Synthesis, crystal structure and molecular orbital investigation of the first platinum complex of piroxicam †

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The first platinum complex [PtCl$_2$(dmso)(HL)] of the widely used anti-inflammatory drug piroxicam (HL = 4-hydroxy-2-methyl-*N*-(2-pyridyl)-2*H*-1,2-benzothiazine-3-carboxamide 1,1-dioxide; dmso = dimethyl sulfoxide) was obtained from K$_2$[PtCl$_4$]. Its crystal structure reveals that the metal atom is linked to the pyridyl nitrogen atom. A Pt ··· H–N (amide) interaction is present and made possible by the orientation of the HL molecule which brings the N(amide)–H bond above the co-ordination plane and almost parallel to the N (pyridyl)–Pt vector. The amide hydrogen was located from the Fourier-difference-synthesis and its position refined. The Pt ··· H distance is 2.35 Å (0.25–0.55 Å shorter than the sum of the van der Waals radii), whereas the ν(N–H) vibration band is red-shifted by about 90 cm^{-1} upon complexation. An extended-Hückel molecular orbital analysis revealed that a mixing of d$_{z^2}$(Pt) and p$_z$[N(amide)] atomic orbitals occurs, whereas electrostatic Pt ··· H attractive forces can play a significant role.

Interest in neutral complexes of platinum(II) arises from the high anticancer activity of *cis*-[Pt(NH$_3$)$_2$Cl$_2$] (cisplatin) and related species. However, the antineoplastic activity of platinum(II) compounds is not restricted to cisplatin-type complexes and the preparation of new compounds is important to investigate potential activities, better to understand the structure–activity relationship, and to shed light on the drug–biosystem interaction.[1]

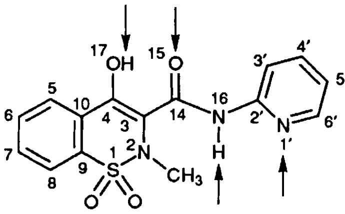
Piroxicam[4-hydroxy-2-methyl-*N*-(2-pyridyl)-2*H*-1,2-benzothiazine-3-carboxamide 1,1-dioxide; feldene, Pfizer] is an extensively used anti-inflammatory, anti-arthritic drug of the carboxamide family (Scheme 1). The drug, which has a variety of possible donor sites such as N(1′), N(2), O(17), O(15), may act as a monodentate and/or chelating agent, and its ligating ability towards some first-row transition-metal and zinc(II) and cadmium(II) ions has recently been investigated.[2] The oxygen-radical-scavenger activity of the copper(II) derivative has also been studied.[3] The structural investigation of metal–piroxicam complexes is important to analyse both the ligating ability of the drug and the effects of co-ordination on the conformation of the HL/L$^-$ molecules. Complexes [PtX$_2$(L′)(HL)] (X = halide, L′ = easily removable ligand) can be of interest both for the potential anticancer activity derived from the PtX$_2$ function or from the metal-linked HL moiety (*e.g. via* platinum– and/or HL–nucleic acid interaction), and for anti-inflammatory tests. Furthermore, weak forces as those of the Pt^{II} ··· Pt^{II} and Pt^{II} ··· H(N/C) type and hydrogen bonds are important for the stability of a number of compounds[4,5] and help to understand the activation of H–N and H–C bonds.[5]

Here I report on the synthesis and structural characterization of [PtCl$_2$(dmso)(HL)] (dmso = dimethyl sulfoxide) which is the first complex of piroxicam with any of the third series of d-block elements to be analysed *via* X-ray diffraction.

Experimental

Materials

Piroxicam was a gift from Pfizer Italia spa; K$_2$[PtCl$_4$] was obtained from Janssen (Belgium), dimethyl sulfoxide, *n*-butanol and PhCl from Merck (Germany).



Scheme 1 Neutral piroxicam HL in the 4,16-*EZE* conformation

Preparation of *trans*-[PtCl$_2$(dmso)(HL)]

A mixture of K$_2$[PtCl$_4$] (200 mg, 0.48 mmol) and dmso (4 cm^3) was stirred at room temperature for about 0.5 h. The white precipitate (KCl) was filtered off, and the yellow filtrate added to a solution of HL (166 mg, 0.5 mmol) in dmso (4 cm^3). The mixture was stirred at 110 °C for 0.5 h (it turned orange) and then Bu^{n}OH (35 cm^3, 110 °C) slowly added. A fine pale yellow crystalline solid formed. The final suspension was left to cool to room temperature. The solid was filtered off and washed with a small amount of dmso, Bu^{n}OH (twice) and diethyl ether, and finally dried under vacuum at 40 °C for 24 h. Yield *ca.* 50% (Found: C, 30.60; H, 2.90; Cl, 10.1; N, 6.50; Pt, 28.1; S, 9.30. Calc. for C$_{17}$H$_{19}$Cl$_2$N$_3$O$_5$PtS$_2$: C, 30.25; H, 2.85; Cl, 10.50; N, 6.20; Pt, 28.90; S, 9.50%). The complex is insoluble in all of the common solvents tested and is just slightly soluble in dmso and hot chlorobenzene. Single crystals (yellow) suitable for X-ray diffraction were obtained from a solution prepared by dissolving the microcrystalline compound (10 mg) in chlorobenzene (40 cm^3) at reflux.

Crystal-structure determination

A well formed prism (0.25 × 0.35 × 0.35 mm) was selected and mounted on a glass fibre for the X-ray data collection, which was carried out on a Siemens P4 automatic diffractometer operating at 22 °C. Crystallographic data are reported in Table 1. Unit-cell parameters were obtained by least-squares refinement of the values of 25 carefully centred and randomly selected reflections (2θ 10–30°). The intensities were corrected for Lorentz, polarization and absorption effects (ψ-scan technique based on the reflections −1 1 3, 3 −1 −4 and 6 0 −14). The structure solution and refinement (space group, $P2_1/c$, no. 14, from systematic absences; mean $|E^2 - 1|$ = 0.925, 0.968 for centrosymmetric and 0.736 for non-centrosymmetric space

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† 4-Hydroxy-2-methyl-*N*-(2-pyridyl)-2*H*-1,2-benzothiazine-3-carboxamide 1,1-dioxide.

groups) were performed through Patterson and Fourier methods. Two independent complex molecules are present in the asymmetric unit. The Pt, Cl, S, O, N and C atoms were treated anisotropically, the H atoms isotropically. The full-matrix least-squares cycles converged to $R = 0.0458$ and $R' = 0.0477$. Atoms H(16a), H(17a) and H(17b) were located through the Fourier-difference synthesis whereas all the other H atoms were set in calculated positions. The scattering factors were those of SHELX 76[6] and SHELXS 86[7] and of ref. 8. The isotropic thermal parameters for H(17a) and H(17b) and the H(16a) proton were fixed at 0.08 and 0.06 Å^2, respectively. The atomic coordinates are listed in Table 2. All the calculations were carried out on VAX 6610 and IBM 3090 machines using SHELXS[6,7] and PARST[9] computer packages.

Complete atomic coordinates, thermal parameters, and bond lengths and angles have been deposited at the Cambridge Crystallographic Data Centre; see Instructions for Authors, *J. Chem. Soc., Dalton Trans.*, 1996, Issue 1.

Table 1 Crystal data for *trans*-[PtCl$_2$(dmso)(HL)]

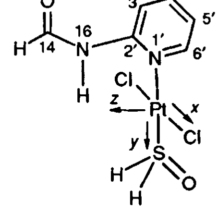
Formula	$C_{17}H_{19}Cl_2N_3O_5PtS_2$
M	675.5
Crystal system	Monoclinic
Space group	$P2_1/c$ (no. 14)
a/Å	16.685(4)
b/Å	12.560(3)
c/Å	21.941(5)
β/°	103.79(3)
U/Å^3	4466(2)
Z	8
F(000)	2608
D_c/g cm^{-3}	2.01
λ(Mo-Kα)/Å	0.710 73
μ/cm^{-1}	67.45
Total number of reflections	6160
Number of observed reflections [$F > 4\sigma(F)$]	4277
$R = \Sigma\|\|F_o\| - \|F_c\|\|/\Sigma\|F_o\|$	0.0458
$R' = \Sigma w^{\frac{1}{2}}\|\|F_o\| - \|F_c\|\|/\Sigma w^{\frac{1}{2}}\|F_o\|$	0.0477
$w = a/[\sigma^2(F) + bF^2]$	$a = 0.9381, b = 0.002\,618$
Parameters refined	585

Infrared spectroscopy

The IR spectra were recorded *via* the KBr pellet technique on an FT-IR Perkin-Elmer model 1600 spectrometer.

Molecular orbital calculations

Extended-Hückel (EH) type molecular-orbital calculations were carried out using the ICONC&INPUTC package[10] implemented on a VAX 6610 computer. The parameters used were those standard in the program. The distance-dependent weighted Wolfsberg–Helmholz formula[10,11] was applied. In order to simplify the analysis, the molecule *trans*-[PtCl$_2$(H$_2$SO){NC$_5$H$_4$(NHCOH)-2}] (Scheme 2) was studied



Scheme 2 Representation of the molecule *trans*-[PtCl$_2$(H$_2$SO){NC$_5$H$_4$(NHCOH)-2}] showing the coordinate system used

Table 2 Atomic coordinates (× 10^4) for the non-hydrogen atoms of *trans*-[PtCl$_2$(dmso)(HL)] with e.s.d.s in parentheses. The coordinates of the H(16) atoms are also included

	Molecule a			Molecule b		
Atom	X/a	Y/b	Z/c	X/a	Y/b	Z/c
Pt	1135.4(6)	1036.2(8)	1113.9(7)	4301.0(6)	5760.0(8)	3690.0(8)
Cl(1)	1154(3)	−671(3)	806(2)	3773(2)	4270(3)	4059(2)
Cl(2)	828(3)	2702(3)	1413(2)	4826(3)	7316(3)	3403(2)
S(1)	3091(2)	822(3)	3260(2)	2177(2)	5932(3)	1747(1)
S(d)	2253(2)	1632(3)	852(2)	4800(2)	4778(3)	3022(2)
O(1)	3586(6)	1565(8)	3021(5)	2022(5)	5032(7)	2101(4)
O(2)	3094(6)	−269(7)	3085(5)	2814(6)	5819(7)	1400(4)
O(d)	2118(7)	2123(11)	227(5)	5566(6)	4232(9)	3288(5)
O(15)	300(5)	−153(7)	3258(4)	1468(6)	7812(8)	3453(4)
O(17)	1381(6)	−190(7)	4302(4)	343(5)	7612(7)	2409(4)
H(17)	817(89)	−583(111)	3947(67)	572(88)	7762(111)	2907(68)
N(1′)	65(7)	493(9)	1335(5)	3806(6)	6617(8)	4307(4)
N(2)	2135(7)	1231(8)	3079(5)	2434(5)	6937(7)	2227(4)
N(16)	711(7)	415(9)	2382(5)	2768(6)	7133(8)	3506(4)
H(16)	1256(77)	717(94)	2184(55)	3166(6)*	6844(8)*	3220(4)*
C(2′)	−20(8)	291(10)	1912(6)	3096(7)	7160(9)	4132(5)
C(3′)	−757(8)	−44(9)	2026(6)	2759(10)	7644(11)	4582(6)
C(4′)	−1455(9)	−119(10)	1526(7)	3164(11)	7604(12)	5202(6)
C(5′)	−1362(11)	100(14)	924(8)	3899(11)	7065(14)	5383(6)
C(6′)	−592(9)	415(13)	835(7)	4193(9)	6599(11)	4927(6)
C(3)	1634(7)	620(9)	3381(6)	1763(8)	7253(9)	2503(5)
C(4)	1890(8)	355(11)	3994(7)	980(6)	7309(9)	2167(5)
C(5)	2909(11)	531(12)	5032(7)	−4(8)	7350(11)	1128(7)
C(6)	3720(12)	772(14)	5373(7)	−222(9)	7057(13)	491(8)
C(7)	4296(12)	1077(13)	5074(8)	307(9)	6482(14)	250(7)
C(8)	4109(9)	1141(11)	4427(7)	1042(11)	6108(14)	606(6)
C(9)	3334(8)	883(10)	4075(7)	1251(9)	6391(10)	1245(6)
C(10)	2705(9)	598(11)	4381(6)	741(7)	7017(10)	1510(6)
C(13)	1989(9)	2392(10)	3097(8)	2909(9)	7830(11)	2028(7)
C(14)	817(9)	255(10)	3024(6)	1975(8)	7439(10)	3189(5)
C(1d)	2978(12)	645(18)	867(13)	4041(10)	3833(12)	2641(8)
C(2d)	2818(12)	2455(17)	1429(9)	4879(11)	5511(15)	2352(7)

* The H(16b) atom was set in its calculated position.

Table 3 Selected bond distances (Å) and angles (°) for *trans*-[PtCl$_2$(dmso)(HL)]

Bond	Molecule a	Molecule b	Average	Bond	Molecule a	Molecule b	Average
Pt–Cl(1)	2.303(4)	2.296(4)	2.300	N(1′)–C(2′)	1.332(18)	1.344(15)	1.338
Pt–Cl(2)	2.288(4)	2.291(4)	2.290	N(1′)–C(6′)	1.356(16)	1.360(15)	1.358
Pt–S(d)	2.210(4)	2.224(4)	2.217	N(2)–C(3)	1.412(18)	1.450(17)	1.431
Pt–N(1′)	2.075(12)	2.049(10)	2.062	N(2)–C(13)	1.481(16)	1.497(18)	1.489
Pt · · · H(16)	2.34(12)	2.36(1)*	2.35	N(16)–C(2′)	1.405(15)	1.351(14)	1.378
S(1)–O(1)	1.427(11)	1.429(9)	1.428	N(16)–C(14)	1.394(18)	1.394(15)	1.394
S(1)–O(2)	1.424(10)	1.454(10)	1.439	N(16)–H(16)	1.16(14)	1.08(2)*	1.12*
S(1)–N(2)	1.632(11)	1.635(9)	1.634	C(3)–C(4)	1.352(18)	1.340(16)	1.346
S(1)–C(9)	1.740(15)	1.767(13)	1.754	C(4)–C(10)	1.453(18)	1.447(16)	1.450
S(d)–O(d)	1.469(12)	1.445(11)	1.457	C(9)–C(10)	1.420(22)	1.384(20)	1.402
S(d)–C(1d)	1.727(22)	1.791(15)	1.759	C(3)–C(14)	1.474(18)	1.480(16)	1.477
S(d)–C(2d)	1.730(19)	1.767(18)	1.749	C(2′)–C(3′)	1.378(21)	1.387(20)	1.383
O(15)–C(14)	1.215(19)	1.227(17)	1.221	C(3′)–C(4′)	1.400(18)	1.369(18)	1.385
O(17)–C(4)	1.384(19)	1.352(16)	1.368	C(4′)–C(5′)	1.393(25)	1.373(24)	1.383
O(17)–H(17)	1.18(13)	1.08(14)	1.13	C(5′)–C(6′)	1.401(25)	1.349(22)	1.375
S(d)–Pt–Cl(1)	92.1(2)	90.9(1)	91.5	N(2)–C(3)–C(4)	121(1)	122(1)	122
S(d)–Pt–Cl(2)	91.5(2)	93.7(1)	92.6	N(2)–C(3)–C(14)	120(1)	117(1)	119
S(d)–Pt–N(1′)	178.3(3)	177.7(3)	178.0	C(4)–C(3)–C(14)	119(1)	121(1)	120
Cl(1)–Pt–Cl(2)	176.2(2)	175.0(1)	175.6	H(17)–O(17)–C(4)	112(7)	109(7)	111
Cl(1)–Pt–N(1′)	88.1(3)	87.0(3)	87.5	C(3)–C(4)–O(17)	121(1)	124(1)	123
Cl(2)–Pt–N(1′)	88.2(3)	88.5(3)	88.4	C(3)–C(4)–C(10)	124(1)	122(1)	123
N(1′)–Pt · · · H(16)	65(3)	65.1(3)*	65	C(10)–C(4)–O(17)	115(1)	114(1)	115
Pt–S(d)–O(d)	115.6(5)	115.5(5)	115.6	C(4)–C(10)–C(9)	118(1)	121(1)	120
Pt–S(d)–C(1d)	112.5(8)	110.0(6)	111.2	S(1)–C(9)–C(10)	117(1)	117(1)	117
Pt–S(d)–C(2d)	111.0(8)	111.9(6)	111.4	C(3)–C(14)–O(15)	124(1)	121(1)	123
Pt–N(1′)–C(2′)	125.2(8)	123.0(7)	124.1	C(3)–C(14)–N(16)	112(1)	116(1)	114
Pt–N(1′)–C(6′)	114.2(10)	118.9(9)	116.6	O(15)–C(14)–N(16)	124(1)	123(1)	124
Pt · · · H(16)–N(16)	123(6)	118.7(7)	121*	N(16)–C(2′)–N(1′)	114(1)	113(1)	114
O(1)–S(1)–O(2)	119.4(7)	117.2(6)	118.3	N(16)–C(2′)–C(3′)	124(1)	127(1)	126
O(1)–S(1)–N(2)	108.9(6)	108.3(5)	108.6	N(1′)–C(2′)–C(3′)	122(1)	120(1)	121
O(1)–S(1)–C(9)	109.7(6)	110.6(6)	110.1	C(2′)–C(3′)–C(4′)	119(1)	120(1)	120
O(2)–S(1)–N(2)	107.6(6)	107.5(5)	107.6	C(3′)–C(4′)–C(5′)	118(1)	120(1)	119
O(2)–S(1)–C(9)	107.7(6)	110.2(6)	109.0	C(4′)–C(5′)–C(6′)	120(1)	117(1)	119
N(2)–S(1)–C(9)	102.2(6)	101.9(5)	102.0	C(5′)–C(6′)–N(1′)	120(1)	124(1)	122
C(3)–N(2)–S(1)	111.7(8)	111.7(7)	111.7	C(2′)–N(1′)–C(6′)	120(1)	118(1)	119
C(3)–N(2)–C(13)	114(1)	116(1)	115	O(d)–S(d)–C(1d)	106(1)	109(1)	108
C(2′)–N(16)–C(14)	127(1)	127(1)	127	O(d)–S(d)–C(2d)	112(1)	110(1)	111
S(1)–N(2)–C(13)	117.4(9)	117.9(8)	117.6	C(1d)–S(d)–C(2d)	99(1)	98(1)	99

* The H(16b) atom was set in its calculated position.

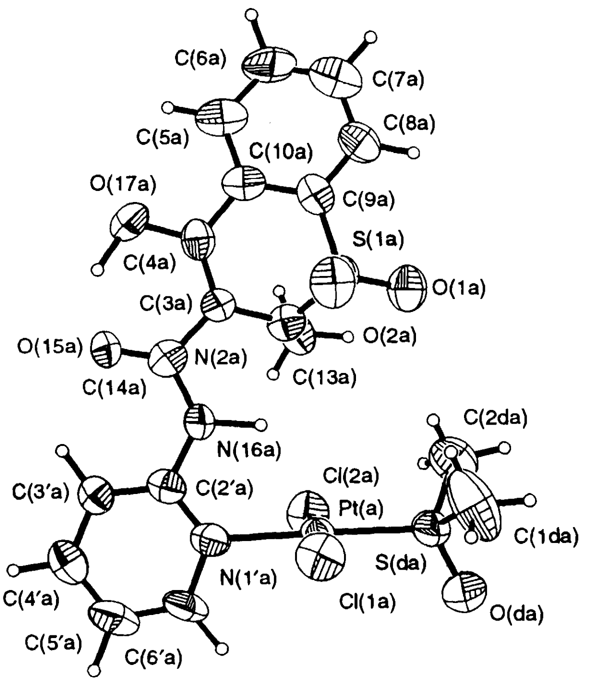


Fig. 1 One of the two complex molecules found in the asymmetric unit of the crystals of *trans*-[PtCl$_2$(dmso)(HL)]. The ellipsoids of the non-hydrogen atoms enclose 50% probability

in place of *trans*-[PtCl$_2$(dmso)(HL)]. The model molecule was constructed from the piroxicam complex using the molecular graphics package MacroModel[12] (graphics output: obtained *via* an Evans & Sutherland PS390 machine). Its geometry was kept fixed for all the calculations.

Results and Discussion

Selected bond lengths and angles are given in Table 3, and a drawing of one of the two molecules of the asymmetric unit is in Fig. 1. All the corresponding bond lengths and angles for the two molecules are equal within three times the estimated standard deviations (e.s.d.s). Each platinum atom is linked to two *trans* chloride ions, to the N(1′) atom from the pyridyl group and to the sulfur atom of a dmso molecule. The Pt–Cl, Pt–N and Pt–S bond distances average 2.294(3), 2.062(10) and 2.217(3) Å, respectively, in agreement with the values usually found for platinum complexes.[4,13–19] The geometry around the metal ion is almost square planar, the largest deviation from canonical values being the angle Cl(1b)–Pt–Cl(2b) [175.0(1)°]. The metal atom deviates by 0.027(2) Å (average) from the plane of the four donors. It is noteworthy that this deviation is towards the H(16) atom in both molecules. The distance of the H(16) atoms from the co-ordination planes is 2.1(1) Å (average), whereas the dihedral angle between the co-ordination plane and the N(2)C(3)[C(4)]C(14)[O(15)]N(16)-C(2′)C(3′)C(4′)C(5′)C(6′)N(1′) chain (see Scheme 1 and Fig. 1) of the HL ligand is 99.2(1) and 94.9(1)° for the two molecules, respectively. The Cl(2a)–Pt(1)–N(1′a)–C(2′a) and Cl(2b)–Pt(2)–N(1′b)–C(2′b) torsional angles are −78(1) and 81(1)°, respectively.

The H(16) atoms of both molecules have a short contact with the metal centre (average 2.35 Å; sum of the van der Waals radii 2.6–2.9 Å[20]). The N(16)–H(16) and the N(1)–Pt vectors are nearly parallel, the angles between the two lines being 8(5) and 16(1)° for molecule a and b, respectively. All these observations are evidence in favour of some Pt···HN linking interaction. The mean values of the Pt···H–N [121(3)°], H(16)–N(16)–C(2′) [114(3)°], H(16)–N(16)–C(14) [118(1)°], N(16)–C(2′)–N(1′) [114(1)°] and N(16)–C(2′)–C(3′) [126(1)°] angles are consistent with the Pt···HN linkage. The Pt–N(1′)–C(2′), Pt–N(1′)–C(6′), and N(1′)–Pt–S(d) angles average 124.1(7), 116.6(7), 182.0(3)° (on the side of N–H), respectively, in agreement with some crowding of the N(2)[C(13)]SO_2 portion of HL and the Cl^- ligands [*e.g.* Cl(12)···H(133) 3.01(2) Å; sum of van der Waals radii, 2.9–3.3 Å[20]].

It should be noted that the 360° rotation of the HL molecule around the Pt–N(1′) bond is not free because of the repulsive forces between some atoms of HL and the Cl^- ligands. For a Cl(2)–Pt–N(1′)–C(2′) angle (χ) equal 0 (the co-ordination square and the pyridyl ring almost coplanar) there are very short intramolecular contacts. In the case that all the bond lengths and angles are fixed at the values found in the solid-state structure, the N(16)···Cl(2) and C(6′)···Cl(1) intramolecular distances are 2.05(2) and 2.77(2) Å, respectively, much below the sum of the van der Waals radii (3.2–3.4 and 3.3–3.6 Å,[20] respectively). The trend of the N(16)···Cl(2) distance and of the N(16)–H(16)···Cl(2) angle as a function of χ is shown in Fig. 2. It is evident that a χ value of about −50° should provide a significant N(16)···Cl(2) intramolecular hydrogen bond [d(N···Cl) = 2.90 Å, angle 110°]. The N(16)···Cl(2) distance of 3.61(1) Å and the N(16)–H(16)···Cl(2) angle of 110(2)° found in molecule a indicate that the N(16)–H···Cl(2) interaction is, at best, very weak. This shows again that the Pt···H–N linking interaction is operative. The existence of an M···H–N (M = Pt[5,21–24] or Pd[21,23,25]) interaction has recently been a matter of investigation and debate. The interest arises because M···H–N/C interactions can cause H–N/C activation and because the linkage can influence the stability and reactivity of the metal complexes.[24]

The piroxicam molecule in the present complex is neutral, protonated at O(17) and has a 4,16-*EZE* conformation as that found in the solid-state structure of free piroxicam.[26] A recent molecular mechanics analysis showed that the *ZZZ* conformation is more stable [by *ca.* 3 kcal mol^{-1} (*ca.* 12.5 kJ mol^{-1})] than the *EZE* one;[3] the N(16)–H···O(17) hydrogen bond being one of the leading effects which favour *ZZZ*. Packing forces such as intermolecular hydrogen bonds and van der Waals interactions can explain the preference for *EZE* in the solid state. The existence of the Pt···HN interaction in the present structure obviously favours the *EZE* conformation.

A comparison of the geometrical parameters of the piroxicam moieties of known structures shows that those of the C(14)/C(10) portion in *trans*-[$PtCl_2$(dmso)(HL)] are very similar to those found for neutral free piroxicam, in agreement with the same protonation status and the same general *EZE* conformation. Some differences are found in the C(14)/N(1′) fragment as a consequence of the metal co-ordination to N(1′). For instance the C(14)–N(16) bond length [1.394(17) Å] of this platinum(II) complex is closer to the relevant value of the zwitterionic form [1.385(6) Å[27]] than to that of the neutral [1.353(4) Å[26]] or of the anionic [1.365(4) Å[28]] molecules. However, it is interesting that the N(16)–C(2′)–N(1′) bond angle is much the same in the platinum complex and in the free HL molecule, even though the sum of the van der Waals radii for Pt and N(16) (3.2–3.4 Å) is higher than the Pt···N(16) contact distance (3.10 Å). This is one more observation consistent with a Pt···HN attractive interaction.

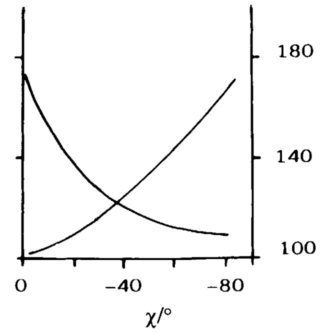


Fig. 2 Values of the N(16)···Cl(2) intramolecular distance (*d*) and of the N(16)–H···Cl(2) angle (α) plotted against the Cl(2)–Pt–N(1′)–C(2′a) (χ) torsional angle for *trans*-[$PtCl_2$(dmso)(HL)]. The values were obtained using MacroModel[12] by keeping fixed all the bond distances and angles

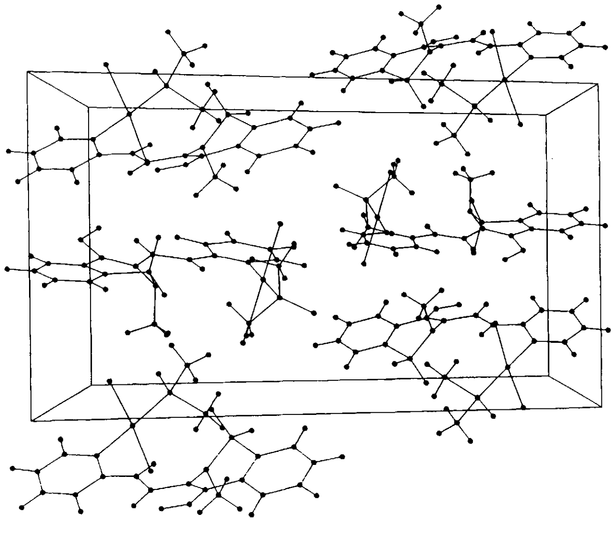


Fig. 3 View of the molecular packing along the crystallographic *a* axis

The *E* conformation of the 4,14 chain of the HL ligand is stabilized by an intramolecular O(17)–H···O(15) hydrogen bond [d(O···O) = 2.58(1) and 2.60(1) Å; angles 129(11) and 140(11)° for the two molecules, respectively]. Furthermore, two weak intermolecular hydrogen bonds involve the H(17) atoms: namely O(17a)–H···O(15b) ($x, y - 1, z$) and O(17b)–H···O(15a) ($x, y + 1, z$) [*d*(O···O) = 3.15(1) and 3.38(1) Å; angles 105(8) and 113(9)° for the two molecules, respectively]. No stacking interaction involving the pyridyl or the C(5)/C(10) rings could be revealed (Fig. 3). There are no Pt···Pt contacts below 4 Å.

Infrared spectroscopy

The Pt···H–N interaction is also identifiable through infrared spectroscopy in the solid state (Fig. 4). The ν(N–H) band is at 3250 cm^{-1}, some 90 cm^{-1} lower than that of free HL (3340 cm^{-1}). It also broadens upon co-ordination. Similar effects were found for *trans*-[$PtCl_2\{o\text{-}Ph_2PC_6H_4NHC(O)Ph\}_2$],[29] *cis*-[Pt{$o\text{-}Ph_2PC_6H_4NC(O)C_6H_4$}{$o\text{-}Ph_2PC_6H_4NHC(O)Ph$}]·$C_6H_5$Me,[21] and for [Ni(CO){$NH(C_2H_4PPh_2\text{-}2)_3$}]$^+$[30] where a Pt···HN interaction was considered present.

EHMO calculations

The frontier orbitals do not have significant Pt, N(16) and H(16) atomic orbital character. One molecular orbital (MO), with high p_z(Pt), p_y[N(16)] and s[H(16)] character, lies some 1140 kJ mol^{-1} above the highest occupied molecular orbital

Table 4 Selected molecular orbitals (decreasing energies) for the model molecule *trans*-$[PtCl_2(H_2SO)\{NC_5H_4(NHCOH)\text{-}2\}]$ [only those with some N(16) and Pt character are reported]. Coefficients of atomic orbitals higher than 0.15 are reported. The HOMO and the lowest unoccupied molecular orbital (LUMO) are given for comparison. The coordinate system is that in Scheme 2

MO	Coefficients of the atomic orbitals				*E*/eV*
22	0.30p_y Pt	0.66p_z Pt	−0.27p_z Cl(1)	−0.29p_z Cl(2)	0.94
	0.28p_z S	0.27s O(d)	0.22p_z O(d)	−0.18p_z N(1′)	
	−0.56p_y N(16)	0.16p_z N(16)	−0.31p_y C(2′)	−0.18p_z C(2′)	
	−0.20p_y C(3′)	−0.16p_z C(4′)	−0.23p_z C(6′)	0.37s H(16)	
27(LUMO)	0.15d_{xy} Pt	0.55p_x N(1′)	−0.19p_x C(2′)	−0.42p_x C(3′)	−8.71
	0.59p_x C(4′)	−0.55p_x C(6′)			
28(HOMO)	−0.84d_{xy} Pt	0.27d_{xz} Pt	0.39p_y Cl(1)	−0.41p_y Cl(2)	−10.84
31	−0.15d_{z^2} Pt	−0.23d_{yz} Pt	0.22p_x O(15)	−0.57p_y O(15)	−12.14
	−0.67p_z O(15)	−0.23p_z N(16)			
42	−0.18d_{yz} Pt	−0.34p_y Cl(1)	0.19p_z Cl(1)	−0.41p_y Cl(2)	−14.65
	0.23d_z Cl(2)	−0.19p_y S	0.25p_z O(d)	0.17p_y N(16)	
	−0.18p_y C(2′)	0.21p_y C(3′)	−0.17p_y C(4′)	−0.17p_y C(6′)	
43	0.23d_{xy} Pt	0.38p_y Cl(1)	−0.25p_y Cl(2)	−0.23p_x O(15)	−14.78
	0.19p_x N(1′)	−0.31p_x N(16)	0.23p_x C(4′)	−0.28p_x C(14)	
45	0.22d_{xy} Pt	−0.23d_{xz} Pt	0.20p_x Cl(1)	0.40p_y Cl(1)	−15.08
	0.38p_z Cl(2)	0.18p_x O(15)	0.38p_x N(16)		
47	0.27d_{xy} Pt	0.36d_{xz} Pt	0.25p_y Cl(1)	0.43p_z Cl(1)	−15.18
	−0.37p_y Cl(2)	−0.40p_z Cl(2)	0.16p_x N(16)		

* eV ≈ 1.60×10^{-19} J.

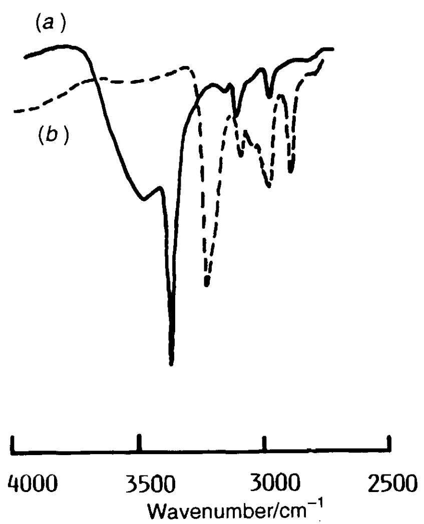


Fig. 4 Infrared spectra (KBr pellets), in the 4000–2500 cm^{-1} region of (*a*) HL and (*b*) *trans*-$[PtCl_2(dmso)(HL)]$

(HOMO) (Table 4, number 22). However, various occupied MOs with some metal (d_{z^2}, d_{xy}, d_{xz} and d_{yz}), p_z[N(16)], p_y[O(15)] and p_z[O(15)], without any appreciable H(16) character were computed for the *trans*-$[PtCl_2(H_2SO)\{NC_5H_4(NHCOH)\text{-}2\}]$ model system (numbers 31, 42, 43, 45 and 47). Among the latter, that (31) closer to the frontier region is 130 kJ mol^{-1} more stable than the HOMO and has d_{z^2}(Pt), d_{yz}(Pt) and p_z[N(16)] character.

The calculated atomic charges of the Pt and H(16) atoms are −0.32 and +0.18 respectively. This suggests that electrostatic forces can play a significant role in the Pt ··· H(16) interaction, in agreement with previously reported investigations.[22,30]

In conclusion a new metal complex of piroxicam is presented. Its crystal and molecular structure shows that the pyridyl nitrogen is the preferred donor, instead of the hydroxy and amide oxygen and benzothiazine nitrogen atom. This study reveals also that the drug molecule can adopt the *EZE* conformation when complexed, in addition to the *ZZZ* one previously found for copper(II) and cadmium(II) complexes.[2] Finally this work adds a new example to the scanty batch of compounds for which the Pt ··· H–N interaction was noted and reported. Some electron density from the metal centre (at least *via* d_{z^2} and d_{yz}) is possibly passed to the NH function which exhibits a bond weakening (IR spectrum, Fig. 4). An electrostatic Pt ··· H attraction then enforces the affinity of the metal centre towards the NH group.

Work is planned in this laboratory to investigate the reactivity of the complex, particularly with nucleobases, nucleotides and nucleic acids, and to perform appropriate tests for anti-inflammatory activity.

Acknowledgements

I thank MURST (Ministero dell'Universitá e della Ricerca Scientifica e Tecnologica, Roma) for financial support, and Pfizer Italia (Roma) for the gift of piroxicam.

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Received 6*th July* 1995; *Paper* 5/04392A