X-Ray Crystal Structure of a 2:2 Chloroterpyridineplatinum(II)–Adenosine-5′-monophosphate Intercalation Complex

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Summary Chloroterpyridineplatinum(II) forms a 2:2 intercalation complex with adenosine-5′-monophosphate (AMP), the geometry of which has been revealed through a single crystal *X*-ray diffraction study.

METAL complexes can bind to nucleic acids by covalent attachment to donor atoms of the bases or the sugar phosphate backbone, by ionic interactions, or by intercalation. The last binding mode, frequently observed for antibiotics and drugs such as actinomycin D,[1] has been demonstrated for a family of cationic, planar complexes of platinum(II) having 2,2′-bipyridine (bpy), 2,2′,2″-terpyridine (terpy), or related ligands.[2] One of these platinum metallointercalators has been shown to inhibit genetic recombination in pneumococci.[3] Here we report the synthesis and structure of the 2:2 intercalation complex formed between [(terpy)PtCl]$^+$ (I) and adenosine-5′-monophosphate (AMP). The characterization of this complex is important in understanding its binding, and that of other intercalators, to oligo- and poly-nucleotides.

Orange crystals of the 2:2 complex were obtained by slow evaporation of an aqueous solution containing 0·1 M AMP (sodium salt) and 0·1 M [(terpy)PtCl]Cl·2H_2O.[4] The crystals are monoclinic with $a = 37·69(3)$, $b = 10·316(8)$, $c = 16·03(1)$ Å, $\beta = 93·23(3)°$, $Z = 4$, $M = 1702·1$, space group $C2$; 3424 independent reflections were measured [graphite monochromatized Mo-K_α four-circle diffractometry: $2\theta \leqslant 42°$; $I_{obs} > 3\sigma(I_{obs})$; intensities corrected for Lorentz and polarization effects and for absorption]. The structure was solved by the conventional heavy atom method and refined by least-squares to a final value of $R = 0·048$. The molecular structure is shown in the Figure.†

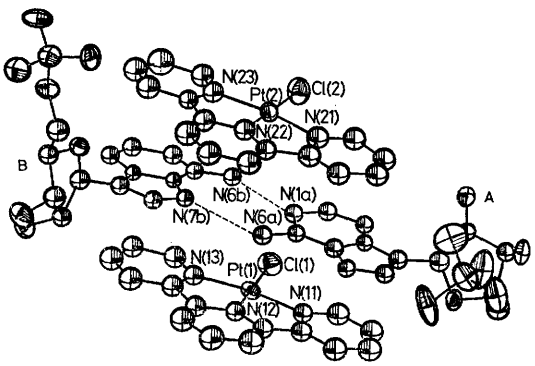

FIGURE. Geometry of the 2:2 (I)–AMP intercalation complex showing one crystallographic asymmetric unit and omitting the water molecules in the lattice (- - - -, hydrogen bond). Translation of this unit in the vertical direction produces additional head-to-head stacking of the [(terpy)PtCl]$^+$ species.

The crystallographic asymmetric unit contains two molecules of (I), a hydrogen-bonded AMP base pair, and 4·5 water molecules. The base pair is intercalated between two [(terpy)PtCl]$^+$ cations which in turn are stacked on one another in the crystal lattice. The result is a reverse kind of nearest neighbour exclusion effect[2b] where the usual

† The atomic co-ordinates for this work are available on request from the Director of the Cambridge Crystallographic Data Centre, University Chemical Laboratory, Lensfield Road, Cambridge CB2 1EW. Any request should be accompanied by the full literature citation for this communication.

-BP-BP-I-BP-BP-I- (BP = base pair; I = intercalator) sequence found in polynucleotides saturated with simple intercalators now becomes -I-I-BP-I-I-BP-. Since neither the nucleotide nor the platinum complex is linked into a helix in the present example, the neighbour exclusion effect must have its origin in electrostatic and stacking forces. These may be more important in the neighbour exclusion mode of drug binding to polynucleotides than has recently been emphasized. It is interesting that the head-to-head self-stacking of (I) in the intercalation complex differs from the head-to-tail stacking pattern observed in structural studies of the related complexes $[(terpy)Pt(SCH_2CH_2OH)]^+$,[5] $[(terpy)PdCl]^+$,[4,6] and the red form of $[(bpy)PtCl_2]$.[7]

The cation (I) consists of platinum co-ordinated to the tridentate terpyridine ligand and to a chlorine atom. The co-ordination geometry is essentially square planar with distortions arising from constraints of the terpyridine ligand, as found in several related structures.[4-6] The AMP base pair has several interesting features. The inter-base hydrogen-bonding is of the rarely observed hybrid Watson–Crick–Hoogsteen variety,[8] where N(1) of one adenine base and N(7) of the other adenine base are used as hydrogen-bond acceptors from the N(6) amino-groups (Figure). The two ribose rings crystallize in different conformations. Ring A has the common C(2′)-*endo* sugar pucker with $\chi = 40°$ and the *anti* base and *gauch*$^+$ conformation ($\psi = 39°$) about the C(4′)–C(5′) bond.[9] Ring B exhibits the very rare C(4′)-*exo* pucker, with the base *anti* ($\chi = 70°$) but with a different, *trans* ($\psi = -175°$), conformation around the C(4′)–C(5′) bond. This result is consistent with the trend[10] that distortion of the nucleotide from its preferred conformation occurs more readily about the backbone C(4′)–C(5′) bond than the glycosidic C(1′)–N(9) linkage. Complete structural results and a more detailed analysis of the stereochemistry will be reported elsewhere.

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