Crystal Structure of *N*-3-Pyridinyl-methanesulfonamide and *trans*-Diiodobis(*N*-3-pyridinyl-methanesulfonamide)platinum(II)

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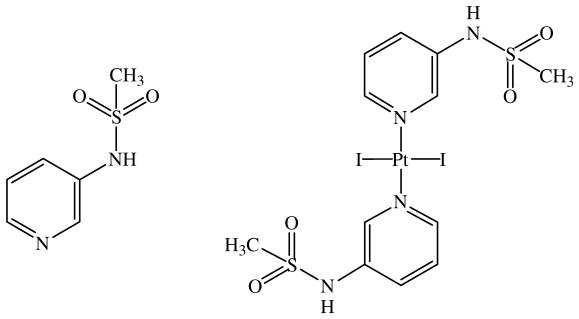
Crystals of *N*-3-pyridinyl-methanesulfonamide, PMSA (monoclinic, $P2_1/c$, $a = 5.6436(7)$, $b = 33.875(4)$, $c = 8.3356(10)$ Å, $\beta = 96.885(2)^\circ$) contain two non-equivalent molecules differing considerably in their conformations. The structure is stabilized by a network of hydrogen bonds, the strongest one being between the pyridine N atom and the sulfonamide H atom. Crystals of *trans*-[Pt(PMSA)$_2$I$_2$] (monoclinic, $C2/c$, $a = 22.912(2)$, $b = 5.2397(5)$, $c = 17.3376(17)$ Å, $\beta = 92.631(2)^\circ$) contain centrosymmetric complex molecules in which PMSA is coordinated *via* the pyridine N atom, and Pt has a planar coordination. A system of hydrogen bonds of the types N–H···O and C–H···O links the complex molecules.

Key words: *N*-3-Pyridinyl-methanesulfonamide, Platinum(II), Crystal Structure

Introduction

Farrell *et al.* established [1] that when the ammonia ligands in the molecule of the anticancer agent cisplatin, *cis*-[Pt(NH$_3$)$_2$Cl$_2$], are replaced by planar ligands like pyridine, the cytotoxicity of the *trans*-isomers of the resulting complexes is comparable to that of cisplatin, while the *cis*-analogues are inactive. This finding lead to the development of the *trans*-platinum complexes with planar heterocyclic N-donor ligands as a new class of non-conventional platinum antitumor agents which retain their activity against cisplatin-resistant cells [2 – 5].

The antitumor activity of sulfonamide derivatives [6, 7] and its relation with the processes of enzyme inhibition attract much attention in the last years. In this direction, the most studied targets of enzyme inhibition by sulfonamides are carbonic anhydrases [7], cyclooxygenase-2 [8, 9] and topoisomerases [10, 11]. Sulfonyl derivatives of pyridine and related heterocycles display versatile pharmacological activity based on the inhibition of carbonic anhydrases [7c] or cyclooxygenase-2 [8]. As shown by Supuran *et al.*, [7c, 12] numerous metal complexes with sulfonamide ligands act as carbonic anhydrase inhibitors.



1 **2**

Fig. 1. Structural formulae of PMSA (**1**) and *trans*-[Pt(PMSA)$_2$I$_2$] (**2**).

Recently [13a], we studied the conformational features (by molecular mechanics and HF *ab initio* calculations) and infrared spectra of *N*-3-pyridinyl-methanesulfonamide (PMSA). In continuation of our studies on the design of new platinum complexes as potential anticancer agents [14], a series of Pd(II) and Pt(II) complexes of PMSA was synthesized by us and characterized spectroscopically [13b]. The crystal structure of neither the free ligand nor its complexes has been studied so far.

Table 1a. Selected bond lengths (Å) and angles (deg) for **1**.

N(1)-C(1)	1.335(5)	C(1)-C(2)	1.382(6)
C(2)-C(3)	1.376(6)	C(3)-C(4)	1.375(6)
C(4)-C(5)	1.361(7)	N(1)-C(5)	1.331(6)
C(2)-N(2)	1.406(5)	S(1)-N(2)	1.613(5)
S(1)-O(1)	1.419(3)	S(1)-O(2)	1.427(3)
S(1)-C(6)	1.741(6)	N(1A)-C(1A)	1.333(5)
C(1A)-C(2A)	1.375(6)	C(2A)-C(3A)	1.380(6)
C(3A)-C(4A)	1.371(7)	C(4A)-C(5A)	1.364(7)
N(1A)-C(5A)	1.322(5)	C(2A)-N(2A)	1.417(5)
S(2)-N(2A)	1.619(4)	S(2)-O(1A)	1.418(4)
S(2)-O(2A)	1.428(3)	S(2)-C(6A)	1.749(7)
C(1)-C(2)-N(2)	117.4(4)	C(3)-C(2)-N(2)	124.8(4)
C(1)-N(1)-C(5)	116.3(4)	C(2)-N(2)-H(2)	117(4)
S(1)-N(2)-C(2)	127.9(3)	S(1)-N(2)-H(2)	114(4)
N(2)-S(1)-O(1)	109.3(2)	N(2)-S(1)-O(2)	105.5(2)
N(2)-S(1)-C(6)	106.1(3)	O(1)-S(1)-O(2)	119.5(2)
O(1)-S(1)-C(6)	108.3(3)	O(2)-S(1)-C(6)	107.3(2)
C(1A)-C(2A)-N(2A)	119.7(3)	C(3A)-C(2A)-N(2A)	122.8(4)
C(1A)-N(1A)-C(5A)	117.2(4)	C(2A)-N(2A)-H(2A)	115(3)
S(2)-N(2A)-C(2A)	122.7(3)	S(2)-N(2A)-H(2A)	113(3)
N(2A)-S(2)-O(1A)	109.5(2)	N(2A)-S(2)-O(2A)	105.46(19)
N(2A)-S(2)-C(6A)	106.7(3)	O(1A)-S(2)-O(2A)	118.1(2)
O(1A)-S(2)-C(6A)	106.9(3)	O(2A)-S(2)-C(6A)	109.7(3)
S(1)-N(2)-C(2)-C(1)		167.8(3)	
S(1)-N(2)-C(2)-C(3)		−13.6(7)	
O(1)-S(1)-N(2)-C(2)		−33.8(5)	
O(2)-S(1)-N(2)-C(2)		−163.5(4)	
C(6)-S(1)-N(2)-C(2)		82.8(5)	
S(2)-N(2A)-C(2A)-C(1A)		−138.1(4)	
S(2)-N(2A)-C(2A)-C(3A)		44.9(6)	
O(1A)-S(2)-N(2A)-C(2A)		−59.7(4)	
O(2A)-S(2)-N(2A)-C(2A)		172.3(3)	
C(6A)-S(2)-N(2A)-C(2A)		55.7(5)	

Here we report the single crystal X-ray diffraction analysis of PMSA (**1**) and of the complex *trans*-$[Pt(PMSA)_2I_2]$ (**2**) (Fig. 1) which appears to be the first structurally characterized metal complex of this ligand.

Results and Discussion

Selected geometric parameters for the molecules of compounds **1** and **2** are collected in Table 1. A perspective view of the two crystallographically non-equivalent asymmetric molecules of the free ligand, **1a** and **1b**, is shown in Fig. 2. The bond lengths and bond angles have the usual values compared with other *N*-aryl- (hetaryl-) substituted sulfonamides [15 – 18]; they are in satisfactory agreement with the theoretically calculated values (HF *ab initio* optimization of a single molecule with the 3-21G(*) basis set) [13a]. The conformers **1a** and **1b** differ considerably with respect to the bond angles around the sulfonamide nitrogen atom. Thus, in **1a**, the sulfonamide N(2) atom is almost fully planarized (sp^2 hybridization, sum of the bond angles 358.9°), as predicted by the *ab initio* calculations [13a]. In **1b** the sulfonamide N(2A) atom has a flattened-pyramidal configuration (sum of the bond angles 350.7°), like in other similar sulfonamides [15, 16]. It is interesting to note that a complete planarization for the sulfonamide N atom has been observed in the Zn(II) complex of methanesulfonic acid hydrazide [19a], in distinct with the non-coordinated ligand [19b] and with its Co(II) and Ni(II) complexes [19c]. The second significant difference between the two independent PMSA molecules concerns the torsion angles about the S–N(2) and N(2)–

Table 1b. Selected bond lengths (Å) and angles (deg) for **2**.

N(1)-C(1)	1.341(12)	C(1)-C(2)	1.389(12)
C(2)-C(3)	1.393(12)	C(3)-C(4)	1.371(13)
C(4)-C(5)	1.361(13)	N(1)-C(5)	1.346(12)
C(2)-N(2)	1.413(10)	S-N(2)	1.625(7)
S-O(1)	1.422(7)	S-O(2)	1.424(7)
S-C(6)	1.750(18)	Pt-I(1)	2.6071(7)
Pt-N(1)	2.032(7)		
C(1)-C(2)-N(2)	121.6(7)	C(3)-C(2)-N(2)	120.1(7)
C(1)-N(1)-C(5)	120.9(7)	C(2)-N(2)-H(2)	117.52
S-N(2)-C(2)	124.8(6)	S-N(2)-H(2)	117.64
N(2)-S-O(1)	108.6(4)	N(2)-S-O(2)	104.4(4)
N(2)-S-C(6)	106.0(7)	O(1)-S-O(2)	118.4(4)
O(1)-S-C(6)	110.5(7)	O(2)-S-C(6)	108.1(7)
C(1)-N(1)-Pt	119.0(6)	C(5)-N(1)-Pt	120.1(6)
I(1)-Pt-N(1)	90.0(2)	I(1a)-Pt-N(1)	90.0(2)
S-N(2)-C(2)-C(1)		43.1(11)	
S-N(2)-C(2)-C(3)		−138.3(7)	
O(1)-S-N(2)-C(2)		−51.6(8)	
O(2)-S-N(2)-C(2)		−178.7(7)	
C(6)-S-N(2)-C(2)		67.2(10)	
I(1)-Pt-N(1)-C(1)		−68.9(6)	
I(1)-Pt-N(1)-C(5)		111.3(6)	

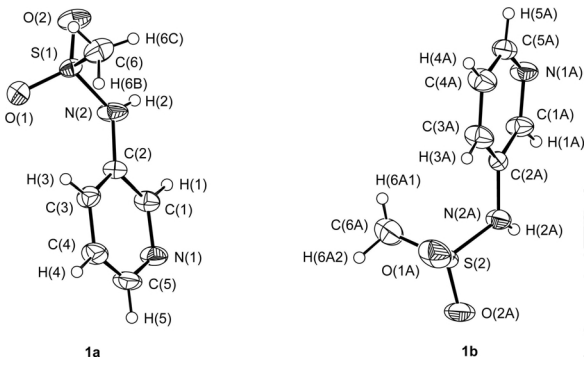


Fig. 2. Molecular structure of PMSA (**1**) with the atom numbering scheme of the two independent molecules (**1a** and **1b**). Thermal ellipsoids are drawn at the 40% probability level.

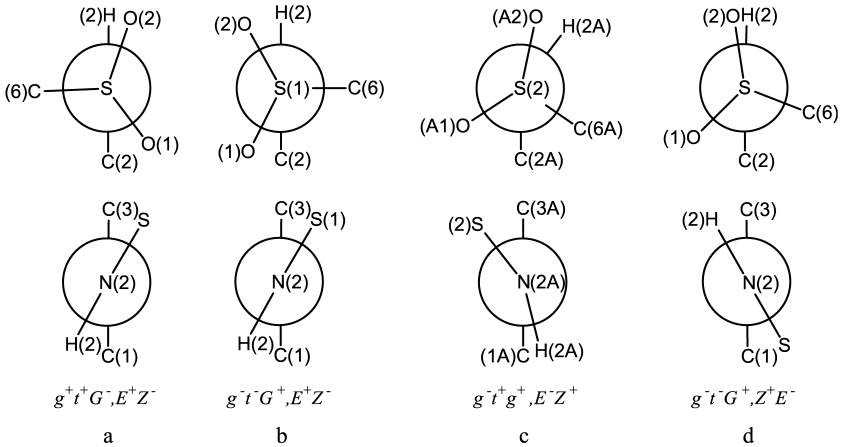


Fig. 3. Newman projections of: a) the *ab initio* optimized minimum-energy conformation of an isolated PMSA molecule [13a] (note: here the numbering of O(1) and O(2) is the opposite of that used in [13a]); b) and c) the two independent molecules (**1a** and **1b**, respectively) in the crystal structure of PMSA, d) The PMSA ligand in the crystal structure of *trans*-$[Pt(PMSA)_2I_2]$ (**2**). The first three letters in the notations of the conformations refer to the torsion angles O(1)−S−N(2)−C(2), O(2)−S−N(2)−C(2) and C(6)−S−N(2)−C(2), respectively: *t* = *trans* (torsion angle between 120 and 180°)), *g* – *gauche* with torsion angle between 0 and 60°, *G* = *gauche* with torsion angle between 60 and 120°, with the corresponding sign. The remaining two letters refer to the torsion angles S−N(2)−C(2)−C(1) and H(2)−N(2)−C(2)−C(1), respectively (*E* = *entgegen*, *Z* = *zusammen*).

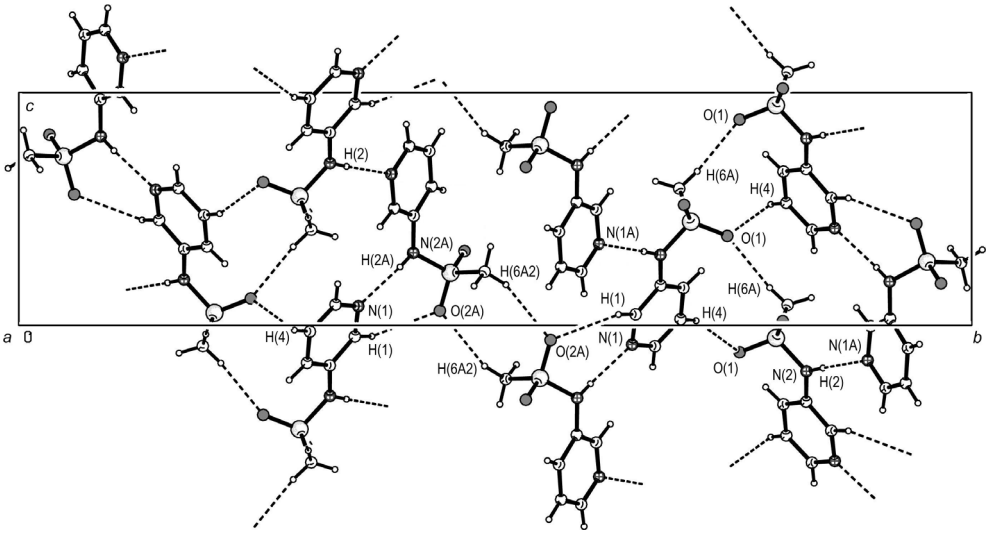


Fig. 4. A view of the packing of PMSA (**1**) within the unit cell, showing most of the hydrogen bonds.

C(2) bonds, giving rise to the different conformations $g^-t^-G^+$, E^+Z^- and $g^-t^+g^+$, E^-Z^+ for **1a** and **1b**, respectively, as shown in Fig. 3b, c. It is noteworthy that the *ab initio* optimized structure of PMSA closely approaches that of **1a**. Thus, at qualitative level the conformations with respect to the S–N bond are mirror images, and these with respect to the N–C(2) bond are the same (Fig. 3a, b)

Fig. 4 shows the crystal packing of **1**. The parameters of the hydrogen bond network for **1** and **2** are collected in Table 2. In both conformers **1a** and **1b**, the γ-hydrogen atoms of the pyridine ring form an intramolecular hydrogen bond with a sulfonyl oygen atom (C(3)–H(3)···O(1) and C(3A)–H(3A)···O(1A), respectively). Two types of intermolecular hydrogen bonds connect the conformers **1a**: between the

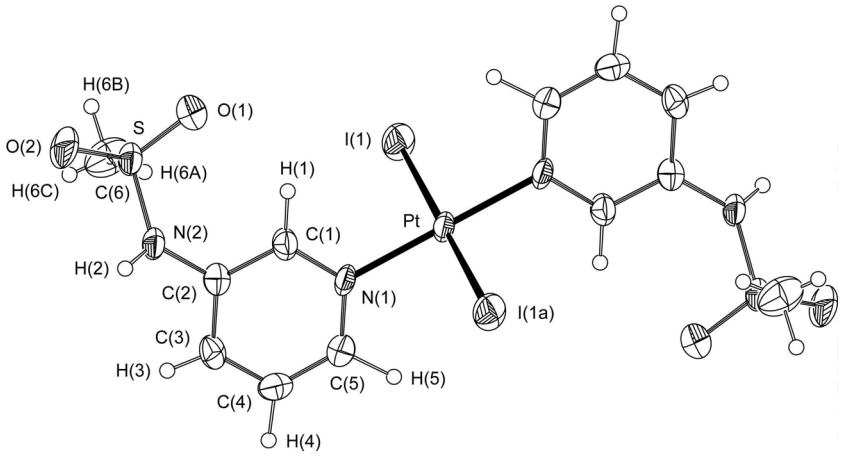


Fig. 5. Molecular structure of *trans*-[Pt(PMSA)$_2$I$_2$] (**2**) with the atom numbering scheme. Thermal ellipsoids are drawn at the 40% probability level.

Table 2. Distances and angles for the intra- and intermolecular hydrogen bonds of compounds **1** and **2**[a].

D−H···A	D-H [Å]	H···A [Å]	D···A [Å]	∠ D-H···A [deg]
	1			
C(3)-H(3)···O(1)	0.90(4)	2.55(4)	3.043(5)	116(3)
C(3A)-H(3A)···O(1A)	0.89(4)	2.44(4)	3.041(6)	126(3)
C(4)-H(4)···O(1)^{i}	0.94(4)	2.58(4)	3.467(6)	157(3)
C(6)-H(6A)···O(1)^{ii}	0.89(5)	2.40(6)	3.285(7)	173(5)
C(6)-H(6B)···O(2)^{iii}	0.96(6)	2.31(6)	3.216(6)	158(5)
C(6A)-H(6A2)···O(2A)^{iv}	0.98(6)	2.59(6)	3.519(8)	158(5)
C(1)-H(1)···O(2A)	0.98(6)	2.60(4)	3.332(6)	132(3)
N(2)-H(2)···N(1A)^{v}	0.69(4)	2.27(5)	2.946(6)	165(5)
N(2A)-H(2A)···N(1)	0.78(4)	2.13(4)	2.897(5)	168(4)
	2			
C(1)-H(1)···O(1)	1.01(7)	2.26(7)	2.961(12)	125(5)
C(6)-H(6B)···O(1)^{vi}	0.99(14)	2.53(12)	3.31(2)	136(10)
N(2)-H(2)···O(2)^{vii}	0.860	2.360	2.868(10)	118.0

[a] Symmetry transformations: ^{i} $1+x, 1/2-y, 1/2+z$; ^{ii} $x, 1/2-y, -1/2+z$; ^{iii} $1+x, y, z$; ^{iv} $-x, -y, 1-z$; $^{v)}$ $-1+x, y, -1+z$; ^{vi} $1/2-x, 3/2-y, 1-z$; ^{vii} $1/2-x, -1/2+y, 1/2-z$.

methyl and sulfonyl group (C(6)–H(6A)···O(1) and C(6)–H(6B)···O(2)), and between a β-hydrogen atom of the pyridine ring and the sulfonyl group (C(4)–H(4)···O(1)). The conformers **1b** form centrosymmetric hydrogen-bonded dimers of the type DA=AD in expense of a pair of bonds C(6A)–H(6A2)···O(2A) involving the methyl and sulfonyl groups. The two different conformers **1a** and **1b** are linked between each other by two types of hydrogen bonds – a short bond of the type N–H···N involving the imino hydrogen and the pyridine nitrogen atom (H(2)···N(1A) = 2.27 Å and H(2A)···N(1) = 2.13 Å), and a longer one C(1)–H(1)···O(2A) (H(1)···O(2A) = 2.60 Å) connecting a pyridine α-hydrogen with a sulfonyl oxygen atom. Thus, the different conformations of the molecules **1a** and **1b** give rise in the different intermolecular contacts.

The analysis of the IR spectra of **1** in solution and in the solid state gave us earlier [13a] the reason to assume the existence of a strong intermolecular hydrogen bond between the pyridine N atom and the acidic H atom of the sulfonamide group. The present X-ray structural analysis approved this suggestion.

A view of the complex molecule **2** is depicted in Fig. 5. The two PMSA ligands in *trans*-configuration are bound to the platinum by the pyridine nitrogen atom. The donor atoms are coplanar and form a D_{2h} tetragon (N_2I_2) with the platinum in the center. The point group of the entire complex molecule is C_i. The Pt–I and Pt–N bond lengths (2.607 and 2.032 Å, respectively) are in the ranges reported for *trans*-diiodo complexes of Pt(II) with pyridine-type ligands [20–22]. The bond lengths and bond angles of the pyridine ring, as well as of the methanesulfonamide fragment in **2** are not affected considerably by the coordination. The sulfonamide nitrogen atom is fully planarized (sum of the bond angles 360°) like in **1a**. The conformation of the sulfonamide residue in **2** ($g^-t^-G^+, Z^+E^-$, Fig. 3d) differs, however, significantly as compared with the free ligand with respect to the torsion angles about the N(2)–C(2) bond (Table 1). This could be a result of the different type of hydrogen bonding (*vide infra*).

Like in other complexes of the type *trans*-[ML$_2$X$_2$] (M = Pt, Pd; L = pyridine-like ligand; X = Cl, Br, I) [1b, 20–27], the planes of the pyridine rings are not perpendicular to the coordination plane, but are rotated in the opposite directions, the dihedral angles being 69 and −69°. The experimentally established geomet-

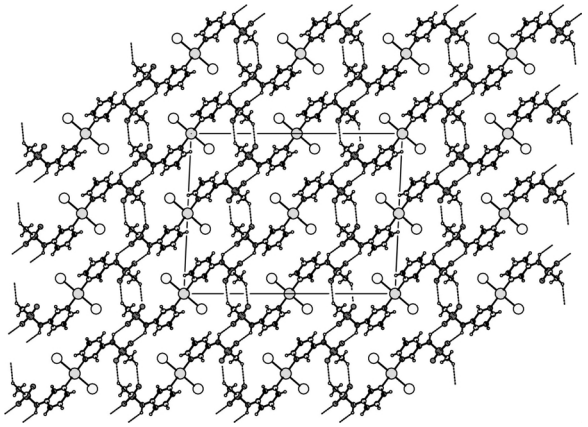


Fig. 6. A view of the extended hydrogen bonding network of *trans*-[Pt(PMSA)$_2$I$_2$] (**2**) along the *b* axis.

ric parameters for the coordination node of **2** appeared quite similar to the values ascribed to them in [13b] for the purposes of the normal coordinate analysis and the interpretation of the far IR spectrum of the complex.

The crystal packing of **2** is presented in Fig. 6. The O(1) atom forms an intraligand hydrogen bond with H(1) atom of the pyridine ring. The complex molecules are connected centrosymmetrically *via* two couples of hydrogen bonds of the pattern DA=AD. The first couple involves the methyl group and the O(1) atom (C(6)–H(6B)$\cdots$O(1)), and the second one (the shorter) – the imino-hydrogen and O(2) atom (N(2)–H(2)$\cdots$O(2)).

Conclusion

The single crystal X-ray diffraction analysis of the pharmacologically interesting compounds PMSA and *trans*-[Pt(PMSA)$_2$I$_2$] confirmed most of the conclusions regarding their structure, made earlier [13] on the basis of computational and spectroscopic results. The existence of a strong intermolecular hydrogen bond between the pyridine nitrogen and the sulfonamide hydrogen atom, previously suggested from the IR spectra of PMSA, was now proved by the X-ray analysis. Hydrogen-bonded assemblies of this type are of interest for supramolecular chemistry and crystal engineering [28], and could be related to molecular crystals with increased solid-state electric conductivity [29].

Experimental Section

The ligand PMSA (**1**) was prepared from methanesulfonylchloride and 3-aminopyridine by the method of Jones and Katritzky [30], and purified with charcoal [13a]. Crystal suitable for X-ray diffraction was selected from the crystalline mass obtained after the recrystallization of the product from hot water. Latter we found that well-formed, large (up to 7 mm) crystals of PMSA can be obtained by long concentration at room temperature of a solution of the compound in a methanol water (2:1) mixture.

The complex *trans*-[Pt(PMSA)$_2$I$_2$] (**2**) was synthesized by reacting [Pt(PMSA)$_4$]Cl$_2$ and KI in *N*,*N*-dimethylformamide, and recrystallizing the crude product from acetone [13b]. Crystal specimens for X-ray diffraction were obtained as follows. 5 – 7 mg of the recrystallized product were dissolved in 2 ml of hot acetone, and the solution was carefully layered over carbon tetrachloride (*ca.* 5 ml) in a short tube. The tube was stoppered, and avoiding shaking was left

Table 3. Crystal data and structure refinement for compounds **1** and **2***.

Compound	**1**	**2**
Empirical formula	$C_6H_8N_2O_2S$	$C_{12}H_{16}I_2N_4O_4PtS_2$
M	172.21	793.31
T [K]	293(2)	293(2)
λ [Å]	0.71073	0.71073
Crystal system	monoclinic	monoclinic
Space group	$P2_1/c$ (No 14)	$C2/c$ (No 15)
a [Å]	5.6436(7)	22.912(2)
b [Å]	33.875(4)	5.2397(5)
c [Å]	8.3356(10)	17.3376(17)
β [deg]	96.885(2)	92.631(2)
V [Å^3]	1582.1(3)	2079.2(3)
Z	8	4
D_{calcd} [Mg m^{-3}]	1.446	2.534
μ [mm^{-1}]	0.359	9.942
$F(000)$	720	1456
Crystal size, mm	$0.3\times0.4\times0.5$	$0.4\times0.4\times0.3$
θ Range for data coll. [deg]	2.40 to 26.37	1.78 to 26.37
Limiting indices h,k,l	$-7\le h\le 7$, $-42\le k\le 42$, $-10\le l\le 10$	$-28\le h\le 28$, $-6\le k\le 6$, $-21\le l\le 21$
Reflections collected	12360	7868
Independent reflections	3207	2123
R_{int}	0.0473	0.0605
Refinement method	– Full-matrix-block – least-squares on F^2 –	
Data / restraints / params.	3207 / 0 / 263	2123 / 0 / 144
Goodness-of-fit on F^2	1.237	1.071
Final R Indices ($I>2\sigma(I)$)	$R_1=0.0803$, $wR_2=0.1546$	$R_1=0.0452$, $wR_2=0.0869$
R Indices (all data)	$R_1=0.1014$, $wR_2=0.1629$	$R_1=0.0603$, $wR_2=0.0916$
Largest diff. peak and hole [e Å^{-3}]	0.480 and −0.346	1.185 and −1.240

* Crystallographic data for the structures have been deposited with the Cambridge Crystallographic Data Centre, CCDC-229268 and CCDC-229269. Copies of the data can be obtained free of charge on application to The Director, CCDC, 12 Union Road, Cambridge CB2 1EZ, UK (Fax: int.code +(1223)336-033; e-mail for inquiry: fileserv@ccdc.cam.ac.uk).

in a refrigerator (0 °C). After 7 – 10 days the yellow crystals were collected on a filter, washed with ether and dried *in vacuo*.

X-ray diffraction data were collected on a Bruker Smart Apex diffractometer with graphite-monochromated Mo-K_α radiation in the $\omega - 2\theta$ mode [31, 32]. Cell constants were determined by using 25 reflections in the range $2.40 < \theta < 27.18^\circ$ and $2.35 < \theta < 26.57^\circ$ for **1** and **2**, respectively. Lorentz and polarization effects were corrected. Data reduction and analysis were carried out with the Bruker Smart programs. The structure was solved by direct methods (program SHELXS97) and refined by the full-matrix least-squares method on all F^2 data using the WinGX version of SHELXL97 programs [31, 32]. Anisotropic thermal parameters were used for all non-hydrogen atoms. All hydrogen atoms for **1** and **2** were located through Fourier-difference synthesis, except N(2)−H for **2** was set in calculated position. Molecular graphics were performed using PLATON2001 [33]. A summary of the crystal data, experimental details and refinement results is presented in Table 3.

Acknowledgements

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