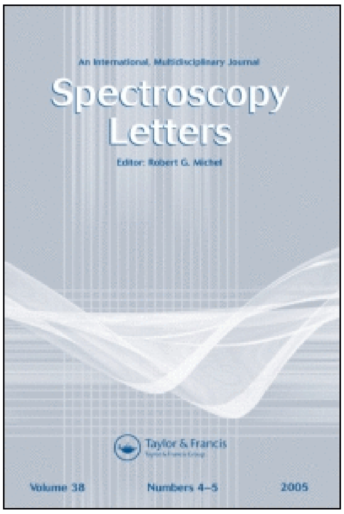

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Claudia C. Wagner[a]; Enrique J. Baran[a]
[a] Centra de Química Inorgánica (CEQUINOR, CONICET/UNLP), Facultad de Ciencias Exactas, Universidad Nacional de La Plata, Argentina

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VIBRATIONAL SPECTRUM OF A PLATINUM COMPLEX OF PIROXICAM

Key Words: Platinum(II); Piroxicam; Infrared Spectrum; Raman Spectrum.

Claudia C.Wagner and Enrique J.Baran*

Centro de Química Inorgánica (CEQUINOR, CONICET/UNLP), Facultad
de Ciencias Exactas, Universidad Nacional de La Plata, C.Correo 962,
1900-La Plata, Argentina

ABSTRACT. The infrared and Raman spectra of a platinum complex of the antiinflammatory drug piroxicam (Pir) and dimethylsulfoxide (DMSO) of composition [$PtCl_2Pir(DMSO)$] were recorded and briefly discussed on the basis of its structural characteristics. The metal-to-ligand vibrations are analyzed in detail.

INTRODUCTION

Piroxicam (4-hydroxy-2-methyl-N-2-(pyridyl)-2H-1,2-benzothiazine-3-carboxamide 1,1-dioxide, Fig.1) is a well known and very effective antiinflammatory drug [1].

Recently, a neutral piroxicam complex of platinum could be prepared and thoroughly characterized [2]. This is the first example of a piroxicam complex of a metal of the third transition metal series, and such type of complexes are of interest due to its possible antineoplastic activity [3-5].

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*Author to whom correspondence should be addressed

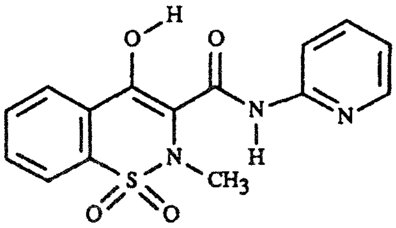

Fig.1. Structure of piroxicam.

The crystal structure of this new complex, of composition [$PtCl_2Pir(DMSO)$], reveals that the coordination around Pt(II) is almost square planar. The metal ion is linked to two *trans* chloride ions, to the pyridyl nitrogen atom of piroxicam and to the sulfur atom of a dimethylsulfoxide molecule [2].

It is very interesting to gain a wider insight into the general physicochemical properties of this new complex. Therefore, in the present paper, we report our results on its vibrational spectroscopic properties from an analysis of its infrared and Raman spectra.

EXPERIMENTAL

Pharmaceutical grade piroxicam (Schweizerhall), K_2PtCl_4 from Aldrich, DMSO from Merck, and n-butanol from Mallickrodt were used as supplied. The complex was obtained as described earlier, by reaction of hot DMSO solutions of K_2PtCl_4 and piroxicam, and precipitation by addition of n-butanol [2].

The infrared spectra in the range between 4000 and 200 cm^{-1} were recorded with a Perkin Elmer 580 B spectrophotometer, using the KBr pellet technique. Infrared spectra in the region between 600 and 100 cm^{-1} were also measured with a Bruker FTIR model 113v instrument, with the powdered samples dispersed in polyethylene discs. The Raman spectra were obtained with a Bruker IF66 FTIR spectrophotometer provided with the FRA 106 Raman accessory. The samples were excited with the 1064 nm line of a Nd:YAG laser (power = 100 mW).

RESULTS AND DISCUSSION

In the spectral range between 4000 and 700 cm^{-1} the spectra of free piroxicam and of the complex are very similar. Only minor intensity changes and small band shifts could be detected. This behavior is not totally unexpected, as coordination involves only the pyridyl N-atom [2].

As the IR and Raman spectra of piroxicam and of some of its metallic complexes have been discussed in detail in a previous paper [6] it seems unnecessary to repeat this analysis here. Thus, in Table 1 we present only a brief assignment of the most characteristic and important bands found in this region. Some additional comments on this assignment and on the spectral changes observed after complexation are given below.

The well-defined IR bands of piroxicam at 3394 and 3338 cm^{-1} are assigned to the ν(N-H) and ν(O-H) stretching vibrations respectively [6,7]. In the complex, both bands are displaced to lower frequencies. The ν(N-H) mode is only seen as a weak shoulder at 3244 cm^{-1}, whereas the intensity of the hydroxyl stretching is considerably lowered. The important displacement of the ν(N-H) band is consistent with the existence of a strong Pt$\cdots$HN attractive interaction, as revealed by the structural analysis [2].

After complexation, the so-called amide **I** band, which represents mainly the ν(C=O) stretching mode [6,7,9], is slightly displaced to higher wavenumbers in the IR spectrum, whereas in the Raman spectrum it is less affected.

The amide **II** and the amide **III** bands, which in secondary amides are probably mixed motions involving the N-H in plane bending and the C-N stretching vibration [6], are practically not affected.

TABLE 1

Assignment of the most characteristic IR and Raman bands of piroxicam and of [$PtCl_2$Pir(DMSO)] in the range between 4000 and 700 cm^{-1}

Piroxicam		[$PtCl_2$Pir(DMSO)]		
IR	Raman	IR	Raman	Assignment
3394 s		3244 sh		ν(O-H)
3340 vs		3224 m		ν(N-H)
1633 vs	1606 vs	1651 s	1598 vs	amide **I**
1579 s	1576 m	1574 m	1575 w	amide **II**
1529 vs	1522 vs	1513 vs	1517 s	
1471 w	1474 m	1470 w	1468 w	see text
1436 vs	1434 vs	1435 vs	1438 m	
1352 vs		1348 s	1344 w	$\nu_{as}(SO_2)$
1310 vs	1310 w	1309 s	1313 m	amide **III**
1182 vs	1176 m	1179 m	1162 m	$\nu_s(SO_2)$
1094 m	1090 vw	1090 w	1085 vw	δ(OH)
830 vs	830 m	824 m	826 m	
773 vs	780 w	781 m	780 w	see
763 m	764 vw	765 w	762 m	text
732 vs	736 vw	730 m	733 w	
691 s	695 vw	689 w	693 m	δ(NH)

vs: very strong; s: strong; m: medium; w: weak; vw: very weak.

The group of strong bands in the region between 1530 and 1430 cm^{-1} involves mainly (C-C) and (C=N) stretchings, as well as CH_3–deformational modes [6]. On the other hand, the block of bands between 830 and 730 cm^{-1} are assigned to δ(CH) and ring modes [6,8].

In relation to the typical DMSO bands, the strong ν(S=O) vibration, which in the free compound lies at 1042 cm^{-1} in both the IR and Raman spectra [10], and is expected to be displaced to higher energy after coordination [11,12], is surely overlapped with a strong piroxicam band which in the free ligand is observed at 1150 cm^{-1} [6] and which in the complex appears somewhat broadened at 1153 cm^{-1} with a shoulder at 1127 cm^{-1}. Some other important DMSO bands in the 1300-1450 cm^{-1} and 700 cm^{-1} regions [10] are also overlapped with piroxicam features.

The spectral range below 700 cm^{-1} is of special interest because in this region the different metal-to-ligand vibrations are expected. Fig.2 shows the infrared spectra of free piroxicam and of the investigated complex between 700 and 40 cm^{-1}. The band positions, together with the proposed assignments of some of the most important and characteristic vibrations in this region, are presented in Table 2.

The very strong 626/620 cm^{-1} doublet of free piroxicam is probably of complex nature, involving δ(OCN) and out-of-plane δ(CO) modes, as previously discussed [6]. But, on the other hand, from the spectroscopic behavior of simple metallic complexes of pyridine, it is known that after complexation the vibrations in the high frequency region are not appreciably shifted, whereas the characteristic ring deformations found at 604 and 405 cm^{-1} in free pyridine are shifted to higher frequencies [11,13]. In the IR spectrum of the complex only one band, at 620 cm^{-1}, is found in this region; whereas a new feature located at 653 cm^{-1} is observed which we tentatively assign to one of the mentioned pyridine deformational modes. The other one is clearly observed as a new IR band at 441 cm^{-1} (435 cm^{-1} in the Raman spectrum).

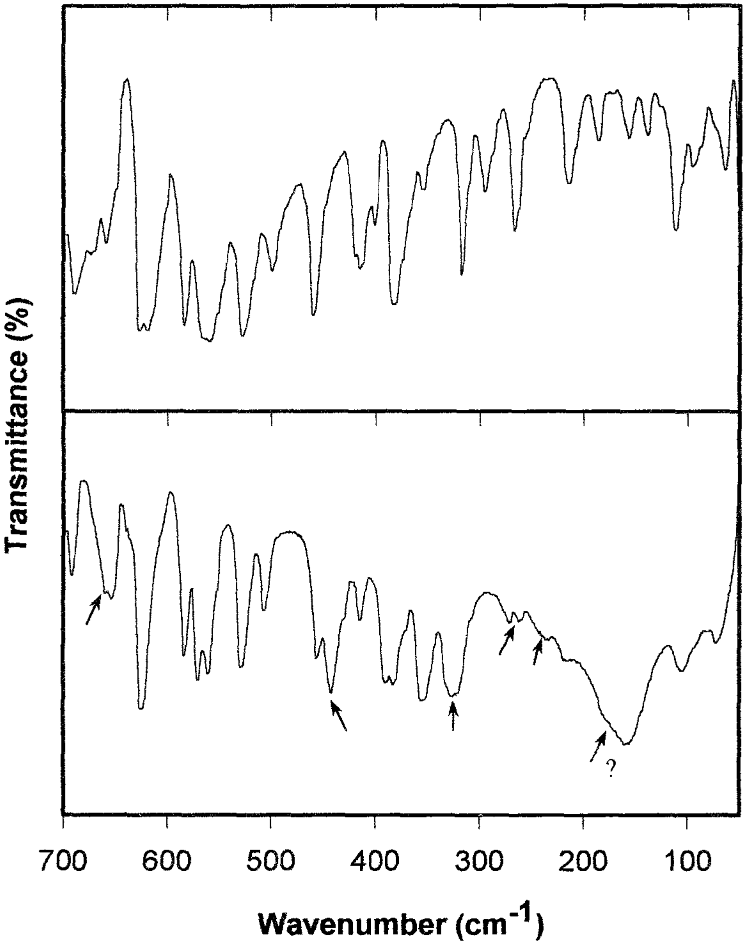

Fig.2. IR spectra between 700 and 40 cm^{-1} of piroxicam (above) and of [$PtCl_2$Pir(DMSO)] (below) (The metal-to-ligand vibrations are marked with arrows).

TABLE 2

IR and Raman spectra of piroxicam and of [$PtCl_2Pir(DMSO)$] in the range between 700 and 40 cm^{-1}.

Piroxicam		[$PtCl_2Pir(DMSO)$]		
IR	Raman	IR	Raman	Assignment
691 s	695 vw	689 s	693 m	δ (NH)
658 m	654 w	660 sh	658 m	
		653 s		δ(CCC)py
626vs/620vs	624 w	623 vs	620 w	
582 vs	581 w	582 vs	580 vw	
563 sh		569 vs	565 w	
557 vs		559 vs	556 w	
525 vs	510 vw	526 vs	520 vw	
497 w		504 m		
456 vs	457 vw	454 m	458 w	
		441 s	435 w	δ(CCC)py
420sh/411s	405 s	413 w	406 s	
397 w		388 s		
378 vs	375 m	379 s	378 m	
350 w	351 m	351 vs	350 m	
313 vs	310 w	325sh/320vs	320w/309w	ν(Pt-Cl)
291 m	293 w		298 m	
		268 w		
261 s	257 w	256 w	260 w	ν(Pt-N)
		231 w	236 w	ν(Pt-S)
208 s	207 w	212 w	206 m	
181 w	183 w		186 s	
151 w	166m/153s	153,vs,br	171 m	
136 w	124 m		148 m	
106 s	104 m	98 m	127 s	
89w/80sh	90 vs		85 vs	
59 m/43vs		65 w		

vs: very strong; s: strong; m: medium; w: weak; vw: very weak; sh: shoulder; br; broad.

The Pt-Cl stretching band appears as a shoulder in both the IR and Raman spectra (325 and 320 cm^{-1}, respectively). Only one band is seen for this vibration, as expected for a *trans* ligand arrangement [11] and it is found in the same region as in other Pt(II) chloro complexes [11].

The ν(Pt-N) vibration is found in the same region as in some pyridine complexes [11].

The assignment of the Pt-S stretching vibration is more difficult to made. We propose to assign the weak IR band at 231 cm^{-1} to this mode but it is also possible that this vibration lies under the strong and broad IR band centered at 153 cm^{-1}.

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