.5)	128.7 (+4.4)	156.5 (+2.6)	27.8(CH_3) (+1.0)	199.5 (+2.0)	n.o.	44.0	41.0	10.5
	-CN	156.5 (+2.8)	114.2 (+3.0)	145.4 (+4.9)	129.0 (+4.3)	157.1 (+3.4)	115.7(CN) (−1.8)		n.o.	49.0	41.0	11.8
	-OH	145.0 (+7.3)	156.1 (−1.8)	128.5 (+0.2)	128.9 (+2.2)	141.3 (+4.6)			n.o.	52.5	47.3	[g]
	-I	158.3[c] (+1.8)[b]	95.3 (−2.6)	148.8 (+4.0)	128.5 (+2.3)	152.1 (+3.0)			n.o.	53.8	42.5	[g]
	-Br	153.7 (+2.3)[b]	123.3 (+1.7)	144.9 (+5.7)	129.3 (+3.8)	152.0 (+3.1)			n.o.	57.5	44.0	≃10
	-Cl	152.1[d] (+3.2)	135.9 (+3.2)	142.1 (+4.5)	129.3 (+.3.9)	151.8[d] (+2.9)			n.o.	58.0	44.5	10.5
pyrimidine		160.9[h] (+1.2)	–	160.9[h] (+3.2)	125.4 (+3.1)	161.2[h] (+3.5)			≃22(C6)[h]	–	34.8(C5)	[f]
4-methylpyrimidine		159.3[h] (+1.6)	–	173.4 (+4.1)	125.3 (+2.2)	160.2[h] (+2.1)	24.7(CH_3) (+9.5)		20.0(C6)[h]	–	35.5(C5)	9.5(C4)
5-methylpyrimidine		159.1[h] (+3.6)	– –	161.5 (+3.5)	136.7 (+3.4)	160.1[h] (+2.1)	16.1 (−0.1)		[i]	–	[i]	[i]

Parentheses denote shifts relative to free ligand, (+) downfield, (−) upfield shift. [a]Relative to internal dioxane at 67.73 ppm from TMS. [b]Shifts of free ligand from refs. [34, 35]. [c]Solvent dimethylsulphoxide. [d]Shifts not unambiguous. [e]Not observed. [f]Poorly resolved. [g]Unresolved. [h]Assignment not unambiguous. [i]Sensitivity problems due to poor solubility.

TABLE VI. ^{1}H Nmr Data for *cis*-$[Pt(NH_3)_2(X)_2](ClO_4)_2$ in $^{2}H_2O$ (X = 6-Membered Heterocycle).

Compound		Chemical Shift, ppm from DSS					$^{n}\lvert J_{^{195}Pt-^{1}H}\rvert$ Coupling Constants/(Hz)	
X	R	H2	H6	H4	H5	Other	^{3}J(H2)	^{3}J(H6)
3R-pyridine	-CH_2OH	8.89[e] –	8.81[a] –	8.93[b] –	7.61[c] –	[g] (CH_2)	39.0	≃40
	-CH_3	8.68[e] (+0.11)	8.61[d] (+0.09)	7.86[b] (+0.17)	7.44[c] (+0.15)	2.37[e](CH_3)	40.0	39.1
	-H	8.80[a] (+0.21)	8.80[a] (+0.21)	8.02[b] (+0.27)	7.56[c] (–0.19)	–	39.0	39.0
	-$COOCH_3$	9.44[e] –	9.06[d] –	8.55[b] –	7.43[c] –	4.10[e](CH_3)	40.0	37.5
	-$COCH_3$	9.42[e] (+0.11)	9.06[d] (+0.10)	8.55[b] (+0.12)	7.45[c] (–0.23)	2.70[e] (CH_3)	40.0	37.5
	-CN	9.34[e] –	9.12[d] –	8.43[b] –	7.79[c] –		≃40	≃37
	-OH	8.39[a] (–0.17)	8.31[c] (–0.04)	≃7.5[f] (+0.12)	≃7.5[f] (–0.03)	–	≃42	≃38
	-I	9.19[a] (+0.40)	8.80[c] (+0.24)	8.38[b] (+0.25)	7.37[c] (–0.13)	–	39.5	37.5
	-Br	9.08[e] (+0.29)	8.82[d] (+0.05)	8.24[b] (+0.06)	7.52[c] (–0.20)	–	40.0	37.8
	-Cl	8.95[a] (+0.16)	8.78[d] (+0.10)	8.10[b] (+0.11)	7.57[c] (0.00)	–	41.0	38.7
pyrimidine		9.57 (+0.45)	9.17 (+0.36)	8.92 (+0.11)	7.74 (+0.15)		24.3	39.2
4-methylpyrimidine		9.34 (+0.42)	8.88 (+0.29)	–	7.58 (+0.15)	2.59 (+0.08)	24.1	37.6
5-methylpyrimidine		9.34 (+0.44)	9.01 (+0.40)	8.76 (+0.15)	–	2.34 (+0.03)	22.0	36.9

Parentheses denote complexation shift, (+) deshielded, (–) shielded; free pyridine data (solvent DMSO) from ref. [33]. [a]Doublet, resolved $J_{H_2H_4} \simeq 1.2$–1.7 (Hz). [b]Poorly resolved doublet $J_{H_4H_5} \simeq 7.0$–8.5 (Hz). [c]Doublet of doublets $J_{H_5H_6} \simeq 4.8$–6.3 (Hz), $J_{H_2H_5}$ not resolved. [d]Doublet $J_{H_2H_6}$ not resolved. [e]Singlet. [f]Multiplet, H_4H_5 resonances superimposed. [g]Obscured by ^{2}HOH resonance.

TABLE VII. ^{13}C Nmr Data for Some *cis*-$[Pt(NH_3)_2(X)_2](ClO_4)_2$ in DMSO-d_6 Containing $Cr(acac)_3$ (≃ 0.01 *M*).

Compound		Chemical Shift, ppm from TMS[a]							$^{n}\lvert J_{^{195}Pt-^{13}C}\rvert$ Coupling Constants/(Hz)		
X	Y	C2	C4	C5	C6	Other			^{2}J	^{3}J	Other
pyrimidine	ClO_4^-	160.7[b]	160.7[b]	125.2	161.5[b]	–			[c]	33.0(C5)	[c]
4-methylpyrimidine	ClO_4^-	159.4[b]	171.7	123.8	161.6[b]	24.8(CH_3)			[c]	≃23[d](C5)	[c]
5-methylpyrimidine	ClO_4^-	159.0[b]	160.8[b]	134.6	160.8[b]	16.1(CH_3)			[c]	32.0(C5)	[c]
		C2	C9	C8	C4	C5[b]	C6[b]	C7			
benzimidazole[e]	ClO_4^-	145.3	139.9	132.2	117.7	124.4	125.3	114.0	[c]	[c]	[c]

[a]Relative to DMSO at 40.4 ppm from TMS [34]. [b]Resonance broad, assignment not unambiguous. [c]No coupling resolved/observed. [d]Poorly resolved. [e]Assignment by analogy with spectrum in water, all lines much broader in DMSO (see text), traces of unbound benzimidazole appear.

of known Swain–Lupton [36] and Taft [37] substituent constants, no clear correlation was obtained. The only correlation between substituent effects and coupling constants we obtained was qualitative. These substituents that withdraw π-electrons by an inductive effect ($\sigma_I > 0$) [38], but are capable of resonance interaction which is electron releasing to the aromatic ring ($R^n < 0$), show largest increase in $^3J_{Pt-C3}$. For substituents -Cl, -Br, -I, -OH, the $^3J_{Pt-C3}$ value is between 52.5 and 58.0 Hz while for -CN, $-COCH_3$ and $-COOCH_3$ an intermediate value is obtained (44.0–45.0 Hz). The latter substituents are all inductively electron withdrawing ($\sigma_I > 0$) while having a positive resonance parameter ($R^n > 0$) *i.e.* tend to withdraw π-electron density from the aromatic ring. Finally, where the substituent is $-CH_3$ or $-CH_2OH$, $^3J_{Pt-C3}$ is 41.9 Hz and 41.5 Hz respectively, while that of the unsubstituted pyridine is 42.5 Hz. The methyl group has $\sigma_I > 0$ (inductively electron supplying) and is thought to release electrons through resonance interactions ($R^n < 0$).

Turning to the pyrimidine complexes, one observes that $^3J_{Pt-C5}$ decreases in magnitude relative to the corresponding pyridine coupling constant, while additionally, $^2J_{Pt-C6}$ becomes observable. For the 4-methyl-pyrimidine case one also observes $^4J_{(Pt-C4)}$ of 9.5 Hz. No coupling to C2, between the two nitrogen atoms is observed (Fig. 2). In DMSO, one only observes $^3J_{Pt-C5}$ type coupling as is evident from Table VII. These couplings are also somewhat smaller than the corresponding data obtained in water as solvent. In general the ^{13}C spectra in DMSO show broader lines, for example in water the *cis*-$[Pt(NH_3)_2$-(4-methylpyrimidine)$_2](ClO_4)_2$ complex shows line widths from 4–7 Hz, while the corresponding line widths in DMSO are 8–16 Hz.

In general we were unable to obtain satisfactory ^{13}C spectra using DMSO as solvent. Coupling of the order of 20 Hz would be lost in the base of the main resonance. In the ^{13}C spectrum of *cis*-$[Pt(NH_3)_2$-(benzimidazole)$_2](ClO_4)_2$ in H_2O extensive coupling was observed, Table II, including a ^2J of 50 Hz. The corresponding spectrum in DMSO, Table VII, showed no resolved coupling to Pt. Either the coupling constants are much reduced in DMSO and thus lost in the broad central resonance or exchange with DMSO removes the coupling. Resonances due presumably to solvolysis products were observed in the spectrum after several hours accumulation. Similar solvolysis reaction particularly with chloro complexes have been observed [39].

Discussion

It is evident that a great deal of information about the nature of platinum binding to nitrogen heterocycles can be obtained from their respective ^{13}C nmr spectra. Previous studies on pyridine and bipyridyl platinum complexes [18] concluded that the lack of easy discrimination among two and three bond platinum to carbon spin–spin coupling constants may lessen their potential diagnostic value. Others have attempted to use ^{13}C chemical shifts induced on complexation as compared to protonation shifts [16, 17] to examine the nature of platinum binding to nucleosides in particular, but did not report coupling constant data. The use of DMSO as solvent has been widespread [11, 15, 16, 40] in the study of platinum and palladium interactions with nucleosides. Despite its generally excellent solvent properties, DMSO unfortunately co-ordinates readily to Pt(II) and Pd(II) either via oxygen or sulphur [41, 42]. Furthermore as has recently been conclusively shown, extensive solvolysis of *cis*-$[Pt(NH_3)_2Cl_2]$ occurs [39]. The existance of *cis/trans* isomerisation processes has been recognised for some time with the appearance of some detailed studies [15, 43–45]. This suggests that in some cases conditions of fast chemical exchange may be satisfied with regard to bound/unbound DMSO. Such exchange processes lead to the loss of coupling constant data. Such considerations may account for our failure to obtain useful ^{13}C nmr results with complexes of nucleosides such as *cis*-$[Pt(nucleoside)_2Cl_2]$ dissolved in DMSO. Indeed even using the system suggested by Kong [15, 43] in which *cis*-$[Pt(DMSO)_2Cl_2]$ and an aromatic amine are thought to equilibrate to mixtures of *cis* and *trans* $[Pt(DMSO)(amine)Cl_2]$ type complexes proved intractable with regard to ^{13}C nmr whenever DMSO as solvent was used.

The use of water as solvent proved preferable in many respects as is evident from results given above. Water binds to platinum only weakly and thus *cis*-$[Pt(NH_3)_2X_2]Y_2$ type complexes are readily obtainable, being stable in solution for at least 24 hours.

5-Membered Heterocycles

Chemical shifts

In interpreting the ^1H and ^{13}C chemical shifts of the various imidazole analogues, indeed all above complexes of the general configuration *cis*-$[Pt(NH_3)_2$-$X_2]Y_2$ consideration must be given to the fact that the nitrogen heterocycles are apparently not free to rotate about the Pt–N bond. Drieding models indicate at least, that such rotations are expected to have a high energy barrier for free rotation. Furthermore, from the simplicity of ^1H and ^{13}C nmr spectra it is apparent that the complexes have an effective two fold (C_{2v}) symmetry axis bisecting the N Pt N bond. X-ray crystallographic data [46, 47] for the cations *cis*-$[Pt(NH_3)_2(guanosine)_2]^{2+}$ and *cis*-$[Pt(NH_3)_2$-$(IMP)_2]^{2-}$ have confirmed this. It is also evident from such crystal structures that the dihedral angle between the two purine planes is *ca.* 70° for the

guanosine complex. In the absence of lattice constraints as exist in the solid state it may be reasonably expected that the N Pt N angle is close to 90° while the planes through the imidazolyl moieties are approximately perpendicular to the square plane.

Although a number of theoretical studies concerning the nature of the electronic structure of aromatic heterocycles have been undertaken [48, 49, 52, 53], these have been limited mainly to comparative studies of perturbations induced by ligand protonation in the case of nitrogen heterocycles.

Consideration of Tables I and II shows that with very few exceptions all ^{1}H and ^{13}C resonances experience a downfield shift. In contrast, protonation of neutral imidazole results in an upfield shift of C2 and C4, 5 while proton chemical shifts move downfield relative to the non-protonated species [48]. Similar trends have been observed for benzimidazole [49]. On co-ordination to platinum the tautomeric proton exchange for imidazole is no longer possible and C4 and C5 resonate at 128.3 and 119.1 ppm respectively (Table II).

The asssignment is based on that of 1-methylimidazole (1-MeIMD) and its corresponding *cis*-$[Pt(NH_3)_2(1\text{-MeIMD})_2]Cl_2$ complex. Roberts *et al.* [50] have assigned the ^{13}C spectrum of 1-methylimidazole with the aid of $Eu(fod)_3$ and $Pr(fod)_3$ shift reagents. Comparison of the bound and unbound shifts of 1-methylimidazole with similar data for imidazole, 2-methylimidazole and benzimidazole lead to the assignment as in Table II. In addition we used 5-(2-hydroxyethyl)-4-methylthiazole as a further model for the assignments in which case C4 and C5 are nonequivalent, the ^{13}C spectrum for thiazole having been previously assigned [34]. Additionally the proton undecoupled ^{13}C spectrum of 1-methylimidazole supports the above assignment. We observe $^{3}J_{C5-H2} < 4$ Hz, $^{2}J_{C5-H4} = 15.8$ Hz and for C4 the couplings are $^{3}J_{C4-H2} = 10.1$ Hz, $^{2}J_{C5-H5} \simeq 10$ Hz, in good agreement with a recent report [51].

$^{195}Pt-^{13}C$ coupling constants

As shown Pt–C coupling constants in which an imidazolyl moiety is involved in co-ordination the observed trend in the coupling constants is $^{2}J_{Pt-C2} > {}^{3}J_{Pt-C5} > {}^{2}J_{Pt-C4} \simeq {}^{3}J_{Pt-C(CH_3)}$. This pattern is also observed for benzimidazole as well as for inosine and guanosine (Table IV). In fact, the coupling constants observed for inosine and guanosine complexes served to confirm our assignment of the ^{13}C nmr parameters for the imidazole compounds. Such similarity between imidazoles, benzimidazoles and purine analogues is not unexpected in view of the similarity in π-electron density as calculated by Mahanti [53] using the Hückel molecular orbital method. It was concluded in the latter study that fusing an imidazole ring to a pyrimidine system did not introduce any major perturbations to either ring system.

A study of the protonation effects on the electronic structure of imidazole, benzimidazole and purine systems [48, 49] may serve as a basis for understanding the qualitative trends in $^{n}J_{Pt-C}$ constants. On protonation of imidazole the σ-charge densities and Mulliken overlap populations do not change dramatically but there is a significant change in the corresponding π-electron parameters [48].

Protonation at the 'pyridine' nitrogen, N3, increases the π-electron density at that site considerably at the expense of the π-bond order between C2–N3 as well as the π-density C2. The π-bond overlap population between N3–C4 also decreases markedly while the π-bond order between C4–C5 increases. Similar effects may be reasonably anticipated for platinum co-ordination in the absence of extensive $\sigma-\pi$ conjugation and π metal-ligand interaction. The insignificance of such $\sigma-\pi$ conjugation effects has been suggested from a study of *trans*-phenylplatinum-(II) derivatives [54].

The above comparison suggests a significant $^{n}J_{Pt-C}$ coupling constant dependence on the π-bond orders; however, due to the delocalization of the π electrons it is difficult to separate contributions into J^{σ} and J^{π} terms. According to present theory, coupling between various elements particularly between heavy metals and ^{13}C, ^{1}H is considered to be dominated by the Fermi contact term. For direct metal carbon coupling constants $^{1}J_{M-C}$ is a function of the S-electron densities at the respective nuclei, as well as the fractional S character of the metal orbital forming the carbon metal bond [34, 55, 56].

6-Membered Heterocycles

Chemical shifts

Similar considerations as advanced above for 5-membered aromatic heterocycles must be applied to the understanding of the chemical shifts of the pyridine and pyrimidine platinum complexes. Vrieze [21] has given a detailed study of the bonding properties of *trans*-$[PtCl_2XY]$ type compounds in which Y = 4R-pyridines, X = CO, C_2H_2. It was concluded that the major contribution to the chemical shifts of the pyridine carbon atoms are σ_P, the paramagnetic shielding constant, and σ_d, the diamagnetic contribution due to the platinum atom. In our case, however, the ring currents of pyridine undoubtedly contribute to the observed shifts. Secondly, it appears from Vrieze's study that σ_P depends on low lying charge transfer transitions from $Pt(5d_{xy})$ to pyridine π^* orbitals which are rotationally allowed. In complexes such as *cis*-$[Pt(NH_3)_2(pyridine)_2](ClO_4)_2$ the two rings are most probably at right angles to the square plane and thus charge transfer transitions are rotationally forbidden leading to smaller downfield shifts of the pyridine carbons on complexation than would otherwise be the case.

Since pyridine and pyrimidine have similar chemi-

cal and electronic properties [53] it is not surprising that no important difference between complexes of these two ligands are found with regard to chemical shifts.

Coupling constants

As already seen only $^3J_{Pt-C}$ and $^4J_{Pt-C}$ coupling constants are seen for pyridine. An attempt to perturb the electronic structure by introducing substituents at position 3 in pyridine in order to possibly observe two bond coupling constants especially at C2 failed. We could not observe any $^2J_{Pt-C}$ couplings. This contrasts with the results of Vrieze [21] who obtained the order $^3J_{Pt-C3} > {}^2J_{Pt-C2,6} > {}^4J_{Pt-C4}$ using 4-substituted pyridines in *trans*-[$Pt(Cl_2)$-(4Rpyr)CO]. Other workers have observed a similar general trend, that heavy metal-carbon coupling constants vary in the order $^1J > {}^3J > {}^2J > {}^4J$ as for example in phenylplatinum(II) derivatives [54], phenylmercury(II) [57] and phenylthallium(III) compounds [58].

Our results show that there is only a qualitative correlation between the nature of the substituent and the $^3J_{Pt-C}$ coupling constant at the substituted carbon as already mentioned above. The lack of a suitable theoretical basis as to the nature of long range metal-carbon coupling constants partly transmitted through π-electrons precludes a detailed understanding of the factors determining our coupling constants. The complexity of metal–pyridine bonding becomes evident from extended Hückel MO calculations carried out for *trans*-dichlorodiamminoplatinum(II) and dichloromercury(II) complexes [59].

It has been noticed that for pyridine C3, C5 carry the highest π-electron density while for pyrimidine, C5 has the highest π-electron density [53]. However, as seen for the imidazoles above the π-density alone does not account for the magnitudes of the coupling constants, since the intervening bonding orbital populations undoubtedly play a significant part.

Finally, it may be seen that for the pyrimidines a $^2J_{Pt-C}$ coupling constant becomes visible. In this case the order $^3J > {}^2J > {}^4J$ seems to hold true, however our assignment of C2 and C6 is not unambiguous in these compounds.

Unfortunately we could not obtain any coupling constant data for *cis*-[$Pt(NH_3)_2$(cytidine)$_2$]$(ClO_4)_2$. On dissolving the complex in water and addition of a drop of dioxane an intense purple colour developed and the subsequent ^{13}C spectrum was complicated (Table IV). It is apparent that a number of different species exist in solution, with fast exchange processes probably leading to the loss of coupling data. The ^1H nmr spectrum shows only very broad resonances. The exact nature of the species is being further investigated as this example is undoubtedly a variation of the "platinum blues" whose structure has eluded workers up till now [24].

Conclusions

Valuable information may be obtained from the ^{13}C nmr parameters of platinum(II) complexes with 5- and 6-membered aromatic heterocycles.

(*a*) For the imidazole heterocycles the relative order of the platinum to carbon coupling constants follows the trend $^2J_{Pt-C2} > {}^3J_{Pt-C4} > {}^2J_{Pt-C5}$.

(*b*) Pyrimidine moieties show similar trends of $^nJ_{Pt-C}$ coupling constants as do the corresponding pyridine platinum complexes.

(*c*) The nature of the substituent in the 3-substituted pyridine platinum complexes has a significant effect on the $^3J_{Pt-C}$ constant at the substituted carbon. Qualitatively, the highly electron withdrawing groups tend to increase the magnitude of $^3J_{Pt-C}$.

(*d*) The use of DMSO as a solvent for such studies should be avoided, as solvolysis/exchange effects reduce the ^{13}C nmr resolution.

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References

1 B. Rosenberg, L. Van Camp and T. Krigas, *Nature, 205,* 698 (1965).
2 B. Rosenberg, L. Van Camp, J. R. Trosko and V. H. Mansour, *Nature, 222,* 385 (1969).
3 B. Rosenberg, *Cancer Chemotherapy Reports part 1, 59 (3),* 589 (1975).
4 B. Rosenberg and H. C. Harder, *Int. J. Cancer, 6,* 207 (1970).
5 J. Drobnik and P. Horacek, *Biochim. Biophys. Acta, 254,* 341 (1971).
6 J. J. Roberts and J. M. Pascoe, *Nature, 235,* 282 (1972).
7 P. J. Stone, A. D. Kelman and F. M. Sinex, *Nature, 251,* 736 (1974).
8 J. P. Macquet and T. Theophanides, *Inorg. Chim. Acta, 18,* 189 (1976).
9 L. G. Marzilli, *Prog. Inorg. Chem., 23,* 255 (1977).
10 S. Mansy, B. Rosenberg and A. J. Thomson, *J. Am. Chem. Soc., 95,* 1633 (1973).
11 N. Hadjiliadis, P. Kourounakis and T. Theophanides, *Inorg. Chim. Acta, 7,* 226 (1973).
12 Pi-Chang Kong and T. Theophanides, *Inorg. Chem., 13,* 1981 (1974).
13 Pi-Chang Kong and T. Theophanides, *Inorg. Chem., 13,* 1167 (1974).
14 Pi-Chang Kong and T. Theophanides, *Bioinorg. Chem., 5,* 51 (1975).
15 Pi-Chang Kong, D. Iyanuremye and F. D. Rochon, *Bioinorg. Chem., 6,* 83 (1976).
16 F. Coletta, R. Ettorre and A. Gambaro, *J. Mag. Res., 22,* 453 (1976).
17 D. J. Nelson, P. L. Yeagle, T. L. Miller and R. B. Martin, *Bioinorg. Chem., 5,* 353 (1976).
18 S. T. Chow and R. B. Martin, *Inorg. Nucl. Chem. Letters, 10,* 1131 (1974).

19 H. C. Clark and J. E. H. Ward, *Can. J. Chem., 52,* 570 (1974).
20 D. G. Cooper and J. Powell, *Inorg. Chem., 16,* 142 (1977).
21 M. A. M. Meester, D. J. Stufkens and K. Vrieze, *Inorg. Chim. Acta, 15,* 137 (1975).
22 G. Y. H. Chu and R. S. Tobias, *J. Am. Chem. Soc., 98,* 2641 (1976).
23 G. Y. H. Chu and R. S. Tobias, *ibid., 98,* 2641 (1976).
24 G. Y. H. Chu, R. E. Duncan and R. S. Tobias, *Inorg. Chem., 16,* 2625 (1977).
25 G. Y. H. Chu, S. Mansy, R. E. Duncan and R. S. Tobias, *J. Am. Chem. Soc., 100,* 593 (1978).
26 S. Mansy, G. Y. H. Chu, R. E. Duncan and R. S. Tobias, *ibid., 100,* 607 (1978).
27 J. Lettvin and A. D. Sherry, *J. Mag. Res., 28,* 459 (1977).
28 L. E. Erickson, J. E. Sarneski and C. N. Reilley, *Inorg. Chem., 14,* 3007 (1975).
29 'Inorganic Syntheses', *7,* 239, McGraw–Hill, New York (1963).
30 I. E. Balaban and F. L. Pyman, *J. Chem. Soc., CXXI(1),* 947 (1922).
31 K. W. Lee and D. S. Martin, Jr., *Inorg. Chim. Acta, 17,* 105 (1976).
32 C. G. van Kralingen and J. Reedijk, *Inorg. Chim. Acta, 30,* 171 (1978).
33 R. F. M. White and H. Williams in 'Physical Methods in Heterocyclic Chemistry', Academic Press (1971) IV(4), 207 (and references therein).
34 J. B. Stothers, 'Carbon-B NMR Spectroscopy' Academic Press, New York (1972).
35 H. L. Retcotoky and R. A. Friedel, *J. Phys. Chem., 72,* 290 (1968).
36 L. G. Swain and E. C. Lupton, *J. Am. Chem. Soc., 90,* 4328 (1968).
37 R. W. Taft, *J. Phys. Chem., 64,* 1805 (1960).
38 D. R. Coulson, *J. Am. Chem. Soc., 98,* 3111 (1976).
39 S. J. S. Kerrison and P. J. Sadler, *Chem. Comm., 861* (1977).
40 R. Ettorre, *Inorg. Chim. Acta, 25,* L9 (1977).
41 J. H. Price, A. N. Williamson, R. F. Schramm and B. B. Wayland, *Inorg. Chem., 11,* 1280 (1972).
42 W. Kitching, C. J. Moore and D. Doddrell, *Inorg. Chem., 9,* 541 (1970).
43 Pi-Chang Kong, D. Iyamuremye and F. D. Rochon, *Can. J. Chem., 54,* 3224 (1976).
44 J. H. Price, J. P. Birk and B. B. Wayland, *Inorg. Chem., 17,* 2245 (1978).
45 R. Romeo and M. L. Tobe, *Inorg. Chem., 13,* 1991 (1974).
46 C. C. Chiang, T. Sorrell, T. J. Kistenmacher and L. G. Marzilli, *J. Am. Chem. Soc., 100,* 5102 (1978).
47 R. W. Gellert and R. Bau, *J. Am. Chem. Soc., 97,* 7379 (1975).
48 R. J. Pugmire and D. M. Grant, *J. Am. Chem. Soc., 90,* 4232 (1968).
49 R. J. Pugmire and D. M. Grant, *J. Am. Chem. Soc., 93,* 1880 (1971).
50 J. Elguero, C. Marzin and J. D. Roberts, *J. Org. Chem., 39,* 357 (1974).
51 W. F. Reynolds and C. W. Tzeng, *Can. J. Biochem., 55,* 576 (1977).
52 W. Adams, A. Grimison and G. Rodriquez, *Tetrahedron,* 23, 2513 (1967).
53 M. K. Mahanti, *Ind. J. Chem., 15B,* 168 (1977).
54 H. C. Clark and J. E. H. Ward, *J. Am. Chem. Soc., 96,* 1741 (1974).
55 B. E. Mann, *Adv. Organomet. Chem., 12,* 135 (1974).
56 R. M. Lynden-Ball and R. K. Harris, 'Nuclear Magnetic Resonance Spectroscopy', Studies in Modern Chemistry Series, Nelson (1969).
57 N. K. Wilson and R. D. Zehr, *J. Mag. Res., 21,* 437 (1976).
58 L. Ernst, *J. Organometal Chem., 82,* 319 (1974).
59 T. Ibusuki and Y. Saito, *Inorg. Chim. Acta, 19,* 87 (1976).
60 M. C. Thorpe and W. C. Coburn, *J. Mag. Res., 12,* 225 (1973).