Integrative Assembly of Heteroleptic Tetrahedra Controlled by Backbone Steric Bulk

Jacopo Tessarolo, Haeri Lee, Eri Sakuda, Keisuke Umakoshi, and Guido H. Clever*

ABSTRACT: A bent fluorenone-based dipyridyl ligand LA reacts with PdII cations to a solvent-dependent dynamic library of [Pd4LA]4 assemblies, constituted by a [Pd4LA]6 ring and a [Pd4LA]4 tetrahedron as major components, and a [Pd6LA]12 octahedron as minor component. Introduction of backbone steric hindrance in ligand LB allows exclusive formation of the [Pd4LB]12 octahedron. Combining equimolar amounts of both ligands results in integrative self-sorting to give an unprecedented [Pd4LA4LB]6 tetrahedron. Key to the non-statistical assembly outcome is exploiting the structural peculiarity of the [Pd4L8] tetrahedral topology, where the four lean ligands occupy two doubly bridged edges and the bulky ligands span the four remaining, singly bridged edges. Hence, the system finds a compromise between the entropic drive to form an assembly smaller than the octahedron and the enthalpic prohibition of pairing two bulky ligands on the same edge of the triangular ring. The emission of luminescent LA is maintained in both homoleptic [Pd3LA6] and heteroleptic [PdL6LA4].

Coordination-driven self-assembly provides a powerful tool to design and synthesize discrete nanostructured objects with accessible cavities.1−2 The resulting metallo-supramolecular assemblies are promising candidates for mimicking functional host systems found in nature, such as enzymes. The dynamic nature of many transition metal–ligand interactions, characterized by precise geometry and directionality, combined with a polytopic ligand structure, allow us to design and self-assemble a plethora of compounds with different shapes, sizes, and properties. Embedded functions, depending on either individual building blocks or their synergistic interaction,3−7 may involve host–guest interactions,8−10 photoswitching,11−12 chirality,13−15 chromophore effects,16−19 or catalysis,20−23 just to name a few.

Besides the formation of single components, dynamic systems consisting of several structures with different topologies may be the result of a self-assembly reaction.24−29 So far, most reported metallo-supramolecular compounds carry only one type of ligand, limiting the possibility to exploit applications arising from the implementation of multiple functionalities. To overcome this problem, we propose to increase structural complexity via the non-statistical integration of a set of different ligands. A first step in this direction is represented by homoleptic assemblies where the same ligand occupies two or more non-identical positions. For example, Lützen reported a [Pd4L4]@[Pd4L4] cage-in-ring assembly.30 Shionoya differentiated metal positions, thus desymmetrizing a porphyrin ligand.31 Our group investigated the controlled formation of [Pd4L4X4] bowls (X = solvent, halides) featuring two different ligand environments.32,33 Recently, structural complexity has been increased using non-symmetric ligands.34−37 A further approach relies on the structural diversity of [Pd4L8] assemblies with bis-pyridyl ligands, making it possible to form rings,38 interpenetrated double cages,39,40 or a tetrahedron-like arrangement, featuring four edges composed of a single ligand and two doubly bridged edges.5,41−43

Complexity further increases when chemically different ligands are placed in defined positions, yielding heteroleptic species. To overcome the formation of a statistical mixture,44 several strategies have been applied, e.g., exploiting hydrogen-bonding,45 templating guests,46 shape complementarity,47−53 or covalent bridges between ligands.54−56 Herein, we report a system where a bis-monodentate, flat ligand L4 self-assembles with PdII to give a series of [Pd4La]n architectures in a solvent-dependent process. Introduction of steric congestion into its backbone gives the bulky ligand LB, allowing us to exclusively form a large [Pd4L12] octahedron. A similar approach was reported by Severin and Hiraoka based on clathrochelate metallo-ligands.55,56 We now show that combining lean ligand LA and bulky derivative LB opens a new strategy to form unprecedented [Pd4LA4LB]6 heteroleptic structures. Key to clean, integrative self-sorting is the presence of two non-equivalent edge types in the [Pd4L8] tetrahedron, combined with control over steric pressure in the ligand backbones.

Ligands LA and LB were synthesized by Suzuki cross-coupling starting from 2,7-dibromo-9-fluorenone and 2,7-dibromo-9,9-dihexylfluorene, respectively, with 3-pyridineboronic acid pinacol ester (Supporting Information (SI)). Using 9-substituted fluorene-based backbones makes it possible to obtain non-linear bis-pyridyl ligands, bearing the C==O or...
alkyl substituents pointing toward one side of the molecule. This generates two binding modes: convex ($\theta \approx 90^\circ$) with nitrogen donors pointing away from the substituent(s), and concave ($\theta \approx 40^\circ$) pointing in the same direction (Scheme S4). A similar backbone design was reported to lead to Fe-based helicates and tetrahedra, 57−60 as well as knots and Borromean rings.61

At first, we studied the self-assembly of homoleptic species. Combination of ligand LA with PdII in a 2:1 ratio led to a solvent-dependent dynamic library of compounds with different nuclearity (Figure 1a). In CD$_3$CN, two major components are formed, a [Pd$_3$LA$_6$] triangular ring and a [Pd$_4$LA$_8$] tetrahedron. After coordination to PdII, $^1$H NMR signals are downfield shifted and split into three sets, as clearly observed for proton HIV, with a 1:1:2 ratio (Figure 1b). NOESY-NMR allows us to identify two independent sets of signals (SI), while DOSY-NMR shows the presence of two species in solution, with hydrodynamic radii of 11.04 and 12.19 Å, respectively (SI). This is consistent with the formation of a [Pd$_3$LA$_6$] ring and a [Pd$_4$LA$_8$] tetrahedron, the latter generating two sets of $^1$H NMR signals due to two non-equivalent ligand positions. Support comes from high-resolution ESI-MS analysis, showing a series of signals for [Pd$_3$LA$_6$(BF$_4$)$_m$]$^{m+}$ ($n = 2–4; m = 4–2$) and [Pd$_4$LA$_8$(BF$_4$)$_m$]$^{m+}$ ($n = 4, 5; m = 4, 3$) (Figure 1c).

Interestingly, the signal at $m/z = 1336.2$ reveals the presence of [Pd$_4$LA$_8$(BF$_4$)$_4$]$^{2+}$ as major and higher-nuclear [Pd$_6$LA$_{12}$(BF$_4$)$_8$]$^{4+}$ as minor components (Figure 1c, inset). Self-assembly in DMSO-$d_6$ results in only [Pd$_3$LA$_6$] ring formation, as confirmed by $^1$H NMR (Figure 1d), DOSY-NMR ($R_H = 13.20$ Å), and ESI-MS analysis (SI). The structures for all three [Pd$_n$LA$_m$] components have been determined by single-crystal X-ray diffraction (SCXRD) analysis (Figure 2). Needle-shaped crystals of the trimetallic [Pd$_3$LA$_6$] were obtained by vapor diffusion of toluene into a DMSO solution. The compound has the expected triangular geometry, where PdII metal centers occupy the vertices while pairs of ligands sit on the edges (Figure 2a). The carbonyl backbone substituent adopts two positions, one pointing outside the ring cavity while the other points toward the π-surface of the neighboring ligand. The distance between the fluorenone oxygen and the S-membered ring centroid of LA is

![Figure 1](https://doi.org/10.1021/jacs.1c01931)

Figure 1. (a) Self-assembly of Pd$^{II}$ and LA forms a [Pd$_n$LA$_m$] solvent-dependent library. (b) $^1$H NMR (CD$_3$CN, 500 MHz) spectra of [Pd$_3$LA$_6$] (triangles)/[Pd$_4$LA$_8$] (squares) and LA. (c) ESI-MS spectrum of [Pd$_n$LA$_m$] in CH$_3$CN; inset shows the isotopic patterns for [Pd$_3$LA$_6$(BF$_4$)$_4$]$^{2+}$ and [Pd$_6$LA$_{12}$(BF$_4$)$_8$]$^{4+}$. (d) $^1$H NMR (DMSO-$d_6$, 500 MHz) of [Pd$_3$LA$_6$] and LA.

![Figure 2](https://doi.org/10.1021/jacs.1c01931)

Figure 2. SCXRD structures of (a) [Pd$_3$LA$_6$] ring (left), highlighting the C=O−π interaction (right); (b) [Pd$_4$LA$_8$] tetrahedron (left), highlighting edge 1 (red), edge 2 (orange), and the C=O−π interaction (right); (c) [Pd$_6$LA$_{12}$] octahedron (one enantiomer shown); and (d) [Pd$_6$LB$_{12}$] octahedron. Counterions, solvent molecules, hydrogen atoms, and disorder are omitted for clarity. Color code: Pd, metallic blue; N, blue; O, red; C, gray.)
3.07 Å, suggesting the incompatibility of a bulkier backbone substituent with this structure. Diffusion of ethyl acetate into a DMF solution yielded single crystals of [Pd₆L₆]ₙ, yielding a tetrahedral structure with Pd⁴⁺ centers on the vertices and ligands bridging the edges (Figure 2b). In this case, L⁴ occupies two non-equivalent positions: four edges (“edge 1”) are composed of one ligand, while the two remaining edges (“edge 2”) accommodate a pair of ligands. In edge 1, the carbonyl substituent points outside the tetrahedral cavity, with L⁴ adopting a convex binding mode (θ ≈ 80°). In edge 2, the carbonyl group of one L⁴ points toward the π-surface of its neighbor (C=O–π-C₆ centroid = 3.53 Å), while the other carbonyl group points inside the cavity, featuring a concave binding mode (θ ≈ 40°). Finally, diffusion of 1,4-dioxane into the [Pd₆L₆]ₙ (n = 3, 4, 6) CH₂CN solution resulted in single crystals of [Pd₆L₆]₁₂, suitable for synchrotron diffraction analysis. The compound crystallizes in the R3 space group as a pair of enantiomeric [Pd₆L₆]₁₂ octahedra (Figure 2c). Pd⁴⁺ cations occupy the vertices, while the edges feature one ligand L⁶ each, with all carbonyl groups pointing outside the cavity. Comparing the three [Pd₆L₆]ₙ structures suggests that only the octahedron, the sole structure without C=O–π interactions, should be able to accommodate sterically demanding ligands on all edges.

To explore this possibility, L⁶ was synthesized by replacing the 9-fluorenone with a 9,9-dihexylfluorenone backbone. Self-assembly of L⁶ with Pd⁴⁺ cations in a 2:1 stoichiometry led to the formation of a single species, identified as a [Pd₆L₆]₁₂ octahedron (Figure 3a). Upon complexation of Pd⁴⁺, the ¹H NMR signals of L⁶ are downfield shifted and slightly broadened (Figure 3b). DOSY analysis confirmed a single species in CD₂CN (r₁ = 15.22 Å) and DMSO-d₆ (r₁ = 18.66 Å, SI), while pointing to differences in the solvent shell dynamics around the heavily alkyl-decorated [Pd₆L₆]₁₂ species. The high nuclearity was confirmed by HR-ESI-MS, where a series of peaks for [Pd₆L₆(BF₄)]ₙ⁺ (n = 3–6; m = 9–6) were identified (Figure 3c). Moreover, single crystals were obtained from vapor diffusion of toluene into a DMSO solution. The compound crystallizes as an octahedron with a structure analogous to that of [Pd₆L₆]₁₂. L⁶ sits on the edges and coordinates in the convex mode, and all hexyl chains point outside the cavity (Figure 2d). From these results we inferred that the steric bulk in the backbones of L⁶ prevents two ligands from being direct neighbors on the same edge, thus averting formation of entropically favored homoleptic species [Pd₆L₆] or [Pd₆L₆].

Looking at the [Pd₆L₆]ₙ tetrahedral structure (Figure 2b) reveals that while edge 2 must fit two ligands, edge 1 can accommodate a single ligand with a bulkier backbone, adopting a convex binding mode with substituents pointing outside the cavity. Based on this assumption, we postulated the formation of an unprecedented heteroleptic [Pd₆L₆L₆]₄ tetrahedron, with four L₆ sitting on edges 1, while ligands L⁶ occupy edges 2. Hence, Pd⁴⁺, L₆, and L⁶ were mixed in a 1:1:1 ratio in DMSO-d₆ at 70 °C for 1 h, indeed resulting in the exclusive formation of a [Pd₆L₆L₆]₄ heteroleptic tetrahedron (Figure 4b). ¹H NMR signals show downfield shifting, without signs of any homoleptic assemblies (Figure 4c). The presence of both L⁶ and L₆ within the same structure is supported by NOESY-NMR, showing a number of cross-signals, e.g., between H₄ and H₂ (SI). DOSY-NMR clearly shows a single species (r₁ = 15.11 Å), bigger than [Pd₆L₆]⁴⁺, but smaller compared to [Pd₆L₆]₁₂ in the same solvent (Figure S36). Furthermore, in the ESI-MS spectrum, a series of peaks for [Pd₆L₆L₆(BF₄)]ₙ⁺ (n = 1–5; m = 7–3) were identified (Figure 4d). Due to the dynamic nature of the metallo-supramolecular system, the same result was obtained in the fashion of a “cage-to-cage transformation” when two equimolar solutions of [Pd₆L₆]⁴⁺ and [Pd₆L₆]₁₂ were mixed (Figure S33). Despite a longer reaction time (Figure S34) than starting from free ligands plus Pd⁴⁺, in agreement with our previous findings, this proves that [Pd₆L₆L₆]₄ is a thermodynamic product.

Structural analysis of single crystals, from benzene vapor diffusion into DMSO, ultimately proved the formation of a [Pd₆L₆L₆]₄ heteroleptic tetrahedron (Figure 4a). To the best of our knowledge, this is the first example of such a [M₂L₄]₄ tetrahedron. As postulated, four ligands L⁶ are accommodated on edges 2, with the C=O group either pointing inside the cavity or facing the π-surface of neighboring L₆ (C=O–π-C₆ centroid = 3.38 Å, Figure 4a). In addition, four ligands L₆ are sitting on edges 1, adopting a convex binding mode with hexyl chains pointing outside the cavity (Figure 4a, purple backbone).

Next, we investigated guest binding of one aliphatic and two aromatic bis-sulfonates (Scheme S5) with [Pd₆L₆]⁴⁺ and [Pd₆L₆L₆]₄ in DMSO-d₆. In all cases, ¹H NMR titrations show interaction of the guests with the cage’s inner cavity, indicated by a shift of inward-pointing protons (SI). Signal broadening and onset of precipitation prevented us from determining association constants. ESI-MS analysis, however, suggests that the maximal number of hosted guests is

Figure 3. (a) Self-assembly of Pd⁴⁺ and L⁶ to form [Pd₆L₆]₁₂. (b) ¹H NMR (DMSO-d₆, 500 MHz) spectra of [Pd₆L₆]¹⁺ and L⁶. (c) ESI-MS spectrum of [Pd₆L₆]₁² with isotopic pattern of [Pd₆L₆(BF₄)]¹⁺ shown in the inset.
controlled by the assembly size. While for [Pd₃LA₆] we only observed interaction with one guest, for tetrahedra [Pd₄LA₈] and [Pd₄LA₄LB₄] binding of two guests was detected, and large octahedron [Pd₆LB₁₂] was even found to bind up to three guest molecules (SI).

Finally, we investigated the photophysical properties of the systems (Figure 5). In DMSO, LA shows an emission band centered at 555 nm that is blue-shifted to 532 nm upon PdII complexation in either homoleptic [Pd₃LA₆] or heteroleptic [Pd₄LA₄LB₄]. While this indicates that the emissive properties of ligand LA are retained in the heteroleptic tetrahedron, our platform allows to introduce additional functionality through modification of LB. It is worth noting that in Pd-mediated assemblies luminescence quenching is frequently observed, and only few examples of emissive cages have been reported so far.

To conclude, we report a new strategy for the non-statistical, integrative self-assembly of a previously unreported [ML₄LA₄] heteroleptic cage topology. Key factors are the use of bis-monodentate ligands, able to adopt a concave or convex binding mode, the precise introduction of backbone steric hindrance, and a balance between the entropic tendency to form small assemblies and the enthalpic disadvantage to pair bulky substituents on a single edge. The preservation of ligand emission properties in the Pd-mediated assemblies opens potential toward application as multifunctional devices and materials in fields such as chiroptical sensing, donor–acceptor systems, and photocatalysis.

ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge at https://pubs.acs.org/doi/10.1021/jacs.1c01931.

Accession Codes

CCDC 2061340, 2061344, 2061345, 2061347, 2061350, and 2061351 contain the supplementary crystallographic data for this paper. These data can be obtained free of charge via www.ccdc.cam.ac.uk/data_request/cif, or by emailing data_request@ccdc.cam.ac.uk, or by contacting The Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge CB2 1EZ, UK; fax: +44 1223 336033.

AUTHOR INFORMATION

Corresponding Author

Guido H. Clever – Department of Chemistry and Chemical Biology, TU Dortmund University, 44227 Dortmund, Germany; orcid.org/0000-0001-8458-3060; Email: guido.clever@tu-dortmund.de

Authors

Jacopo Tessarolo – Department of Chemistry and Chemical Biology, TU Dortmund University, 44227 Dortmund, Germany
Haeri Lee – Department of Chemistry, Hannam University, Daejeon 34054, Republic of Korea
Eri Sakuda – Department of Chemistry and Chemical Biology, TU Dortmund University, 44227 Dortmund, Germany

Figure 4. (a) SCXRD structure of [Pd₄LA₄LB₄] (left), highlighting LA (orange) and LB (purple) positions and the C=O–π interaction (right). Counterions, solvent molecules, hydrogen atoms, and disorder are omitted for clarity. Color code: Pd, metallic blue; N, blue; O, red; C, gray. (b) Self-assembly of PdII with LA and LB forms [Pd₄LA₄LB₄]. (c) ¹H NMR (DMSO-d₆, 500 MHz) spectra of [Pd₄LA₄LB₄] and a 1:1 mixture of LA and LB. (d) ESI-MS spectrum of [Pd₄LA₄LB₄], with isotopic pattern of [Pd₄LA₄LB₄(BF₄)₃]⁺ shown in the inset.

Figure 5. Absorption spectra of ligands and cages (5.0 × 10⁻⁴ M referred to ligand concentration; DMSO) and normalized emission spectra of LA, [Pd₃LA₆], and [Pd₄LA₄LB₄] (1.4 × 10⁻⁴ M; λₑₓ = 430 nm).
Division of Chemistry and Materials Science, Graduate School of Engineering, Nagasaki University, Nagasaki 852-8521, Japan; orcid.org/0000-0001-9882-7628
Keisuke Umakoshi — Division of Chemistry and Materials Science, Graduate School of Engineering, Nagasaki University, Nagasaki 852-8521, Japan; orcid.org/0000-0002-2027-6333

Complete contact information is available at: https://pubs.acs.org/10.1021/jacs.1c01931

Notes
The authors declare no competing financial interest.

ACKNOWLEDGMENTS

This work was supported by the European Research Council (ERC Consolidator grant 683083, RAMSES). We acknowledge DESY (Hamburg, Germany), a member of the Helmholtz Association HGF, for access to PETRA III and thank Dr. Anja Burbhardt for assistance in using synchrotron beamline P11 (I-1018090). E.S. thanks the JSPS program for Advancing Strategic International Networks to Accelerate the Circulation of Talented Researchers and JSPS for KAKENHI Grant No. JP20H05834. The authors thank Dr. Julian J. Holstein for functionalized Tetraphenylethylene M12L24 Nanospheres: Fluorescence Emission Inside a Confined Space. J. Am. Chem. Soc. 2019, 141, 9673–9679.

Regeni, I.; Chen, B.; Frank, M.; Baksì, A.; Holstein, J. C.; Clever, G. H. Coal-Tar Dye-based Coordination Cages and Helicates. Angew. Chem., Int. Ed. 2021, 60, 5673–5678.

Marti, D. R.; Escudero, D.; Jacqueline, D.; Cordes, D. B.; Slawin, A. M. Z.; Frucht, H. A.; Warriner, S. L.; Colman, E. Z. Homochiral Emissive A6 and A8[Fe4Pd10] Supramolecular Cages. Chem. - Eur. J. 2017, 23, 14358–14366.

Sun, Y.; Yao, Y.; Wang, H.; Fu, W.; Chen, S.; Maha transition to the formation of a new type of complex with strong fluorescence. J. Am. Chem. Soc. 2018, 140, 12819–12828.

Cullen, W.; Takezawa, H.; Fujita, M. Demethylation of Cyclopropanes via Photoinduced Guest-to-Host Electron Transfer in an M4L4 Cage. Angew. Chem., Int. Ed. 2019, 58, 9171–9173.

Yoshizawa, M.; Klosterman, J. K.; Fujita, M. Functional Molecular Flasks: New Properties and Reactions within Discrete, Self-Assembled Hosts. Angew. Chem., Int. Ed. 2009, 48, 3418–3438.

Murase, T.; Horiiuchi, S.; Fujita, M. Naphthalene Diels–Alder in a Self-Assembled Molecular Flask. J. Am. Chem. Soc. 2010, 132, 2866–2867.

Hong, C. M.; Bergman, R. G.; Raymond, K. N.; Toste, F. D. Self-Assembled Tetrahedral Hosts as Supramolecular Catalysts. Acc. Chem. Res. 2018, 51, 2447–2455.

Zhang, T.; Zhou, L.-P.; Guo, X.-Q.; Cai, L.-X.; Sun, Q.-F. Adaptive Self-Assembly and Induced-Fit Transformations of Anion-Binding Metal-Organic Macrocycles. Nat. Commun. 2017, 8, 15989–15996.

Riddell, I. A.; Smulders, M. M. J.; Clegg, J. K.; Hristova, Y. R.; Breiner, B.; Thoburn, J. D.; Nitschke, J. R. Anion-Induced Reconstitution of a Self-Assembling System to Express a Chloride-Binding Co10L15 Pentagonal Prism. Nat. Chem. 2012, 4, 751–756.

Riddell, I. A.; Hristova, Y. R.; Clegg, J. K.; Wood, C. S.; Breiner, B.; Nitschke, J. R. Five Discrete Multinuclear Metal-Organic Assemblies from One Ligand: Deciphering the Effects of Different Templates. J. Am. Chem. Soc. 2013, 135, 2723–2733.

Hasenknopf, B.; Lehn, J. M.; Boumediene, N.; Dupont-Gervais, A.; Van Dorselaer, A.; Kneisel, B.; Fenske, D. Self-Assembly of Tetrahedral and Hexanuclear Circular Helicates. J. Am. Chem. Soc. 1997, 119, 10956–10962.

Hasenknopf, B.; Lehn, J.; Kneisel, B. O.; Baum, G.; Fenske, D. Self-Assembly of a Circular Double Helicate. Angew. Chem., Int. Ed. Engl. 1996, 35, 1838–1840.
(29) Roy, B.; Saha, R.; Ghosh, A. K.; Patil, Y.; Mukherjee, P. S. Versatility of Two Diamidazole Building Blocks in Coordination-Driven Self-Assembly. *Inorg. Chem.* 2017, 56, 3579–3588.

(30) Kaseborn, M.; Holstein, J. J.; Clever, G. H.; Lützen, A. A Rotaxane-like Cage-in-Ring Structural Motif for a Metallosupramolecular Pd4L14 Aggregate. *Angew. Chem., Int. Ed.* 2018, 57, 12171–12175.

(31) Nakamura, T.; Ube, H.; Shiro, M.; Shionoya, M. A Self-Assembled Multiporphyrin Cage Complex through Three Different Zinc(II) Center Formation under Well-Balanced Aqueous Conditions. *Angew. Chem., Int. Ed.* 2013, 52, 720–723.

(32) Chen, B.; Horiiuchi, S.; Holstein, J. J.; Tessarojo, J.; Clever, G. H. Tunable Fullerenne Affinity of Cages, Bowls and Rings Assembled by Pd(II) Coordination Sphere Engineering. *Chem. - Eur. J.* 2019, 25, 14921–14927.

(33) Chen, B.; Holstein, J. J.; Horiiuchi, S.; Hiller, W. G.; Clever, G. H. Pd(II) Coordination Sphere Engineering: Pyridine Cages, Quinoline Bowls, and Heteroleptic PdII Binding One or Two Fullerenes. *J. Am. Chem. Soc.* 2019, 141, 8907–8913.

(34) Lewis, M. J. J.; Tarzia, A.; White, A. J. P.; Jelks, K. E. Conformational Control of Pd4L4 Assemblies with Unsymmetrical Ligands. *Chem. Sci.* 2020, 11, 677–683.

(35) Ograt, D.; Yuasa, J. Dynamic Open Coordination Cage from Non-Symmetrical Imidazole-Pyridine Ditopic Ligands for Turn-On/Off Anion Binding. *Angew. Chem., Int. Ed.*, 2019, 58, 18424–18428.

(36) Lewis, J.; Crowley, J. Metallol Supramolecular Self-Assembly with Reduced Symmetry Ligands. *ChemPlusChem* 2020, 85, 815–827.

(37) Samantray, S.; Krishnaswamy, S.; Chaud, D. K. Self-Assembled Conjoined-Cages. *Nat. Commun.* 2020, 11, 880–891.

(38) Suzuki, K.; Kawano, M.; Fujita, M. Solvato-Controlled Assembly of Pd4L4 and Pd4L6 Coordination “Boxes”. *Angew. Chem., Int. Ed.*, 2007, 46, 2819–2822.

(39) Frank, M.; Johnstone, M. D.; Clever, G. H. Interpenetrated Cage Structures. *Chem. - Eur. J.* 2016, 22, 14104–14125.

(40) Schulte, T. R.; Holstein, J. J.; Schneider, L.; Adam, A.; Haberhauer, G.; Clever, G. H. A New Mechanically-Interlocked [Pd4L4] Cage Motif by Dimerization of Two Peptide-based Labelmotis. *Angew. Chem., Int. Ed.*, 2020, 59, 22489–22493.

(41) Chand, D. K.; Biradha, K.; Kawano, M.; Sakamoto, S.; Yamaguchi, K.; Fujita, M. Dynamic Self-Assembly of an M1L6 Molecular Triangle and an M1L68 Tetrahedron from Naked PdI4 Ions and Bis(3-pyridyl)-Substituted Arenes. *Chem. - Asian J.* 2006, 1, 82–90.

(42) Tateishi, T.; Kojima, T.; Hiraoka, M. Multiple Pathways in the Self-Assembly Process of a Pd4L4 Coordination Tetrahedron. *Inorg. Chem.* 2018, 57, 2686–2694.

(43) Klein, C.; Gütz, C.; Bogner, M.; Topič, F.; Rissman, K.; Lützen, A. A New Structural Motif for an Enantiomerically Pure Metallosupramolecular Pd4L4 Aggregate by Anion Templating. *Angew. Chem., Int. Ed.*, 2014, 53, 3739–3742.

(44) Bloch, W. M.; Clever, G. H. Integrative Self-Sorting of Coordination Cages Based on ‘Naked’ Metal Ions. *Chem. Commun.* 2017, 53, 8506–8516.

(45) Preston, D.; Barnsley, J. E.; Gordon, K. C.; Crowley, J. D. Controlled Formation of Heteroleptic [Pd2(L1)2(L2)2]4+ Cages. *J. Am. Chem. Soc.* 2016, 138, 10578–10585.

(46) Yamashina, M.; Yuki, T.; Sei, Y.; Akita, M.; Yoshizawa, M. Anisotropic Expansion of an M6L4 Coordination Capsule: Host Capability and Frame Rearrangement. *Chem. - Eur. J.* 2015, 21, 4200–4204.

(47) Li, J.-R.; Zhou, H.-C. Bridging-Ligand-Substitution Strategy for the Preparation of Metal–Organic Polyhedra. *Nat. Chem.* 2010, 2, 893–898.

(48) Sun, Q.; Sato, S.; Fujita, M. An M1L1212(C2)2 Cantellated Tetrahedron: A Case Study on Mixed-Ligand Self-Assembly. *Angew. Chem., Int. Ed.* 2014, 53, 13510–13513.

(49) Bloch, W. M.; Abe, Y.; Holstein, J. J.; Wandtke, C. M.; Dittrich, B.; Clever, G. H. Geometric Complementarity in Assembly and Guest