Synthesis and preliminary DNA-binding studies of diimineplatinum(II) complexes containing 3- or 4-pyridineboronic acid†

H. Y. Vincent Ching,[a] Jack K. Clegg[b] and Louis M. Rendina*[a]

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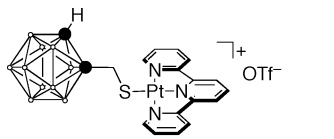
A series of platinum(II) complexes of the type $[Pt(NN)(pyB)_2](NO_3)_2$ (NN = bipy, phen; pyB = 3- or 4-pyridineboronic acid) were successfully prepared and fully characterised by 1D- and 2D-multinuclear NMR spectroscopy and ESI-MS. Using VT ^{1}H NMR spectroscopy, rotational isomers for $[Pt(NN)(3\text{-}pyB)_2](NO_3)_2$ were identified and the free energies of activation for rotation of 3-pyB about the Pt–N bond were determined to be $\Delta G^{\ddagger}_{310} = 69.2 \pm 0.1$ kJ mol^{-1} and $\Delta G^{\ddagger}_{305} = 66.0 \pm 0.1$ kJ mol^{-1} for $[Pt(bipy)(3\text{-}pyB)_2](NO_3)_2$ and $[Pt(phen)(3\text{-}pyB)_2](NO_3)_2$, respectively. The 3- and 4-pyB ligands readily deboronate in boiling H_2O to afford $[Pt(NN)(py)_2](NO_3)_2$; the structure of $[Pt(phen)(py)_2]^{2+}$ (as its PF_6^- salt) was confirmed by X-ray crystallography. Preliminary thermal denaturation studies revealed only minimal interactions between $[Pt(NN)(pyB)_2](NO_3)_2$ and calf-thymus DNA and is attributed to hydroxylation of the boronic acid groups at pH 7.4 to afford the corresponding zwitterionic boronate species. This was confirmed by means of variable pH ^{1}H and ^{11}B{^{1}H} NMR spectroscopy.

Introduction

DNA metallointercalation was first reported by Lippard and co-workers using $[Pt(terpy)(SCH_2CH_2OH)]^+$ and $[Pt(terpy)Cl]^+$ (terpy = 2,2′:6′,2″-terpyridine).[1] Recently, the DNA intercalation of platinum(II) complexes containing bidentate diimines such as 2,2′-bipyridine (bipy), 1,10-phenanthroline (phen) and dipyrido[3,2-*a*:2′,3′-*c*]phenazine (dppz), has also been thoroughly investigated and the complexes have all exhibited strong affinities toward DNA.[2–6] Related complexes containing a *closo*-thioalkylcarborane ligand and a platinum(II)–terpy unit or chelating diimine ligands such as bipy and phen were reported as potential DNA metallointercalators for boron neutron capture therapy (BNCT).[7–10]

Preliminary DNA-binding studies demonstrated that the platinum(II)–carborane complex **1** was able to intercalate calf-thymus DNA but not to the same degree as the analogous $[Pt(terpy)(SCH_2CH_2OH)]^+$ and this was proposed to be the result of steric hindrance due to the bulky *closo*-carborane functionality.[7] Nevertheless, cell uptake and cytotoxicity experiments with **1** and related complexes revealed promising results.[8] Unfortunately, the aqueous solubility of **1** proved to be extremely limited due to the lipophilicity of the *closo*-carborane moiety. The addition of a pendant glycerol moiety to the carborane cage afforded the related species **2** with far greater water solubility than **1** but its synthesis proved to be formidable owing to the considerable number of synthetic steps involved.[10] Simple boronated ligands such as boronic acids are rare in coordination chemistry but 3- and 4-pyridineboronic acids have been shown to coordinate metal ions such as Co^{3+} and Zn^{2+} to afford both molecular polygons and polyhedra.[11–13] Such ligands offer the possibility of readily incorporating boron into DNA metallointercalators such as those based on planar platinum(II)–diimine complexes without the need to undertake extensive syntheses and perhaps also address the issue of low water-solubility that is normally associated with other boron moieties such as the *closo*-carboranes. Herein we report the synthesis, characterisation and preliminary DNA-binding studies of complexes of the type $[Pt(NN)(pyB)_2](NO_3)_2$ (NN = bipy, phen; pyB = 3- or 4-pyridineboronic acid) containing 3- or 4-pyridineboronic acid.



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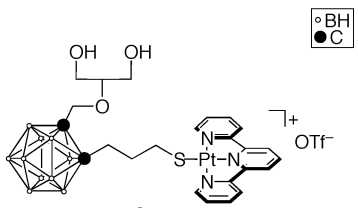

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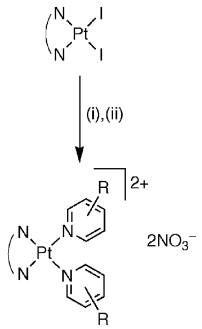
Results and discussion

Treatment of $[PtI_2(NN)]$ with two equivalents of $AgNO_3$ afforded the labile species $[Pt(NO_3)_2(NN)]$[14] to which two equivalents of 3- or 4-pyridineboronic acid were then added to give the target complexes $[Pt(NN)(pyB)_2](NO_3)_2$ (**3**–**6**) in good yield (Scheme 1). The complexes were fully characterised by 1D-multinuclear (^{1}H, ^{13}C{^{1}H}, ^{11}B{^{1}H}, and ^{195}Pt{^{1}H}) and 2D (HSQC and HMBC)

[a]*School of Chemistry, The University of Sydney, Sydney, NSW, 2006, Australia. E-mail: rendina@chem.usyd.edu.au; Fax: +61 2 9351 3329; Tel: +61 2 9351 4781*
[b]*Crystal Structure Analysis Facility, School of Chemistry, The University of Sydney, Sydney, NSW, 2006, Australia*

† Electronic supplementary information (ESI) available: An analysis of the crystal packing and tables of X-ray data for **7**. See DOI: 10.1039/b618668h



3 NN = bipy, R = 3-B(OH)$_2$
4 NN = phen, R = 3-B(OH)$_2$
5 NN = bipy, R = 4-B(OH)$_2$
6 NN = phen, R = 4-B(OH)$_2$

Scheme 1 *Reagents*: (i)$AgNO_3$; (ii) 3- or 4-pyB.

NMR spectroscopy and ESI mass spectrometry. The $^{11}B\{^1H\}$ NMR spectra of **3–6** revealed a broad singlet at approximately δ 19 for all four compounds. The resonance was shifted more upfield than those signals observed for free arylboronic acids, which typically show chemical shifts in the range δ 25–33.[15] Although solvent polarity effects may play a minor role in the observed differences in chemical shifts, it is more likely to be the result of polarization effects associated with the cationic metal centre and is consistent with the trends observed in the ^1H and $^{13}C\{^1H\}$ NMR data. $^{195}Pt\{^1H\}$ NMR spectroscopy proved very useful in confirming the coordination of the N-donor ligands as a single resonance at approximately δ −2540 was observed for all four complexes, consistent with a PtN_4 coordination sphere.[16]

At room temperature, the ^1H NMR spectra of **3** and **4** in CD_3OD solution displayed some broadened aromatic resonances pertaining to the 3-pyridineboronic acid ligands. This phenomenon was investigated further using variable temperature (VT) ^1H NMR spectroscopy (Fig. 1). For **3**, the resonance assigned to the H4″ proton appeared as a doublet, but as the temperature was decreased the signal broadened before separating into a partially overlapping set of doublets with a coalescence temperature (T_c) of *ca.* 290 K. This phenomenon was also observed for the H6″ resonance which coalesced at *ca.* 310 K. Similarly for **4**, coalescence of the peaks was observed at *ca.* 290 and 310 K for the H6′ and H1′ resonances, respectively. Notably, no signal broadening was observed for the 4-pyridineboronic acid analogues **5** and **6** at ambient temperatures. All these observations are consistent with an intramolecular rearrangement process between the *s-trans* and *s-cis* rotamers, *e.g.* **3a** and **3b**, respectively (Scheme 2). The interchange between the two species resulting from rotation about the Pt–N bond of the coordinated pyridine ligand would be hindered by the steric bulk of the boronic acid groups and also the partial double-bond character of the Pt–N bond.[17] At low temperatures, both species were observed in solution by NMR spectroscopy but, at elevated temperatures, the rotational exchange was faster than the NMR timescale, hence only the time-averaged resonances pertaining to these two conformations were observed. An accurate measurement of the relative population of the two rotamers was not possible due to the close proximity of the two sets of resonances. However, assuming the rates of interconversion between the rotamers are approximately equal, an estimation of the free energy of activation ($\Delta G^{\ddagger}$) can be derived

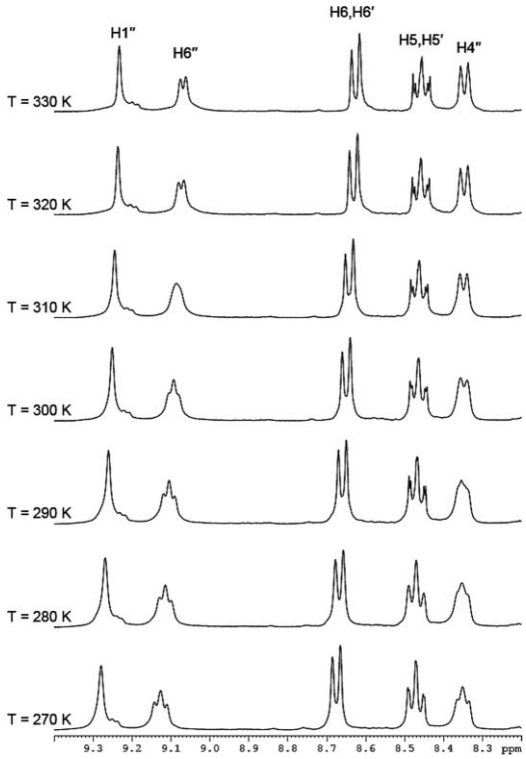
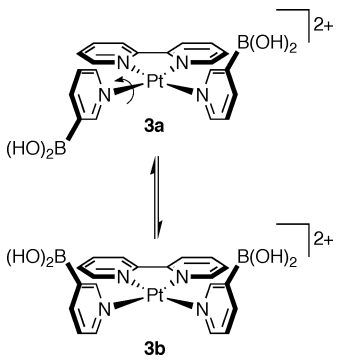


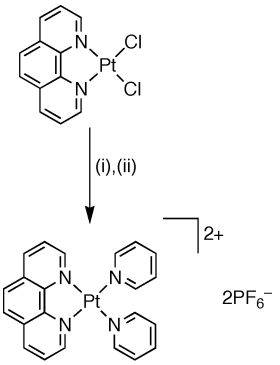
Fig. 1 Variable-temperature (VT) ^1H NMR spectrum of **3** in CD_3OD solution.



Scheme 2

from T_c using a modified Eyring equation.[18] For **3**, $\Delta G^{\ddagger}_{310} = 69.2 \pm 0.1$ kJ mol^{-1} and for **4**, $\Delta G^{\ddagger}_{305} = 66.0 \pm 0.1$ kJ mol^{-1} which correlate well with the free energies of activation determined for other platinum(II) complexes containing 3-substituted pyridine ligands.[6,17,19]

Treatment of $[PtCl_2(NN)]$ with two equivalents of 3- or 4-pyridineboronic acid in H_2O under reflux conditions did not afford the expected $[Pt(NN)(pyB)_2]^{2+}$ complexes but rather the deboronated species $[Pt(NN)(py)_2]^{2+}$ (Scheme 3). Precipitation of the cation from solution using a saturated solution of KPF_6 afforded **7** in good yield and purity. The molecular structure of the cation in **7**, as determined by X-ray crystallography, is illustrated in Fig. 2. Although free 3- and 4-pyridineboronic acid are known to be thermally quite stable, the latter is known to decompose into pyridine and boric acid in boiling H_2O and so it appears that hydrolytic cleavage of the B–C bond precedes coordination of pyridine to the metal centre.[21] However, the metal centre may



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Scheme 3 *Reagents*: (i) 3- or 4-pyB, H_2O, Δ; (ii) KPF_6.

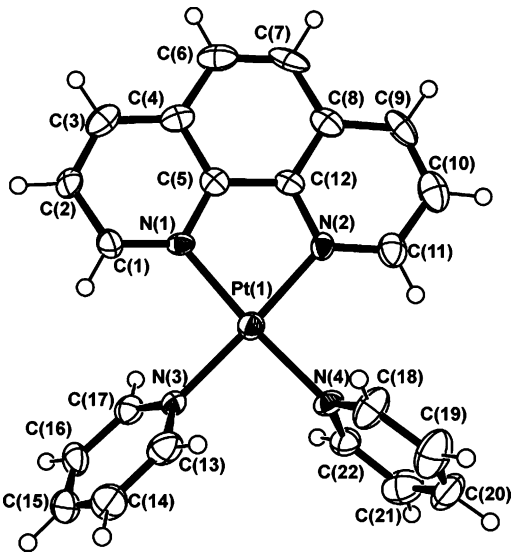


Fig. 2 An ORTEP depiction and atomic numbering scheme of the cation in the X-ray crystal structure of **7** with 50% displacement ellipsoids. Selected bond lengths (Å): N(1)–Pt(1): 2.024(9), N(2)–Pt(1): 2.022(9), N(3)–Pt(1): 2.027(9), N(4)–Pt(1): 2.025(9). Selected bond angles (°): N(3)–Pt(1)–N(2): 175.1(4), N(3)–Pt(1)–N(4): 89.7(4), N(2)–Pt(1)–N(4): 93.8(4), N(3)–Pt(1)–N(1): 94.8(3), N(2)–Pt(1)–N(1): 81.8(3), N(4)–Pt(1)–N(1): 175.4(4).

also play a key role in the deboronation reaction, particularly in the case of 3-pyridineboronic acid.‡ As expected, the structure of the cation in **7** is square planar with the phen ligand acting as a bidentate chelating ligand and the *cis*-pyridine ligands occupying the remaining two sites around the metal centre. The geometry of the metal centre is somewhat distorted from the ideal angles of 90° with the phen ligand having a bite angle (N–Pt–N) of only 81.8(3)°; the angle between the two pyridine ligands (N–Pt–N) is 89.7(4)°. Furthermore, the platinum centre and the nitrogen atoms are not exactly in the same plane, with the bond angles between the *trans* nitrogen atoms at approximately 175°. All the Pt–N bond lengths are within 1% of 2.02 Å. The pyridine ligands are not co-planar with the mean Pt–phen plane; the N(3)-containing pyridine ring is rotated about the Pt(1)–N(3) bond by approximately 60° and the N(4)-containing pyridine ring is rotated about the Pt(1)–N(4) bond by approximately 74° due to the steric bulk associated with the monodentate ligands. There also exists intra-complex edge-to-face π–π stacking between the phen and pyridine ligands. This is shown by the H1–N(3)- and H11–N(4)-containing ring centroid distances of 2.92 Å and 3.15 Å, respectively. The effect of the pyridine ring rotation is also reflected in the extended crystal packing of **7** (see ESI†).

Preliminary DNA thermal denaturation (DNA melting) experiments involving calf-thymus DNA were performed on **3–6** at pH 7.4. The deboronated species **7** was used as a model compound as its avid DNA-binding has been investigated recently.[2] The well-known intercalator ethidium bromide (EtBr) was used as the control. The results of the DNA thermal denaturation experiments are presented in Table 1, and a typical DNA melting plot is presented in Fig. 3. As expected, there was a large ΔT_m (16.5 ± 0.6 °C) observed for EtBr. For **7**, an even larger ΔT_m value (27.0 ± 0.6 °C) was determined and, like EtBr, its strong propensity to intercalate DNA has been demonstrated by means of other spectroscopic methods.[2] Interestingly, none of the four boronic acid complexes exhibited large ΔT_m values, with the largest ΔT_m (2.6 ± 0.6 °C) being observed for **4**. It is unlikely that the small ΔT_m values are the result of steric hindrance between the complexes and DNA because the boronic acid groups, particularly those found in the 4-pyridineboronic acid derivatives **5** and **6**, are located remotely from the intercalating diimine ligands. Furthermore, **5** and **6** did

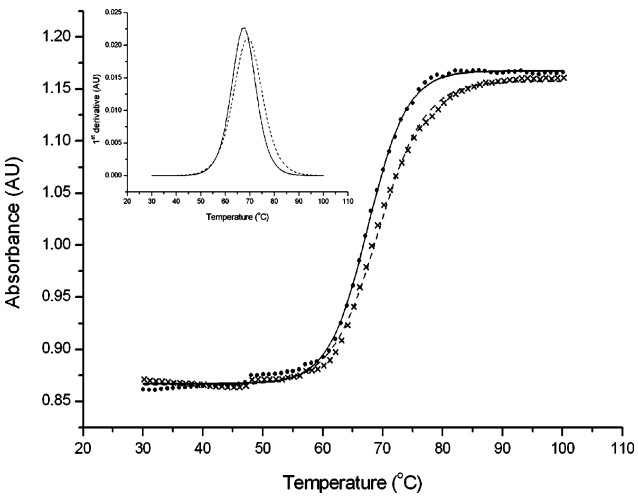


Fig. 3 Calf-thymus DNA melting curves in the presence (---) and absence (—) of **6** at pH 7.4. The first derivative plot (inset) allowed for an accurate determination of T_m.

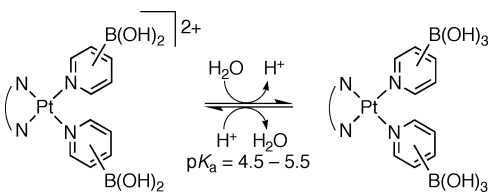
Table 1 ΔT_m values for EtBr and **3–7** in the presence of calf-thymus DNA at pH 7.4

Compound	ΔT_m/°C	Compound	ΔT_m/°C
EtBr	16.5 ± 0.6	**5**	0.5 ± 0.7
3	0.8 ± 0.6	**6**	1.0 ± 0.6
4	2.6 ± 0.6	**7**	27.0 ± 0.6

‡ Coordination of the 3- or 4-pyridineboronic acid ligands to the metal centre would lead to a weakening of the B–C bond as a result of a metal-induced polarization effect. This would certainly enhance the electrophilic nature of the boron centre and make it more susceptible to nucleophilic attack by H_2O. Notably, complex **6**, for example, undergoes a slow hydrolysis reaction in hot H_2O to afford **7** and other (unidentified) minor products.

not exhibit any increased ΔT_m values compared to **3** and **4**. Indeed, an opposite trend is observed.

The marginal DNA-binding characteristics observed for complexes **3–6** led to a study of their speciation in an aqueous medium as a function of pH. It is known that the speciation of free 4-pyridineboronic acid, for example, is pH dependent.[11,20] At high pH values, hydroxylation of the boronic acid functionality occurs to afford the tetrahedral boronate moiety, while at low pH protonation occurs at the nitrogen atom and at intermediate pH values 4-pyridineboronic acid exists as a zwitterion. 3-Pyridineboronic acid also behaves in a similar manner.[20] To verify this type of pH-dependent behaviour was indeed occurring, variable pH (VpH) ^{1}H NMR spectroscopy was performed on **5**. The resonances assigned to the pyridine ring protons H2″ and H3″ were shifted dramatically as a function of pH. At lower pH values (*i.e.* pH 1–5), both signals were located downfield, whereas at higher pH values (*i.e.* > pH 5) the boronate species dominates in solution and the corresponding aromatic signals were shifted *ca.* 0.2 ppm upfield, consistent with an increased electron density in the pyridine ring. This trend was also observed in the VpH ^{11}B{^{1}H} NMR spectra of **5**. Furthermore, from the VpH NMR data the pK_a value for **5** has been determined to be 4.81 ± 0.03, which is comparable to the values reported for the boronic acid ionization of 3-pyridiniumboronic acid (pK_a = 4.0),[20] 4-pyridiniumboronic acid (pK_a = 3.6 and pK_a = 3.83 ± 0.05),[11,20] *N*-methyl-3-pyridiniumboronic acid (pK_a = 4.4),[21] 2,2′-bipyridinium-4,4′-diboronic acid (pK_a = 3.9)[22] and 2,2′-bipyridinium-4-boronic acid (pK_a = 3.2).[22] Consequently, at the pH of the buffered solution used in the DNA-binding experiments (7.4), the boronic acid groups exist predominately in their anionic boronate form which means **3–6** are zwitterionic in solution and thus electrostatic interactions with DNA are unfavoured owing to their overall neutral charge (Scheme 4). Hence, DNA intercalation would not be particularly favoured and only minor changes in the DNA melting temperatures were observed for each of the complexes.§



Scheme 4

Conclusions

A series of platinum(II) complexes containing a chelating diimine (bipy, phen) and 3- or 4-pyridineboronic acid ligands was successfully prepared and fully characterised by techniques including multinuclear NMR spectroscopy and ESI-MS. Using VT ^{1}H NMR spectroscopy, rotational isomers for [Pt(NN)(3-pyB)$_2$](NO$_3$)$_2$ were identified and the free energies of activation for rotation of the monodentate ligand about the Pt–N bond were determined. Preliminary thermal denaturation studies revealed only minimal interactions between **3–6** and calf-thymus DNA and is attributed to hydroxylation of the boronic acid groups at a biological pH range to afford the corresponding zwitterionic boronate species. This was confirmed by means of variable pH ^{1}H and ^{11}B{^{1}H} NMR spectroscopy. We are currently exploring the synthesis and DNA-binding characteristics of related complexes of the type [Pt(NN)L(pyB)]$^{2+}$ (L = py and NH$_3$, for example) and their sugar–boronate ester derivatives, and the results of this work will be reported in due course.

§ It is very unlikely the boronic acid functionalities in the complexes covalently bind to the 3′-OH group of the deoxyribose ring in DNA resulting in the small ΔT_m values observed.[30]

Experimental

All reactions were carried out at atmospheric pressure under nitrogen unless otherwise stated and manipulations were performed using conventional Schlenk techniques. *N*,*N*-Dimethylformamide (DMF) was pre-dried with MgSO$_4$ and anhydrous CuSO$_4$, followed by distillation at reduced pressure. Diethyl ether was distilled from sodium wire. All reagents were obtained commercially and used as received without further purification.

^{1}H (400.13 MHz), ^{13}C{^{1}H} (100.6 MHz), ^{11}B{^{1}H} (128.40 MHz) and ^{195}Pt{^{1}H} (85.69 MHz) NMR spectra were recorded on a Bruker AVANCE DPX400 spectrometer at 300 K. ^{1}H and ^{13}C{^{1}H} NMR spectra were referenced either to TMS (δ 0.00) or to residual solvent resonances as an internal reference. ^{11}B{^{1}H} and ^{195}Pt{^{1}H} NMR spectra were referenced to the external standards BF$_3$·Et$_2$O (δ 0.00) and 0.1 M Na$_2$[PtCl$_6$] in D$_2$O (δ 0.00), respectively.

Low resolution mass spectra (ESI-MS) were obtained on a Finnegan LCQ MS detector equipped with Finnegan LCQ data processing software using HPLC grade MeOH. Elemental analyses were performed by the Chemical and Microanalytical Services (CMAS), Victoria (Australia).

2,2′-Bipyridinediiodoplatinum(II) and diiodo-1,10-phenanthrolineplatinum(II) were prepared by the method of Wimmer and Castan.[23]

Syntheses

2,2′-Bipyridinebis(3-pyridineboronic acid)platinum(II) nitrate (3). AgNO$_3$ (0.140 g, 0.826 mmol) was added to [Pt(bipy)I$_2$] (0.250 g, 0.413 mmol) in DMF (100 mL) at 50 °C. The mixture was kept in the absence of light and stirred overnight at room temperature. The AgI precipitate was removed by filtration, and 3-pyridineboronic acid (0.102 g, 0.826 mmol) was added to the clear filtrate. After stirring at room temperature for 2 d, diethyl ether (~300 mL) was added and **3** was collected by filtration. The product was recrystallised by careful diffusion of diethyl ether into a methanol solution of **3**, filtered off and then dried *in vacuo* (0.210 g, 71%). ^{1}H NMR (CD$_3$OD): δ 9.25 (s, 2H, H2″), 9.09 (s, 2H, H6″), 8.65 (d, $^3J_{H3,H4}$ = 8.1 Hz, 2H, H6, H6′), 8.46 (m, 2H, H4, H4′), 8.35 (d, $^3J_{H,H}$ 2H, H4, H4″), 7.71 (m, 6H, H5, H5′, H5″, H6, H6′). ^{13}C{^{1}H} NMR (CD$_3$OD): δ 158.42 (C2, C2′), 157.70 (C2″), 153.26 (C6″), 150.92 (C6, C6′), 147.62 (C4″), 129.63 (C5, C5′), 128.59 (C5″), 125.77 (C3, C3′). ^{11}B{^{1}H} NMR (CD$_3$OD): δ 19.7. ^{195}Pt{^{1}H} NMR (CD$_3$OD): δ −2535. ESI MS: *m*/*z* 299 [M − 2NO$_3$]$^{2+}$.

1,10-Phenanthrolinebis(3-pyridineboronic acid)platinum(II) nitrate (4). AgNO$_3$ (0.145 g, 0.790 mmol) was added to [PtI$_2$(phen)] (0.250 g, 0.397 mmol) in DMF (100 mL) at 50 °C. The mixture was kept in the absence of light and stirred at room temperature

overnight. The AgI precipitate was removed by filtration and 3-pyridineboronic acid (0.98 g, 7.97 mmol) was added to the filtrate. After stirring at room temperature for 2 d, diethyl ether (~300 mL) was added and **4** was collected by filtration. The product was recrystallised by careful diffusion of diethyl ether into a methanol solution of **4**, filtered off and then dried *in vacuo* (0.186 g, 63%). ^{1}H NMR (CD_3OD): δ 9.26 (m, 2H, H2′), 9.12 (d, $^{3}J_{H,H} = 4.8$ Hz, 2H, H6′), 9.07 (d, $^{3}J_{H2,H3} = 8.3$ Hz, 2H, H2, H9), 8.36 (s, 2H, H5, H6), 8.34 (m, 2H, H4′), 8.14 (d, $^{3}J_{H3,H4} = 4.9$ Hz, 2H, H4, H8), 8.21 (dd, $^{3}J_{H2,H3} = 8.3$ Hz, $^{3}J_{H3,H4} = 4.9$ Hz, 2H, H3, H8), 7.71 (m, 2H, H5′). ^{13}C{^{1}H} NMR (CD_3OD): δ 157.78 (C2′), 152.89 (C6′), 151.94 (C4, C7), 148.89 (C13, C14), 147.63 (C4′), 142.82 (C2, C9), 132.67 (C11, C12), 129.54 (C5, C6), 128.47 (C5′), 127.61 (C3, C8). ^{11}B{^{1}H} NMR (CD_3OD): δ 19.7. ^{195}Pt{^{1}H} NMR (CD_3OD): δ −2545. ESI MS: m/z 310 $[M - 2NO_3]^{2+}$.

2,2′-Bipyridinebis(4-pyridineboronic acid)platinum(II) nitrate (5). The same method described for **3** was followed with the exception that 4-pyridineboronic acid (0.102 g, 0.826 mmol) was used instead of the 3-derivative. Yield 0.203 g, 67%. ^{1}H NMR (CD_3OD): δ 9.03 (d, $^{3}J_{H2'',H3''} = 6.1$ Hz, 4H, H2″), 8.65 (d, $^{3}J_{H3,H3'} = 8.1$ Hz, 2H, H3, H3′), 8.47 (m, 2H, H4, H4′), 7.89 (d, $^{3}J_{H2'',H3''} = 6.1$ Hz, 4H, H3″), 7.72 (m, 4H, H5, H5′, H6, H6′). ^{13}C{^{1}H} NMR (CD_3OD): δ 158.39 (C2, C2′), 151.85 (C2″), 150.93 (C6, C6′), 143.80 (C4, C4′), 133.59 (C5, C5′), 129.70 (C3″), 125.80 (C3, C3′). ^{11}B{^{1}H} NMR (CD_3OD): δ 19.7. ^{195}Pt{^{1}H} NMR (CD_3OD): δ −2533. ESI MS: m/z 299 $[M - 2NO_3]^{2+}$.

1,10-Phenanthrolinebis(4-pyridineboronic acid)platinum(II) nitrate (6). The same method described for **4** was followed with the exception that 4-pyridineboronic acid (0.98 g, 7.97 mmol) was used instead of 3-derivative. Yield 0.240 g, 81%. ^{1}H NMR (CD_3OD): δ 9.10 (d, $^{3}J_{H2',H3'} = 6.4$ Hz, 4H, H2′), 9.07 (dd, $^{4}J_{H2,H4} = 1.2$ Hz, $^{3}J_{H2,H3} = 7.8$ Hz, 2H, H2, H9), 8.35 (s, 2H, H5, H6), 8.12 (dd, $^{4}J_{H2,H4} = 1.2$ Hz, $^{3}J_{H3,H4} = 5.4$ Hz, 2H, H4, H7), 8.03 (dd, dd, $^{3}J_{H2,H3} = 7.8$ Hz, $^{3}J_{H3,H4} = 5.4$ Hz, 2H, H3, H8), 7.92 (d, $^{3}J_{H2',H3'} = 6.4$ Hz, 4H, H3′). ^{13}C{^{1}H} NMR (CD_3OD): δ 152.10 (C2′), 151.93 (C4, C7), 148.85 (C13, C14), 142.88 (C2, C9), 133.59 (C3′), 132.66 (C11, C12), 129.57 (C5, C6), 127.70 (C3, C8) ^{11}B{^{1}H} NMR (CD_3OD): δ 19.7. ^{195}Pt NMR (CD_3OD): δ −2541. ESI MS: m/z 311 $[M - 2NO_3]^{2+}$.

1,10-Phenanthrolinebis(pyridine)platinum(II) hexafluorophosphate (7). 3- or 4-pyridineboronic acid (0.50 g, 4.07 mmol) was added to a suspension of $[PtCl_2(phen)]$ (0.600 g, 1.35 mmol) in water (100 mL). After refluxing the mixture overnight, the volume of the clear, colourless solution was reduced and micro-filtered through 0.45 μm Sartorius™ Minisart®. A saturated solution of KPF_6 was then added to form an off-white precipitate which was recrystallised by diffusion of CH_2Cl_2 into an acetone solution of **7**, filtered off and dried *in vacuo* (0.645 g, 58%). ^{1}H NMR (acetone-d_6): δ 9.48 (dd, $^{4}J_{H2',H4'} = 1.4$ Hz, $^{3}J_{H2',H3'} = 6.5$ Hz, 4H, H2′), 9.26 (dd, $^{4}J_{H2,H4} = 1.1$ Hz, $^{3}J_{H2,H3} = 8.3$ Hz, 2H, H4, H8), 8.53 (s, 2H, H5, H6), 8.48 (dd, $^{4}J_{H2,H4} = 1.1$ Hz, $^{3}J_{H3,H4} = 5.4$ Hz, 2H, H4, H8), 8.40 (td, $^{4}J_{H2',H4'} = 1.4$ Hz, $^{3}J_{H3',H4'} = 7.8$ Hz, 2H, H4′), 8.21 (dd, $^{3}J_{H2,H3} = 8.3$ Hz, $^{3}J_{H3,H4} = 5.4$ Hz, 2H, H3, H8), 7.95 (dd, $^{3}J_{H2',H3'} = 6.5$ Hz, $^{3}J_{H3',H4'} = 7.8$ Hz, 4H, H3′).

X-Ray diffraction study

Data for **7** were collected at 150(2) K to approximately 56° 2θ on a Bruker SMART 1000 diffractometer employing graphite-monochromated Mo-K_α radiation generated from a sealed tube (0.71073 Å). Data integration and reduction were undertaken with SAINT and XPREP[24] and subsequent computations were carried out using the WinGX-32 graphical user interface.[25] The structure was solved by direct methods using SIR97.[26] Multi-scan empirical absorption corrections were applied to data sets using the program SADABS.[27] Data were refined and extended with SHELXL-97.[28] All atoms were refined anisotropically. Carbon-bound hydrogen atoms were included in idealised positions and refined using a riding model. An ORTEP[29] depiction of the cation in **7** is provided in Fig. 2.

X-Ray data for **7**: Formula $C_{22}H_{18}F_{12}N_4P_2Pt$, M 823.44, monoclinic, space group $P2_1/c$ (#14), $a = 8.6210(12)$, $b = 25.904(4)$, $c = 11.7424(17)$ Å, $\beta = 97.255(2)°$, $V = 2601.3(7)$ Å^3, $D_c = 2.103$ g cm^{-3}, $Z = 4$, crystal size 0.280 × 0.187 × 0.110 mm, colour colourless, habit shard, temperature 150(2) K, λ(Mo-K_α) 0.71073 Å, μ(Mo-K_α) 5.625 mm^{-1}, T(SADABS)$_{min,max}$ 0.307, 0.539, $2\theta_{max}$ 56.56, hkl range −11 11, −33 34, −15 15, N 23301, N_{ind} 6151(R_{merge} 0.0601), N_{obs} 5185($I > 2\sigma(I)$), N_{var} 370, residuals¶ $R1(F)$ 0.0848, $wR2(F^2)$ 0.1553, GoF(all) 1.385, $\Delta\langle\pi\tau\rangle$ $\rho\langle/\pi\tau\rangle_{min,max}$ −3.878, 1.867 e$^-$ Å^{-3}.

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For crystallographic data in CIF or other electronic format see DOI: 10.1039/b618668h

Thermal denaturation (DNA melting) experiments

The melting temperatures (ΔT_m) were determined using calf-thymus DNA (Sigma) in 1×10^{-3} M phosphate buffer (pH 7.4), containing 1.2×10^{-5} M of metal complex and 1.5×10^{-2} M NaCl. Melting curves were recorded at 260 nm on a CARY-50 UV-vis spectrophotometer using a stoppered semi-micro (1200 μL) quartz cuvette with a path length of 10 mm. The temperature increase was at a rate of 0.5 °C min^{-1} using a CARY temperature controller, with data collection at 1 min intervals. The experiments were performed in triplicate for EtBr and **3–7**.

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¶ $R1 = \sum\|F_o| - |F_c\|/\sum|F_o|$ for $F_o > 2\sigma(F_o)$; $wR2 = (\sum w(F_o^2 - F_c^2)^2/\sum(wF_c^2)^2)^{1/2}$ all reflections; $w = 1/[\sigma^2(F_o^2) + (0.03P)^2 + 0.3P]$ where $P = (F_o^2 + 2F_c^2)/3$.

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