

## A New Mode of Theophyllinate Anion–Metal Bonding: N(7),N(9)-Bridging in Theophyllinate Complexes of Trimethylplatinum(IV)

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**Summary** The theophyllinate anion forms a trimeric complex with trimethylplatinum(IV) which contains Pt–N(7),–N(9)–Pt bridges and a weak, direct (C–6)O–Pt bond.

THERE has been much interest in the interaction of metal ions with 6-oxopurines, in part because the anti-cancer action of *cis*-PtCl<sub>2</sub>(NH<sub>3</sub>)<sub>2</sub> is thought to involve co-ordination to a guanosine residue in DNA.<sup>1</sup> The anion derived from theophylline (I) (Hthp) has often been used as a model ligand in studying the interaction of 6-oxopurines with metal ions.<sup>2,3</sup> In guanosine, N(9) is substituted by ribose. In the theophyllinate anion, co-ordination at N(9) is sterically hindered by the N(3)-methyl group,

and has not been observed previously. Numerous X-ray crystal structure determinations have shown that the theophyllinate anion normally bonds to metal ions through N(7), usually with (C–6)O also involved in intramolecular H-bonding with an adjacent O–H or N–H group.<sup>2</sup>

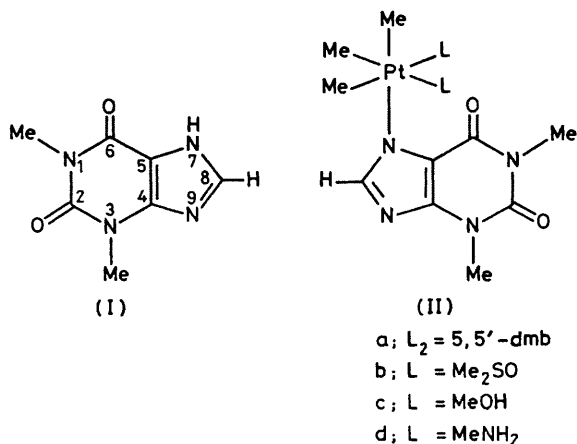
Since the chemical and spectroscopic properties of methylplatinum(IV) compounds make them excellent probes for the co-ordination behaviour of relatively complex ligands,<sup>4</sup> we have investigated the reactions of these compounds with theophylline (I). The complex PtMe<sub>3</sub>–(5,5'-dmb)(NO<sub>2</sub>) reacts with Na(thp) in acetone-water to give PtMe<sub>3</sub>(5,5'-dmb)(thp) (5,5'-dmb = 5,5'-dimethyl-2,2'-bipyridyl). Significant coupling between H(8) and <sup>195</sup>Pt

TABLE. Important n.m.r. data.<sup>a</sup>

Compound	Solvent	Temp. /°C	<sup>1</sup> H				<sup>13</sup> C				
			Relative intensity	Pt–Me <i>J</i> (Pt–Me)	<i>trans</i> - Ligand	H(8) $\delta$ <i>J</i> (Pt–H)	C(8) $\delta$ <i>J</i> (Pt–C)	C(6) $\delta$ <i>J</i> (Pt–C) <sup>b</sup>	C(5) $\delta$ <i>J</i> (Pt–C) <sup>b</sup>	C(4) $\delta$ <i>J</i> (Pt–C) <sup>b</sup>	C(2) $\delta$
Na(thp)	D <sub>2</sub> O	28	—			7.56	145.9	158.2	112.3	149.4	153.1
(IIa)	CDCl <sub>3</sub>	28	0.36	1	69.8	N(7)	7.02				
			1.39	2	69.8	5,5'-dmb	[6.0]				
(IIb)	(CD <sub>3</sub> ) <sub>2</sub> SO	23	0.89	1	66.5	N(7)	7.41				
			1.08	2	73.0	Me <sub>2</sub> SO	[6.2]				
(IIc) <sup>c</sup>	CD <sub>3</sub> OD	–30	0.85	1	66.4	N(7)	7.46				
			1.01	2	79.0	MeOH	[6.2]				
(IId)	CDCl <sub>3</sub>	28	0.65	1	67.9	N(7)	7.37	149.0	159.1	112.2	151.5 <sup>d</sup>
			0.75	2	68.3	NH <sub>2</sub> Me	[8.1]	[19.1]			151.8 <sup>d</sup>
(III)	CDCl <sub>3</sub>	–30	0.74	1	69.6	N(7)	7.44				
			1.16	1	73.1	N(9)	[4.4]				
			1.50	1	80.3	(C–6)O					
		28	br s				7.44	144.3	163.1	118.5	147.6
							[4.3]	[21.6,12.2]	[2.6]	[5.9]	[6.6,1.8]
(IV)	NaOD–	28	1.08	1	71.6	N(7)	7.25				
	D <sub>2</sub> O		0.53	1	73.2	N(9) <sup>d</sup>	[6.9]				
			0.36	1	74.6	OH <sup>d</sup>					

<sup>a</sup> Chemical shifts are in p.p.m. downfield from Me<sub>4</sub>Si (except <sup>1</sup>H chemical shifts in D<sub>2</sub>O, relative to trimethylsilylpropane-3-sulphonate); coupling constants are in Hz. Data reported are for saturated solutions. Only for (IIc) in CD<sub>3</sub>OD are spectra significantly concentration-dependent. <sup>b</sup> Where coupling to Pt is observed. <sup>c</sup> Weak peaks from [PtMe<sub>3</sub>(thp)]<sub>3</sub> are also present, which decrease relative to those from (IIc) with dilution. <sup>d</sup> These assignments could be reversed.

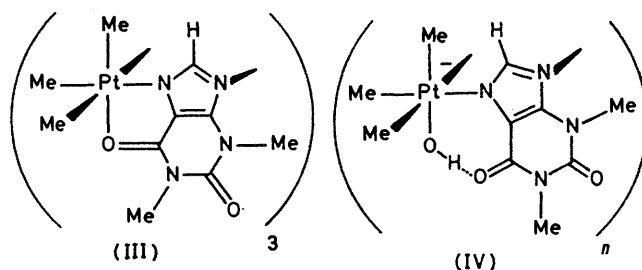
( $I = \frac{1}{2}$ , 34% abundance) is observed in the  $^1\text{H}$  n.m.r. spectrum (Table), consistent with the N(7)-bound theophyllinate group, as in (IIa). No intramolecular H-bond involving (C-6)O is possible in (IIa). The similarity of the two different Pt-Me coupling constants indicates that the the N(7)-bound theophyllinate group is 'pyridine-like' in its bonding to the Pt atom.



The complex  $\text{fac-}[\text{PtMe}_3(\text{H}_2\text{O})_3]^+$  (as the sulphate) reacts with  $\text{Na}(\text{thp})$  in water and immediately gives a precipitate having the empirical formula  $\text{PtMe}_3(\text{thp})\text{H}_2\text{O}$ . Anhydrous  $\text{PtMe}_3(\text{thp})$  may be obtained by heating this material at  $110^\circ\text{C}$  under reduced pressure. When this complex is dissolved in co-ordinating solvents ( $\text{Me}_2\text{SO}$ ,  $\text{MeOH}$ ),  $^1\text{H}$  n.m.r. spectra (Table) and molecular weight measurements indicate that the major species are monomeric complexes (IIb) and (IIc), respectively. In chloroform, the average molecular weight from nine determinations by vapour pressure osmometry over the molar concentration range (based on the monomer formula)  $0.005\text{--}0.05\text{ M}$  was 1286 {cf. calc. mol. wt. for  $[\text{PtMe}_3(\text{thp})]_3$ , 1258}. No significant variation with concentration was observed. The complex is also trimeric in dichloromethane (average mol. wt. from two determinations, 1245). Its  $^1\text{H}$  n.m.r. spectrum in  $\text{CDCl}_3$  at  $28^\circ\text{C}$  shows a sharp singlet from H(8), with  $J(\text{Pt-H})$  4.3 Hz. At this temperature the methyl groups attached to Pt give only a broad central resonance. At  $-30^\circ\text{C}$ , the aromatic resonance is unchanged, but the Pt-Me region shows three singlets, each with 'satellites' (Table). In the  $^1\text{H}$ -decoupled  $^{13}\text{C}$  n.m.r. spectrum at  $28^\circ\text{C}$ , the C(8) and C(4) central resonances are each flanked by two sets of satellites, arising from coupling to two different Pt atoms.

We considered the possibility that, on dissolution,  $\text{PtMe}_3(\text{thp})$  had reacted with traces of water in the solvent to give  $[\text{PtMe}_3(\text{thp})(\text{H}_2\text{O})]_3$ . This is, however, unlikely, since anhydrous  $\text{PtMe}_3(\text{thp})$  crystallizes from chloroform solution. Also, an n.m.r. sample prepared with rigorous exclusion of water gave an identical spectrum to that obtained using commercial  $\text{CDCl}_3$ .

On the basis of these observations, we propose that  $[\text{PtMe}_3(\text{thp})]_3$  (III) is a cyclic trimer having the structure shown in the Figure. Imidazolate bonding between metal ions has recently received much attention in compounds proposed as models for the active site of cytochrome oxidase.<sup>5</sup> N(9)-metal bonding is common for



purines unsubstituted at N(3),<sup>2</sup> but has not previously been observed for N(3)-methyl purines. It is clear from models that, in an octahedral complex, severe steric hindrance from the N(3)-methyl group can be avoided only if the metal ion bound to N(9) is substantially out of the plane of the purine ring. This is expected to cause a weakening of the metal-N(9) bond, which, in (III), is reflected in the low value of  $J[\text{Pt-N}(9)\text{-C}(8)]$ , 12.2 Hz, compared with  $J[\text{Pt-N}(7)\text{-C}(8)]$ , 21.6 Hz, and in the high value of  $J(\text{Pt-Me})$  *trans* to N(9), 73.1 Hz, compared with  $J(\text{Pt-Me})$  *trans* to N(7), 69.9 Hz.

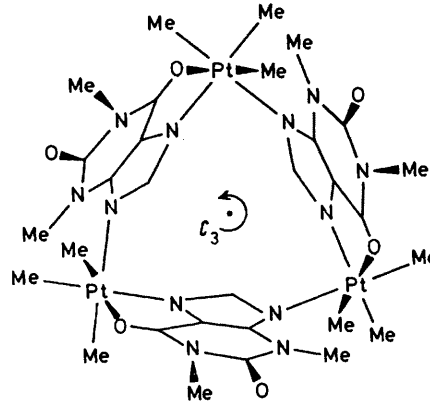


FIGURE. Proposed structure for (III) viewed from 'below', along the  $C_3$  axis.

$J(\text{Pt-Me})$  *trans* to (C-6)O (80.3 Hz) corresponds to a relatively weak Pt-O bond [cf. 73.6 Hz *trans* to (C-8)O in an 8-hydroxyquinolate complex<sup>6</sup>].  $J[\text{Pt-C}(6)]$ , 2.6 Hz, is also low. In the one solid-state structure of a copper complex where an N(7), (C-6)O-chelated theophyllinate group has been found, the Cu-O distance is 2.919 (3) Å, indicating a very weak Cu-O interaction.<sup>7</sup>

The coalescence of the Pt-Me resonances when the temperature is raised would result from breaking of the Pt-O(C-6) bond, followed by rapid intramolecular rearrangement of the five-co-ordinate complex. The N(7),-N(9) bridges remain intact during the exchange, since C(8) remains coupled to two Pt nuclei. Rapid exchange reactions are often observed in n.m.r. spectra of trimethylplatinum(IV) complexes with one or more weakly bound ligands.<sup>4,8</sup>

The complex (III) reacts with an excess of methylamine to give  $\text{PtMe}_3(\text{thp})(\text{NH}_2\text{Me})_2$  (IIId), which is monomeric in chloroform and is less soluble than (III). For C(8), for which the nuclear Overhauser effect provides a relaxation mechanism, coupling of 19.1 Hz to only one Pt atom is observed. Signals from the other C atoms are less intense,

and 'satellites' from coupling to  $^{195}\text{Pt}$  are not observed. Attempts to prepare a monomethylamine derivative [which might contain a simple N(7),(C-6)O chelate] resulted only in mixtures of (III) and (IIId).

The complex (III) dissolves in dilute NaOD-D<sub>2</sub>O solution. Three different Pt-Me peaks are observed in the  $^1\text{H}$  n.m.r. spectrum, none of which has a Pt-Me coupling large enough to correspond to a methyl group *trans* to co-ordinated H<sub>2</sub>O or theophyllinate (C-6)O (Table). Formulations such as  $[\text{PtMe}_3\{\text{N}(7)\text{-thp}\}(\text{OH})_2]^{2-}$ ,  $[\text{PtMe}_3\{\text{N}(7)\text{-thp}\}(\text{OH})(\text{H}_2\text{O})]^-$ , or  $[\text{PtMe}_3\{\text{N}(7), (\text{C}-6)\text{O-thp}\}(\text{OH})]^-$  can thus be eliminated. The only structure consistent with the spectrum is a cyclic oligomer in which each Pt atom is co-ordinated

to N(7) of one theophyllinate group, N(9) of another, and the hydroxide group, as in (IV), which is probably stabilized by Pt-OH... (C-6)O hydrogen-bonding. A trimer is likely, but this cannot be confirmed by molecular weight measurements for this ionic species. Unfortunately, the complex slowly decomposes in solution, which has prevented us from obtaining a satisfactory  $^{13}\text{C}$  n.m.r. spectrum. We have also prepared dimethylplatinum(IV) analogues of (IV),  $[\text{PtMe}_2\text{X}(\text{thp})(\text{OH})]_n^-$  (X = Br or OH), in solution.

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