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Isomerism with Metallacalix[4]arenes of the Nonsymmetrical Pyrimidine Nucleobase Cytosine: How Connectivity and Rotamer State Determine the Topology of Multinuclear Derivatives

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Two cyclic octanuclear complexes, **2** and **3**, of cation composition $[\{Pd(bpy)\}_8C_4]^{8+}$ (bpy = 2,2′-bipyridine) form side by side when $[Pd(bpy)(H_2O)_2]^{2+}$ and cytosine (H_2C) are reacted in water. The two complexes are isomers, composed of central metallacalix[4]arene backbones to which four additional Pd(bpy) units are bonded pairwise to exocyclic groups of the C^{2-} ligands. As a consequence of differences in the N1−N3 connectivity patterns of the two central Pd_4C_4 rings and 1,3-alternate rotamer states of cytosinate in both compounds, the spatial arrangements of exocyclic groups are distinctly different, leading to two Pd_3 stacks and two Pd_1 entities in **2**, yet to four Pd_2 stacks in **3**.

Metallacalix[4]arenes are a class of metallacycles[1] in which *cis* square-planar metal entities, typically *cis*-a_2M^{II} (with M = Pt or Pd and a = am(m)ine or other ligands), replace the CH_2 groups of classical calix[*n*]arenes and ditopic N-heterocyclic ligands substitute for the phenol rings.[2] In a way, they represent a subgroup of the so-called heterocalixaromatics, in which O or NR groups replace CH_2 groups.[3] The concept of coordination-driven self-assembly[1] can be applied to metallacalix[*n*]arene synthesis particularly well if the N-heterocyclic ligand is symmetrical. Thus, the C_{2v} symmetric anion of 2-hydroxypyrimidine (2-pymo$^-$) readily reacts with *cis*-a_2Pd^{II} to give metallacalix[*n*]arenes with $n = 4$ or 6.[4,5] Things are more complicated if the ligands are of low symmetry because then the possibility of linkage isomer formation exists.[6] For example, with C_s-symmetrical pyrimidine (pym) nucleobases (uracil, thymine, and cytosine), four principle linkage isomers I−IV are possible for metallacalix[4]arenes, which can occur in numerous subsets differing in rotamer states (cone, partial cone, 1,3-alternate, and 1,2-alternate) of the heterocyclic ligands (Figure 1).

Among the first reported examples of a metallacalix[4]arene was one containing $enPt^{II}$ (en = ethylenediamine) and unsubstituted uracil, $[\{enPt(HU\text{-}\mathit{N1},\mathit{N3})\}_4](NO_3)_4$ (**1**) (with HU = uracil monoanion).[2] It crystallizes as a type I isomer (cf. Figure 1), with the N1 and N3 positions strictly alternating. The 1,3-alternate state of the four HU rings is stabilized by intramolecular OH···O hydrogen bonds between the HU rings, which occur as rare hydroxo tautomer forms in **1**.

A special feature of **1** is its ability to have these acidic OH protons readily substituted by four transition-metal ions, which become chelated by pairs of O2 and O4 donor sites with the connectivity pattern and the 1,3-alternate state of **1** preserved.[7]

Here we present the results of a study in which $[Pd(bpy)(H_2O)_2]^{2+}$ (bpy = 2,2′-bipyridine) was reacted with unsubstituted cytosine (H_2C). As it turns out, two isomeric complexes (**2** and **3**) containing eight $(bpy)Pd^{II}$ units and four dianionic cytosine ligands (C^{2-}; Scheme 1) are formed in this reaction. While one of these crystallizes as discrete octanuclear species $[\{Pd(bpy)\}_8(C)_4]$ $(NO_3)_8\cdot 25H_2O$ (**2**),[8] the other isomer cocrystallizes with a half-molecule of $Pd(bpy)(NO_3)_2$, hence as $[\{Pd(bpy)\}_8(C)_4]_2(NO_3)_{16}\cdot Pd(bpy)(NO_3)_2\cdot 60H_2O$ (**3**).[9] The crystals were separated by hand under a microscope, with isolated yields of 12% (**2**) and 42% (**3**). The

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(8) Crystal data for $[\{Pd(bpy)\}_8(C)_4](NO_3)_8\cdot 25H_2O$ (**2**): $C_{96}H_{126}N_{36}O_{53}Pd_8$, monoclinic, $C2/c$, $a = 35.201(4)$ Å, $b = 21.7600(9)$ Å, $c = 22.296(3)$ Å, $\beta = 128.958(19)°$, $Z = 4$, fw = 3483.53 g mol^{-1}, $V = 13280(2)$ Å^3, $D_{calcd} = 1.742$ Mg m^{-3}, λ(Mo Kα) = 0.710 73 Å, $\mu = 1.159$ mm^{-1}, 29 754 measured reflections (14 679 observed), R1(F_o) = 0.0666 [$I > 2\sigma(I)$], wR2(F_o^2) = 0.2002 (all data), GOF = 0.953.

(9) Crystal data for $[\{Pd(bpy)\}_8(C)_4]_2(NO_3)_{16}\cdot Pd(bpy)(NO_3)_2\cdot 60H_2O$ (**3**): $C_{202}H_{280}N_{76}O_{122}Pd_{17}$, triclinic, $P\bar{1}$, $a = 22.1984(6)$ Å, $b = 25.6905(7)$ Å, $c = 29.3466(8)$ Å, $\alpha = 113.454(3)°$, $\beta = 91.271(2)°$, $\gamma = 112.288(3)°$, $Z = 2$, fw = 7533.82 g mol^{-1}, $V = 13907.6(6)$ Å^3, $D_{calcd} = 1.799$ Mg m^{-3}, λ(Mo Kα) = 0.710 73 Å, $\mu = 1.180$ mm^{-1}, 127 203 measured reflections (64 803 observed), R1(F_o) = 0.1050 [$I > 2\sigma(I)$], wR2(F_o^2) = 0.3439 (all data), GOF = 1.001.

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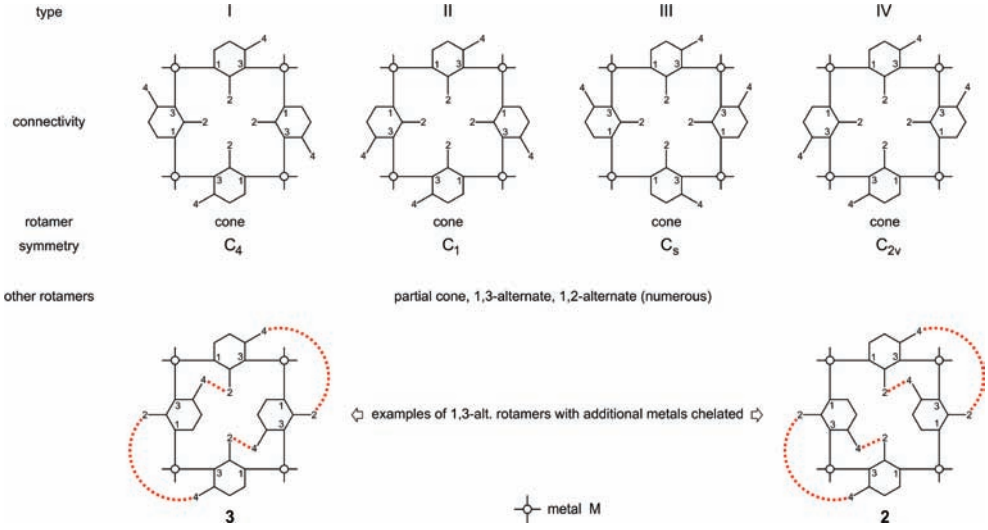
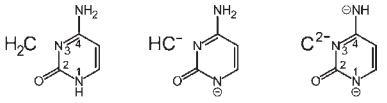


Figure 1. Four principle linkage isomers of metallacalix[4]arenes I−IV derived from C_s-symmetrical pyrimidine ligands with cone forms (top) and two 1,3-alternate forms (of I and IV, bottom) shown. Chelation of four additional metal entities to the 1,3-alternate forms leads to **2** and **3**. In all cases, the pym ligands are perpendicular to the paper plane. Sections of pym ligands within the M_4 square are up; sections outside the M_4 square are down.

Scheme 1



two isomeric cations of **2** and **3** differ in connectivities (type IV in **2** and type I in **3**) but have identical rotamer structures, namely, 1,3-alternate. Hence, all four cytosine rings are mutually *head*−*tail*. In both cations, the cytosine ligands are dianionic (C^{2-}), with N1 and the exocyclic amino group N4 deprotonated. The difference in topology of the two cations is a result of the differences in mutual spatial dispositions of the exocyclic groups O2 and N4 of the cytosine rings, to which the four other (bpy)Pd^{II} entities are bonded (Figure 1, lower part). In **2**, the four exocyclic groups of two adjacent cytosines are in favorable orientations to bind *two* (bpy)Pd^{II} residues, thereby producing two stacks of Pd_3 (Figure 2). These Pd_3 stacks, with Pd···Pd distances of 2.8007(12) Å (Pd2···Pd3) and 2.8164(7) Å (Pd4···Pd5), are reminiscent of that seen in a trinuclear PdPtPd compound with 1-methylcytosinato ligands.[10] Each Pd_3 stack forms a rooflike entity with two cytosinate ligands, and the two "roofs" are connected by two Pd ions (Pd1 and Pd1′), which are bonded to C−*N1* sites. Cation **2** possesses an inversion center and, therefore, two symmetry-related halves. Besides, because of their topology, cations of **2** are chiral. Both enantiomers are present in the crystal in equal quantities. Salient structural features of cation **2**, in addition to the Pd2···Pd3 and Pd4···Pd5 distances, are as follows: Pd1···Pd2, 4.8803(9) Å; Pd1···Pd5, 4.7657(11) Å; Pd2−Pd3−Pd2, 170.08(4)°; Pd5−Pd4−Pd5, 171.15(4)°; Pd5−Pd1−Pd2, 124.57(2)°. The rooflike-disposed cytosine bases form a dihedral angle of 88.4°, with distances between opposite rings ranging from 3.476(12) Å for C5a···C5b to 5.716(12) Å for C2a···C2b and even 6.733(9) Å for the exocyclic O2a···O2b. N3-coordinated bases to Pd3 (A) and Pd4 (B) form almost perpendicular dihedral angles: 90.0° and 82.3°,

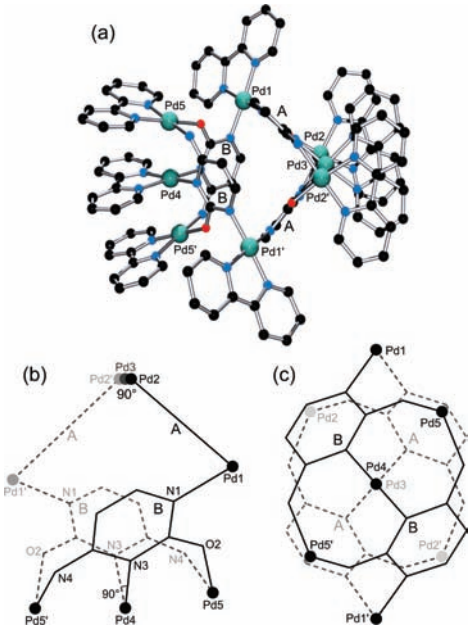


Figure 2. Full (a) and partial views (b and c) of cation **2**.

respectively. Cytosine bases (A and B) bonded to Pd1 through N1 form an angle of 74.5°. Stacking of the three bpy ligands shows slightly smaller torsion angles [8.0(3)−14.3(3)°] than both previously reported cases.[11]

The largely different topology of cation **3** (Figure 3) stems from the fact that the type I connectivity pattern has the exocyclic groups of C^{2-} ligands oriented such that only a single additional metal [(bpy)Pd^{II}] can be accommodated above or below the Pd atoms of the central metallacycle in a chelating fashion. As a result, the basic structure of **3** is analogous to that seen in Pt_8 or mixed Pt_4M_4 complexes containing four uracil anions,[7] hence with pairs of metal ions in the corners of the square. A similar situation is realized in a mixed Pt_2Pd_6 cycle with alternating uracil and cytosine rings

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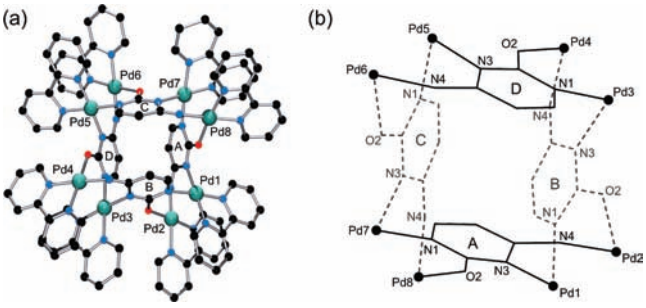

Figure 3. Top view (a) and schematic view (b) of cation **3**.

and a type I connectivity pattern.[12] Other than with **2**, cations of **3** are not chiral. Both cations included in the asymmetric unit are almost identical, with minor geometrical alterations. The distances between pairs of Pd atoms in **3** range from 2.8329(15) Å (Pd3···Pd4) to 2.8684(18) Å (Pd7···Pd8). Albeit short and comparable with or shorter than Pd−Pd contacts in other dinuclear complexes for which weak d^8-d^8 bonding interactions have been postulated,[13] these intermetallic distances are significantly longer than those seen within the Pd_3 stacks of **2**.[14] Disposition of the four cytosine bases within the central core of **3** displays an arrangement similar to that shown in **2**. In fact, a formal (but not possible) conversion from the topology of **2** to the topology of **3** could be achieved by transferring the exocyclic amino group from C4 to C6 in a pair of opposite cytosine rings.

The way cations **3** are arranged in the crystal lattice is of interest (Figure 4). The cocrystallizing $Pd(bpy)(NO_3)_2$ connects two cations of **3** in such a way as to produce an array of five Pd atoms. The distances between the central Pd [of $Pd(bpy)(NO_3)_2$] with the Pd atoms of the coordinated $(bpy)Pd^{II}$ units are longer (Pd4···Pd17, 3.409 Å; Pd16···Pd17, 4.669 Å) than those between Pd atoms included in the cations of **3** [Pd3···Pd4, 2.8329(15) Å; Pd15···Pd16, 2.8537(15) Å]. In contrast to the difference between Pd distances involving Pd17 (Δd = 1.26 Å), $\pi-\pi$ stackings between bpy rings are similar, however: Pd3−Pd4, 3.5 Å; Pd4−Pd17, 3.4 Å; Pd17−Pd16, 3.4 Å; Pd16−Pd17, 3.5 Å.[15]

The ^{1}H NMR spectra of **2** and **3** in D_2O are given in the Supporting Information. In both compounds, the cytosine−H5 doublets (**2**, 6.45 ppm; **3**, 6.46 ppm; ^3J = 7.02 Hz) occur furthest upfield and are well-separated from all other resonances. The integrated intensities of all signals are consistent with compositions of **2** and **3**.[16] In the spectrum of **2**, three doublet-of-doublets of equal intensities and the same

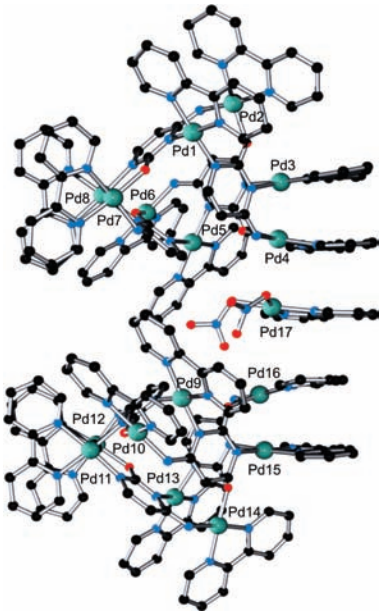

Figure 4. Section of the crystal lattice of **3**, with two octanuclear cations interacting with the extra $Pd(bpy)(NO_3)_2$.

intensity as cytosine−H5 are observed. The chemical shifts of these resonances (6.95, 7.18, and 7.26 ppm) are characteristic of bpy−H5 signals of stacked $(bpy)Pd^{II}$ units.[17] For **3** with its four Pd_2 stacks, likewise four bpy−H5 doublet-of-doublets are expected, two for each $(bpy)Pd^{II}$ entity. Three of these are observed (6.88, 7.27, and 7.33 ppm), while the fourth one is buried under the other bpy resonances.

In conclusion, two isomeric octanuclear $(bpy)Pd^{II}$ complexes with four bridging cytosinate ligands are presented. Although in both compounds the nucleobases function as tetradentate ligands through N1, O2, N3, and N4 sites, the spatial dispositions of the eight metals are markedly different. The origin of this difference stems from the linkage isomerism of the four cytosine bases and the differential availability of their two exocyclic donor sites (O2 and N4H) for additional metal chelation.

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Supporting Information Available: Crystallographic data, synthesis, and ^{1}H NMR spectra of **2** and **3**. This material is available free of charge via the Internet at http://pubs.acs.org. CCDC 773773 (**2**) and 773774 (**3**) contain the supplementary crystallographic data for this paper, which have been deposited with the Cambridge Crystallographic Data Centre. The coordinates can be obtained, upon request, from the Director, Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge CB2 1EZ, U.K.

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