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Spectral Evidence and DFT Calculations on the Formation of Bis(2,2′-bipyridine)platinum(II)−N-Base Adducts

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The formation of 1:1 adducts of $Pt(bpy)_2^{2+}$ (bpy = 2,2′-bipyridine) with various N bases (B) has been ascertained in water at ambient temperature by spectrophotometric titration and electrospray ionization mass spectroscopy. A pseudo-five-coordinated complex, $[Pt(bpy)_2(B)]^{2+}$ with a monodentating bpy, is proposed based on density functional theory calculation. The formation constants (K_c) increase with the nucleophilicity of B except for sterically hindered N-bases, indicating an associative ligand-substitution mechanism.

Artificially designed interactions between metal complexes and biomolecules are attracting attention with a view to their use in bio/genome analysis and advanced medical therapy.[1] The incorporation of metal coordination in molecular recognition provides a great advantage when designing a wide variety of sensor molecules for efficient detection and for stabilization of the receptor−target complex. A coordination bond has a hybrid character consisting of ionic, covalent, and charge-transfer interactions sensitive to molecular orientation and electronic states, which reflect the spectroscopic, electrochemical, and magnetic properties of the complex. Organic ligands can attract a target molecule through, for example, donor–acceptor, Coulombic, dipole–dipole, $\pi-\pi$, and hydrophobic interactions, after appropriate structural modifications. The accompanying metal−target interaction results in a substantial electronic change and the formation of a new bond between them. The polytopic interaction caused by the cooperative action of ligands and metal is more beneficial with regard to stabilizing the receptor−target complex in highly polar circumstances such as in water.

Some square-planar platinum(II) complexes are known to be DNA intercalators with high antitumor activity.[2] A simplified scheme for the well-known cisplatin or *cis*-diaminodichloroplatinum(II)[3] is the formation of G−G inter- and intrastrand cross-links in which platinum binds coordinatively to the 7-N of the nucleobases after chloride hydrolysis in water (G = guanine). Similar reactivity has been reported and discussed for $Pt(N^N)Cl_2$ and $Pt(N^N^N)Cl^+$ complexes through the displacement of Pt^{II} (N^N and N^N^N are N-donor chelates). The ligand substitution of Pt^{II} largely follows an associative bimolecular S_N2 process through a five-coordinated transition state[4] or an optionally dissociative S_N1 mechanism with a three-coordinated intermediate in a sterically hindered system.[5] The lability and substitution of platinum(II) complexes are strongly associated with the chemical structures of complexes and reactants and the molecular environment, e.g., the aromaticity of chelates,[6] the nucleophilic base interactions,[7] the trans effect,[8] the electronic effect of the π-acceptor ligand,[9] and steric crowdedness.[10] Platinum(II) reactions have also been investigated using quantum chemical calculations.[11]

We focus on $Pt(\alpha\text{-diimine})_2^{2+}$ as a candidate for a nucleobase sensor to be embedded in conductive nanowires with a view to realizing electronic detection devices.[12] Although the coordination sites of $Pt(\alpha\text{-diimine})_2^{2+}$ are fully occupied, the associative substitution reactions on the square-planar metal involving attack of a nucleophile along the z axis will contribute to the development of further reactions for various target molecules. In fact, it is known that

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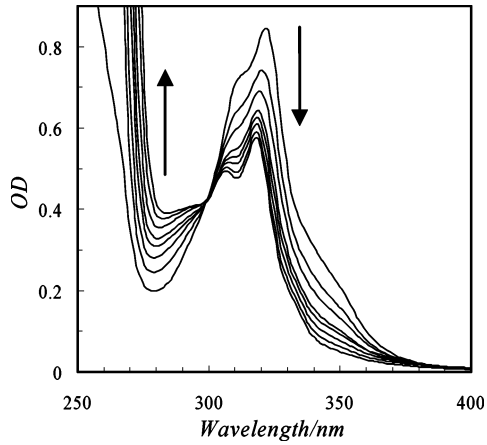

Figure 1. UV–visible absorption changes of $Pt(bpy)_2^{2+}$ upon portional addition of py in water at 295 K. Arrows indicate the direction of the OD change, while [py] increases from 0 to 30 mM. [$Pt(bpy)_2^{2+}$](initial) = 3.4×10^{-5} M.

$Pt(bpy)_2^{2+}$ suffers from the addition of OH^- or forms $Pt(bpy)_2L^{2+z}$ complexes in water (bpy = 2,2′-bipyridine; L = Cl^-, SCN^-, SO_4^{2-}, pyridine (py), etc., with ionic charge z).[13] Cusumano et al. demonstrated the DNA intercalation of $Pt(bpy)_2^{2+}$, $Pt(bpy)(py)_2^{2+}$, $Pt(terpy)(Rpy)^{2+}$, and $Pt(quaterpy)^{2+}$ (terpy = 2,2′:6′,2″-terpyridine; quaterpy = 2,2′:6′,2″:6″,2‴-quarterpyridine; R = H, CH_3), and the binding constants were well explained in terms of aromatic planar surface extension except that $Pt(bpy)_2^{2+}$ required partial intercalation.[14] These results encourage us to survey the inherent reactivity of $Pt(bpy)_2^{2+}$ versus organic nucleophiles. In this Communication, we report facile adduct formation between $Pt(bpy)_2^{2+}$ and a variety of N bases (B) including pyridines, pyrimidines, purines, and quinolines in water at ambient temperature through a partial ligand-substitution reaction. Interestingly, the elimination of bpy is a minor process in this system because the ligating structure of one bpy switches from bidentate to monodentate. This feature will result in an important recognition mode when coupled with conventional host–guest or donor–acceptor chemistry; i.e., even a very weak receptor−target interaction can be sustained or amplified under metal−target bond assistance.[15]

Figure 1 shows typical UV–visible absorption changes of $Pt(bpy)_2^{2+}$ that occurred with the portional addition of py. A clear isosbestic point exists, while MS signals associated with 1:1 adducts $(Pt(bpy)_2(py))^{z+}$ (z = 1, 2) and fragmented $(Pt(bpy)(py))^+$ are evident for the py-added solutions, as shown in Figure 2. Equivalent results were obtained for other $Pt(bpy)_2^{2+}$−B systems. Neither the consecutive insertion of the second py nor the formation of higher 1:n (n > 1) adducts has been found under our electrospray ionization mass spectroscopy (ESI-MS) condition.

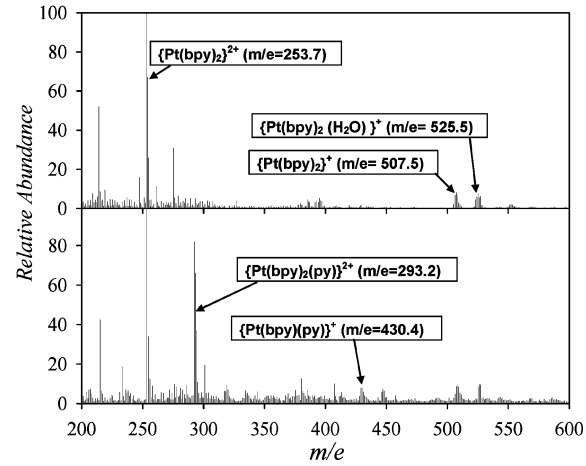

Figure 2. ESI-MS spectra of aqueous solutions of $Pt(bpy)_2^{2+}$. [Pt] = 4.2×10^{-5}M, [py] = none (upper), and [py] = 0.5 mM (lower). Possible species and observed (calculated) *m/e* values are as follows: $(Pt(bpy)_2)^{2+}$, *m/e* = 254.2 (253.7); $(Pt(bpy)_2(py))^{2+}$, *m/e* = 292.8 (293.2); $(Pt(bpy)(py))^+$, *m/e* = 430.2 (430.4). The calculated *m/e* values are illustrated.

Table 1. Formation Constant K_c of $Pt(bpy)_2^{2+}$−B Adducts

no.	N base	pK_a [a]	$10^{-2}K_c$ [b] M^{-1}
1	pyridine	5.17	2.7
2	3-methylpyridine	5.68	8.6
3	4-methylpyridine	6.00	6.1
4	4-methoxypyridine	6.47	7.0
5	3-cyanopyridine	1.45	0.13
6	4-cyanopyridine	1.90	0.42
7	4-hydroxypyridine	3.23	0.72
8	quinoline	4.80	3.8
9	isoquinoline	5.40	9.0
10	pyridazine	2.33	0.51
11	pyrimidine	1.30	0.14
12	4,4′-bipyridine	4.82	5.4
13	adenine	9.75	145
14	acyclovir	3.30[c]	2.1
15	uracil	0.60	0.13
16	cytosine	4.58	0.59
17	2-methylpyridine	5.96	0.54
18	2-hydroxypyridine	1.25	0.13
19	methylpyridine-2-carboxylate	2.21	0.10
20	methylpyridine-4-carboxylate	3.26	0.21
21	2-methoxypyridine	3.06	0.19
22	2,6-dimethylpyridine	6.71	0.21

[a] NH forms.[18] [b] In water at 295 K. [c] Guanine's value.

Then UV-absorption data were subjected to Benesi−Hildebrand analysis[16] to elucidate the formation constant (K_c) for $(Pt(bpy)_2(B))^{2+}$ by using Ketelaar's method.[17] The results are summarized in Table 1. $\log K_c$ vs pK_a[18] is plotted in Figure 3 as an index of nucleophilicity or the σ-donating ability of B. K_c ranges from $\sim 1 \times 10^1$ to 1×10^4 M^{-1} and shows a strong dependence on pK_a. B can be categorized into two groups: a linearly dependent group (a) and a depressed group (b). Group b consists of α-substituted bases suffering from the depression of adduct formation as represented by 2-methylpyridine. Adenine exhibits superb reactivity, which

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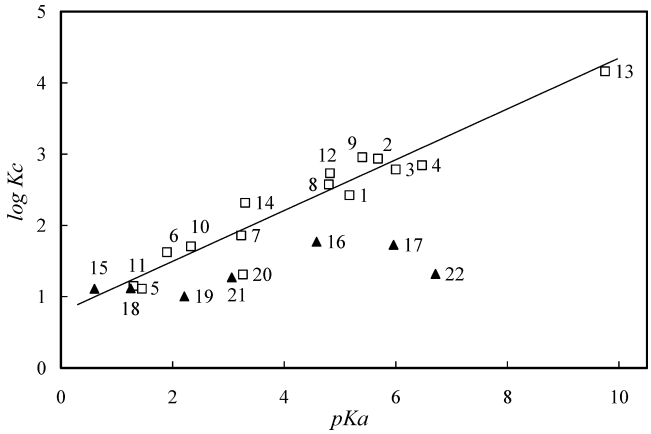

Figure 3. Plots of log K_c vs pK_a for various $Pt(bpy)_2^{2+}$−B pairs. Squares and triangles represent base groups a and b, without and with an adjacent substituent at the α position to coordinating N, respectively (see the main body). The line was obtained from a least-squares fitting for entries 1–12.

is attributed to the high nucleophilicity of 9-N in the purine skeleton. However, a new interaction mode between platinum(II) and adenine has been described,[19] and the effect should be further investigated. The reactivity of acyclovir or 9-(2-hydroxyethoxy)methylguanine will be reduced by coordination through 7-N.

Because no adducts have been crystallized for crystallographic investigation, we consider the molecular structures and electronic states by using DFT calculations.[20] Presumably, five-coordinated structures were examined, but no stable bond formation was obtained. Instead, we propose a pseudo-five-coordinated complex with a dangling bpy (Figure 4) as a result of a partial ligand exchange between py and one N(bpy). The stabilization is significant, and nearly 1 eV is acquired at a Pt−N(py) distance of 2 Å, while the dissociative Pt−N(dangling bpy) distance is ∼3 Å. Such stabilization is considered to originate from the release of a steric hindrance, i.e., torsion and strain owing to the van der Waals repulsion between two pairs of facing 6(6′)-H of bpy in square-planar $Pt(bpy)_2^{2+}$. A similar structure has been proposed by McInnes et al. for the reactions between $Pt(bpy)_2^{2+}$ and a relatively strong nucleophile (HO^-, $S_2O_3^{2-}$, or CN^-) in water from ^{195}Pt NMR experiments.[21] Lowering of the C_2-symmetric structure was also observed in our ^1H NMR experiments

Figure 4. Proposed structure of the $(Pt(bpy)_2(py))^{2+}$ complex generated by DFT calculations. Distances for coordinating Pt−N bonds are between 2.05 and 2.10 Å, while that of Pt−N(dangling pyridine) is much longer (2.96 Å), resulting in a pseudo-five-coordinated structure.

upon the addition of py-d_5. Fanizzi et al. reported that the coordination mode of Me_2phen (2,9-dimethyl-1,10-phenanthroline) in the *trans*-$Pt^{II}I_2(Me_2phen)(L)$ complex shifts from bidentate to monodentate depending on the π-accepting ability of L.[22] According to the X-ray crystallographic data, the Pt−N bond distances are 2.24 and 2.24 Å for L = C_2H_4 (strong π acceptor) and 2.04 and 2.68 Å for L = py (weak π acceptor). The latter values are consistent with the calculated Pt−N distances 2.05 and 2.96 Å as for the dangling bpy of the $(Pt(bpy)_2(py))^{2+}$ complex. We conclude that the pseudo-five-coordinated complex is readily formed as a result of the very fast equilibrium between $Pt(bpy)_2^{2+}$ and B when mixed in water at ambient temperature. Complex formation depends on the σ-donating power of B, but group b bases with a hindered N donor are less reactive. The results suggest that the insertion of B proceeds with an associative mechanism. It should be noted that no adducts were observed in $Pt(terpy)(py\text{-}d_5)^{2+}$ + py or CH_3CN systems in the ESI-MS investigation.[23] $Pt(terpy)(py)^{2+}$ has little releasable excess energy, and the tridentate coordination is stable.

Our results imply that two bpy ring systems in $Pt(bpy)_2^{2+}$ are potentially nonequivalent, probably because of a lack of effective π back-donation: only a slight overlap is anticipated between one d_{xy} orbital and two spatially separated p_x orbitals in the same molecular plane *yz*. The σ-donation ability is crucial to attaining a stable complex. Thus, a Pt−N bond from one side of bpy is weakened and easily replaced by the nucleophilic attack of an N base.

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Supporting Information Available: Listing of ESI-MS, photometric titration, graphical analysis, DFT calculations, and synthesis and identification of $Pt(bpy)_2(PF_6)_2$. This material is available free of charge via the Internet at http://pubs.acs.org.

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