Synthesis and NMR Assignments of some Platinum(II) Complexes of 3-Aryl-5,5-dimethyl-2-pyrazolines

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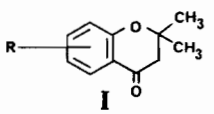
Abstract

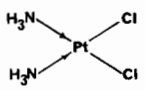
The synthesis of platinum(II) complexes of 3-aryl-5,5-dimethyl-2-pyrazolines has been examined in an attempt to obtain analogues of the biologically active so called 'cisplatin' complexes. The ^{1}H and ^{13}C NMR and IR spectral data for the complexes synthesized are presented and discussed, together with the physical data of some isolated complexes to support the arguments suggested by the spectroscopy.

Introduction

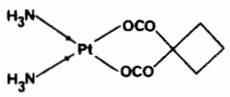
In our recent article [1], we examined the reactions between Zeise's salt and tert-amine *N*-oxides, and as part of our study on the synthesis of some naturally occurring 2,2-dimethylchroman-4-one derivatives (**I**) [2], we are interested in a potential reaction between 3-aryl-5,5-dimethyl-2-pyrazolines (**V**) and the *cis*-$[PtCl_2(DMSO)_2]$ complex in order to obtain complexes analogous to the cisplatin complexes (**II**–**IV**).



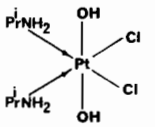
I



II
cisplatin



III
carboplatin



IV
iproplatin

Considerable interest has developed recently in the synthesis and biological evaluation of platinum complexes of nitrogenous derivatives of five-membered heterocycles [3]. These syntheses have been supported by the discovery that most of these complexes have a broad spectrum of biological properties including antibacterial and antitumour activities [4–6].

These results encouraged our attempted synthesis of platinum(II) complexes (**VI**) of 2-pyrazolines (**V**), which could be regarded as structural analogues to some biologically active palladium–pyrazole complexes [7]. Compounds **V** have been prepared from the reaction of 2,2-dimethyl-chroman-4-ones (**I**) with hydrazine hydrate and characterized at our laboratories [2].

Experimental

General

Natural abundance, proton-decoupled FT ^{13}C NMR spectra were recorded at ambient temperature on a Bruker-WH90 DS spectrometer, operating at 22.63 MHz, equipped with an aspect 2000, 32 K computer. The pulse widths of 6 s and 3 s delay were used, and between *ca.* 1000 to 5000 scans (depending on the nature of the compound) were accumulated with 16 K data points for a spectral width of 4807 Hz. ^{1}H NMR spectra were recorded on the same spectrometer, using the deuterium signal of the solvent as a field lock signal.

IR spectra were recorded on an SP2000 spectrometer at a range between 200 and 4000 cm^{-1} using Nujol mull.

Analyses of the complexes were carried out on a CHN Analyser, type 1106 (Carlo Erba).

Preparation of Starting Materials

3-Aryl-5,5-dimethyl-2-pyrazolines (V)

These compounds were prepared from the reaction between 2,2-dimethylchroman-4-ones and hydrazine hydrate and characterized as described in our previous report [2].

cis-Dichlorobis(dimethylsulphoxide)platinum(II)

This complex, *i.e. cis*-$[PtCl_2(DMSO)_2]$ was prepared and characterized as described in the literature [8].

Preparation of Complexes VI

The complexes were prepared according to Scheme 1, and here we describe in detail the prepara-

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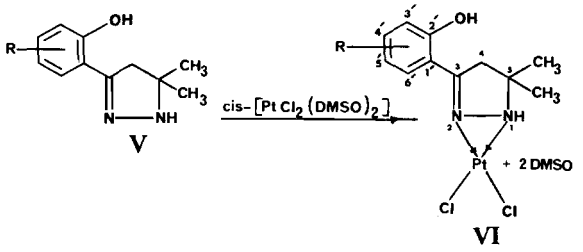

a, R = 4′-OCH_3 e, R = 3′,4′-$(CH_3)_2$
b, R = 4′,5′-$(OCH_3)_2$ f, R = 3′,5′-$(CH_3)_2$
c, R = 4′,6′$(OCH_3)_2$ g, R = 4′,6′-$(CH_3)_2$
d, R = 3′,4′,5′-$(OCH_3)_3$ h, R = 4′,5′-$(CH_3)_2$

Scheme 1. Reactions of pyrazoline compounds with *cis*-$[PtCl_2(DMSO)_2]$.

tion and full characterization of only two complexes, **VIc** and **VIg** as a model for the others.

The platinum complex *cis*-$[PtCl_2(DMSO)_2]$ (0.211 g, 0.50 mmol) was suspended in chloroform (15 ml) and the pyrazoline ligand **Vc** (0.135 g, 0.54 mmol) or **Vg** (0.12 g, 0.55 mmol) was dissolved in chloroform (10 ml) and immediately added to the suspension under nitrogen. The mixture was warmed carefully until a clear yellow solution formed which after standing for only a few minutes turned turbid. It was stirred for *ca.* 24 h. The mixture was reduced in volume to *ca.* 5 ml and the resulting yellow solid was filtered off, washed with n-hexane several times and dried *in vacuo* for several hours.

Results and Discussion

The platinum complexes (**VI**) were obtained from the reaction of pyrazoline compounds (**V**) with *cis*-$[PtCl_2(DMSO)_2]$ in chloroform (Scheme 1).

The more recent article by Saha *et al.* [7] dealt with the preparation of palladium complexes containing pyrazole-derived ligands. However, they believe that the ligand molecule behaves as an (*N,N*) bidentate ligand in its 'imidol' form. Our findings are in agreement with the fact that the platinum metal coordinates similarly through both nitrogens of the pyrazolines. The structures of complexes **VI** were determined on the basis of elemental analyses and spectroscopic data (IR, ^1H and ^{13}C NMR).

Infra Red Assignments

The IR data of complexes **VIc** and **VIg** are listed in Table I. The ν(Pt–Cl) appeared as a double band at 335 and 350 cm^{-1}, for example, which assigned a *cis*-platinum complex [9], as the *trans* gives only a single band. In addition, the ν(Pt–N) for these complexes appeared as double bands at 470 and 480 cm^{-1}, for example, which again confirms the presence of a *cis*-complex with two different nitrogens. Other IR stretching frequencies such as C=C and C=N also appeared in the spectra (Table I), and the ν(N–H) is overlapped with the ν(–OH) to give a broad band at more than 3000 cm^{-1}.

^1H NMR Assignment

All the complexes (**VIa–VIh**) are highly insoluble in most solvents, however, they are appreciably soluble in donor solvents, e.g. DMSO. Therefore, they were dissolved in DMSO-d_6 for recording the NMR spectra. The special feature of the ^1H NMR spectra of the pyrazoline complexes (**VIa–VIh**) (Table II) is that the methyl groups (C5-CH_3) resonate as a singlet at a slightly higher field (δ1.28–1.38 ppm) than that (δ1.38–1.42 ppm) in chromanone (**I**) [2]. The spectrum of the other hydrogens in the molecule was almost similar to that of the ligand (**V**). The methylene protons appear in the range δ2.5–2.62 ppm as a singlet and typical aromatic multiplets near δ6.6–7.6 ppm are consistent with the structures **VIa–VIh**.

^{13}C NMR Assignments

We decided to examine the ^{13}C NMR spectra of complexes **VIa–VIh** in more detail in order to check the assignments of the structures (Table III).

We examined complexes **VIc** and **VIe–VIg** as a model for the complexes **VIa–VIh**. By single frequency off-resonance decoupling experiments (sford), signal intensities and comparisons to structurally

TABLE I. The Properties of the Platinum Complexes VIc and VIg

Complex	Colour	Melting point (dec.) (°C)	Analyses: found (calc.) (%)			Characteristic IR data (cm^{-1})[a]			
			C	H	N	ν(Pt–Cl)	ν(Pt–N)	ν(C=N)	ν(C=C)
VIc	yellow	220–226	29.87 (30.23)	3.33 (3.49)	5.25 (5.43)	335, 350m	470, 482m	1530s	1625s (sh)
VIg	yellow–orange	228–232	31.99 (32.23)	3.61 (3.27)	5.45 (5.79)	345br	440, 455w	1560w	1612m

[a]m. medium; s, small; w, weak; br, broad; sh, shoulder.

TABLE II. The ^{1}H NMR Data[a] (δ[b] (ppm) and J (Hz)) for Complexes **VIa–VIh**

Complex	(C5-CH_3)[c]	(H-4)[c]	Ar–H	R–H	δ N–H
VIa	1.38	2.52	H-5′(6.6, dd, J = 8 and 1) H-3′(6.4, d, J = 1) H-6′(7.8, d, J = 8)	3.78, S, 3H, OCH_3	8.4
VIb	1.30	2.50	H-3′(6.42, s) H-6′(7.3, s)	3.72, s, 3H, CH_3 3.74, s, 3H, CH_3	8.4
VIc	1.38	2.62	H-5′(6.12, d, J = 1) H-3′(6.22, d, J = 1)	3.8, s, 3H, OCH_3 3.86, s, 3H, OCH_3	7.8
VId	1.35	2.52	H-4′(6.4, s)	3.81, s, 9H (3-OCH_3)	8.38
VIe	1.30	2.53	H-6′(7.6, d, J = 8) H-5′(6.75, d, J = 8)	2.05, s, 3H, CH_3 2.2, s, 3H, OCH_3	8.3
VIf	1.30	2.52	H-6′(7.51, broad) H-4′(6.85, borad)	2.15, s, 3H, CH_3 2.25, s, 3H, CH_3	8.3
VIg	1.35	2.5	H-3′ (6.6, broad, 2H) H-5′	2.6, s, 6H, (2-CH_3)	8.25
VIh	1.28	2.5	H-6′(7.61, s) H-5′(6.62, s)	2.15, s, 6H (2-CH_3)	8.2

[a]Spectra were recorded using DMSO-d_6 as solvent. [b]Downfield from internal TMS. [c]Singlet (2H) for H-4 and (6H) for two methyl groups.

TABLE III. ^{13}C NMR Chemical Shifts[a] for Complexes **VIc** and **VIe–VIg**

Carbon	Compound **Vb**[b]	Complexes			
		VIc	**VIe**	**VIf**	**VIg**
C-3	143.2	158.6	153.4	155.9	156.95
C-4	33.7	37.6	38.6	37.2	37.4
C-5	74.9	75.9	75.8	76.2	76.7
C-1′	101.3	110.7	116.9	116.7	116.1
C-2′	150.0	159.3	155.5	154.5	156.9
C-3′	112.6	94.2	121.8	122.7	116.5
C-4′	147.5	160.1	137.5	137.45	139.3
C-5′	137.9	94.2	124.5	128.3	125.8
C-6′	105.0	162.8	121.8	120.8	139.9
C5-CH_3	26.6	26.3	26.8	26.8	26.8
R	55.8	56.1	19.7	17.8	21.8
	55.4	55.3			

[a]Spectra were recorded using DMSO-d_6 as solvent. Downfield from internal TMS. [b]Data for the free ligand are listed here for comparison.

related compounds, the chemical shift assignments of these complexes were achieved. The multiplets at δ = 155.9–158.6 ppm and 75.8–76.6 ppm were distinguished by their appearance as a singlet in the sford spectra and assigned to quaternary carbons, *i.e.* C-3 and C-5 respectively of the pyrazole moiety. The lone singlet (sford) in the range δ37.2–38.6 ppm was unambiguously assigned to C-4. The special feature of the ^{13}C NMR spectra of the platinum complexes of pyrazoline is that the heterocyclic carbons of the pyrazole moiety (C3, C4 and C5) in complexes **VI** resonate at lower field than that in the ligand (**V**). This means that the presence of a platinum metal coordinated to a nitrogen-containing ring causes a pronounced downfield shift in the ring carbons in comparison with the corresponding carbocyclic analogue (Table III).

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