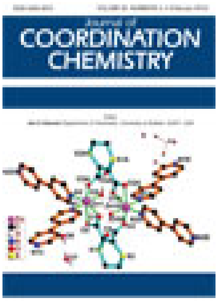

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trans-Dichloro(η^2-ethylene) (*N*-3-pyridinylmethanesulfonamide)platinum(II). Crystal structure, spectroscopic, and thermoanalytical characterization, and cytotoxicity assays

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The organometallic complex, *trans*-[$PtCl_2(\eta^2-C_2H_4)$(PMSA)] (**1**), where PMSA = *N*-3-pyridinylmethanesulfonamide, has been synthesized and characterized by elemental analysis, molar electric conductivity, IR, electronic, and NMR (^1H, ^{13}C, and ^{195}Pt) spectroscopy, and thermal analysis. X-ray crystallography revealed that in **1** [monoclinic, $P2_1c$, $a = 5.1260(1)$, $b = 19.1600(4)$, $c = 12.7990(3)$ Å, $\beta = 97.242(2)^\circ$, $Z = 4$] Pt(II) shows planar coordination geometry with PMSA coordinated *via* the pyridine. The ethylene is virtually perpendicular to the $PtCl_2N$ plane with the pyridine ring twisted relative to this plane by 47°. In *in vitro* assays, PMSA, K[$PtCl_3(\eta^2-C_2H_4)$] · H_2O, and **1** do not exhibit appreciable cytotoxic activity against human K562 and HepG2 tumor cell lines.

Keywords: Platinum(II) complex; Coordinated ethylene; Sulfonamide; Crystal structure

1. Introduction

The new generation of clinically used metal-based anticancer drugs – carboplatin, oxaliplatin, and nedaplatin [1] – follows the paradigm of the parent compound, cisplatin, with respect to the chemical structure, reactivity, and mechanism of cytostatic action [2]. Nevertheless, there is an increased interest in platinum and other metal complexes that do not strictly conform to the rules derived over the years for cytostatically/cytotoxically active cisplatin analogs [2d, e, 3]. Such drugs should retain

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their activity against cisplatin-resistant tumors [3]. Interest in non-conventional or non-classical platinum cytotoxic agents was inspired by the finding of Farrell *et al*. [4] concerning the cytotoxic activity of platinum complexes with *trans*-configuration containing pyridine-type ligands. The following years witnessed increased attention to *trans*-platinum complexes, which became a promising and rapidly growing group of non-classical platinum antitumor agents [5].

On the other hand, the cytotoxic effect and its relation to carbonic anhydrase activity of sulfonamide derivatives enjoy considerable attention in the work of Supuran [6] and other researchers [7]. The molecule *N*-3-pyridinylmethanesulfonamide (PMSA, figure 1) combines structural features of both the above groups of cytotoxic agents – pyridine ring and sulfonamide residue. We performed a Hartree–Fock (HF) *ab initio* quantum chemical and infrared (IR) spectroscopic studies of PMSA [8a], were first to synthesize and structurally characterize Pd(II) and Pt(II) complexes of this ligand [8b, c], and revealed that its Pt(II) complexes of both *cis*- and *trans*-configuration exhibit cytotoxic activity [8d].

$K[PtCl_3(\eta^2\text{-}C_2H_4)]\cdot H_2O$ (Zeise's salt, ZS) – the first reported organometallic compound [9] – reacts with pyridine-like [10–18] and other *N*- [10, 19–23] and *O*-donor ligands [11, 24] (L) to give *trans*-$[PtCl_2(\eta^2\text{-}C_2H_4)(L)]$. Pt(II) complexes with η^2-coordinated ethylene [25] and other olefin ligands [26, 27] have been tested for cytotoxicity, and some of them have shown significant effect.

In continuation of our studies, here we report the preparation, crystal structure, spectroscopic, and thermoanalytical characterization, as well as the results of cytotoxicity assays of the new organoplatinum complex *trans*-$[PtCl_2(\eta^2\text{-}C_2H_4)(PMSA)]$ (**1**, figure 1).

2. Experimental

2.1. *Materials and physical measurements*

PMSA was synthesized from 3-aminopyridine and methanesulfonylchloride according to Jones and Katritzky [28], and purified as described in [8a]. $K[PtCl_3(C_2H_4)]\cdot xH_2O$

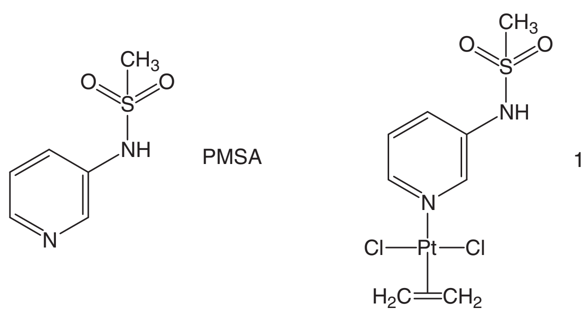

Figure 1. Structural formulae of *N*-3-pyridinylmethanesulfonamide (PMSA) and *trans*-$[PtCl_2(\eta^2\text{-}C_2H_4)(PMSA)]$ (**1**).

was purchased from Sigma. The remaining reagents and solvents, used without purification, were commercial products with qualification *purum* or *pro analysi*.

Elemental analyses (C, H, and N) were performed on a Perkin-Elmer 240 B microanalyser. The melting range (uncorrected) was measured in a capillary tube on a Stuart Scientific melting point apparatus SMP3. The molar electric conductivity (Λ_m) was measured in methanol (specific conductivity, $\Lambda = 9.0 \times 10^{-7}\,\Omega^{-1}\,cm^{-1}$) at 25°C, employing a WTW conductivity bridge and a calibrated dip type cell, on a Crison Conductimeter Basic 30.

NMR spectra were recorded at 20°C in CD_3OD, $(CD_3)_2CO$, and $CDCl_3$ solutions. ^1H spectra were recorded on Bruker Avance II+ 600 (BBO or TBI probe head) and Bruker DRX-250 (QNP probe head) spectrometers operating at 600.13 and 250.13 MHz, respectively. ^{13}C and ^{195}Pt spectra were recorded on the Bruker Avance II+ 600 apparatus at 150.90 and 129.01 MHz, respectively. The ^1H and ^{13}C NMR chemical shifts are given relative to TMS, while in the case of the ^{195}Pt NMR chemical shift of 1.2 mol L^{-1} Na_2PtCl_6 in D_2O solution was used as external standard [29]. The precise assignment of ^1H and ^{13}C NMR spectra was accomplished by measurement of 2-D homonuclear correlation (COSY), DEPT-135, and 2-D inverse detected heteronuclear (C–H) correlations (HSQC and HMBC). The delay for evolution of one bond couplings was optimized for 145 Hz, while the delay for evolution of long-range couplings was optimized for 8 Hz. The ^1H NMR chemical shifts of pyridine protons and their coupling constants were refined with the LAOCOON PC iterative program based on the LAOCN3 algorithm [30].

IR spectra were registered in the solid state as KBr (4000–400 cm^{-1}) and CsI discs (400–130 cm^{-1}) on a Bruker IFS 113 spectrophotometer. The electronic spectra of methanol solutions were recorded on a Shimadzu 160 A spectrophotometer. The thermal behavior of **1** was studied in nitrogen using the simultaneous TG/DTG-DTA technique, from ambient to 980°C, using a Setaram Model Setsys-1200 thermogravimetric analyzer. The sample with a weight of about 15 mg was heated in platinum crucibles at a heating rate 10°C min^{-1}.

The structural identification of the residue was performed by powder X-ray diffraction (XRD) analysis using a 2-circle Rigaku Ultima$^+$ diffractometer (40 kV, 30 mA, Cu-Kα radiation) with Bragg–Brentano geometry.

2.2. *Preparation of trans-[$PtCl_2(\eta^2$-$C_2H_4)$(PMSA)] (1)*

The method is analogous to that given by Orchin and Schmidt [11]: $K[Cl_3Pt(C_2H_4)] \cdot xH_2O$ (0.30 g, 0.78 mmol, calculated on the basis of monohydrate) was dissolved in water (2 mL); the solution was filtered and the filter washed with water (2 mL). PMSA (0.13 g, 0.75 mmol) was dissolved in water (5 mL) upon heating. After cooling to room temperature, the solution was added dropwise (by filtering through the filter already used, *vide supra*) upon stirring to the solution of $K[PtCl_3(C_2H_4)] \cdot xH_2O$. A lemon-yellow fine crystalline precipitate appeared immediately. The filter was washed with water (3 mL) and the stirring continued for 3 h at room temperature. The filtrate was filtered, washed with a small amount of water, and dried *in vacuo* over P_2O_5. Yield: 0.30 g (86%).

Melting range: 155–160°C (decomp.). Elemental Anal. Calcd for $C_8H_{12}Cl_2N_2O_2PtS$ (466.25): C, 20.61; H, 2.59; N, 6.01. Found: C, 20.70; H, 2.58; N, 5.97. $\Lambda_m = 4.3\,\Omega^{-1}\,mol^{-1}\,cm^2$ ($9.87 \times 10^{-4}\,mol\,L^{-1}$ solution).

Crystals suitable for XRD analysis were prepared as follows. *ca* 30 mg of **1** was dissolved in methanol (3 mL) and water (1.5 mL) was added. The solution was left at room temperature not tightly closed. After 2 h long needle-shaped crystals appeared, were collected on a filter and dried as above.

2.3. *X-ray crystal structure analysis*

XRD data were collected at 120 K with an Oxford Diffraction Xcalibur E diffractometer using graphite-monochromated Mo-Kα radiation ($\lambda = 0.71073$ Å). The unit cell determination and data integration were carried out using CrysAlisPro [31]. Intensity data were corrected for Lorentz and polarization effects and for absorption. The structure was solved by direct methods with SHELXS-97 [32] and refined by full-matrix least-squares on F^2 using SHELXL-97 [32], with anisotropic displacement parameters for the non-hydrogen atoms. The C-bound hydrogen atoms were placed in calculated positions and refined as riding on the carrier with isotropic displacement parameters equal to $1.2 \times U_{eq}$ of the relevant carbon. The hydrogen of N–H was located in a difference Fourier map and its position refined. Molecular graphics were generated with Mercury 1.4 software [33]. Crystal data and some further details concerning X-ray analysis are given in table 1.

2.4. *Cytotoxicity assays*

Cell lines. Human leukemia cells K562 (ATCC, CCL-243) and HepG2 human liver hepatocellular cells were cultured in DMEM (Dilbecco's Modified Eagle Medium, Applichem, Germany) supplemented with 10% (v/v) FBS (Lonza, Switzerland), penicillin ($100\,\mu g\,mL^{-1}$), streptomycin ($100\,\mu g\,mL^{-1}$), and $4\,mmol\,L^{-1}$ l-glutamine (Biowhittaker Lonza, Switzerland) at 37°C in a humidified atmosphere of 5% CO_2 and 95% air. Cells were routinely checked for mycoplasma contamination by DAPI staining (Roche Diagnostics, Mannheim, Germany) and found free of it.

Cell survival. The compounds (PMSA, ZS, and **1**) were dissolved in methanol to obtain stock solutions, which were then diluted with cell culture media to obtain the desired concentrations. For the drug sensitivity assay, cells were harvested and cultured for 24 h in fresh medium and were subsequently plated into 96-well microtiter plates (Nunc, Wiesbaden, Germany) at a density of 5×10^4 cells/well (100 µL). Sensitivity of the cell lines to different concentrations of the tested compounds was determined at 24, 48, or 72 h of drug exposure using the MTT assay of Mosmann [34]. The MTT-formazan product was dissolved in isopropanol and the absorption at 550/630 nm was measured on an ELISA plate reader (Bio-Tek Instruments Inc., USA). The growth-inhibitory effect of the compounds was expressed as percentage of viable cells with respect to the control with solvent (methanol).

Table 1. Crystal data and structure refinement for **1**.

Empirical formula	$C_8H_{12}Cl_2N_2O_2PtS$
Formula weight	466.25
Temperature (K)	120(2)
Crystal system	Monoclinic
Space group	$P2_1/c$
Unit cell dimensions (Å, °)	
a	5.1260(1)
b	19.1600(4)
c	12.7990(3)
β	97.242(2)
Volume (Å^3), Z	1247.01(5), 4
Calculated density (Mg m^{-3})	2.483
Absorption coefficient (mm^{-1})	11.83
F(000)	872
Crystal color, shape, size (mm^3)	Lemon-yellow, needle, $0.8 \times 0.02 \times 0.02$
θ range for data collection (°)	3.2–28.8
Limiting indices	$-6 \le h \le 6$; $-22 \le k \le 22$; $-15 \le l \le 15$
Reflections collected	9272
Independent reflections	2187
R_{int}	0.035
Data/restraints/parameters	2187/0/148
Goodness-of-fit on F^2	0.953
Final R indices [$I > 2\sigma(I)$]	$R_1 = 0.0185$, $wR_2 = 0.0379$
R indices (all data)	$R_1 = 0.0242$, $wR_2 = 0.0386$
Largest difference peak and hole (e Å^{-3})	0.669 and −0.753

3. Results and discussion

ZS reacts rapidly with PMSA in aqueous solution to give **1** in a good yield, as a yellow crystalline precipitate, soluble in methanol, ethanol, dichloromethane, and chloroform, and practically insoluble in water. Well-shaped crystals are readily obtained from methanol solution diluted with water. The molar electric conductivity of the complex measured in methanol is consistent with a non-ionic structure [35]. Although in the crystalline state **1** is stable under normal conditions, its solutions were found to decompose slowly upon standing at room temperature, judging by the deposition of a brownish product.

3.1. *Crystal structure of 1*

The molecular structure of **1** is depicted in figure 2 and selected geometric parameters are collected in table 2. The Pt(II) is in an almost planar surrounding of two *trans*-positioned chlorides, the pyridine N of PMSA and the middle of the CC bond of η^2-coordinated ethylene, the latter being virtually perpendicular to the plane defined by N(1), Pt, Cl(1), and Cl(2) (dihedral angle 89°; see figure 2C). The two Pt–Cl bond lengths in **1** differ by 0.033 Å and are comparable to those in ZS [36] and in analogous complexes containing pyridine-like ligands [12, 16, 18, 20]. The latter also holds for the Pt–C and $(C–C)_{ethylene}$ bond lengths. In general, there is no significant difference in the geometric parameters of the coordination node of **1** (bond lengths and bond angles around the platinum and orientation of the ethylene ligand) in comparison with analogous complexes [12, 16, 18, 20].

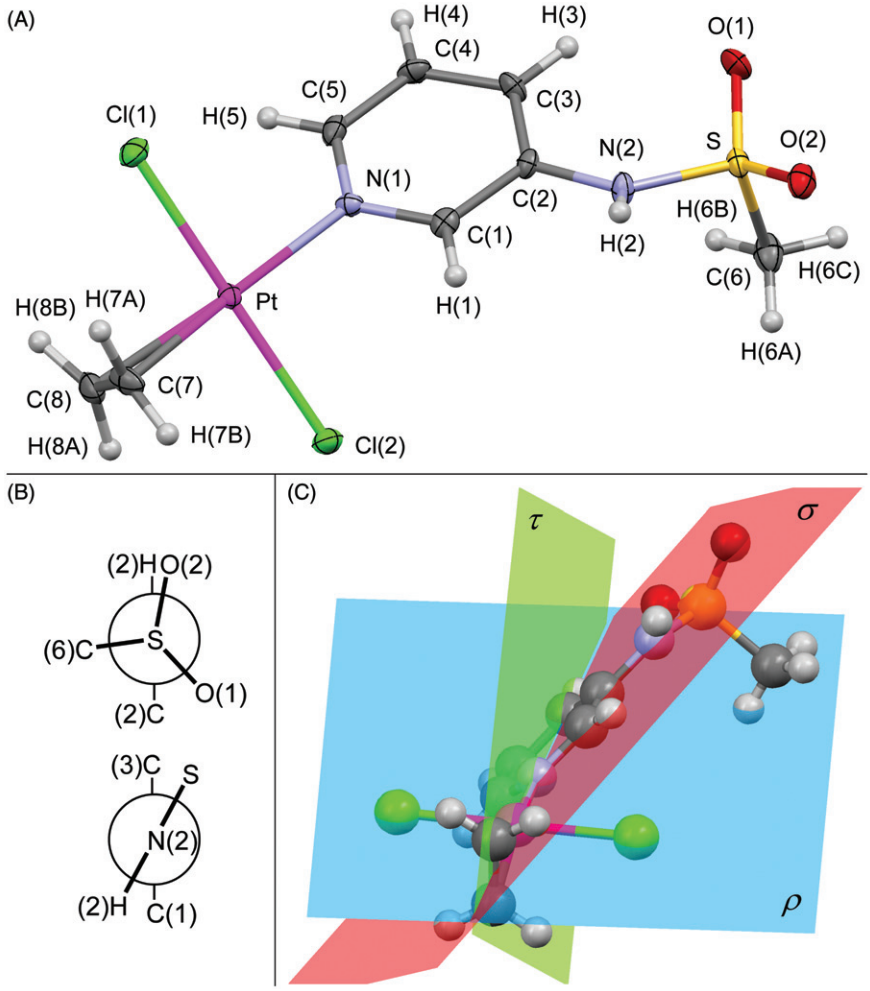

Figure 2. (A) Molecular structure of *trans*-[$PtCl_2(\eta^2$-$C_2H_4)$(PMSA)] (**1**) with the atom numbering. Thermal ellipsoids are drawn at the 50% probability level. (B) Newman projections along the S–N(2) and N(2)–C(2) bonds. (C) View of the least-squares planes in the molecule. Equations of the least-squares planes in crystal coordinates (x, y, z) and RMS deviations of fitted atoms (Å): ρ[N(1)–Pt–Cl(1)–Cl(2)]: $-4.3777(0.0040)x - 8.6912(0.0239)y + 4.6157(0.0054)z = 0.1236(0.0014)$, 0.0038; σ[Pt–N(1)–C(1)–C(2)–C(3)–C(4)–C(5)]: $3.3029(0.0051)x + 11.0023(0.0104)y + 5.3732(0.0189)z = 2.8777(0.0050)$, 0.0107; τ[Pt–N(1)–C(7)–C(8)]: $0.3637(0.0217)x + 6.9544(0.0467)y + 11.6822(0.0222)z = 4.0501(0.0018)$, 0.0064.

The geometry of the pyridine ring in **1** is quite similar to that in free PMSA and *trans*-[PtI_2(PMSA)$_2$] [8a, c]. The Pt–N bond length of 2.074 Å corresponds well with the value found in complexes of the type *trans*-[$PtCl_2(\eta^2$-$C_2H_4)$(L)] (L = substituted pyridines) [12, 18], but longer compared to *trans*-[PtI_2(PMSA)$_2$] (2.032 Å) [8c] and to other Pt(II) complexes with substituted pyridine ligands [37–40]. This should be attributed to the strong *trans*-effect of ethylene [41]. The pyridine ring in **1** (figure 2C) is twisted by 47° relative to the coordination plane and this twist angle is nearly the same as in *trans*-[$PtCl_2(\eta^2$-$C_2H_4)$(L)] (L = 4-methylpyridine) [12b], but is smaller than that in *trans*-[PtI_2(PMSA)$_2$] (69°) [8c]. The main difference in the geometry of the sulfonamide

Table 2. Selected geometric parameters for **1**.

Bond lengths (Å)			
N(1)–C(1)	1.344(5)	C(1)–C(2)	1.389(5)
C(2)–C(3)	1.377(6)	C(3)–C(4)	1.388(6)
C(4)–C(5)	1.380(5)	N(1)–C(5)	1.334(5)
C(2)–N(2)	1.412(5)	N(2)–S	1.635(3)
S–O(1)	1.426(3)	S–O(2)	1.435(3)
S–C(6)	1.759(4)	C(7)–C(8)	1.364(6)
Pt–N(1)	2.074(3)	Pt–Cl(1)	2.2837(11)
Pt–Cl(2)	2.3167(10)	Pt–C(7)	2.163(4)
Pt–C(8)	2.163(4)		
Bond angles (°)			
C(1)–C(2)–N(2)	115.7(4)	C(3)–C(2)–N(2)	125.0(4)
C(1)–N(1)–C(5)	119.4(3)	C(2)–N(2)–H(2)	115(4)
C(2)–N(2)–S	128.8(3)	H(2)–N(2)–S	115(4)
N(2)–S–O(1)	108.1(2)	N(2)–S–O(2)	104.0(2)
N(2)–S–C(6)	107.1(2)	O(1)–S–O(2)	119.8(2)
O(1)–S–C(6)	108.6(2)	O(2)–S–C(6)	108.5(2)
C(1)–N(1)–Pt	119.9(3)	C(5)–N(1)–Pt	120.6(3)
N(1)–Pt–Cl(1)	89.2(1)	N(1)–Pt–Cl(2)	90.6(1)
Cl(1)–Pt–Cl(2)	179.46(4)	N(1)–Pt–C(7)	161.2(1)
N(1)–Pt–C(8)	162.0(1)	C(7)–Pt–C(8)	36.8(2)
Cl(1)–Pt–C(7)	89.7(1)	Cl(1)–Pt–C(8)	90.3(1)
Cl(2)–Pt–C(7)	90.4(1)	Cl(2)–Pt–C(8)	90.1(1)
Torsion angles (°)			
S–N(2)–C(2)–C(1)	159.5(3)	S–N(2)–C(2)–C(3)	–20.1(6)
O(1)–S–N(2)–C(2)	36.1(4)	O(2)–S–N(2)–C(2)	164.4(3)
C(6)–S–N(2)–C(2)	–80.7(4)	C(1)–N(1)–Pt–Cl(1)	134.3(3)
C(1)–N(1)–Pt–Cl(2)	–45.3(3)	C(5)–N(1)–Pt–Cl(1)	–47.8(3)
C(5)–N(1)–Pt–Cl(2)	132.6(3)	C(1)–N(1)–Pt–C(7)	47.7(6)
C(1)–N(1)–Pt–C(8)	–137.5(5)	C(5)–N(1)–Pt–C(7)	–134.4(5)
C(5)–N(1)–Pt–C(8)	40.4(6)	C(7)–C(8)–Pt–Cl(1)	–89.1(2)
C(7)–C(8)–Pt–Cl(2)	90.5(2)	C(7)–C(8)–Pt–N(1)	–177.2(4)
Dihedral angles between least-squares planes[a] (°)			
$\rho-\sigma$ 47.0(1)	$\rho-\tau$ 89.3(2)	$\sigma-\tau$ 43.7(3)	

[a]See figure 2 for details.

group in **1** in comparison with crystalline PMSA and *trans*-[$PtI_2(PMSA)_2$] [8c] concerns the torsion angles around the S–N(2) and N(2)–C(2), which leads to different conformations. The conformation of the sulfonamide residue in **1** (figure 2B) is qualitatively the same as that in the *ab initio* optimized structure of an isolated PMSA molecule [8a, c].

As shown in figure 3, the centrosymmetric unit cell of **1** contains four molecules. The molecules related by unit translation along the *a*-axis form chains *via* N–H ··· Cl hydrogen bonds (H(2) ··· $Cl(2)^i = 2.58(4)$ Å, N(2) ··· $Cl(2)^i = 3.307(4)$ Å, <N(2)–H(2) ··· $Cl2^i = 170(5)°$; symmetry code ^{i}: $x-1$, y, z). Sulfonamide oxygen atoms are involved in C–H ··· O interactions, with the shortest H ··· O distance of 2.33 Å being to the ethylene ligand.

3.2. *NMR spectra*

3.2.1. ^{1}H and ^{195}Pt NMR spectra. Analysis of the ^{1}H NMR spectrum of **1** is illustrated in figure 4. ^{1}H and ^{195}Pt NMR spectroscopic data for **1** and PMSA in

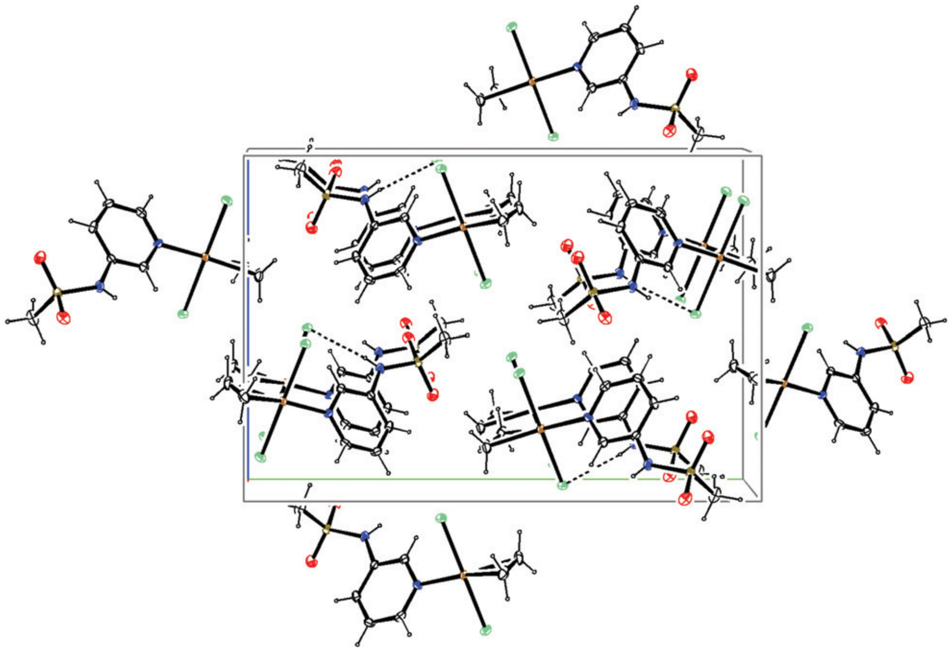

Figure 3. Crystal packing of *trans*-[$PtCl_2(\eta^2$-$C_2H_4)$(PMSA)] (**1**) viewed along the *a*-axis with NH···Cl hydrogen bonds shown as dashed lines.

different solvents are collected in table 3. The assignments were verified by literature data on PMSA and its Pt(II) complexes [8b], complexes of the type *trans*-[$PtCl_2$ $(\eta^2$-$C_2H_4)$(L)] [11, 13, 17c, 21, 22, 24], as well as other Pt(II) complexes with pyridine ligands [40c–e, 42]. The signal of the NH proton was not observed in spectra taken in CD_3OD and $CDCl_3$, probably because of exchange with the solvent and/or with traces of water. The ethylene protons give only one signal, which is consistent with the data on fast rotation of the pyridine and ethylene ligands in similar systems [11]. The signal is accompanied by a satellite doublet due to coupling with ^{195}Pt (figure 4). The $^2J_{PtH(ethylene)}$ coupling constants (table 3) are in agreement with reported values for η^2-ethylene Pt(II) complexes [13b, 18, 21, 24]. In spectra recorded in CD_3OD and $(CD_3)_2CO$, no satellite signals were observed for pyridine α-protons H(1) and H(5), attributed to exchange of PMSA with solvent [11]. In the spectrum taken in $CDCl_3$ (250 MHz), the expected satellites are clearly seen (figure 4), with coupling constants $^3J_{PtH}$, in the expected range for Pt(II) pyridine complexes [8b, 11, 18a, 40d, e, 42b].

The ^{195}Pt NMR spectrum of **1** gives a single signal at −2979 ppm, in agreement with literature data for similar species [13a, 42a].

3.2.2. ^{13}C NMR spectra. The assignment of the signals of the carbons was performed by measurement of DEPT and inverse detected C–H correlated HSQC and HMBC (figure S1, Supplementary material) spectra. Figure 5 shows analysis of the ^{13}C spectrum of **1**, and the spectroscopic parameters for PMSA and **1** are summarized in table 4. Relevant literature data [17, 18, 21, 43] were used to confirm the assignments.

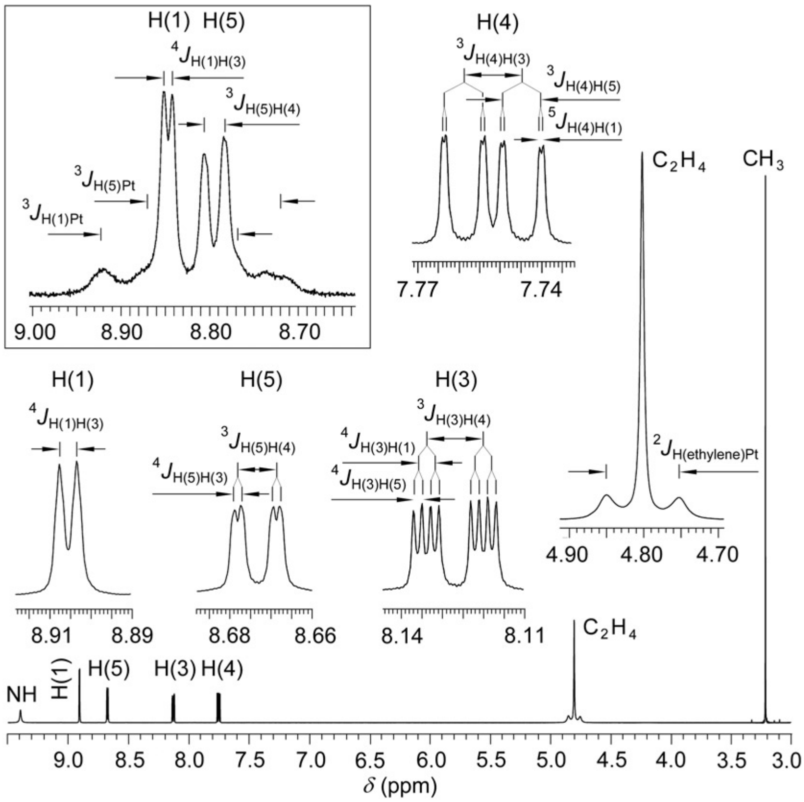

Figure 4. ^{1}H NMR spectrum (600.13 MHz) of *trans*-[$PtCl_2(\eta^2\text{-}C_2H_4)$(PMSA)] (**1**) dissolved in $(CD_3)_2CO$ with assignments and analysis of the multiplets. Framed inset: fragment of the ^{1}H NMR spectrum (250.13 MHz) of the same compound taken in $CDCl_3$.

The signals of pyridine carbons, except C(2), appear as two- to four-fold doublets with one large ($^1J_{CH}$ = 165.5–190.0 Hz) and several much smaller constants ($^2J_{CH}$, $^3J_{CH}$, and $^4J_{CH}$ in the range 11.2–1.2 Hz). The ethylene carbons give a seven-line signal whose interpretation was facilitated by the ^{13}C{H} spectrum (figure S2, Supplementary material). The signal consists of a triplet ($^1J_{CH}$ = 165 Hz) with ^{195}Pt satellites with the same value of the coupling constant $^1J_{CPt}$ (table 4). The chemical shift and $^1J_{CPt}$ value are in agreement with literature data [13b, 17, 21, 22a, 43].

3.3. IR spectra. The 28-atom molecule of **1** has 78 normal vibrations which can be formally divided into four groups of modes: 51 of PMSA, 15 of the ethylene–platinum moiety, 6 of the $PtCl_2N$ fragment, and 6 more – belonging to the rocking, wagging, and torsion modes of PMSA and ethylene–platinum fragment, respectively, toward the remaining part of the molecule. Our previous results from the HF *ab initio* vibrational analysis of PMSA [8a] and IR data for its Pt(II) complexes [8b] were used to identify the bands belonging to the PMSA fragment in **1**. The assignments of bands of the ethylene–platinum residue were grounded on the data about ZS [44] and

Table 3. ^{1}H and ^{195}Pt NMR spectroscopic data for PMSA and *trans*-[$PtCl_2(\eta^2$-$C_2H_4)$(PMSA)] (**1**).

Compound, solvent	Assignment of the signal, chemical shift (δ, ppm), multiplicity, relative intensity[a,b,c]								Coupling constants (^nJ, Hz)[c]
	CH_3	C_2H_4	H(4)	H(3)	H(5)	H(1)	NH	Pt	
PMSA, CD_3OD	3.03 s 3H		7.42 ddd 1H	7.77 ddd 1H	8.31 dd 1H	8.42 dd 1H	[d,e]		$^3J_{H(3)H(4)} = 8.3$, $^3J_{H(4)H(5)} = 4.8$, $^4J_{H(3)H(5)} = 1.4$ $^4J_{H(1)H(3)} = 2.7$, $^4J_{H(1)H(5)} = -0.1$, $^5J_{H(1)H(4)} = 0.7$
1, CD_3OD	3.10 s 3H	4.83 s(d) 4H	7.61 dd 1H	7.98 dd 1H	8.62 d br 1H	8.81 d 1H	[d]		$^3J_{H(3)H(4)} = 8.5$, $^3J_{H(4)H(5)} = 5.6$, $^4J_{H(3)H(5)} = 1.2$ $^4J_{H(1)H(3)} = 2.5$, $^4J_{H(1)H(5)} = -0.0$, $^5J_{H(1)H(4)} = 0.0$ $^2J_{PtH(ethylene)} = 57.8$
1, $(CD_3)_2CO$	3.22 s 3H	4.80 s(d) 4H	7.75 ddd 1H	8.13 ddd 1H	8.67 dd 1H	8.91 d 1H	9.39 s, b 1H	−2979 s	$^3J_{H(3)H(4)} = 8.5$, $^3J_{H(4)H(5)} = 5.7$, $^4J_{H(3)H(5)} = 1.1$ $^4J_{H(1)H(3)} = 2.4$, $^4J_{H(1)H(5)} = 0.5$, $^5J_{H(1)H(4)} = 0.4$ $^2J_{PtH(ethylene)} = 58.4$
1, $CDCl_3$	3.14 s 3H	4.94 s(d) 4H	7.56 dd 1H	8.00 ddd 1H	8.80 dd(d) 1H	8.85 d(d) 1H	[d]		$^3J_{H(3)H(4)} = 8.5$, $^3J_{H(4)H(5)} = 5.7$, $^4J_{H(3)H(5)} = 1.0$ $^4J_{H(1)H(3)} = 2.4$, $^4J_{H(1)H(5)} = -0.1$, $^5J_{H(1)H(4)} = 0.1$ $^2J_{PtH(ethylene)} = 61$, $^3J_{PtH(1)} = 37$, $^3J_{PtH(5)} = 36$

[a]Atom numbering according to figure 2. [b]Notations: b – broad, d – doublet, dd – doublet of doublets, ddd – three-fold doublet, (d) – satellite doublet due to coupling with ^{195}Pt. [c]Chemical shifts and coupling constants for the pyridine protons were optimized by the LAOCOON PC iterative program [30]; RMS errors <0.11 Hz. [d] Signal not detected. [e] In $(CD_3)_2CO$ observed at 8.85 ppm, 1H, s, b [8b].

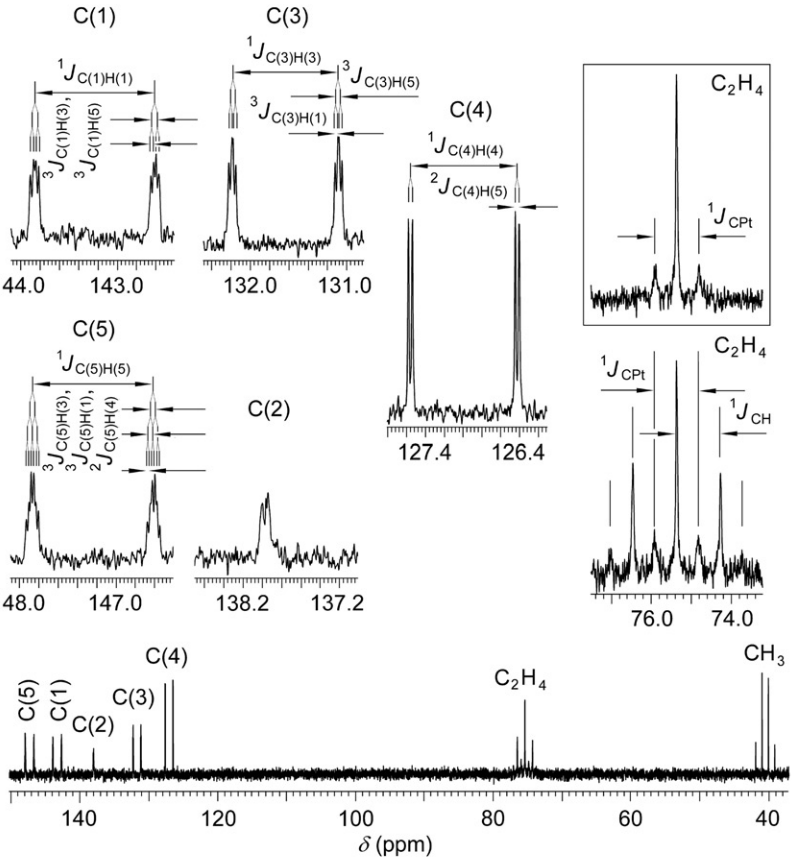

Figure 5. ^{13}C NMR spectrum (150.90 MHz) of *trans*-[PtCl$_2$(η^2-C$_2$H$_4$)(PMSA)] (**1**) dissolved in (CD$_3$)$_2$CO with assignments and analysis of the multiplets. Framed inset: the signal of the ethylene carbons in the ^{13}C{^{1}H} spectrum.

trans-[PtCl$_2$(η^2-C$_2$H$_4$)(py)] [15], and those of the PtCl$_2$N fragment were based on data for *trans*-[PtCl$_2$(η^2-C$_2$H$_4$)(py)] and its analogs with substituted pyridines [10, 11, 17e]. We were able to identify the majority of the IR bands of **1**. Representative IR spectroscopic data for **1** along with comparative data for reference compounds are collected in table 5.

3.4. *Electronic spectra*

Electronic spectral data for PMSA and **1** are given in table 6. Taking into account the electronic spectral data for Pt(II) complexes with pyridine ligands [8b, 17c–e, 46], most of the d–d bands in **1** are expected to be masked by the strong absorption of the pyridine chromophore and by charge-transfer transitions. Only the weak band at 25,000 cm^{-1} could be tentatively ascribed to some of the d–d singlet-triplet transitions [46] ($^3B_2 \leftarrow {}^1A_1$, $^3A_2 \leftarrow {}^1A_1$, $^3B_1 \leftarrow {}^1A_1$ in C_{2v}).

Table 4. ^{13}C NMR spectroscopic data for PMSA and *trans*-$[PtCl_2(\eta^2\text{-}C_2H_4)(PMSA)]$ (**1**).

Compound, solvent	Assignment of the signal, chemical shift (δ, ppm) multiplicity, coupling constants (^nJ, Hz)[a,b]						
	CH_3	C_2H_4	C(4)	C(3)	C(2)	C(1)	C(5)
PMSA, CD_3OD	39.8 q $^1J_{CH} = 138.1$		125.7 ddd $^1J_{C(4)H(4)} = 165.5$ $^2J_{C(4)H(5)} = 8.5$ $^2J_{C(4)H(3)}$, $^4J_{C(4)H(1)} = 1.4, 0.0$	129.3 dddd $^1J_{C(3)H(3)} = 165.4$ $^3J_{C(3)H(5)} = 6.7$ $^3J_{C(3)H(1)}$, $^2J_{C(3)H(4)} = 4.5, 1.2$	137.1 m[c]	142.2 dddd $^1J_{C(1)H(1)} = 181.2$ $^3J_{C(1)H(5)}$, $^3J_{C(1)H(3)} = 11.2, 4.7$ $^4J_{C(1)H(4)} = 1.2$	145.8 dddd $^1J_{C(5)H(5)} = 181.1$ $^3J_{C(5)H(3)}$, $^3J_{C(5)H(1)}$, $^2J_{C(5)H(4)} = 10.6, 7.0, 3.0$
1, CD_3OD	40.4 q $^1J_{CH} = 138.6$	76.0[d] (d) $^1J_{CPt} = 160$	127.2 dd $^1J_{C(4)H(4)} = 170.6$ $^2J_{C(4)H(5)} = 6.6$	131.7 ddd $^1J_{C(3)H(3)} = 169.5$ $^3J_{C(3)H(5)}$, $^3J_{C(3)H(1)} = 5.3, 5.3$	138.7 m[c]	143.5 ddd $^1J_{C(1)H(1)} = 188.2$ $^3J_{C(1)H(5)}$, $^3J_{C(1)H(3)} = 7.7, 5.5$	147.5 dddd $^1J_{C(5)H(5)} = 190.0$ $^3J_{C(5)H(3)}$, $^3J_{C(5)H(1)}$, $^2J_{C(5)H(4)} = 7.4, 7.4, 6.0$
1, $(CD_3)CO$	40.5 q $^1J_{CH} = 138.4$	75.4 t(d) $^1J_{CH} = 165$ $^1J_{CPt} = 165$	127.0 dd $^1J_{C(4)H(4)} = 171.1$ $^2J_{C(4)H(5)} = 6.3$	131.6 ddd $^1J_{C(3)H(3)} = 169.3$ $^3J_{C(3)H(5)} = 6.0$ $^3J_{C(3)H(1)} = 4.9$	138.0 m[c]	143.2 ddd $^1J_{C(1)H(1)} = 188.2$ $^3J_{C(1)H(5)}$, $^3J_{C(1)H(3)} = 8.4, 4.5$	147.2 dddd $^1J_{C(5)H(5)} = 189.8$ $^3J_{C(5)H(3)}$, $^3J_{C(5)H(1)}$, $^2J_{C(5)H(4)} = 7.7, 7.7, 4.4$

[a]Atom numbering according to figure 2. [b]Notations: d – doublet; dd, ddd and dddd – two-, three- and four-fold doublet, respectively; (d) – satellite doublet due to coupling with ^{195}Pt. m – multiplet; q – quartet; t – triplet. [c]Complex multiplet with half-width of *ca* 0.1 ppm. [d]Poorly resolved signal in the non-decoupled spectrum; the value of ^1J refers to the $^{13}C\{^1H\}$ spectrum.

Table 5. Selected IR spectroscopic data for **1**, compared with literature data for reference compounds: wavenumbers ($\widetilde{\nu}$, cm^{-1}) of the fundamental vibrations.

PMSA fragment PMSA[a]	**1**	Assignment[a,b]	PMSA[a]	**1**	Assignment[a,b]
2860–2709 m,b,c[c]	3240 m	ν(NH)	531 s	526 m	$\delta(SO_2)$
1351 s and/or 1341 m	1350 s	$\nu_{as}(SO_2)$	520 s	513 s	$\omega(SO_2)$
1150 vs	1148 vs	$\nu_s(SO_2)$	500	538 sh	t(ring) + π (CN) − py(11)
925 m	932 m	ν(SN)	407 w	419 w	$\rho(SO_2)$
762 m	750 m	ν(CS)	376 w	382 m	δ(SCN)
638 sh	667 m	δ(ring) – py(6b)	313 w	305 w	δ(CN) − py(15)
612 sh	645 w,b	δ(ring) – py(6a)	289 w	285 w	$\tau(SO_2)$
$Pt(\eta^2\text{-}C_2H_4)$ fragment ZS[d]	**1**	Assignment[b,d]	ZS[d]	**1**	Assignment[b,d]
3100	3111 w	ν(CH) – A_2	3005	2982 w and 2957 w	ν(CH) – A_1 and ν(CH) – B_1
3080	3097 w	ν(CH) – B_2	405	428 w	ν(PtC) – A_1
trans-$PtCl_2N$ fragment *trans*-$[Pt(\eta^2\text{-}C_2H_4)(py)]$[e]	**1**	Assignment[b,e]	*trans*-$[Pt(\eta^2\text{-}C_2H_4)(py)]$[e]	**1**	Assignment[b,e]
350 vs, 340 sh	353 s, 340 sh	ν(PtCl) – A_1, B_2	242 m	241 m	ν(PtN)

[a]Data from [8a, b]. [b]Notations for the assignments: as – asymmetric; A_1, B_1, A_2, B_2 – group theory notations assuming C_{2v} symmetry for the *trans*-$PtCl_2(\eta^2\text{-}C_2H_4)Cl_2N$ moiety; py(i) – pyridine ring vibration with number i according to Wilson scheme [45]; s – symmetric; δ – in-plane bending; π – out-of-plane bending; ρ – rocking; τ – twisting; ω – wagging. [c]Here and below, abbreviations: b – broad, c – complex, m – medium, s – strong, sh – shoulder, v – very, w – weak. [d]Data from [44]. [e]Data from [10].

Table 6. Electronic spectral data for PMSA and **1** in methanol solutions: wavenumbers ($\widetilde{\nu}$) and molar extinction coefficients (ε).

Compound	$\widetilde{\nu}$, cm^{-1} (ε, $l\ mol^{-1}cm^{-1}$)
PMSA	44,400 (8690), 36,400 (2820)
1	46,770 (18,520), 43,500 sh (12,760), 39,000 sh (3980), 35,700 (4480), 25,000 sh (35)

3.5. *Thermal analysis*

The thermoanalytical curves recorded simultaneously in nitrogen (weight loss – TG, derivative weight loss – DTG, and heat flow – DTA) of **1** are given in figure S2, "Supplementary material." The thermal decomposition of the compound is a multi-step complex process with three different areas of weight loss, each starting before the end of the previous one. The decomposition is mainly endothermic and begins almost together with the melting of the compound at 147°C, as evidenced from the symmetric sharp endothermic peak on the DTA curve. The experimental weight loss of 5.5% in the temperature range from ambient to 200°C with a DTG_{max} at 180°C coincides with the weight loss of an ethylene molecule (C_2H_4) with theoretical value of 6.0%. The second sudden weight loss of 30.0% until 550°C, DTG_{max} at 205°C and 282°C, coincides with

Table 7. Growth-inhibitory effect[a] of PMSA, ZS, and **1** on human hepatocellular liver carcinoma Hep72 and human leukemic K562 cell lines.

HepG2 cells

Compound	Time of treatment (h)									
	24					48				
	Concentration (μmol L^{-1})					Concentration (μmol L^{-1})				
	50	125	250	500	1000	50	125	250	500	1000
PMSA	100 (22)	102 (24)	98 (18)	94 (19)	87 (19)	98 (10)	97 (12)	95 (12)	101 (15)	98 (13)
ZS	100 (4)	99 (11)	99 (5)	96 (5)	99 (10)	103 (10)	104 (13)	106 (9)	103 (8)	96 (9)
1	102 (14)	103 (8)	104 (10)	105 (10)	101 (13)	102 (18)	101 (11)	97 (17)	99 (11)	96 (13)

K562 cells

Compound	Time of treatment (h)									
	24					72				
	Concentration (μmol L^{-1})					Concentration (μmol L^{-1})				
	50	125	250	500	1000	50	125	250	500	1000
PMSA	99 (13)	98 (7)	98 (13)	103 (15)	96 (8)	98 (7)	101 (12)	97 (7)	99 (8)	90 (5)
ZS	91 (26)	100 (28)	92 (28)	96 (22)	87 (18)	96 (17)	104 (8)	88 (8)	87 (5)	52 (4)
1	104 (8)	105 (8)	102 (8)	102 (7)	101 (16)	101 (20)	100 (15)	96 (22)	92 (27)	118 (21)

[a]Growth-inhibitory effect expressed as percentage of viable cells with respect to the control with solvent (methanol). Standard deviations are given in parentheses.

elimination of some products (methanol, water, and 3-aminopyridine) from the PMSA ligand with a calculated value of 30.9%. Upon increasing the temperature, the unstable intermediate undergoes further decomposition from 550°C to 980 °C (DTG_{max} at 810°C, DTA exothermic peaks at 815°C and 903°C). The amount of the solid residue at 980°C, estimated from the TG curve, 50.0%, could be attributed to the expected PtS or metallic Pt (calculated values 48.7 or 41.8%, respectively). This finding agrees with the thermal decomposition of Pt(II) complexes of *N*-allyl-*N'*-pyrimidin-2ylthiourea, where PtS was the end product at 800°C [47]. The powder XRD pattern of the thermal decomposition's residue of **1**, however, proved this to be cubic Pt, contaminated with carbon coming from the pyrolysis of PMSA in the inert atmosphere.

3.6. *Cytotoxicity assays*

The cytotoxic effect of **1** together with PMSA and ZS was examined against human leukemia K562 cell line and human HepG2 hepatocellular line. The results of cell survival assays at various drug concentrations and exposure times are presented in table 7. Neither the free ligand nor **1** showed any cytotoxicity against the two cell lines up to 1000 μmol L^{-1}. Only ZS exhibited a slight cytotoxic effect against K562 leukemic cells after 72 h of exposure, but only at concentrations of 500 and 1000 μmol L^{-1} ($87 \pm 5\%$ and $52 \pm 4\%$ inhibition of cell growth, respectively).

4. Conclusion

The first organoplatinum complex of *N*-3-pyridinylmethanesulfonamide has been synthesized and its structure is confirmed by single-crystal X-ray crystallography, detailed spectroscopic, and thermoanalytical methods. The new complex together with its precursors, the free ligand, and ZS, were tested for cytotoxic activity against two human tumor cell lines, but appeared practically inactive.

Supplementary material

CCDC 845938 contains the supplementary crystallographic data for **1**. This data can be obtained free of charge *via* http://www.ccdc.cam.ac.uk/consts/retreiving.html or from the Cambridge Crystallographic Data Center, 12 Union Road, Cambridge CB2 EZ2, UK (Fax: +44 1223 336033; E-mail: deposit@ccdc.cam.ac.uk).

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