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Molecular recognition. Electrostatic effects in supramolecular self-assembly†

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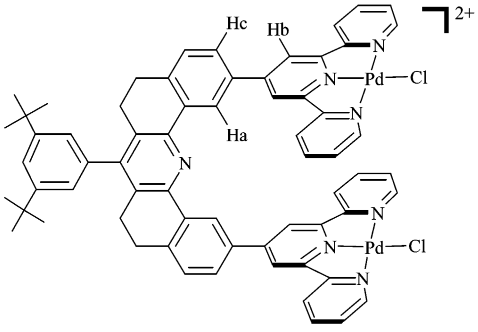
A di-positively charged metal-based receptor is shown to form 1 : 1 or 2 : 1 association complexes with rigid, linear two-site guests depending on the site separation, suggesting that electrostatic repulsion controls the association nuclearity.

One of the currently active areas of supramolecular chemistry is in the use of transition metal complexes for self-assembly.[1] The thermodynamic stability but kinetic lability of many transition metal bonds allows for the generation of complex structures under thermodynamic control. When such structures possess cavities, guest molecules can be incarcerated and stabilized by a variety of weak forces[2] leading to stable but kinetically labile[3] host–guest complexes. It is conceivable, however, that the weak forces of molecular recognition, rather than hydrogen or coordinate bonds, could be deployed for the construction of complex molecular architectures. This is the subject of this communication.



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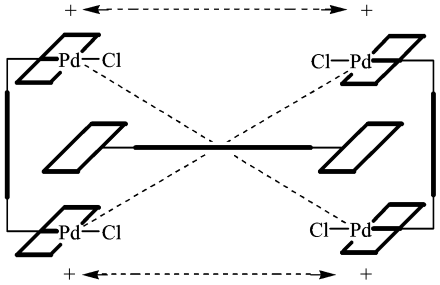
The charged receptor,[4] **1** (PF_6^- salt), is capable of incarcerating a variety of guests[2] within the molecular cleft formed by the two parallel disposed terpyridyl-palladium–chloro$^+$ (terpy-Pd–Cl$^+$) units, a circumstance that may allow for the use of weak molecular recognition forces in self-assembly. It is possible to entertain a variety of complex structures which could be assembled by the interaction of **1** with molecules bearing multiple binding sites, the simplest of which is the assembly, **2**, formed by rigid, linear, di-site linkers.

Several multisite linker systems of various geometries were prepared but most were insufficiently soluble and, if solublizing groups were incorporated, these groups could interfere with host–guest formation. The platinum complex, **3**, forms stable complexes with **1** mainly because of metal–metal interaction between the Pt atom of the guest and the Pd atoms of the receptor, **1**.[5] The two analogous di-site linkers, **4** and **5**, were sufficiently soluble in dimethylformamide (DMF) to allow for study of the potential self-assembly of the type **2**.

Addition of **3**, **4** or **5** to a solution of **1** in DMF leads to an immediate colour change from yellow to deep red, indicating host–guest formation, that was confirmed by ^1H NMR titration experiments.[6] At 20 °C the ^1H NMR signals are broad in DMF-d_7 solution but become sharp at 70 °C and the stability constants were determined at 70 °C. Titration of **3** with **1** caused shifts in the proton signals of both **3** and **1**; in particular H_a and H_b of **1** and H_d and H_e of **3** gave shifts of up to 0.9 ppm. Proton H_c of **1** showed no detectable shift during titration indicating that the guest lies in the cleft and is not associated with the outside face of a terpy-Pd–Cl$^+$ unit. Similar behaviour is observed when **1** is titrated with **4** and **5**. Following established procedures,[4,6] it was determined that **3** forms a 1 : 1 association complex with **1** and the association constant at 70 °C is 2600 ± 500 M^{-1}. This relatively large constant may result from π–π interactions and charge-induced dipole interactions but the main contribution is probably from metal–metal interactions.[2,4,5,7]



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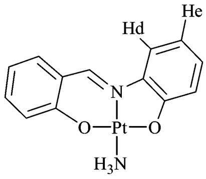

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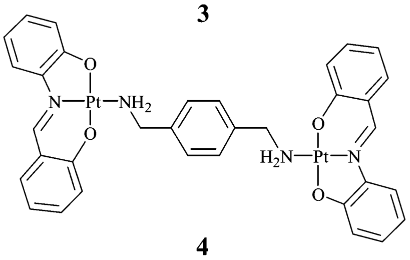

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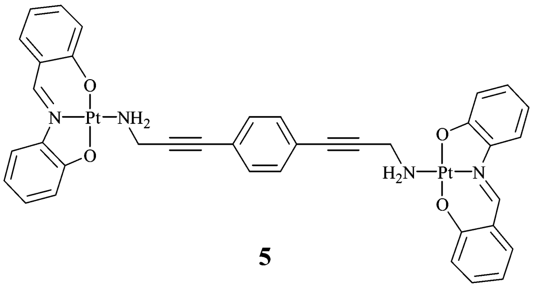

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† Electronic Supplementary information (ESI) available: synthesis and characterization of **4** and **5**, details of determining the stoichiometry and association constants of the host–guest complexes, molecular modelling and electrostatic calculations. See http://www.rsc.org/suppdata/cc/b2/b210957c/

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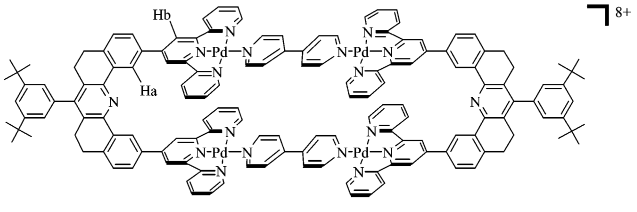
Incremental addition of **1** to the di-site linker, **4**, in DMF-d_7 solution led to ^{1}H NMR shifts similar to those observed in the association of **1** and **3**. At a 1 : 1 ratio of **1** to **4**, the ^{1}H NMR spectrum of the mixture is consistent with binding to both of the linked platinum complexes of **4**, suggesting rapid site exchange. The titration of **1** with **4** shows that only a 1 : 1 association complex is formed. The observed association constant at 70 °C is found to be 2200 ± 200 M^{-1}. Since **4** has two identical sites, the microscopic association constant is 1100 M^{-1} to account for the statistics of binding.[8] When **1** is titrated with the longer di-site linker, **5**, in a similar way, it was found that a 2 : 1 complex formed. The two microscopic association constants were found to be 1000 ± 100 M^{-1} and 200 ± 50 M^{-1} at 70 °C in DMF-d_7 solution.

Were the association constants for each of the two sites in **4** and **5** independent of each other, 2 : 1 association complexes would form with equal binding constants for both guest sites. Molecular modelling† shows that for both **4** and **5** di-association with **1** does not lead to any significant steric interference between the two bound receptors. Further, the rigid structures of **4** and **5** preclude the possibility of the complexes of **4** and **5** from folding about a terpy-Pd–Cl$^+$ unit where one site is inside the cleft and the other is associated with the outside face of the terpy-Pd–Cl$^+$ unit. This is consistent with the ^{1}H NMR data. The most likely source of interaction is electrostatic repulsion between the two charged receptors when a 2 : 1 association complex is formed. In order to obtain an estimate of this interaction, the electrostatic repulsions were calculated as the sum of the four repulsions shown as dotted lines in **2**. The maximum separation between the Pt atoms in **4** is 12.2 Å and in **5** is 18.8 Å. These are also the separations of the Pd atoms in the putative 2 : 1 complexes because of metal–metal interaction. Assuming point charges centred on the Pd atoms of the assemblies, **2**, and a dielectric constant of DMF[9] at 70 °C of 30.67, the electrostatic repulsion between the two receptors associated with **4** is 3.4 kcal mol^{-1} and that for **5** is 2.7 kcal mol^{-1}. The electrostatic repulsion attenuates slowly with increasing receptor separation beyond 15 Å.† Consequently, little electrostatic advantage is gained by extending the linker beyond that of **5**. These calculations are approximate for several reasons including the use of a bulk solvent dielectric constant and the neglect of the effect of possible ion-association between the receptor and the PF_6^- counter ions. At 70 °C the free energy for the first (microscopic) association constant of **5** (or **4**) is -4.7 kcal mol^{-1} and for the second constant of **5** the free energy is -3.6 kcal mol^{-1}, a difference of -1.1 kcal mol^{-1}. The difference in free energy for the two constants for **5** and the calculated (enthalpic) electrostatic interaction is consistent with the assumption that electrostatic interactions are the source of the difference in the first and second association constants with **5** and the formation of a 1 : 1 complex with **4**. In an attempt to reduce the electrostatic repulsion between receptors the shorter di-site linker, **4**, was modified by replacing the two NH_2 groups with S^- groups to give a di-anionic linker. When DMF solutions of this linker were added to the receptor, **1**, an intractable gelatinous precipitate slowly formed, suggesting extended association of the species in solution.

In order to demonstrate that the shorter di-site linker, **4**, is capable of forming a di-receptor association complex, the association constant of **4** with the molecular rectangle,[10] **6** (PF_6^- salt), was determined. The Pt atoms of the linker, **4**, register almost exactly with the Pd atoms in **6**. The molecular rectangle **6** forms quantitatively in acetone solution[10] in which solvent the electrostatic repulsion at 25 °C is calculated to be 21.5 kcal mol^{-1}, that is overcome by the stability of the metal–ligand bonds formed by the 4,4′-dipyridyl linker. It was found that a 1 : 1 complex is formed between **4** and **6** in DMF-d_7 at 70 °C with an association constant of 1500 ± 200 M^{-1}. Large shifts in the H_a and H_b protons at both ends of the receptor, **6**, are observed in the ^{1}H NMR spectra upon association of **4**, suggesting that the guest resides in **6** in the expected manner.



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The results provided here may have significant implications in supramolecular self-assembly. First, the deployment of weak interactions in order to assemble supramolecular structures can be circumscribed by electrostatic interactions that overcome the energy of binding. Electrostatic effects may be the reason that the charged molecular squares of Fujita[1] and Stang[1] do not generally form catenanes[11] in systems where the aromatic linkers might be expected to stabilize catenation. Attractive electrostatic forces, however, have been used to advantage for the incarceration of charged guests in the cavities of oppositely charges hosts.[12] Second, it is possible that the electrostatic repulsions could disrupt the coordinate bonds of highly charged metal based supramolecular structures when like charges are closely spaced. Indeed Stang[13] has reported that a charged molecular rectangle, formed in high dielectric solvents, dissociates its coordinate bonds when transferred to solvents of low dielectric constants. Electrostatic forces are generally much larger than the usual molecular recognition forces[2] and can become comparable to those associated with coordinate bond formation.

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