Inorganica Chimica Acta, 32 (1979) 127–138

Amino Acid Complexes of Platinum(IV). II. Trimethylplatinum(IV) Complexes of α-Substituted Amino Acids – Alanine, Valine, Phenylalanine, and α-Aminoisobutyric Acid

T. G. APPLETON, J. R. HALL, and T. G. JONES

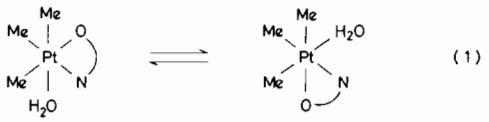
Department of Chemistry, University of Queensland, Brisbane, Australia 4067

Received June 2, 1978

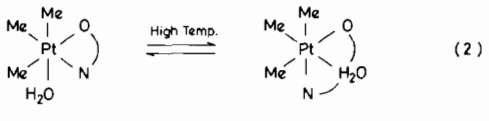
Since there is an asymmetric centre at platinum in complexes $PtMe_3(AA)L$ (H(AA) = amino acid; L = MeOH, 3,5-lutidine) and $PtMe_3(AA)_2$, mixtures of diastereoisomers are formed when the amino acid also contains an asymmetric C-atom. Rapid interconversion of isomers has been studied by variable-temperature NMR. The effects of various substituents on the amino acid on the relative proportions of isomers, and on the chemical behaviour of the compounds have been examined. In lutidine complexes marked upfield shifts are observed for a substituent on the amino acid which is near the aromatic ring.

Introduction

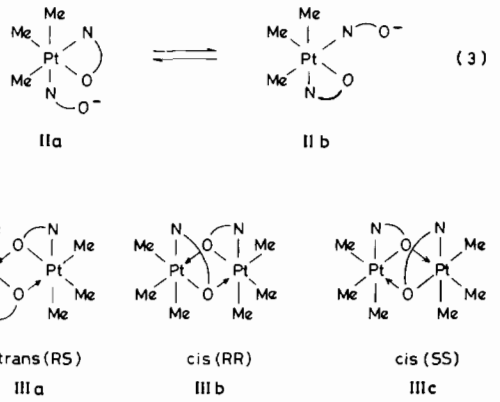
Trimethylplatinum(IV) glycinate complexes have been discussed in a recent paper [1]. Mixture of $PtMe_3(H_2O)_3^+$ with sodium glycinate in water gave $PtMe_3(gly)(H_2O)$ (I), $Na[PtMe_3(gly)_2]$ (II), and $Na_2[PtMe_3(gly)_3]$, while concentration of aqueous solutions of (1) gave the dimer $[PtMe_3(gly)]_2$ (III)*. Variable-temperature NMR was used to study the intermolecular exchange reactions (1)–(3).



(1)



(2)



When the coordinated amino acid is symmetric, as for glycine, (Ia) and Ib) are enantiomers, indistinguishable by NMR. Similarly for (IIa) and (IIb). Of the three possible isomers of $[PtMe_3(gly)]_2$, the *trans* isomer (IIIa) corresponds to a *meso* isomer, with no overall optical activity, while the *cis*-isomers (IIIb) and (IIIc) are enantiomers. When the amino acid contains an asymmetric C-atom, the isomers analogous to (Ia) and (Ib) are diastereoisomers, which should be distinguishable by NMR. Similar statements apply to (IIa) and (IIb), and to (IIIb) and (IIIc). Because of the coordination lability induced by the high trans effect of the methyl ligands, the different isomers should be in equilibrium, and their relative proportions should reflect predominantly the magnitudes of intramolecular steric interactions.

In this paper the behaviour of complexes of the optically active α-amino acids – L-alanine, L-valine, and L-phenylalanine, as well as symmetric α-aminoisobutyric acid, are studied. The kinetics of the exchange reactions will be examined quantitatively in a future publication.

Results and Discussion

Analytical data for compounds isolated are presented in Table I and spectroscopic data in Table II.

*Abbreviations: H(AA) amino acid: Hgly glycine, $NH_2CH_2CO_2H$; Hala α-alanine, $NH_2CHMeCO_2H$; Hval valine, $NH_2CH(CHMe_2)CO_2H$; Hphe Phenylalanine, $NH_2CH(CH_2Ph)CO_2H$; Haba α-aminoisobutyric acid, $NH_2CMe_2CO_2H$; lut 3,5-lutidine, $NC_5H_3Me_2$.

TABLE I. Analytical Data[a].

Compound	C	H	N	Pt	Mol. Wt.[b]
$[PtMe_3(L\text{-}ala)]_2$	22.2 (22.0)	4.6 (4.6)	4.2 (4.3)	59.4 (59.5)	(A) 669 (656) (M) 353
$PtMe_3(L\text{-}ala)(lut)$	35.8 (35.9)	5.6 (5.6)	6.3 (6.4)	44.0 (44.8)	
$Na[PtMe_3(L\text{-}ala)_2]$[c]	24.0 (24.6)	5.4 (4.8)	6.5 (6.4)		
$[PtMe_3(L\text{-}val)]_2$	27.0 (27.0)	5.4 (5.4)	4.0 (3.9)	54.6 (54.8)	(A) 726 (712) (M) 282
$PtMe_3(L\text{-}val)(lut)$	38.8 (38.9)	6.2 (6.1)	6.2 (6.1)	41.5 (42.1)	
$Na[PtMe_3(L\text{-}val)_2]$	31.5 (31.5)	6.0 (5.9)	5.7 (5.7)		
$[PtMe_3(L\text{-}phe)]_2$	35.6 (35.7)	4.8 (4.7)	3.6 (3.5)	48.2 (48.3)	
$PtMe_3(L\text{-}phe)(lut)$[d]	45.1 (44.6)	5.9 (5.5)	5.1 (5.5)	37.1 (38.1)	
$[PtMe_3(aba)]_2$	24.5 (24.6)	5.0 (5.0)	4.2 (4.1)	56.7 (57.0)	
$PtMe_3(aba)(lut)$	37.4 (37.4)	5.9 (5.8)	6.2 (6.2)	43.0 (43.4)	
$Na[PtMe_3(aba)_2]$[c]	28.6 (28.3)	5.7 (5.4)	5.9 (6.0)		

[a]Calc. figures (%) in parentheses. [b]Solvents: A acetone, M methanol. [c]Extremely hygroscopic. [d]Sample retains trace of solvated hexane despite prolonged pumping.

Dimers, $[PtMe_3(AA)]_2$

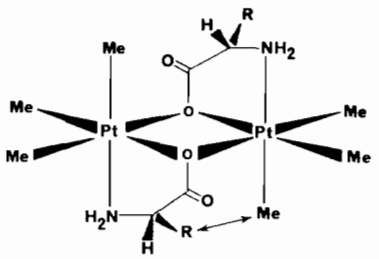
In the glycinate system, $[PtMe_3(gly)]_2$ (III) is never obtained from reaction between $PtMe_3(H_2O)_3^+$ and glycine in the absence of added base [1]. However, for the α-substituted amino acids discussed here, $[PtMe_3(AA)]_2$ does precipitate when concentrated aqueous solutions of $PtMe_3(H_2O)_3^+$ and H(AA) are heated, or allowed to stand. For phenylalanine and α-aminoisobutyric acid, the pure dimer may be obtained in good yield in this way, but for alanine, results are better if base is added (see Experimental).

Like $[PtMe_3(gly)]_2$, $[PtMe_3(aba)]_2$ and $[PtMe_3(L\text{-}phe)]_2$ are essentially insoluble in all common solvents, but $[PtMe_3(L\text{-}ala)]_2$ and $[PtMe_3(L\text{-}val)]_2$ are sufficiently soluble in methanol and acetone for solution measurements to be made. The valine complex is also quite soluble in chloroform, benzene, and hexane.

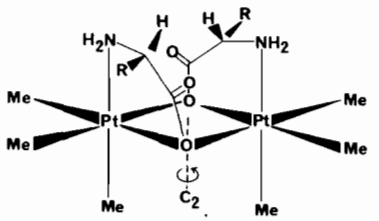
Molecular weight measurements (Table I) indicate that dimers $[PtMe_3(AA)]_2$ are present in acetone, and monomers $PtMe_3(AA)(MeOH)$ in methanol. $[PtMe_3(L\text{-}ala)]_2$ is also very sparingly soluble in water. The poor-quality NMR spectrum obtained in D_2O is qualitatively similar to that in CD_3OD, indicating that monomeric $[PtMe_3(L\text{-}ala)(D_2O)]$ is present.

There are three possible isomers of $[PtMe_3(L\text{-}ala)]_2$ (IVa-c) (R = Me). In the *trans*-isomer (IVa), all six Pt-Me groups are non-equivalent, and the two C-Me groups are also non-equivalent. In each of the *cis* isomers, a C_2 axis may be drawn through the molecule perpendicular to the PtO_2Pt plane, so that there are three distinguishable pairs of Pt-Me groups, and the two C-Me groups are equivalent.

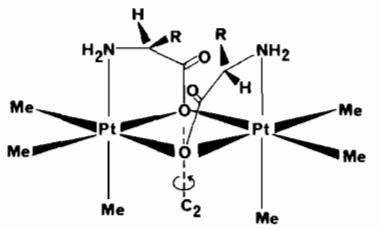
If equal quantities of all three isomers were present, a total of 12 Pt-Me peaks (each with



IVa trans



IVb cis



IVc cis

"satellites" from coupling with ^{195}Pt) and four C-Me doublets (from J_{HCCH_3}) would be expected in the ^1H NMR spectrum. The spectrum in $(CD_3)_2CO$ in fact shows 6 Pt-Me peaks of equal intensity and two C-Me doublets (Table II), so that all of the possible isomers are not present. The spectrum is consistent with the presence of either the *trans* isomer (IVa) alone, or a

TABLE II. Spectroscopic Data.

Compound	PMR Spectra[a]										IR Spectra	
	Solvent	Temp. °C	Pt–CH_3				C–CH_3		N–CH δ	Other Resonances	ν(C=O) cm^{-1}	δ(NH_2) cm^{-1}
			Trans Group[b]	Relative Intensity	δ	$^2J_{Pt-CH_3}$	δ	$^3J_{HCCH_3}$				
$[PtMe_3(L\text{-ala})]_2$	$(CD_3)_2CO$	28	O(bridge)	1	0.90	79.8	1.44	7.5	~4.0		1600	1570
			O(bridge)	1	0.84	79.4	1.48	7.1				
			N	1	0.83	65.9						
			O(chelate)	1	0.79	77.8						
			N	1	0.77	65.5						
			O(chelate)	1	0.76	77.9						
$PtMe_3(L\text{-ala})(CD_3OD)$	CD_3OD	−45	CD_3OD(A)	1	0.96	82.4	1.38	7.5	~3.6			
			CD_3OD(B)	1	0.89	81.9	1.40	7.2				
			O(ala)(C)	2	0.75	76.6						
			N(D)	2	0.70	66.4						
		63					1.44	7.4				
$PtMe_3(L\text{-ala})$(lut)	CD_3OD	28	N(lut)	1	0.90	71.2	1.34	7.3	~2.85	*lut*: δCH_3 2.37	1618	1586
			O	1	0.89	76.8	0.99	7.5	~3.60	δ_{H_α} 8.47		
			O	1	0.88	76.8				J_{Pt-H_α} 12		
			N(lut)	1	0.85	71.0				δ_{H_γ} 7.38		
			N(ala)	1	0.72	69.3						
			N(ala)	1	0.72	69.1						
$Na[PtMe_3(L\text{-ala})_2]$	D_2O	2	O(A+B)	2	0.67	79.4	1.33	7.3	~3.53		1600[d]	
			N(chel)(C)	1	0.67	69.5	1.33	7.3				
			N(unidentate) (D)	1	0.63	70.7	1.42	7.5				
			N(unidentate) (E)	1	0.61	72.1	1.43	7.5				
			N(chel) (F)	1	0.59	68.8						
		57	O	1	0.68	77.8	1.35	7.2	~3.5			
			N	1	0.63	69.5	1.37	7.5				
			N	1	0.62	69.2						

TABLE II. *(Continued)*

Compound	PMR Spectra[a]										IR Spectra	
	Solvent	Temp. °C	Pt–CH_3				C–CH_3		N–CH δ	Other Resonances	ν(C=O) cm^{-1}	δ(NH_2) cm^{-1}
			Trans Group[b]	Relative Intensity	δ	$^2J_{Pt-CH_3}$	δ	$^3J_{HCCH_3}$				
Na[$PtMe_3$(D-ala)(L-ala)][e]	D_2O	2	O	2	0.68	78.6	f	f	f			
			N(unidentate)	1	0.68	71.7						
			N(unidentate)	1	0.65	~73.5						
			N(chel)	1	0.61	~70.5						
			N(chel)	1	0.53	70.5						
		58	O	1	0.68	78.5						
			O	1	0.66	78.2						
			N	2	0.64	70.8						
			N	2	0.59	70.5						
[$PtMe_3$(L-val)]$_2$	$CDCl_3$	28	N	1	0.92	66.9	1.07	6.5	~4.0	C–H_βδ 2.94, 255	1590	1565
			O	1	0.92	79.1	1.12	6.8		NH_2δ ~ 2.2		
			N	1	0.87	67.5	1.05	6.8				
			O	1	0.87	78.7	0.88	~7				
			O	1	0.83	77.7						
			O	1	0.76	79.1						
	$(CD_3)_2CO$	28	O	1	0.87	80.0	0.92	7.2	~3.38	C–H_βδ ~ 2.48		
			O	1	0.86	79.6	1.16	7.0				
			N	1	0.79	67.8						
$PtMe_3$(L-val)(CD_3OD)	CD_3OD	−39	CD_3OD	1	0.93	82.5	0.84	7.0	~3.39	C–H_βδ ~ 2.45		
			CD_3OD	2	0.88	82.9	0.89	7.0				
			O(val)	3	0.79	76.5	~1.05	7.0				
			N	3	0.72	67.7	~1.05	7.0				
		59					0.93	7.1	~3.38	C–H_βδ ~ 2.48		
										$^3J_{H_\alpha CCH_\beta}$ 3.6		
							1.06	7.2		$^3J_{H_\beta CCH_3}$ 7.5		
$PtMe_3$(L-val)(lut)	CD_3OD	28	O	1	0.91	75.7	0.97	7.0	f	*lut*: δ_{CH_3} 2.36	1592[d]	
			O	1	0.89	76.2	0.93	7.0		δ_{H_α} 8.30		
			N(lut)	1	0.85	70.5	0.88	7.0		J_{PtNCH_α} obscured		
			N(lut)	1	0.84	71.1	0.31	7.0		δ_{H_γ} 7.61		
			N(val)	1	0.74	68.5						
			N(val)	1	0.73	68.4						

$Na[PtMe_3(L\text{-val})_2]$	D_2O	2	O	2	0.67	78.0	[f]	[f]	3.25	C–$H_\beta\delta$ 1.97, 2.37	1600	1560
			N(unidentate)	2	0.60	71.7			3.53			
			N(chelate)	2	0.56	68.9						
			O	1	0.69	78.9						
			N(chelate)	1	0.64	69.3						
			N(unidentate)	1	0.58	71.7						
		59	O	1	0.68	79.0	0.87	7.2	[g]			
			N	1	0.62	71.1	0.94	7.2				
			N	1	0.58	69.9	0.97	7.2				
							1.02	7.2				
$PtMe_3(L\text{-phe})(lut)$	$CDCl_3$	28	N(phe)	2	0.88	71.9			[f]	Major isomer:	1605	1575
			N(lut)	2	0.78	69.8				*lut* δ_{CH_3} 2.29	1550	
			O	3	0.75	76.1				δ_{H_α} 8.02 J_{Pt-H_α} 11.4		
			N(lut)	1	0.83	69.9				δ_{H_γ} 7.37		
			N(phe)	1	0.68	70.5				C_6H_5 7.03		
										Minor isomer:		
										lut δ_{CH_3} 2.32		
										δ_{H_α} 8.23, J_{Pt-H_α} 10.5		
										δ_{H_γ} 7.44		
										C_6H_5 7.26		
$PtMe_3(aba)(lut)$	$CDCl_3$	28	N	1	0.90	70.1	1.51			*lut* δ_{CH_3} 2.37	1612	1560
			N	1	0.85	69.8	0.87			δ_{H_α} 8.33 J_{PtH_α} 12		
			O	1	0.78	74.2				δ_{H_γ} 7.48		
										NH_2: AB pattern		
										δ_{H_A} 2.73, δ_{H_B} 2.48, J_{AB} = 10.5		
$Na[PtMe_3(aba)_2]$	D_2O	2.5	N	1	0.73	72.5	1.50					
			N	1	0.71	69.2	1.41					
			O	1	0.67	77.4	1.33					
							1.33					

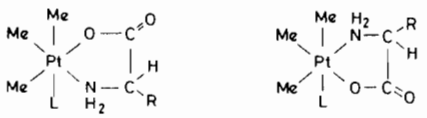
[a]Chemical shifts in p.p.m. downfield from DSS (D_2O) or TMS (other solvents). Coupling constants in Hz. [b]Labels given correspond to those in Figure. [c]±0.2 Hz. [d]One broad peak observed in this region. [e]Peaks corresponding to $PtMe_3(L\text{-ala})_2^-$ also appear in spectrum. [f]Region complex. [g]Overlaps solvent peak.

mixture of equal amounts of the two *cis*-isomers. Since, from examination of models, steric interactions would increase in the order (IVa) $\lesssim$ (IVb) $\ll$ (IVc), it is most likely that the solution contains only the *trans*-isomer (IVa). The spectrum does not vary with temperature, up to the boiling point of acetone. The methine proton region is complex.

The NMR spectra of $[PtMe(L\text{-val})]_2$ in $CDCl_3$ (Table II) and C_6D_6 show six Pt-Me peaks of equal intensity, and four doublets from the C-Me groups. This is consistent with the presence of the *trans* isomer (IVa) alone*. The major steric interaction in this isomer would occur between one of the isopropyl groups and one of the Pt-Me groups (indicated by arrows). In $(CD_3)_2CO$, only three Pt-Me peaks, and two C-Me doublets are observed. It is most likely that the *trans* isomer (IVa) is also present in this solvent, with "accidental" degeneracy of the peaks, rather than the *cis* isomer (IVb) alone.

Methanol Complexes, $PtMe_3(AA)(MeOH)$

The variable-temperature NMR spectra of a solution of $[PtMe_3(L\text{-ala})]_2$ in CD_3OD are shown in Figure 1. The spectrum at –45 °C shows four peaks in the Pt-Me region, intensity ratio 1:1:2:2, with Pt–CH_3 coupling constants 82.4, 81.9, 76.6, and 66.4 Hz respectively (Figure 1a). These values are as expected [1] for methyl groups *trans* to methanol (A and B), alanate O (C) and alanate N (D) respectively. Thus, the two isomers of $PtMe_3(L\text{-ala})(CD_3OD)$, (Va and b) (R = Me, L = CD_3OD) are present in approximately equal amounts. As would be expected, the chemical shifts of the Pt-Me groups *trans* to methanol, which are *cis* to either H or Me across the chelate ring, are most sensitive to the isomeric difference. The expected two C-Me doublets are also observed.



In CD_3OD, the protons bound to N are slowly replaced by deuterium. The spectra in Figure 1 are of a deuterated sample. The methine proton for each isomer would be expected to be a quartet from $HCCH_3$ coupling, with satellites from ^{195}Pt coupling. It is apparent from Figure 1a that two such patterns overlap in this region of the spectrum, but Pt–N–C–H coupling could not be resolved.

*It should be noted that, even in free valine, the two methyl groups of the isopropyl substituent are inequivalent, owing to the proximity of an asymmetric C-atom.

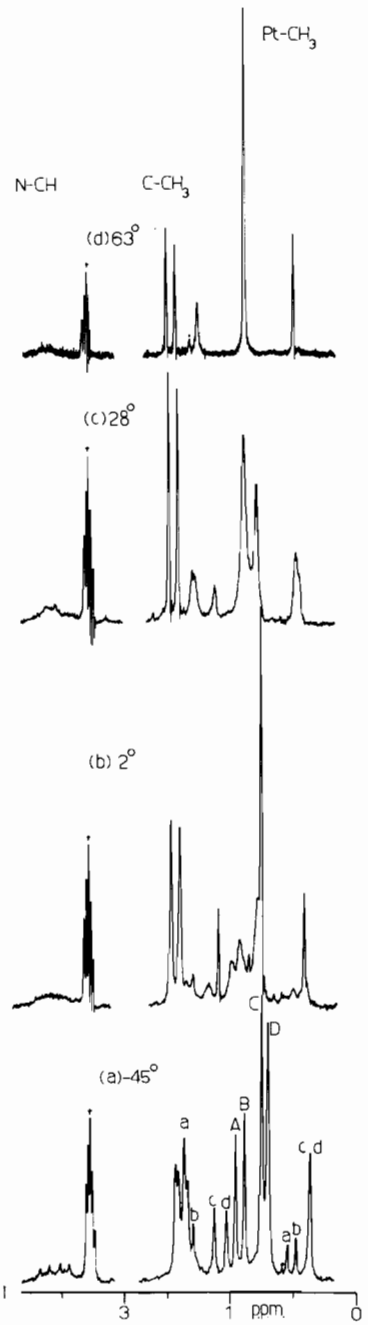
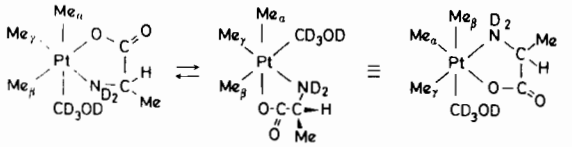


Figure 1. Variable-temperature 100 MHz PMR spectra of $PtMe_3(L\text{-ala})(CD_3OD)$ in CD_3OD. † Solvent resonance.

As the solution is warmed, the exchange reaction (4) commences, analogous to reaction (1) observed for $PtMe_3(gly)(H_2O)$ (I). A mechanism for this reaction, involving the five-coordinate intermediate, $PtMe_3(AA)$, has been previously proposed [1]. When this reaction is sufficiently fast, signals due to separate isomers (Va) and (Vb) will no longer be observed in the NMR spectrum. There is now only one averaged environment for the C-Me groups, and consequently, at 2 °C (Figure 1b) only one doublet is observed.



Va Vb (4)

The effect of the exchange on the platinum-methyl groups is to transform a methyl group *trans* to methanol into one *trans* to alanate O, and *vice-versa.* Thus, peak A would coalesce with one component of peak C, and peak B with the other component of C. Since the peaks due to methyl *trans* to N in the two isomers are already "accidentally" coincident at D, this peak remains sharp. Corresponding changes take place in the "satellites". Broad Pt-Me peaks (except for D) are observed at 2 °C (Figure 1b).

As long as the coordination site of the N-atom remains fixed, no symmetry element relates Me_α and Me_β. If the exchange reaction (4) became sufficiently fast, three sharp Pt-Me resonances would be expected. Before this stage is reached, a second exchange reaction, corresponding to reaction (2), begins to become significant. All three Pt-Me groups now become equivalent, and a sharp singlet with "satellites" is observed at 63 °C.

Similar behaviour is observed for $PtMe_3$(val)-(CD_3OD). At −39 °C, four Pt-Me resonances are again observed, but the intensity ratio is 1:2:3:3, indicating that two isomers (Va and b) (R = i-Pr, L = CD_3OD) are present, with one favoured over the other. The larger isopropyl substituent is more sensitive to the difference in bulk between coordinated methanol and a methyl group. Of the two ligands methanol is larger, but the Pt–O bond is probably significantly longer than Pt–C, so that the favoured isomer cannot be unequivocally assigned. A total of 4 C-Me doublets would be expected, but this region is complicated by overlap with the Pt-Me peaks.

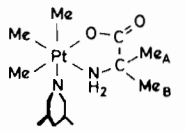
As the temperature is increased, intramolecular exchange reactions occur analogous to those discussed above. By 60 °C, a singlet with satellites is observed for the Pt-Me groups, and two doublets for C-Me (corresponding to one environment for isopropyl groups).

The α-methine proton resonance coincides with the residual $-CHD_2$ resonances. At −39 °C, the isopropyl methine protons give a complex pattern, but at 60 °C, a septet (J_{HCCH_3} 7.5 Hz) of doublets (J_{HCCH} 3.6 Hz) is observed.

Lutidine Complexes, $PtMe_3(AA)(lut)$

All of the dimers $[PtMe_3(AA)]_2$ react with 3,5-lutidine to give $PtMe_3(AA)$(lut). All of the compounds are freely soluble in methanol, and much less soluble in acetone. $PtMe_3(AA)$(lut) (AA = ala, val), like $PtMe_3$(gly)(lut), are only very sparingly soluble in chloroform, but the other complexes (AA = phe, aba) dissolve readily.

There is only one isomer of $PtMe_3$(aba)(lut). Its ^1H NMR spectrum in $CDCl_3$ shows only one set of lutidine peaks, three Pt-Me peaks with satellites, and two C-Me singlets. One C-Me peak occurs at the "normal" chemical shift 1.51 p.p.m., but the other is shifted well upfield to 0.87 p.p.m. The latter signal is probably due to the methyl group on the same side of the chelate ring as the lutidine ligand (Me_B in (VI)). An anisotropic shielding effect is expected if the methyl group lies "above" the plane of the aromatic ring [2], which would be the case if the preferred orientation of the lutidine ligand is as depicted in (VI). For this orientation of the ring, steric interactions would be minimized.



VI

The N–H resonances, uncomplicated by HCNH coupling (although still broadened by partial decoupling from ^{14}N) show an AB pattern (J_{AB} 11 Hz).

The ^1H NMR spectrum of $PtMe_3$(L-ala)(lut) in CD_3OD shows 4 peaks in the Pt-Me region, relative intensities 1:2:1:2, indicating the presence of the two isomers (Va and b) (R = Me, L = lut) in approximately equal proportions. Chemical shift differences between the lutidine resonances are not resolved for the two isomers, but the anisotropic shielding effect of the aromatic ring has a marked effect on the alanine proton shifts. In one isomer (probably Va) the C-Me doublet is much more shielded (0.99 p.p.m.) than in the other isomer (1.34 p.p.m.). There is a corresponding difference in the methine proton shifts (3.60 (isomer (VIa)) and 2.85 (isomer Vb) p.p.m.). Pt–N–C–H coupling was not resolved. No change occurs in the spectrum as temperature is varied up to 70 °C.

For $PtMe_3$(L-val)(lut) in CD_3OD, two sets of Pt-Me resonances of equal intensity are just resolved at 100 MHz. The presence of both isomers (Va and b) (R = $-CHMe_2$, L = lut) in equal amounts contrasts with the preference for one isomer over the other when L = methanol. The expected 4 C-Me doublets are observed. Three occur near 0.9 p.p.m. (overlapping part of the Pt-Me signals) but one, presumably a methyl group in isomer Va which, in the preferred orientation of the isopropyl group is situated above the aromatic ring, has a chemical shift 0.31 p.p.m.

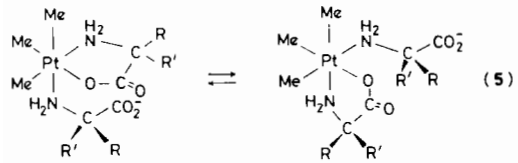
From the Pt-Me region of the spectrum of $PtMe_3$-(L-phe)(lut) in $CDCl_3$ (Table II) it is evident that two isomers are again present, but this time in the approximate ratio 2:1. There are also two well-resolved sets of lutidine resonances, again with relative intensities 2:1. In CD_3OD, peaks due to two isomers (2:1) are again observed. Phenylalanine is the

only amino acid of those studied for which there is a definite preference for one isomer of $PtMe_3(AA)(lut)$ over the other.

Bis(amino acid) Complexes, $Na[PtMe_3(AA)_2]$

Bis(amino acid) complexes $Na[PtMe_3(AA)_2]$ were prepared without difficulty for AA = L-ala, L-val, and aba (see Experimental), but attempts to prepare $Na[PtMe_3(phe)_2]$ were unsuccessful.

In our previous paper [1] it was stated that, when $PtMe_3(gly)_2^-$ undergoes the exchange reaction (3), all the methylene protons become equivalent. From a further consideration of the system, it is now clear that this statement is incorrect. If a complex $PtMe_3(AA)_2^-$ undergoes reaction (5), where AA is symmetric, the two α-substituents attached to one C-atom never become equivalent (although the two coordinated amino acids do). To illustrate, when R is a substituent on a chelate ring, it is on the same side of the ring as the axial Pt-Me, while, when R′ is a substituent on a chelate ring, it is on the opposite side of the ring to the axial Pt-Me.



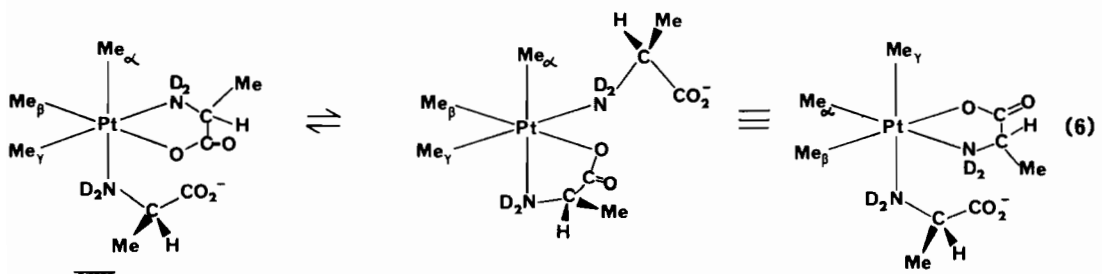
VII a VII b

The question is of academic interest for AA = gly (*i.e.* R,R′ = H), since a broad featureless band is observed in the methylene region at high temperatures, owing to the relatively large chemical shift between protons in chelated and unidentate glycine, and the AB coupling between the methylene protons [1]. For AA = aba (*i.e.*, R,R′ = Me), where there is no coupling between the different methyl protons, it was hoped that the non-equivalence of the two methyl groups might be apparent in the spectra under conditions where reaction (5) is fast. Near 0 °C in D_2O, the spectrum shows three Pt-Me peaks, and three distinguishable C-Me resonances (the two C-Me groups on the unidentate aba are probably not resolved) (Table II). By 28 °C, the Pt-Me region shows two peaks, intensity 2:1, corresponding to methyl groups trans to N and O respectively, and the C-Me peaks have begun to coalesce, thus indicating that reaction (5) is proceeding. Up to this stage, the system parallels $PtMe_3(gly)_2^-$ [1]. Two C-Me resonances should persist in the spectrum as the rate of reaction (5) increases; however, as the temperature increases further, the Pt-Me peaks begin to broaden and coalesce, so that by 56 °C, a broad singlet is observed in this region. This is indicative of intermolecular exchange between free and coordinated aba. For the glycinate complex, such exchange becomes important only at much higher temperatures (>80 °C). As would be expected, the C-Me resonances also coalesce to a broad singlet. At 84 °C, both singlets sharpen considerably. Furthermore, within a few minutes, the Pt-Me peak decreases in intensity relative to C-Me, and $[PtMe_3(aba)]_2$ precipitates in the tube. The increased rate of intermolecular exchange compared with the gly and ala compounds, and the relatively low stability of $PtMe_3(aba)_2^-$, presumably are caused by increased steric interactions in the aba complex.

$Na[PtMe_3(aba)_2]$ is also quite soluble in methanol. In CD_3OD, intermolecular exchange still occurs at temperatures ≥45 °C, although no precipitation of $[PtMe_3(aba)]_2$ occurs.

Variable-temperature ^1H NMR spectra of $Na[PtMe_3(L\text{-}ala)_2]$ in D_2O are illustrated in Figure 2. At 2 °C (Fig. 2(a)), four Pt-Me resonances are observed, with relative intensities 3(A + B + C): 1(D): 1(E): 1(F), with Pt-CH_3 coupling constants (Table II) corresponding to methyl groups *trans* to O(A + B), N(chelated alanate) (C and F), and N(unidentate alanate) (D and E). This indicates that the two isomers (VIIIa and b) are present in approximately equal proportions. Four non-equivalent C-Me groups are expected, and the spectrum shows 3 overlapping doublets, relative intensities 1:1:2.

As the solution is warmed, the exchange reaction (b) begins to occur (*cf.* reaction (3)), which converts isomer (VIIIa) into (VIIIb). This reaction transforms a Pt-Me group *trans* to unidentate alanate into one *trans* to N of chelated alanate and *vice-versa*. When the reaction occurs sufficiently quickly, the two isomers are no longer distinguishable by NMR. Since no symmetry element relates Me_α and Me_γ, they remain inequivalent (*e.g.*, when Me_α is *trans* to



VIII a VIII b

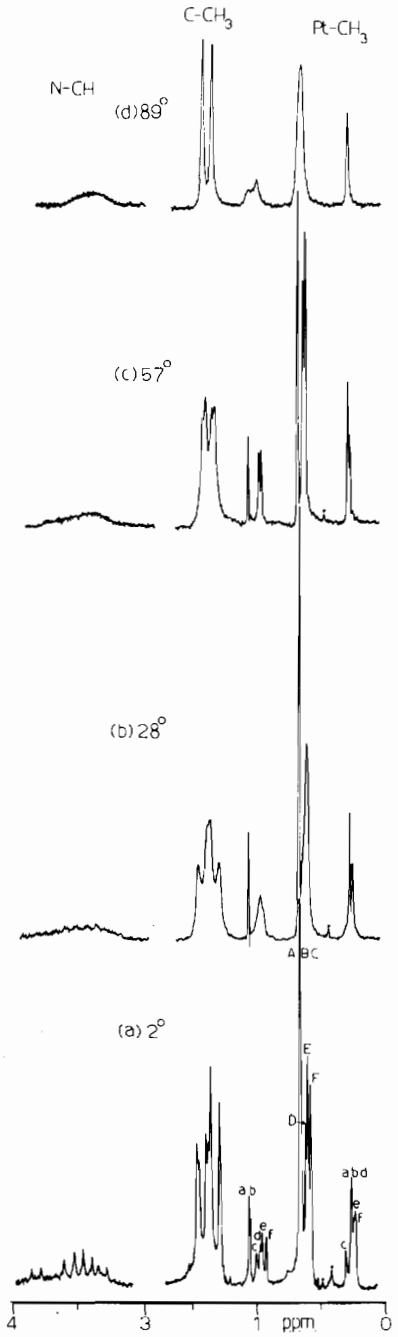


Figure 2. Variable-temperature 100 MHz PMR spectra of $Na[PtMe_3(L\text{-}ala)_2]$ in D_2O. *Impurity.

unidentate alanate (VIIIa) it is on the same side of the chelate ring as C-Me, but when Me_γ is *trans* to unidentate alanate (VIIIb), it is on the opposite side of the chelate ring to C-Me). Similarly, the two C-Me groups remain inequivalent. Consequently, at 57 °C (Fig. 2(c)), 3 Pt-Me peaks and 2 C-Me doublets are observed.

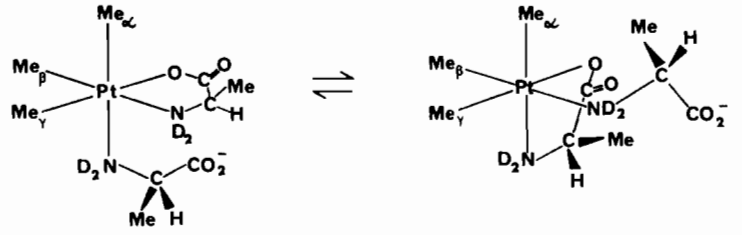
By 89 °C (Figure 2(d)) rapid intermolecular exchange of the coordinated amino acid has caused the C-Me peaks to collapse to a single doublet, and the Pt-Me peaks to coalesce to a broad singlet.

For $[Co(en)_2(L\text{-}ala)]^{2+}$, the alanine methine protons exchange with solvent deuterium, and the amino acid racemizes [3]. Even after standing for several weeks, an aqueous solution of $Na[PtMe_3(L\text{-}ala)_2]$ shows high optical rotation ($[\alpha]_D^{25} = -35.7$), and NMR spectra show no signs of α-H deuteration, or appearance of new peaks corresponding to $Na[PtMe_3(L\text{-}ala)(D\text{-}ala)]$. These peaks would certainly be detectable, since 6 new Pt-Me peaks appear in the NMR spectrum at 2 °C of a sample of $Na[PtMe_3(ala)_2]$ prepared using racemic alanine, as well as the peaks mentioned above for $Na[PtMe_3(L\text{-}ala)_2]$ and $Na[PtMe_3(D\text{-}ala)_2]$ (see Table II). There are two isomers of $PtMe_3(L\text{-}ala)(D\text{-}ala)^-$, (IXa and b) corresponding to S- and R- absolute configurations at platinum respectively. For each isomer there would be 3 inequivalent Pt-Me groups and two inequivalent C-Me groups. No attempt was made to analyse the C-C-Me region of the spectrum, because of its complexity (from all species in solution there are a total of 8 different C-Me groups).

For each of the isomers, the effect of the exchange reaction analogous to reactions (3) and (6) (reactions (7), (8)) is to make the two Pt-Me groups *trans* to N equivalent, and the two C-Me groups equivalent, but, in contrast to the situation with $PtMe_3(L\text{-}ala)_2^-$, the two isomers (IXa and b) are not interconverted by this exchange. Thus, at a temperature when reactions (6), (7), (8) are fast (~60 °C), the spectrum shows in the Pt-Me region, in addition to the 3 peaks from $PtMe_3(L\text{-}ala)_2^-$ and $PtMe_3(D\text{-}ala)_2^-$, four resonances of relative intensity 1:1:2:2, corresponding to methyl groups *trans* to O,O,N,N respectively, from the two isomers of $PtMe_3(L\text{-}ala)(D\text{-}ala)^-$. Unfortunately all the C-Me peaks overlap to give one broadened doublet.

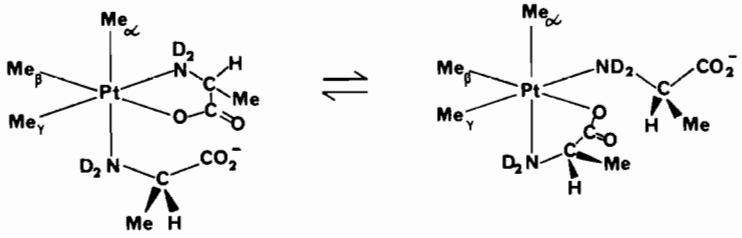
By ~ 90 °C, all Pt-Me resonances have coalesced into one broad singlet (significantly broader than that for $PtMe_3(L\text{-}ala)_2^-$) (Fig. 2(d)), as intermolecular alanate exchange begins to occur.

The spectrum of $Na[PtMe_3(L\text{-}val)_2]$ at 2 °C shows two sets of three Pt-Me groups, one set being half the intensity of the other, indicating the presence of two isomers, (VIIa and b) (R = H, R′ = iPr). It would be expected that (VIIa) would be the less stable isomer. The C-Me peaks are still somewhat broad at 2 °C, and overlap with each other, and with the downfield Pt-Me satellites. As the temperature is raised, reactions analogous to those discussed above for $Na[PtMe_3(L\text{-}ala)_2]$ occur so that at 60 °C, three Pt-Me peaks of equal intensity, and 4 distinct C-Me doublets (corresponding to two non-equivalent isopropyl groups) are observed.



(7)

IX a



(8)

IX b

Conclusions

(i) The variable temperature spectra of compounds $PtMe_3(AA)(CD_3OD)$ and $Na[PtMe_3(AA)_2]$ show that exchange reactions occur analogous to those previously described for glycinate complexes.

(ii) $Na[PtMe_3(aba)_2]$ is significantly less stable toward dissociation of the amino acid ligand than its glycinate analogue, and $Na[PtMe_3(phe)_2]$ could not be prepared.

(iii) For each of the complexes $PtMe_3(AA)L$ (L = CD_3OD, lut) and $PtMe_3(AA)_2^-$, where the α-C atom of the amino acid is an asymmetric centre, the predicted two diastereoisomers are observed in NMR spectra.

(iv) For AA = L-ala, the two isomers are present in each case in equal proportions – that is, overall steric interactions in the two isomers are comparable. This may be achieved by various degrees of distortion in the chelate ring conformation.

(v) For AA = L-val, the two isomers of $PtMe_3$-(L-val)(lut) are present in equal amounts, so that even the bulky isopropyl substituent is unable to discriminate between the steric bulk of methyl and lutidine (once the aromatic ring is so oriented and the ring conformation adjusted to minimize steric interactions). For $PtMe_3(L\text{-val})_2^-$ and $PtMe_3(L\text{-val})(CD_3OD)$ there is a preference for one isomer over the other.

(vi) For the only phenylalanine complex which is soluble, $PtMe_3$(L-phe)(lut), there is a preference for one isomer over the other.

(vii) The protons in an amino acid substituent close to the aromatic lutidine ring in $PtMe_3(AA)$(lut) are shifted to high field in the NMR spectrum.

(viii) Dimers $[PtMe_3(AA)]_2$ (AA = L-ala, L-val) remain as dimers in acetone solution, but in methanol and water (to the limited extent they are soluble) the bridges are cleaved to give monomers.

(ix) Only one isomer (*trans*) exists for $[PtMe_3$-(L-ala)$]_2$ and $[PtMe_3(L\text{-val})]_2$. Stereoselectivity is greater than in the monomers mentioned above, since there are more steric interactions to be considered in the case of the dimers.

Experimental

Materials and Instrumentation

$[PtMe_3I]_4$ and $[PtMe_3]_2SO_4 \cdot 4H_2O$ were prepared by literature methods [4, 5]. Amino acids were used as supplied (B.D.H., except for α-aminoisobutyric acid, Sigma) after a purity check by NMR (and, for L-alanine by optical rotation). 3,5-lutidine was supplied by Aldrich.

NMR and IR instrumentation was as described previously [1]. C, H, and N analyses were performed by J. Kent and P. Nobbs of this department. Pt was analysed by ignition with iodine. Molecular weights were measured using a Hewlett-Packard 302 Mechrolab High Temperature Vapour Pressure Osmometer.

Preparations

Dimers, $[PtMe_3(AA)]_2$

$[PtMe_3(L\text{-ala})]_2$. To 0.1793 g $[PtMe_3]_2SO_4 \cdot 4H_2O$ (0.553 mmol $PtMe_3^+$) in 3 ml water was added dropwise with stirring a solution of 0.0494 g L-alanine (0.561 mmol) and 0.022 g NaOH (0.55

mmol) in 5 ml water. The precipitated $[PtMe_3(OH)]_4$ was filtered off (standing for more than a few minutes should be avoided – $[PtMe_3(L\text{-ala})]_2$ slowly precipitates). The paper was washed with 3 ml water, and the combined filtrate and washings was reduced to approx. 2 ml on the steam bath, during which time colourless crystals formed. The mixture was cooled in a refrigerator overnight. The solid was then filtered off, washed with cold water, and air-dried, then extracted with 20 ml acetone. The filtrate was evaporated to dryness on a steam bath, and the product dried in a drying pistol at 110 °C. Yield 0.0978 g (53.9%).

The product is soluble in acetone and methanol, very sparingly soluble in water, and insoluble in chloroform. Decomposition temperature ~210 °C.

$[PtMe_3(L\text{-val})]_2$. This compound was prepared similarly. Yield 32.4%. It is soluble in acetone, methanol, chloroform, benzene, and hexane, but only very sparingly soluble in water. Decomposition temperature, 230 °C.

$[PtMe_3(L\text{-phe})]_2$. 0.100 g $[PtMe_3]_2SO_4 \cdot 4H_2O$ (0.309 mmol $PtMe_3^+$) and 0.0509 g L-phenylalanine (0.309 mmol) were dissolved in 3 ml water, and the solution was stirred while gently heated. A white precipitate formed. Stirring was continued while the mixture cooled (0.5 hr), then the compound was filtered off, washed with water, then ether, and dried under vacuum. Yield 0.0748 g (60%). The product is very sparingly soluble in water and methanol, and insoluble in acetone, chloroform, benzene, and hexane. Decomposition temperature, ~250 °C.

$[PtMe_3(aba)]_2$. 0.4614 g $[PtMe_3]_2SO_4 \cdot 4H_2O$ (1.423 mmol $PtMe_3^+$) and 0.4592 g α-aminoisobutyric acid (4.45 mmol) were dissolved in 15 ml water. The mixture was heated on a steam bath until the volume was reduced to 7 ml, during which time colourless crystals deposited. The mixture was cooled, and the solid was filtered off, washed with cold water, and air-dried. Yield 0.3756 g (77%). The compound is essentially insoluble in water, methanol, acetone, and chloroform. Decomposition temperature, 240 °C.

Lutidine Adducts, $PtMe_3(AA)(lut)$

The basic preparative method was as described previously for $PtMe_3$(gly)(lut) [1]. A small excess of lutidine was added to a stirred solution (for AA = L-ala, L-val) or a stirred, heated suspension (for AA = L-phe, aba) of $[PtMe_3(AA)]_2$ in methanol. The resultant solution was filtered, then evaporated to dryness. The crude solids so obtained were then purified as outlined below.

$PtMe_3(L\text{-ala})(lut)$. The compound was dissolved in the minimum volume of methanol, 3 ml chloroform was added, and the product was reprecipitated by slow addition of a large volume of hexane. The fine needles were filtered off, washed with hexane, and dried under vacuum. Yield 88%. The compound is soluble in methanol, sparingly soluble in acetone and chloroform. Decomposition temperature, ~240 °C.

$PtMe_3(L\text{-val})(lut)$. This compound was similarly recrystallized from chloroform-methanol/hexane, then from acetone. Yield 70%. Heating or prolonged pumping should be avoided. Its solubility properties are similar to those of the alanato complex. It melts with decomposition at 220–230 °C.

$PtMe_3(L\text{-phe})(lut)$. The compound was twice dissolved in chloroform and reprecipitated by addition of hexane. It was filtered off, washed with hexane, and dried under vacuum. Yield 70%. It is soluble in methanol, chloroform, and acetone. Even after prolonged pumping a trace of solvated hexane remained, evident in NMR spectra and analyses. This compound is the least stable thermally of the lutidine adducts. It melts with evolution of lutidine at 90 °C.

$PtMe_3(aba)(lut)$. The compound was dissolved in chloroform and reprecipitated with hexane. The solid was filtered off, washed with hexane, and dried under vacuum. Yield 78%. It is soluble in methanol, chloroform, and acetone. Decomposition temperature, ~240 °C.

Bis(amino acid) Complexes, $Na[PtMe_3(AA)_2]$

$Na[PtMe_3(L\text{-ala})_2]$. To 0.100 g $[PtMe_3]_2SO_4 \cdot 4H_2O$ (0.309 mmol $PtMe_3^+$) and 0.0549 g L-alanine (0.616 mmol) in 3 ml water was added dropwise with stirring a solution of 0.025 g NaOH (0.62 mmol) in 7 ml water. Precipitated $[PtMe_3(OH)]_4$ was removed by filtration, and the paper washed with water. Evaporation of the combined filtrate and washings to dryness gave a white solid which was extracted repeatedly with 10 ml portions of hot methanol, each portion being filtered to remove Na_2SO_4. The combined filtrate (~150 ml) was then evaporated to dryness, and the resultant white solid dried in a vacuum desiccator over $CaCl_2$. Yield 0.1166 g (86%).

$Na[PtMe_3(L\text{-ala})_2]$ is very soluble in water, sparingly soluble in methanol, and insoluble in chloroform and acetone. It rapidly absorbs moisture from the atmosphere.

$Na[PtMe_3(L\text{-val})_2]$. This compound was prepared similarly (95% yield). It is only slightly hygroscopic.

$Na[PtMe_3(aba)_2]$. 0.2177 g $[PtMe_3(aba)]_2$ (0.636 mmol $PtMe_3^+$) was suspended in 10 ml water, and a solution of 0.063 g α-aminoisobutyric acid (0.611 mmol) and 0.024 g NaOH (0.6 mmol) in 40 ml water was added. The mixture was stirred and heated until

most of the solid had dissolved (0.5 hr), then the filtered solution was evaporated to dryness. The resultant white solid was dissolved in a small volume of methanol. The solution was filtered, then concentrated under reduced pressure, and diethyl ether was added to precipitate the product, which was filtered off, washed with ether, and dried in a vacuum desiccator over silica gel. Yield 0.1765 g (59%). The product is very soluble in water, moderately soluble in methanol, and insoluble in acetone. It is hygroscopic.

An attempt was made to prepare $Na[PtMe_3(L\text{-phe})_2]$ similarly, but the dimer did not dissolve, even after prolonged heating.

Acknowledgements

We thank the Australian Research Grants Committee for supporting this project, Miss L. Lambert for assistance with some of the NMR spectra, and Mr D.A. Hirons for preparation of some of the starting materials.

References

1 Part 1: T. G. Appleton, J. R. Hall and Lambert, *Inorg. Chim. Acta, 29,* 89 (1978).
2 C. E. Johnson and F. A. Bovey, *J. Chem. Phys., 29,* 1012 (1958).
3 D. A. Buckingham, L. G. Marzilli and A. M. Sargeson, *J. Am. Chem. Soc., 89,* 5133 (1967).
4 D. E. Clegg and J. R. Hall, *Inorg. Syn., 10,* 71 (1967).
5 O. M. Ivanova and A. D. Gel'man, *Zhur. Neorg. Khim., 3,* 1334 (1958).