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The X-ray crystal structure of *N*,*S*-bis[(4′-chloro-2,2′:6′,2″-terpyridine)platinum(II)]-2-mercaptoimidazole tris-hexafluorophosphate and tris[(2,2′:6′,2″-terpyridine)platinum(II)]sulfonium tetra-perchlorate†

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Intramolecular stacking of the (4′-chloro-2,2′:6′,2″-terpyridine)platinum(II) moieties occurs in *N*,*S*-bis[(4′-chloro-2,2′:6′,2″-terpyridine)platinum(II)]-2-mercaptoimidazole tris-hexafluorophosphate; *N*,*S*-bis[(2,2′:6′,2″-terpyridine)-platinum(II)]thioacetimine trinitrate is slowly transformed in aqueous solution to the molecular propeller-like tris-[(2,2′:6′,2″-terpyridine)platinum(II)]sulfonium ion.

We have recently shown that (2,2′:6′,2″-terpyridine)platinum(II) complexes are cytotoxic to human ovarian carcinoma and that bis[(2,2′:6′,2″-terpyridine)platinum(II)] complexes with short and rigid linkers are particularly effective.[1] This study has been extended to (2,2′:6′,2″-terpyridine)platinum(II) thiolate complexes.[2] Since intercalation into DNA of such molecules may contribute to their antitumour activity we investigated the crystal structure of *N*,*S*-bis[(4′-chloro-2,2′:6′,2″-terpyridine)platinum(II)]-2-mercaptoimidazole tris-hexafluorophosphate **1** in order to determine whether the two (4′-chloro-2,2′:6′,2″-terpyridine)platinum(II) moieties were stacked. If they are, this might be expected to preclude intercalation into DNA.

As seen in Fig. 1 the two (4′-chloro-2,2′:6′,2″-terpyridine)platinum(II) moieties stack virtually parallel to each other, the platinum–platinum distance being 3.2903 Å.‡ The crystals were obtained from water. This stacking of the (4′-chloro-2,2′:6′,2″-terpyridine)platinum(II) moieties in **1**, is maintained in solution,[3] and should preclude it from intercalating into DNA. This supports the conclusion reported recently that DNA is not the principal target for the antitumour activity of these complexes.[2]

The bis-complex **2**, which was characterised spectroscopically (ESI)† is expected to adopt a similar conformation to **1**. However, unlike **1** and its analogue *N*,*S*-bis[(2,2′:6′,2″-terpyridine)platinum(II)]-2-mercaptoimidazole ion (which were stable), it was observed that on storing the bis-complex **2** in aqueous solution over a period of weeks, decomposition occurred ($t_{1/2}$ = 10.5 days at 20 °C) releasing acetamide and a new complex[4] which was shown by electrospray mass spectrometry to have *m*/*z* = 444 (M^{2+} with isotope distribution for two Pt atoms) consistent with the complex **3** (Scheme 1). The thioacetimine moiety in **2** would be activated by the 2,2′:6′,2″-terpyridine platinum(II) complexes and the tetrahedral intermediate formed from **2** by the nucleophilic attack of water would be expected to collapse to **3** and acetamide. The X-ray

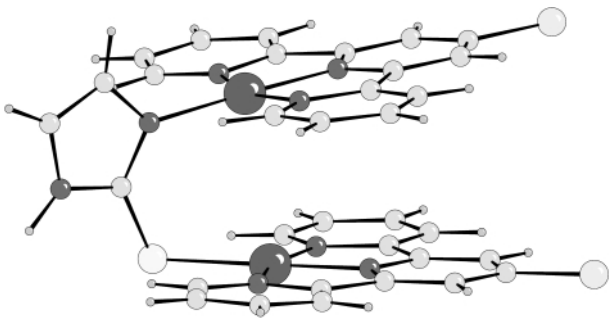
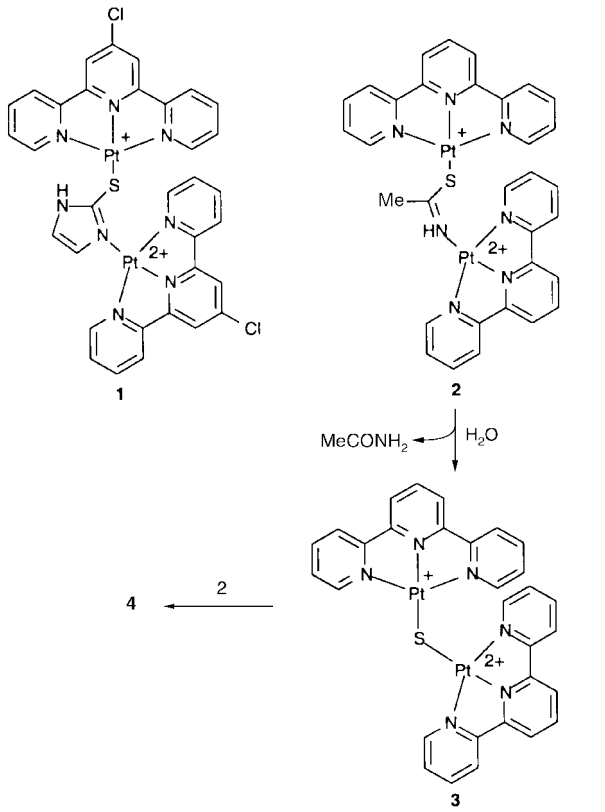


Fig. 1 The X-ray crystal structure of *N*,*S*-bis[(4′-chloro-2,2′:6′,2″-terpyridine)platinum(II)]-2-mercaptoimidazole tris-hexafluorophosphate **1**, showing the stacked (4′-chloro-2,2′:6′,2″-terpyridine)platinum(II) complexes with a Pt–Pt distance of 3.2903 Å and an interplanar angle of 7.5(5)°. The bond lengths to 2-mercaptoimidazole are Pt–S [2.312(4) Å] and Pt–N [2.021(4) Å]. The counter ions and solvent of crystallization are excluded for clarity.

† Electronic supplementary information (ESI) available: spectroscopic data for **1** and **2**. See http://www.rsc.org/suppdata/cc/b1/b103637h/



Scheme 1

 DOI: 10.1039/b103637h

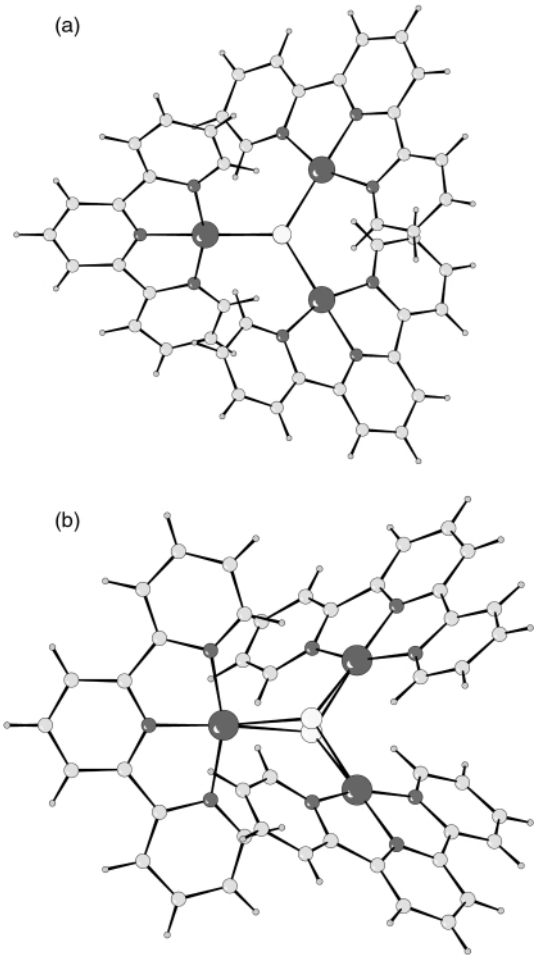


Fig. 2 The X-ray crystal structure of tris[(2,2′:6′,2″-terpyridine)platinum(II)]sulfonium tetra-perchlorate **4**: (a) down the three-fold axis and (b) at an angle to the three-fold axis showing molecules with the same propeller helicity with the sulfur atom above or below the reference plane of the three Pt atoms. The Pt–S bond lengths are 2.32 ± 0.01 Å and the tilt of the three (2,2′:6′,2″-terpyridine)platinum(II) planes is 40 ± 1° to the reference plane of the three Pt atoms. The counter ions and solvent of crystallization are excluded for clarity.

crystal structure of the product [Fig. 2(a)] is clearly not **3**. This tris[(2,2′:6′,2″-terpyridine)platinum(II)]sulfonium salt **4**‡ could be formed from **3** by sulfur abstracting (2,2′:6′,2″-terpyridineplatinum(II) from **2**. Tris[(2,2′:6′,2″-terpyridine)platinum(II)]sulfonium ion **4** would be expected to readily fragment to **3** in the mass spectrometer. Although aliphatic thioethers (*e.g.* methionine)[5] and dimethyl sulfoxide[6] will not ligate to 2,2′:6′,2″-terpyridine)platinum(II) because of the steric hindrance with the 6,6″ hydrogens, the planar nature of the substituents at sulfur in **3** and the longer S–Pt bond compared with the S–C bond make it possible to form **4**.

The X-ray crystal structure shows that the three (2,2′:6′,2″-terpyridine)platinum(II) moieties generate propeller-like helicity which can be right- or left-handed. Sulfur is at the apex of a shallow pyramid, with the S atom 0.354 Å above or below the reference plane formed by the three Pt atoms which are at the apices of an equilateral triangle (Fig. 2). It is not however a stereogenic centre. The three N′–Pt–S bond angles are 172° to accommodate the pyramidalization at sulfur. Thus flipping the molecule through 180° leaves the molecular helicity unchanged but with the sulfur atom on the opposite side of the reference plane formed by the three Pt atoms. Thus each enantiomer (left or right-handed molecular propeller) has crystallised in two orientations in the crystal lattice with equal probability leading to the two positions observed for the sulfur atom [Fig. 2(b)]. The tilt of the (2,2′:6′,2″-terpyridine)platinum(II) moieties from the reference plane of the Pt atoms is 40 ± 1° for each 'blade' of the propeller. Thus the flanking pyridine rings of each (terpyridine)platinum(II) moiety that are on the same side of the reference plane as the sulfur atom are in a different molecular environment from the flanking pyridine rings on the side opposite the sulfur atom. Consequently all ^{1}H resonances of the terpyridines in the NMR spectrum have different chemical shifts and are not resolved.

Propeller-like molecules have been extensively investigated.[7] Because of the necessity for the correlated rotation of the (2,2′:6′,2″-terpyridine)platinum(II) moieties, the tris-[(2,2′:6′,2″-terpyridine)platinum(II)]sulfonium ion forms stable left- and right-handed propeller-like molecules.

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Notes and references

‡ Crystal structure determinations: complex **1**: *Crystal data*: $C_{33}H_{23}Cl_2F_{18}N_8O_2P_3Pt_2S$, M = 1491.63, triclinic, space group $P\bar{1}$, a = 11.9306(1), b = 14.3873(2), c = 15.3729(2) Å, α = 97.1106(5), β = 112.5601(5), γ = 109.7985(5)°, U = 2192.8 Å^3, T = 190 K, Z = 2, μ(Mo-Kα) = 6.773 mm^{-1}, 33327 reflections measured, 8930 unique (R_{int} = 0.032), 7689 observed with $I > 3\sigma(I)$ which were used in all calculations. The final $wR(F)$ was 0.0375 for observed data.

Complex **4**: *Crystal data*: $C_{57}H_{57}Cl_4N_9O_{20}Pt_3S$, M = 973.63, monoclinic, space group $C12/c1$, a = 15.2505(3), b = 24.4126(5), c = 17.3087(3) Å, β = 90.0327(15), U = 6444.1 Å^3, T = 190 K, Z = 4, μ(Mo-Kα) = 6.776 mm^{-1}, 20122 reflections measured, 6940 unique (R_{int} = 0.031), 6004 observed with $I > 3\sigma(I)$ which were used in all calculations. The final $wR(F)$ was 0.0306 for observed data. Owing to the volatility of the solvate the crystal was mounted in a Lindemann tube.

CCDC reference numbers 162979 and 162980. See http://www.rsc.org/suppdata/cc/b1/b103637h/ for crystallographic data in CIF or other electronic format.

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2 K. Becker, C. Herold-Mende, J. J. Park, G. Lowe and R. H. Schirmer, *J. Med. Chem.*, 2001, **44**, in press.
3 The UV–VIS spectrum of **1** in aqueous solution (determined by Dr R. Quarrell) shows absorption bands at λ_{max}/nm (ε/dm^3 mol^{-1} cm^{-1}) 205 (100600), 243 (69050), 273 (52500), 300–360 (charge transfer) and 477 (3260). The broad band at 477 nm is characteristic of stacking of the (4-chloro-2,2′:6′,2″-terpyridine)platinum(II) moieties, see: H.-K. Yip, C.-M. Che, Z.-Y. Zhou and T. C. W. Mak, *J. Chem. Soc., Chem. Commun.*, 1992, 1369; G. Lowe and T. Vilaivan, *J. Chem. Soc., Perkin Trans. 1*, 1996, 1499.
4 Complex **2** (50 mg) was dissolved in water (2 mL) to which was added excess sodium perchlorate, followed by acetone (2 mL). The solution was allowed to evaporate slowly over 3 weeks which gave **4** as red crystals (*ca.* 20 mg).
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