Preparation of Some Platinum-linked Acridines and Crystal Structure of [3,6-Bis(dimethylamino)acridinioethyl]chloro-(*N,N,N',N'*-tetramethylethylenediamine)platinum(II) Perchlorate†

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The cationic platinum complex $[Pt(\eta^2\text{-}C_2H_4)Cl(tmen)]^+$ **1** (tmen = *N,N,N',N'*-tetramethylethylenediamine) reacted with acridines {3,6-diaminoacridine [proflavine, $NC_{13}H_7(NH_2)_2$] and 3,6-bis(dimethylamino)-acridine [acridine orange, $NC_{13}H_7(NMe_2)_2$]} to give platinum species in which the metal is linked to the polycyclic molecule by an ethylene chain. In the case of acridine orange the attack occurs at the endocyclic nitrogen giving the complex $[Pt\{CH_2CH_2NC_{13}H_7(NMe_2)_2\}Cl(tmen)]^+$ **2** which is in equilibrium with the starting species. On the contrary, in the case of proflavine the attack occurs preferentially at the exocyclic aminic groups leading to the formation of $[\{PtCl(tmen)\}_2\{HNC_{13}H_7(NHCH_2CH_2)_2\}]^+$ **3**, which does not dissociate into its constituents. In **3** each NH_2 group of the incorporated proflavine molecule has lost a proton, one of them has been taken up by the endocylic nitrogen, the other by an extra molecule of proflavine. Crystals of **2**, obtained from a dichloromethane solution, were characterized by X-ray crystallography: space group $P2_1/n$, a = 7.700(4), b = 25.446(3), c = 14.858(6) Å, β = 99.08(2)° and Z = 4. The refinement converged to R = 0.0572. The co-ordination around platinum is essentially square planar and the co-ordination plane makes an angle of 29.2(4)° with the plane of the acridine moiety. The acridine rings are infinitely stacked in a head-to-tail fashion. The plane-to-plane distance is about 3.5 Å and the closest Pt • • • Pt distance is 5.178(2) Å.

After the initial reports[1] on the possibility that polycyclic organic molecules interact by intercalation with cellular DNA, and that this mode of interaction operates in several antitumour drugs, there has been growing interest in potentially intercalating systems.[2]

The role of intercalation in the action of a mutagenic, cytotoxic, or antitumour drug is still a debated question. There is evidence that the pharmacological activity of an intercalator depends strongly upon the nature and position of the ring substituents (geometrical isomers can be very different in this respect).[3-5] Therefore intercalation could not be, by itself, the primary cause of drug activity, although it could raise the DNA targeting ability of the molecule. (For this reason studies have been performed in which a rather non-specific alkylating agent, *e.g.* an aniline mustard, has been linked to an intercalator.)[6] A special case is that of metallointercalators. There are several reasons why it could be useful to anchor a metal ion to a DNA intercalating system: metals are easily recognizable in X-ray diffraction patterns and, through their monitoring, the intercalation process could be investigated;[7] metal complexes containing planar aromatic ligands can behave themselves as intercalators;[8] and the anchoring of a positive metal ion to a neutral intercalator can increase the overall binding constant towards DNA, which is a negatively charged polymer.[9]

Since most chemotherapeutic protocols use *cis*-diamminedichloroplatinum(II) (*cis*-DDP) in combination with intercalating drugs,[10] several synthetic strategies have been sought to produce bifunctional molecules in which a *cis*-DDP like residue is anchored to an intercalator, generally of the acridine family.[11-13] The compounds so far synthesised have not shown the expected synergistic effect of the two functionalities present in them, however it has been shown that DNA promotes the interaction between *cis*-DDP and the exocyclic nitrogens of ethidium (3,8-diamino-5-ethyl-6-phenylphenanthridinium) bromide.[14] A platinum–ethidium complex has also been prepared and fully characterized.[15]

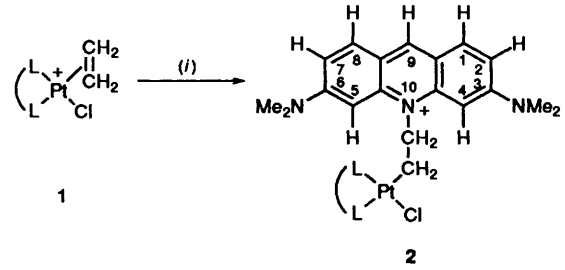
We have exploited the possibility of preparing bifunctional complexes by direct reaction between a nucleophile (the intercalator) and an electrophile (a metal complex). Some cationic platinum(II) complexes of formula $[Pt(\eta^2\text{-olefin})(L\text{–}L)X]^+$ (L–L = dinitrogen donor ligand, X = anionic ligand)[16] show enhanced electrophilicity of the co-ordinated olefin[17] and react with various nucleophiles including deactivated tertiary amines.[18] We allowed $[Pt(\eta^2\text{-}C_2H_4)Cl(tmen)]ClO_4$ **1** (tmen = *N,N,N',N'*-tetramethylethylenediamine) to react with some acridines, such as proflavine [3,6-diaminoacridine, $NC_{13}H_7(NH_2)_2$] and acridine orange [3,6-bis(dimethylamino)acridine, $NC_{13}H_7(NMe_2)_2$]. In both acridine molecules the endocyclic nitrogen is reported to have the highest basicity and therefore to be the preferred site of attack, however also the less basic exocyclic aminic groups could become the sites of attack if the electrophile is sufficiently activated. In the case of proflavine the product of addition to the exocyclic nitrogens could become even more stable than that of addition to the endocyclic nitrogen if the positive charge accumulated on the nitrogen is removed by dissociation of a proton.

In this paper we report the synthesis, chemical properties and structural characterization of some platinum complexes with proflavine and acridine orange.

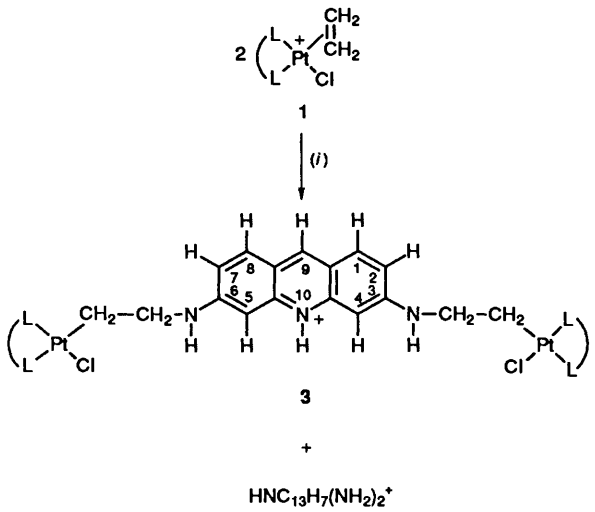
Results and Discussion

Preparation of Complexes.—Compound **1** reacts with acridine orange to give a 1 : 1 adduct **2** in which the site of attack

† *Supplementary data available:* see Instructions for Authors, *J. Chem. Soc., Dalton Trans.*, 1993, Issue 1, pp. xxiii–xxviii.



Scheme 1 (*i*) Acridine orange, CH_2Cl_2, 0 °C



Scheme 2 (*i*) 2 Proflavine, MeOH, 20 °C

has been the endocyclic nitrogen atom, N(10) (Scheme 1). The yield of product is high in aprotic solvents. If, instead, a solvent like methanol is used, the yield of **2** is rather small and the acridine acts mainly as a base favouring the addition of MeO^- anion (or OH^- if the solvent is not anhydrous) to the complexed ethylene. This reaction pattern is in accord with the well established behaviour of **1** in protic media and in the presence of bases of moderate or low nucleophilicity (either for electronic or steric reasons).[17]

When compound **1** is allowed to react with proflavine, independently of the reaction medium and the reagent ratio, the major product is a 2:1 adduct **3** containing two platinum residues and one proflavine molecule which is protonated at the endocyclic nitrogen. The formation of this compound is in accord with Scheme 2. When the reaction is performed in a protic medium, like methanol, compound **3** is the unique reaction product. However, in aprotic media, such as a chlorinated solvent, there is spectroscopic evidence that also the endocyclic nitrogen can interact with the platinum complex, although to a smaller extent.

Complexes of type **2**, formed by addition of **1** to the endocyclic nitrogen of an aromatic base, are generally rather labile and in solution they spontaneously dissociate into the starting materials. However, in the particular case of acridine orange (pK_a = 10), the formation equilibrium is well shifted in favour of the addition product and compound **2** can be prepared and crystallized in a pure form from dichloromethane. In a medium such as Me_2SO there is a slow but complete decomposition of **2** since the parent compound **1**, formed by partial dissociation of **2**, is unstable in this solvent and undergoes a further transformation.

In contrast, compound **3** (addition of the platinum–ethene moiety to the aliphatic nitrogen bases followed by deprotonation of the formed quaternary nitrogens) is very stable. For instance samples are stable indefinitely in the solid state and for hours in dimethyl sulfoxide. The latter result is rather surprising in consideration of the fact that Me_2SO (a solvent largely used also for biological tests) is quite reactive towards platinum and it can enter the metal co-ordination sphere displacing another ligand (for instance the dissolution of **1** in Me_2SO is accompanied by the formation of a new compound in which a Me_2SO molecule has taken the place of the olefin).

In conclusion the different behaviour of compounds **2** and **3** in Me_2SO is the best test of their relative stability. Compound **3** remains unchanged in Me_2SO, on the contrary, **2** decomposes giving rise to the same solvolysis product generated by **1** in this solvent, proving though that **2** participates in a dissociation equilibrium with its constituents.

^1H *NMR Data.*—The ^1H NMR data for complexes **2** and **3** together with values for free and protonated acridines are reported in Table 1. In the case of the acridine orange free base the chemical shifts of the aromatic protons are in the order $H^9 < H^1 < H^2 < H^4$ of increasing field strength. Upon alkylation (compound **2**) or protonation at N^{10}, H^9 and H^1 suffer a relevant downfield shift (slightly bigger for complex **2** than for the protonated base), while H^2 and H^4 exhibit minor changes. The NH signal was not detected in the room-temperature spectrum of monoprotonated acridine orange (in CD_2Cl_2 solution), indicating a scrambling of the proton among the endo- and exo-cyclic nitrogens of similar basicity. When full protonation was achieved by using an excess of acid, two signals for NH, at δ 13.29 and 12.92, with an intensity ratio of 1:2 were observed. The lower-field signal belongs to the proton bound to the endocyclic nitrogen and the latter to the protons bound to the exocyclic aminic groups.

The chemical equivalence of the acridine ring protons H^1 and H^8, H^2 and H^7, and H^4 and H^5 clearly indicates that in complex **2** the metallic moiety has added to the endocyclic nitrogen N^{10}. Furthermore the chemical shift of the β-CH_2 protons is very sensitive to the nature of the attached nucleophile (aromatic nitrogen base or aliphatic amine). In compound **2** the β-CH_2 signal is at δ 4.82, very close to the value of δ 5.06 found for the adduct of complex **1** with quinoline which can mimic, to some extent, the endocyclic nitrogen of acridine orange.

In the case of proflavine (free and monoprotonated base and complex **3**) H^9 is always the most deshielded proton, H^1 then follows; H^2 is always at lower field with respect to H^4 with the only exception of the free base in $CDCl_3$ solution, for which the opposite trend is observed. Moreover in **3** the protonation of the endocyclic nitrogen ($N^{10}H^+$ at δ 11.55 in $CDCl_3$) has caused a significant high field shift for H^2 and H^4 (Δδ ranges from 0.1 for H^2 to 0.8 for H^4), and a considerable low-field shift for the residual proton on the exocyclic nitrogens (Δδ = 2.2). The β-protons of the Pt–$C_\alpha H_2$–$C_\beta H_2$–N moiety resonate at δ 3.11.

Crystal Structure.—The ORTEP[19] diagram showing the complex **2** is given in Fig. 1. Bond distances and angles are reported in Table 2. The estimated standard deviations are relatively high because of the poor quality of the crystal (very thin cracked plates), the ratio between the number of the observed reflections [$F > 3\sigma(F)$] and the refined parameters being < 7:1.

The platinum co-ordination geometry is nearly square planar with the metal atom displaced by 0.029(2) Å from the plane of the donor atoms. All the co-ordination angles are within 5° of the canonical values. The Pt–Cl [2.304(8)], Pt–N(2) [2.07(3)] and Pt–C(16) [2.06(3) Å] bond distances are normal. The Pt–N(1) bond distance [2.22(2) Å] is 0.15 Å longer than Pt–N(2) and is clearly affected by the high *trans* influence of the C(16) donor.

The bond lengths and angles for the acridine ring system are similar to those reported in previous studies.[20] In particular C–C bond distances range from an essentially double-bond character [C(1)–C(2) and C(7)–C(8)] to a quasi-single bond [C(2)–C(3) and C(6)–C(7)]. The quaternization of the N(10) atom increases the C(11)–N(10)–C(14) angle to 124(2)°, close to the mean value (125 ± 3°) found for the protonated endocyclic

Table 1 Proton chemical shifts [δ, downfield from $SiMe_4$; J(Pt–H) in Hz in parentheses when assignable]

		Acridine[a]								tmen		$PtC_\alpha H_2C_\beta H_2N$	
Compound	Solvent	H^9	H^1	H^2	H^4	NH	$N(CH_3)_2$	$N_{endo}H^+$	$N_{exo}H^+$	$N(CH_3)_2$	NCH_2	$C_\alpha H_2$	$C_\beta H_2$
$NC_{13}H_7(NMe_2)_2$	CD_2Cl_2	8.31 (s)	7.71 (d)	7.11 (dd)	7.01 (d)		3.13 (s)						
$^+HNC_{13}H_7(NMe_2)_2$	CD_2Cl_2	8.43 (s)	7.75 (d)	7.09 (dd)	6.97 (d)		3.24 (s)	*b*					
$^+HNC_{13}H_7(NHMe_2^+)_2$	CD_2Cl_2	8.30	7.64 (d)	6.98 (dd)	6.75 (d)		3.14 (s)	13.29	12.92				
2	CD_2Cl_2	8.44 (s)	7.81 (d)	7.15 (dd)	7.00 (d)		3.30 (s)			2.975 (s)	2.89 (m)	1.77 (m, 90)	4.82 (m)
										2.77 (s)	2.63 (m)		
$NC_{13}H_7(NH_2)_2$	$CDCl_3$	8.35 (s)	7.72 (d)	6.88 (d)	7.14 (s)	4.13							
	$(CD_3)_2SO$	8.31 (s)	7.56 (d)	6.83 (d)	6.78 (s)	5.79							
$^+HNC_{13}H_7(NH_2)_2$	$(CD_3)_2SO$	8.69	7.79 (d)	6.93 (dd)	6.67 (d)	7.15		13.35					
3	$CDCl_3$	8.13 (s)	7.44 (d)	6.77 (d)	6.63 (s)	6.32				2.96	2.86	1.70 (88)	3.11
	$(CD_3)_2SO$	8.55 (s)	7.68 (d)	6.90 (d)	6.47 (s)	7.55		13.16		2.81	2.83	1.41	3.15
										2.61	2.59		

[a] The coupling constants for the aromatic protons were: $NC_{13}H_7(NMe_2)_2$ (^3J = 9.24, ^4J = 2.5), $^+HNC_{13}H_7(NMe_2)_2$ (^3J = 8.24, ^4J = 2.4), $^+HNC_{13}H_7(NHMe_2^+)_2$, ($^3J$ = 9.3, ^4J = 2.2), **2** (^3J = 9.3, ^4J = 9.2), $NC_{13}H_7(NH_2)_2$ ($CDCl_3$) (^3J = 8.6, ^4J = 2.0), [$(CD_3)_2SO$] (^3J = 7.5, ^4J < 2.0), $^+HNC_{13}H_7(NH_2)_2$ (^3J = 9.2, ^4J = 2.3), **3** ($CDCl_3$) (^3J = 9.0, ^4J < 2), and [$(CD_3)_2SO$] (^3J = 8.8 Hz, ^4J not detectable). [b] Not observed in the 20 °C spectrum.

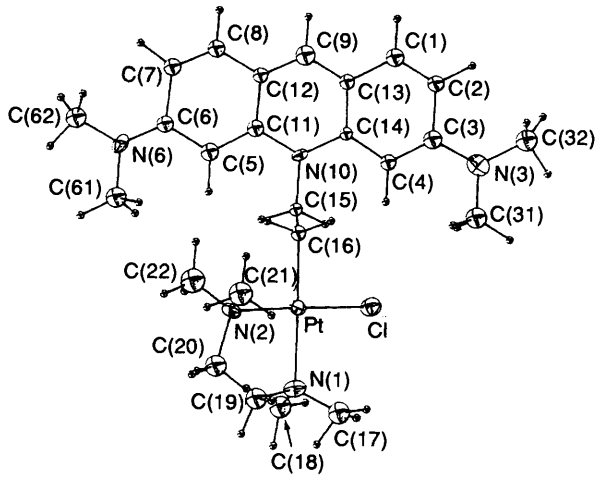


Fig. 1 An ORTEP drawing of complex **2** with the atom labelling scheme. The ellipsoids enclose 30% probability

sp^2 nitrogen atom of a six-membered ring (deprotonated N, 116 ± 3°).[21] Other angles of the acridine system can be considered normal (120 ± 6°).[12]

The aromatic system is planar [maximum deviation 0.06(2) Å for C(4)], whereas the C(15), N(3) and N(6) exocyclic atoms deviate slightly from the aromatic plane [0.01(2), 0.11(2) and 0.01(2) Å, respectively]. The dihedral angle formed by the platinum co-ordination plane and the acridine ring system is 29.2(4)°. The acridine rings are stacked in a head-to-tail fashion along the *a* axis (Figs. 2 and 3) with a distance between the planes of about 3.5 Å which is indicative of strong π overlap (Table 3). The angle between the plane normal and the [100] direction is 25.6(3)°.

The closest intermolecular Pt···Pt distance is 5.178(2) Å. The ClO_4^- ion is not involved in any relevant contact with the complex molecule although relatively short interatomic distances do exist between the oxygen atoms of the perchlorate ion and some methyl groups (both of the ethylenediamine ligand and of the acridine), some methylene groups (of ethylenediamine), and some carbon atoms (of the acridine ring system). The shortest contact is O(2P)···C(2) 3.33(4) Å.

Conclusion

The reactions described allow the preparation, in one step, of platinum complexes in which the metal is linked to an acridine dye by a dimethylene chain. The basicity of the endocyclic nitrogen (which is the highest among the present nitrogen bases) is not such to warrant an irreversible addition product. However, addition to the exocyclic aminic groups of proflavine, followed by dissociation of a proton, allows the formation of a stable compound. A similar situation was obtained with the 9-aminoacridine complexes $[PtCl(NH_3)_2\{HNC_{13}H_8(NH)\}]^+$ and $[Pt(NH_3)_2\{HNC_{13}H_8(NH)\}_2]^{2+}$ reported by Lippard and co-workers.[12] In those compounds, however, the dye was directly bound to the metal through the deprotonated 9-amino group, and the released proton had been taken up by the endocyclic nitrogen N^{10} (one could consider the dye having adopted the tautomeric imino form and used N^9 for co-ordination). In the latter case the electrophile was the metal itself; in our case, a platinum-bonded ethylene which, in the final product, sits across the metal and the dye. The σ carbon–metal bond so formed is expected to exert a strong labilizing effect on the ligand in *trans* position and therefore to enhance the chemical reactivity of the metal. The much longer Pt–N(1) distance with respect to Pt–N(2) was already indicative in this respect. Therefore the reactivity of species like **3** could be different from those of complexes in which the intercalator is either directly co-ordinated to platinum or linked, through a side chain, to a platinum ligand (generally an amine).

Table 2 Bond distances (Å) and angles (°) for $[Pt\{CH_2CH_2NC_{13}H_7(NMe_2)_2\}Cl(tmen)]ClO_4$ **2**

Pt–Cl	2.304(8)	N(3)–C(31)	1.44(4)
Pt–N(1)	2.22(2)	N(3)–C(32)	1.44(4)
Pt–N(2)	2.07(3)	C(4)–C(14)	1.41(3)
Pt–C(16)	2.06(3)	C(5)–C(6)	1.40(4)
N(10)–C(15)	1.49(3)	C(5)–C(11)	1.39(4)
C(15)–C(16)	1.50(3)	C(6)–C(7)	1.52(4)
N(1)–C(17)	1.51(4)	C(6)–N(6)	1.32(3)
N(1)–C(18)	1.46(3)	N(6)–C(61)	1.40(4)
N(1)–C(19)	1.44(3)	N(6)–C(62)	1.46(4)
C(19)–C(20)	1.44(4)	C(7)–C(8)	1.31(3)
N(2)–C(20)	1.55(4)	C(8)–C(12)	1.41(3)
N(2)–C(21)	1.53(4)	C(9)–C(12)	1.34(4)
N(2)–C(22)	1.46(4)	C(9)–C(13)	1.36(4)
C(1)–C(2)	1.31(4)	N(10)–C(11)	1.40(3)
C(1)–C(13)	1.48(4)	N(10)–C(14)	1.41(3)
C(2)–C(3)	1.48(4)	C(11)–C(12)	1.46(4)
C(3)–C(4)	1.36(4)	C(13)–C(14)	1.42(3)
C(3)–N(3)	1.37(4)		
Cl–Pt–N(1)	93.7(7)	C(3)–N(3)–C(31)	124(3)
Cl–Pt–N(2)	178.2(8)	C(3)–N(3)–C(32)	117(3)
Cl–Pt–C(16)	88.5(8)	C(31)–N(3)–C(32)	119(3)
N(1)–Pt–N(2)	84.8(10)	C(5)–C(6)–C(7)	117(3)
N(1)–Pt–C(16)	176.8(9)	C(5)–C(6)–N(6)	122(3)
N(2)–Pt–C(16)	93.0(11)	N(6)–C(6)–C(7)	120(3)
Pt–C(16)–C(15)	115(2)	C(7)–C(8)–C(12)	125(3)
N(10)–C(15)–C(16)	115(2)	C(6)–C(7)–C(8)	119(3)
Pt–N(1)–C(17)	114(2)	C(6)–C(5)–C(11)	121(3)
Pt–N(1)–C(18)	106(2)	C(6)–N(6)–C(61)	124(3)
Pt–N(1)–C(19)	104(2)	C(6)–N(6)–C(62)	119(2)
Pt–N(2)–C(20)	105(2)	C(61)–N(6)–C(62)	116(3)
Pt–N(2)–C(21)	109(2)	C(12)–C(9)–C(13)	125(3)
Pt–N(2)–C(22)	116(2)	C(11)–N(10)–C(14)	124(2)
C(17)–N(1)–C(18)	112(3)	C(11)–N(10)–C(15)	118(2)
C(17)–N(1)–C(19)	110(2)	C(14)–N(10)–C(15)	118(2)
C(18)–N(1)–C(19)	111(3)	C(5)–C(11)–N(10)	123(3)
N(1)–C(19)–C(20)	114(3)	C(5)–C(11)–C(12)	121(3)
N(2)–C(20)–C(19)	114(3)	N(10)–C(11)–C(12)	116(3)
C(20)–N(2)–C(21)	109(2)	C(8)–C(12)–C(9)	125(3)
C(20)–N(2)–C(22)	105(3)	C(8)–C(12)–C(11)	116(3)
C(21)–N(2)–C(22)	112(3)	C(9)–C(12)–C(11)	119(3)
C(1)–C(2)–C(3)	121(3)	C(1)–C(13)–C(9)	124(3)
C(2)–C(3)–C(4)	120(3)	C(1)–C(13)–C(14)	117(2)
C(2)–C(1)–C(13)	121(3)	C(9)–C(13)–C(14)	120(3)
C(2)–C(3)–N(3)	117(3)	C(4)–C(14)–N(10)	122(2)
N(3)–C(3)–C(4)	123(3)	C(4)–C(14)–C(13)	121(2)
C(3)–C(4)–C(14)	120(3)	N(10)–C(14)–C(13)	117(2)

Experimental

Starting Materials.—The complex $[Pt(\eta^2\text{-}C_2H_4)Cl(tmen)]ClO_4$ **1** was prepared according to ref. 22. Dry chlorinated solvents were obtained by distillation from calcium hydride. 3,6-Bis(dimethylamino)acridine (acridine orange) and 3,6-diaminoacridine (proflavine) were purchased from Aldrich in their monoprotonated form, counter ion $ZnCl_4^{2-}$ in the former case and Cl^- in the latter.

The highly insoluble tetrachlorozincate salt of monoprotonated acridine orange (5 g, 13.6 mmol) was suspended in water (200 cm^3) and treated with twice the stoichiometric amount of sodium or potassium hydroxide. An organic phase was added (CH_2Cl_2, 150 cm^3) and the mixture was stirred at room temperature for several hours. The organic phase was then removed, washed with water, dried over anhydrous sodium sulfate, and the solvent evaporated. The solid obtained was the free base, and its purity was checked by ^1H NMR and elemental analysis (Found: C, 76.2; H, 6.9; N, 15.7. Calc. for $C_{17}H_{19}N_3$: C, 76.9; H, 7.2; N, 15.8%).

Commercial proflavine monohydrochloride was recrystallized from water and then treated in the same solvent (2 g, 8.14

Table 3 Selected interatomic distances lower than 3.7 Å relevant to stacking interactions for complex **2**. Estimated standard deviations are 0.04 Å

	$-x, -y, -z+1$		$-x+1, -y, -z+1$
C(1)···C(6)	3.53	C(2)···C(5)	3.51
C(1)···C(7)	3.68	C(2)···C(11)	3.54
C(2)···C(7)	3.65	C(3)···C(11)	3.55
C(4)···C(8)	3.69	C(3)···C(12)	3.62
C(8)···C(13)	3.67	C(4)···C(9)	3.62
C(8)···C(14)	3.52	C(4)···C(12)	3.57
C(9)···C(11)	3.58	C(13)···C(14)	3.58
C(9)···C(12)	3.67		
C(12)···C(13)	3.63		

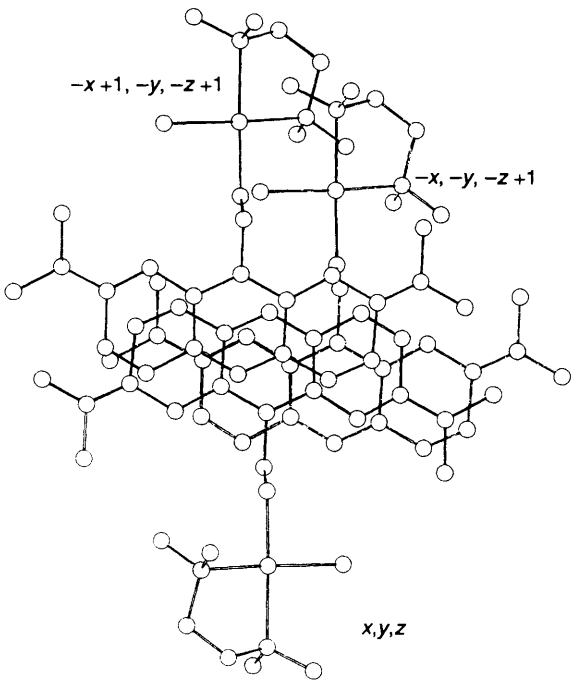


Fig. 2 Diagram showing three stacked complex molecules. The view is almost parallel to the plane normal. Hydrogen atoms are omitted and all the non-hydrogen atoms are represented as isotropic for clarity

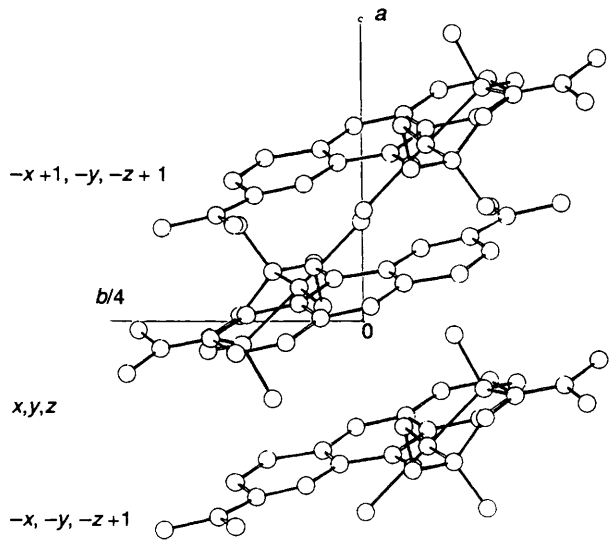


Fig. 3 Diagram showing the stacking interaction viewed along the c^* axis. The hydrogen atoms are omitted and all the non-hydrogen atoms are represented as isotropic for clarity

mmol; in 30 cm^3 water, at 50 °C to increase its solubility) with the stoichiometric amount of sodium hydroxide. The free proflavine, which is not very soluble in water, separated as a dark yellow powder. The mixture was cooled to 0 °C, filtered, and the solid dried in a desiccator. Its purity was checked by ^1H NMR, melting point, and elemental analysis. The proflavine prepared in this way always contained one molecule of water of crystallization (Found: C, 68.2; H, 5.8; N, 18.3. Calc. for $C_{13}H_{11}N_3 \cdot H_2O$: C, 68.7; H, 5.8; N, 18.5%).

Preparation of Complexes.—$[Pt\{CH_2CH_2NC_{13}H_7(NMe_2)_2\}Cl(tmen)]ClO_4$ **2**. Compound **1** (0.5 mmol) was treated with a slight excess of acridine orange in dry CH_2Cl_2 (40 cm^3) at 0 °C. The mixture was stirred for several hours; during this time the poorly soluble **1** gradually dissolved and the solution became a deeper red. The clear solution was then concentrated to a small volume (a few cm^3) and the precipitate which formed was filtered off and dried. The yield of isolated product was 80% referred to platinum. The crude product was always contaminated, as revealed by ^1H NMR data, by small quantities of monoprotonated acridine orange and $[PtCl_2(tmen)]$, moreover these impurities tend to increase with time in CD_2Cl_2 solution. We suggest that, although the equilibrium of formation of **2** (Scheme 1) is well shifted to the right, a small amount of HCl, which can be present in chlorinated solvents, reacts with traces of **1** and free acridine producing neutral $[PtCl_2(tmen)]$, ethylene, and protonated acridine. This process is, however, rather slow and **2** can be crystallized from CH_2Cl_2 (Found: C, 40.0; H, 5.1; Cl, 9.2; N, 9.0. Calc. for $C_{25}H_{39}Cl_2N_5O_4Pt$: C, 40.6; H, 5.3; Cl, 9.6; N, 9.5%). If the reaction between **1** and acridine is carried out in methanol (using the same reagent ratio) a solid material is obtained which is essentially the perchlorate of monoprotonated acridine orange together with a small amount of **2**. Evaporation of the mother-liquor afforded a reddish solid which is essentially $[(tmen)ClPt(CH_2CH_2OCH_2CH_2)PtCl(tmen)]$ containing only a small amount of free acridine.

$[\{PtCl(tmen)\}_2\{HNC_{13}H_7(NHCH_2CH_2)_2\}]ClO_4$ **3**. Compound **1** and proflavine were mixed in aqueous methanol at room temperature [0.5 mmol of each in 10 cm^3 of solvent, water–methanol (1:5 v/v)]. The mixture was stirred for 48 h. The solid phase was then filtered off, washed with methanol and dried. It proved to be compound **3**. The isolated yield was 75% referred to platinum (Found: C, 32.4; H, 4.8; Cl, 9.8; N, 9.0. Calc. for $C_{29}H_{52}Cl_3N_7O_4Pt_2$: C, 32.9; H, 4.9; Cl, 10.0; N, 9.2%). The filtered solution was evaporated to dryness and shown to contain monoprotonated proflavine together with some **3**.

Physical Measurements.—Infrared spectra in the range 4000–400 cm^{-1} were recorded as KBr pellets, in the range 400–200 cm^{-1} as Polythene pellets, on a Perkin Elmer 283 spectrophotometer, proton NMR spectra with Varian XL 200 and Bruker AM 300 spectrometers.

Crystal Structure Determination.—A small and very thin orange plate was selected and mounted on a glass fibre for the data collection on a Delft Instruments FAST TV area detector at the window of a rotating-anode generator equipped with

Table 4 Atomic coordinates ($\times 10^4$) for complex **2**

Atom	*X/a*	*Y/b*	*Z/c*
Pt	1491(2)	640(1)	1242(1)
Cl	3668(11)	20(4)	1230(6)
N(1)	1608(27)	907(11)	−171(16)
N(2)	−486(40)	1194(12)	1210(17)
N(3)	4446(31)	−1447(11)	3344(18)
N(6)	610(28)	2002(10)	4987(16)
N(10)	2664(24)	295(9)	4176(13)
C(1)	3249(36)	−976(12)	5466(21)
C(2)	3835(32)	−1280(11)	4870(18)
C(3)	3963(37)	−1087(13)	3945(22)
C(4)	3534(32)	−583(11)	3712(18)
C(5)	1585(34)	1161(12)	4545(20)
C(6)	1008(34)	1504(12)	5178(18)
C(7)	820(32)	1277(11)	6107(18)
C(8)	1211(31)	783(10)	6277(20)
C(9)	2247(37)	−76(13)	5847(23)
C(11)	2028(30)	642(13)	4776(17)
C(12)	1825(32)	429(10)	5668(18)
C(13)	2831(33)	−416(11)	5253(18)
C(14)	3003(28)	−240(10)	4365(16)
C(15)	2816(28)	491(9)	3246(15)
C(16)	1232(33)	391(11)	2535(18)
C(17)	1674(47)	463(15)	−837(24)
C(18)	3159(43)	1243(14)	−113(24)
C(19)	29(43)	1209(14)	−420(22)
C(20)	−451(43)	1513(14)	321(23)
C(21)	−2260(44)	915(16)	1148(26)
C(22)	−237(49)	1580(16)	1941(27)
C(31)	4915(41)	−1983(13)	3575(23)
C(32)	4476(44)	−1272(15)	2421(23)
C(61)	−66(37)	2347(13)	5578(21)
C(62)	945(41)	2224(14)	4124(22)
Cl(P)	−4564(13)	2456(5)	3155(8)
O(1P)	3960(39)	2730(13)	2834(20)
O(2P)	5550(34)	2448(12)	4114(21)
O(3P)	6922(48)	2672(16)	2927(26)
O(4P)	5057(57)	1994(22)	2768(34)

a molybdenum anode, following procedures previously described.[23] The orientation matrix and cell dimensions were determined using 50 reflections, 25 from each of two zones 90° apart in φ with $\chi = 0$, and refined using 250 reflections with a broad range of θ and φ from the same zones. Reflections in slightly more than one hemisphere were then scanned to obtain the intensity data *via* 190° rotation in ω at $\chi = 0$ and 120° rotation in ω at $\chi = 90°$. 9896 Data were collected at 22 °C.

Crystal data. $C_{25}H_{39}Cl_2N_5O_4Pt$, $M = 727.6$, monoclinic, space group $P2_1/n$, $a = 7.700(4)$, $b = 25.446(3)$, $c = 14.858(6)$ Å, $\beta = 99.08(2)°$, $U = 2875(3)$ Å^3, $Z = 4$, $D_c = 1.681$ g cm^{-3}, $F(000) = 1448$, $\lambda = 0.710\,69$, μ(Mo-Kα) = 51.5 cm^{-1}.

Solution and refinement. The structure solution was performed through the direct methods of SHELX 86,[24] which showed the positions of the Pt, Cl, N and most of the C atoms. The structure was completed using Fourier difference syntheses. Three cycles of full-matrix least-squares refinement (isotropic) brought the *R* index down to 0.095. An absorption correction (DIFABS)[25] was then applied. Three more cycles of full-matrix least-squares refinement (anisotropic for the Pt, Cl and N atoms, isotropic for the C atoms and ClO_4^- anion) reduced the R_F and R' indexes to 0.0572 and 0.0563, respectively. There were 1415 observed reflections ($F > 3\sigma_F$) and 212 parameters were refined. The weighting scheme was $w = a/\sigma^2(F)$; *a* was refined to 0.1310. The H atoms were included in the last refinement through the AFIX options of SHELX 76.[26] The isotropic thermal parameter of groups of H atoms was refined. Neutral atom scattering factors were taken from ref. 27. Atomic coordinates of non-hydrogen atoms are given in Table 4.

Additional material available from the Cambridge Crystallographic Data Centre comprises H-atom coordinates, thermal parameters and remaining bond lengths and angles.

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